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DIABETES TIPO II Y SALUD ORAL.

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Resumen

Introducción: La diabetes es un trastorno metabólico que afecta al organismo provocando hiperglucemia y, como una de sus principales consecuencias, una disminución del sistema inmunológico. Entre las consecuencias de estos problemas inmunológicos, es importante destacar el efecto sobre la salud bucal, ya que existe un mayor riesgo de infecciones bucales en los pacientes diabéticos que también tardan más en sanar.

Objetivo: Establecer la relación existente entre la diabetes con la salud oral.

Metodología: Revisión bibliográfica actualizada.

Resultados: Los resultados analizados indican una relación estrecha entre la diabetes y la salud oral, relacionada principalmente con la inflamación, la pérdida de defensas y la hiperglucemia. La principal consecuencia de una mala salud oral es el desarrollo de complicaciones como la periodontitis, la xerostomía, las infecciones bucales y otros trastornos relacionados con los fenómenos típicos de la patología diabética. Los implantes dentales, pese a ser una solución eficaz, no muestran beneficio significativo frente al no uso de los mismos.

Conclusiones: Es responsabilidad de todos (profesionales de la salud oral, familia, cuidadores y pacientes) el identificar y tratar la diabetes a tiempo, ya sea por métodos de screening o a través de la detección de síntomas y signos típicos de la patología con el fin de trabajar en ella desde el principio y evitar complicaciones relacionadas con el mal tratamiento y la edad.

Abstract

Introduction: Diabetes is a metabolic disorder that affects the body causing hyperglycemia, and, as one of its main consequences, a reduction in the immune system. Among the consequences of these immune problems, its important to highlight the effect on oral health, since there is an increased risk of oral infections in diabetic patients who also take longer to heal.

Objective: To establish the relationship between diabetes and oral health.

Methodology: Updated bibliographic review.

Results: The analyzed results indicate a close relationship between diabetes and oral health, mainly related to inflammation, loss of defenses and hyperglycemia. The main consequence of poor oral health is the development of complications such as periodontitis, xerostomia, oral infections and other disorders related to the typical phenomena of diabetic pathology. Dental implants, despite being an effective solution, do not show significant benefits compared to not using them.

Conclusions: It is the responsibility of everyone (oral health professionals, family, caregivers and patients) to identify and treat diabetes in time, either by screening methods or through the detection of symptoms and typical signs of the disease in order to to work on it from the beginning and avoid complications related to poor treatment and age.

Índice

1. Introducción

1.1.Diabetes mellitus

La Diabetes Mellitus (DM) es un trastorno metabólico que se caracteriza por la presencia de una hiperglucemia crónica normalmente acompañada de otras alteraciones en el metabolismo de carbohidratos, proteínas y lípidos [1]. Los pacientes con diabetes presentan además alteraciones en el sistema inmunológico; así es común observar deficiencias en la función de los leucocitos, que afectan los procesos de adhesión, quimiotaxis y fagocitosis de estas células. Otras alteraciones inmunológicas comunes en los pacientes con DM son la alteración de la actividad bactericida, alteración de la respuesta a la exposición a antígenos y alteración de la función de los linfocitos T [1,2].

La DM se ha convertido en una epidemia mundial, cuyos principales síntomas afectan de manera significativa en la calidad de vida y la longevidad de las personas que la padecen. El número de personas que padecen diabetes ha aumentado desde 108 millones de personas diagnoticadas en 1980 hasta los 422 millones en 2014 [1]. La prevalencia general de diabetes en el caso de los adultos mayores de 18 años ha aumentado del 4,7% en 1980 al 8,5% en 2014 y la Organización Mundial de la Salud (OMS), en sus predicciones, estima que se llegará a un total de 439 millones de personas que sufrirán esta patología en 2030 [1], que se corresponde al 10% de la pooblación adulta mundial. Finalmente, la DM tiene implicaciones económicas debido a los elevados costes sanitarios subyacentes [2].

Existen dos tipos de diabetes las cuales se van a explicar a continuación: Diabetes tipo 1 y diabetes tipo 2.

1.1.1. Diabetes tipo 1

La diabetes mellitus de tipo 1 es una patología caracterizada por un hiperglicemia crónica debido a una deficiencia, o a la total ausencia, en la producción de insulina por parte del páncreas. Normalmente, la disminución en la secreción de insulina se debe a la ausencia o a la destrucción (total o parcial) de las células alpha en los islotes de Langerhans del páncreas responsables de la síntesis de la insulina. De manera general, se suele diagnosticar en niños, adolescentes y adultos jóvenes, pero puede aparecer a cualquier edad [3,4].

La diabetes tipo 1 es una patología de elevada complejidad y en ella participan una amplia combinación de factores, como la susceptibilidad genética, la desregulación inmunológica o la exposición a factores ambientales [3].

Los estudios epidemiológicos han demostrado una mayor incidencia de la enfermedad entre los familiares de individuos con diabetes mellitus tipo 1: 6% en hermanos en comparación al 0,4% en la población general. Es por ello que se consideran los factores genéticos como causa principal de la diabetes mellitus tipo 1 [3].

El modelo inmunológico de diabetes mellitus tipo 1 se desarrolló basándose en una hipótesis basada en el hecho de que la insulina se reconoce como una sustancia no propia en poblaciones que padecen diabetes mellitus tipo 1 y, por ello, es lógico suponer que un defecto en la estructura de la insulina, o una imperfección en el proceso de reconocimiento, es responsable de la enfermedad [3,4]. De hecho, es común considerar la diabetes de tipo 1 como una enfermedad autoinmune.

Otrs estudios han asociado la diabetes mellitus tipo 1 con ciertos tipos de infecciones enterovirales [3]. Así, por ejemplo, el virus Coxsackie B4 contiene una proteína 2C (P2C) que es similar a la enzima descarboxilasa del ácido glutámico, que está presente en los islotes de

Langerhans [3]. La reacción inmunológica contra el virus sería, en este caso, el desencadenante de la destrucción de las células del páncreas responsables de la síntesis y secreción de la insulina.

Otros factores que afectan al desarrollo de la diabetes de tipo I son los factores ambientales[3]. Así, se cree que la exposición a sustancias antigénicas durante la edad temprana en la vida del individuo favorece el desarrollo de la enfermedad. Ciertos ingredientes de la dieta, como la albúmina sérica bovina, la beta-caseína y el gluten, están marcados como factores causantes de la diabetes mellitus tipo 1 [3,4].

Actualmente no existe cura para la diabetes de tipo 1 y el tratamiento de los pacientes consiste en la suministración exógena de insulina para controlar los niveles de azucar en sangre.

1.1.2. Diabetes tipo 2

El 90% de los individuos que padecen diabetes mellitus tipo 2 (no insulinodependiente) y, dentro de esta categoría, alrededor del 10% pueden ser causados por formas monogénicas como la diabetes de madurez de los jóvenes, la diabetes mitocondrial o la diabetes autoinmune de aparición tardía. del adulto, la cual se conoce como una diabetes tipo 1 de aparición tardía [5].

El elevado costo que asumen los pacientes con diabetes tipo 2 surge no solo cuando se establece el diagnóstico, sino al menos 8 años antes [5]. Las complicaciones de la diabetes mellitus son, esencialmente, enfermedades macrovasculares y microvasculares como consecuencia de la aterogénesis acelerada [1,5]. La morbilidad cardiovascular en individuos con diabetes tipo 2 es de dos a cuatro veces superior que la de las personas no diabéticas [6].

A pesar de que el estilo de vida y la sobrealimentación suelen ser los factores patogénicos desencadenantes, los elementos genéticos también están involucrados en la patogenia de la

diabetes tipo 2 [5,6]. Los antecedentes familiares positivos otorgan un riesgo de 2 a 4 veces mayor de diabetes tipo 2, además, entre el 15 y el 25% de los familiares de primer grado de individuos con diabetes tipo 2 desarrollan intolerancia a la glucosa u diabetes [5].

La insulina es un tipo de hormona que se genera en el páncreas cuya función se basa en permitir que el azúcar en sangre entre en las células del cuerpo para utilizarla como fuente de energía [3]. Si se padece de diabetes tipo 2, las células no responden de manera normal a la insulina, fenómeno conocido como resistencia a la insulina [5]. El páncreas produce más insulina para tratar de que las células respondan y, eventualmente, deja de mantener el ritmo, aumentado la cantidad de azúcares presentes en la sangre, lo que prepara el escenario para la prediabetes y la diabetes tipo 2 [5,6]. Los valores de azúcares presentes en sangre son dañinos para el organismo y pueden causar otros problemas de salud graves, como enfermedades cardíacas, pérdida de la visión y enfermedades renales [6].

La diabetes tipo 2 puede ser parcialmente controlada a través de una alimentación saludable y actividad, así como con la receta de insulina por parte de los médicos, otros medicamentos inyectables o medicamentos orales para la diabetes con el fin de ayudar a mantener estables los niveles de azúcares en sangre y evitar complicaciones [5]. También es importante mantener la presión arterial y el colesterol cerca de los objetivos establecidos para cada persona y hacerse las pruebas de detección necesarias [6].

1.2.Diabetes y salud oral

Tanto la diabetes mellitus tipo 1 como la diabetes tipo 2 presentan numerosas posibles complicaciones a largo plazo [6]. Los estudios epidemiológicos muestran que la gravedad de las complicaciones diabéticas suele ser proporcional al grado y duración de la hiperglucemia [1].

Con el aumento de la evidencia científica al respecto, la conexión entre las infecciones bucales y otras enfermedades del cuerpo se está entendiendo y aceptando cada vez más [7]. Las bacterias de las infecciones de las encías pueden pasar al torrente sanguíneo o a las vías respiratorias y trasladarse a otras partes del cuerpo [2]. Estas bacterias tienen el potencial de empeorar o aumentar el riesgo de otros tipos de problemas de salud [6].

Las personas con diabetes son propensas a una variedad de infecciones, incluida la enfermedad de las encías [8]. Las infecciones orales pueden dificultar el control de la diabetes y producir complicaciones, ya que las bacterias de la enfermedad grave de las encías pueden incrementar los valores de azúcares en sangre como el tiempo que el cuerpo lucha contra dichos valores elevados [1,6].

La diabetes y la salud bucal pueden derivar en complicaciones si no se toman las medidas necesarias. La diabetes disminuye la resistencia del cuerpo a las infecciones y retrasa el proceso de curación. Si no se controla, puede inducir al deterioro de los leucocitos, la principal defensa del organismo contra las infecciones. Por ello, las infecciones bucales pueden volverse más graves en personas con diabetes no controlada [7].

La diabetes afecta al reducir el flujo salival y aumentar los niveles de glucosa en la saliva, lo que la convierte en el escenario perfecto para infecciones fúngicas como la candidiasis [7].

Entre las manifestaciones orales relacionadas con la DM descritas se encuentran las siguientes: boca seca, caries, enfermedad periodontal y gingivitis, candidiasis oral, síndrome de boca ardiente (SBA), alteraciones del gusto, cigomicosis rinocerebral (mucormicosis), aspergilosis, liquen plano oral, lengua geográfica y fisurada lengua, retraso en la cicatrización de heridas y aumento de la incidencia de infecciones, disfunción salival, alteración del gusto y otros trastornos neurosensoriales, alteración de la erupción dentaria e hipertrofia parotídea benigna [1].

1.3.Justificación

La diabetes mellitus conlleva múltiples complicaciones, que aumentan cuando el control glucémico del paciente no es correcto [7]. Esto hace que la gestión y la prevención sean vitales. Se ha demostrado que en la diabetes existe en una relación bidireccional con la enfermedad periodontal y puede conducir a otras patologías bucales [1,2,7]. Por ello, los médicos y dentistas deben estar atentos a las diversas manifestaciones bucales de la diabetes para poder realizar un diagnóstico precoz [1,8]. La plena comprensión y conocimiento de la fisiopatología, las manifestaciones y el manejo de los diferentes tipos de infecciones orofaciales relacionadas con la diabetes por parte del dentista hace que la realización de este trabajo sea necesaria para poder evaluar el conocimiento actual a través de la información disponible y establecer posibles puntos de mejora a través de la exposición de los problemas existentes.

2. Objetivos

El objetivo principal del trabajo es, a través de una revisión bibliográfica, establecer la relación existente entre la diabetes, especialmente la de tipo 2, con la salud oral.

A partir del objetivo principal se desarrollaron los siguientes objetivos secundarios:

a) Establecer la relación entre la diabetes y la periodontitis.
b) Relacionar a los odontólogos con la posibilidad de identificar una diabetes no diagnosticada.
c) Determinar otras posibles patologías relacionadas con la salud oral en las que intervenga la diabetes.
d) Relacionar la salud oral con los niños y las personas mayores.
e) Establecer la relación entre los implantes dentales en los pacientes con diabetes.

3. Materiales y métodos

3.1.Estrategia de búsqueda

A la hora de realizar la búsqueda de información para el trabajo se utilizó el MeSH para validar el uso de las palabras clave.

Las palabras clave usadas en la búsqueda fueron las siguientes: “diabetes and periodontitis”, “undiagnosed and diabetes and dentists”, “oral cavity and defects and diabetes”, “Diabetes and children and oral health”, “Diabetes and elderly and oral health” y “Dental implants and patients and diabetes”.

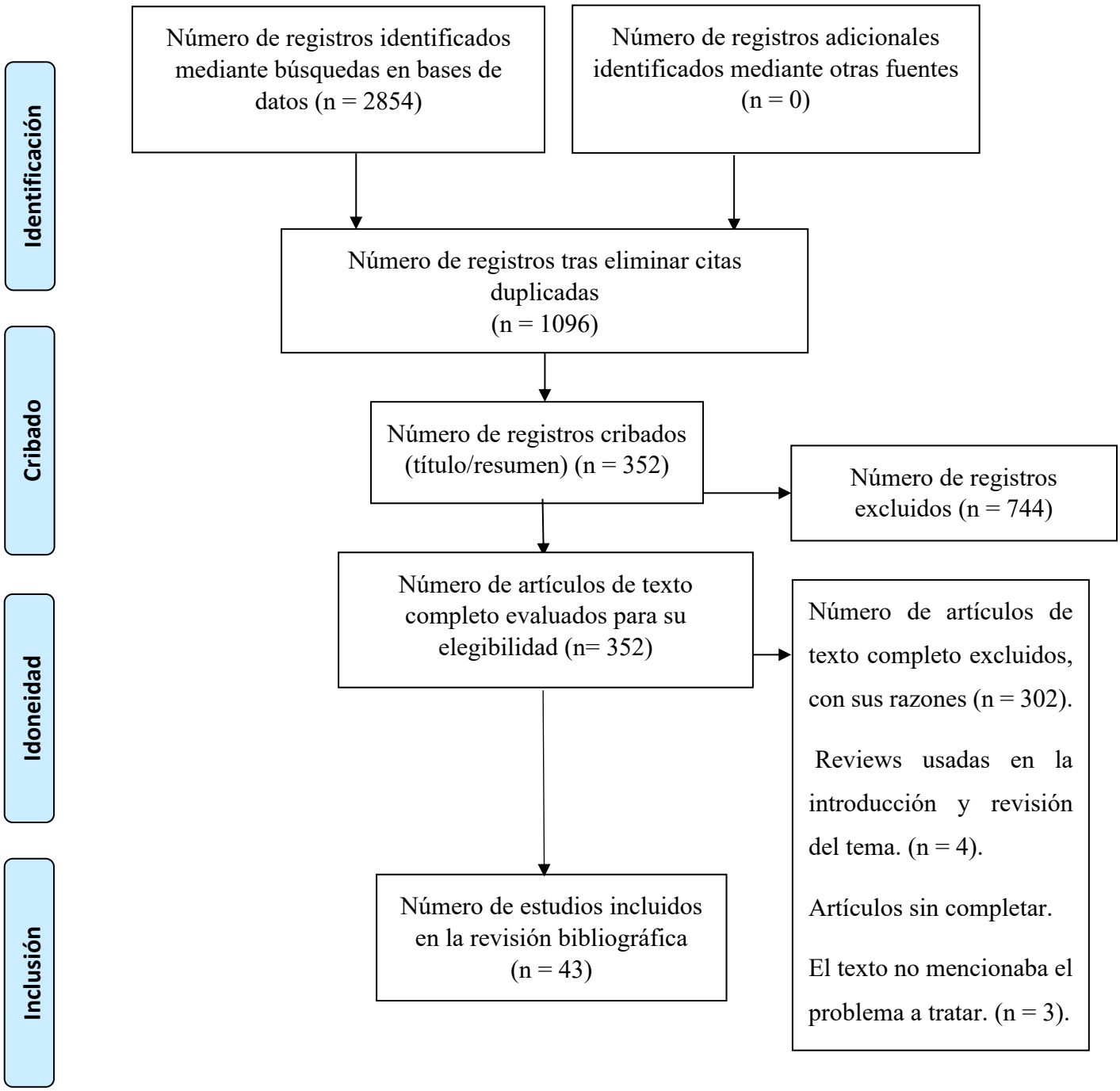
3.2.Criterios de elegibilidad

Los criterios de elegibilidad de los artículos del estudio fueron los siguientes; publicación durante los últimos 10 años (excepto en la relación de la diabetes y la periodontitis debido a que la información al respecto era muy elevada y se acotó la búsqueda a los últimos 5 años), artículos escritos en español o inglés, revisiones bibliográficas, sistemáticas metaanálisis, ensayos clínicos y estudios de casos (excepto en la relación de la diabetes y la periodontitis debido a que la información al respecto era muy elevada y se acotó la búsqueda a solo ensayos clínicos) y artículos en los cuales la investigación no estuviese aún en progreso.

3.3.Recogida de datos

Tras la primera búsqueda, en total se encontraron 2854 resultados, de estos, tras la lectura del título y el resumen, para ver si estaban relacionados con el tema de estudio y si estaban repetidas las referencias, se seleccionaron un total de 352 que cumplían con los criterios de inclusión.

De estos 352 artículos se realizó una segunda criba, primero por el volumen que debía abarcar el trabajo y segundo por una lectura de los mismos, seleccionando, al final, un total de 43 artículos, más 3 adicionales para la introducción del tema.


Identificación
Cribado
Idoneidad
Inclusión
Número de registros identificados mediante búsquedas en bases de datos (n = 2854)
Número de registros adicionales identificados mediante otras fuentes (n = 0)
Número de registros tras eliminar citas duplicadas (n = 1096)
Número de registros cribados (título/resumen) (n = 352)
Número de registros excluidos (n = 744)
Número de artículos de texto completo evaluados para su elegibilidad (n= 352)
Número de artículos de texto completo excluidos, con sus razones (n = 302).
Reviews usadas en la introducción y revisión del tema. (n = 4).
Artículos sin completar.
El texto no mencionaba el problema a tratar. (n = 3).
Número de estudios incluidos en la revisión bibliográfica (n = 43)

3.4.Estudios seleccionados

Base de datos	Palabras clave	Referencia
PubMed	Diabetes and periodontitis	Mauri-Obradors, Elisabet et al. 2018. D'Aiuto, Francesco et al. 2018. Wang, Shunqin et al. 2017. Masi, Stefano et al. 2018. Mizuno, Hirofumi et al. 2017. Geisinger, Maria L et al. 2016. Peniche-Palma, Diana C et al. 2019. Nishioka, Shinji et al. 2019. Kapellas, K et al. 2017. Quintero, Antonio J et al. 2018. Mirza, Sana et al. 2019. Vergnes, Jean-Noel et al. 2018. El-Makaky, Yasser, and Hany K Shalaby. 2020.
PubMed	undiagnosed and diabetes and dentists	Chinnasamy, Alagesan, and Marjory Moodie. 2020. Estrich, C G et al. 2019. Acharya, A et al. 2018. Hegde, Harshad et al. 2019.
PubMed	oral cavity and defects and diabetes	Chałas, R et al. 2016. El Sadik, Abir et al. 2018. Rohani, Bita. 2019. Verhulst, Martijn J L et al. 2019. Cervino, Gabriele et al. 2019. Gómez-Meda, B C et al. 2016.
PubMed	Diabetes and children and oral health	Babatzia, Anastasia et al. 2020. Poudel, Prakash et al. 2018. Rafatjou, Rezvan et al. 2016. Bimstein, E et al. 2019. Renata S. Leite et al. 2015.
PubMed	Diabetes and elderly and oral health	Scannapieco, Frank A, and Albert Cantos. 2016. Peruchi, Carla Thais Rosada et al. 2016. F. Pakize et al. 2020. Altınok, Ali et al. 2016.
PubMed	Dental implants and patients and diabetes	Naujokat, Hendrik et al. 2016. Chambrone, Leandro, and Luiz F Palma. 2019. de Araújo Nobre, M et al. 2016. Souto-Maior, Juliana Raposo et al. 2019. Jiang, Xue et al. 2020. Li, Cui-Xia et al. 2020.
Medline	Elderly and oral health	National Institute of Mental Health, 2017.

4. Resultados y discusión

4.1. Periodontitis y diabetes

La periodontitis es una enfermedad inflamatoria crónica la cual suele estar asociada con la diabetes [9]. Esta patología tiene su origen en una disbiosis de la microbiota oral y se relaciona con una respuesta inmune inflamatoria mal regulada [10]. La respuesta generada a través del incremento del número de bacterias sobre la superficie de los dientes no es solo exclusiva de la cavidad oral, sino que también se relaciona con una inflamación a nivel sistémico [1,10]. El aumento de la carga inflamatoria sistémica en los pacientes con periodontitis está relacionada con un incremento del peligro de enfermedades crónicas como la diabetes [10,11].

La inflamación actúa fomentando la resistencia a la insulina, complicando los problemas cardiovasculares y renales en pacientes con y sin diabetes [12]. Los resultados obtenidos en algunos estudios sobre el tema fortalecen la hipótesis de que la reducción de la inflamación periodontal se relaciona con la reducción de la inflamación sistémica y genera una mejoría de la función vascular y los marcadores metabólicos [10]. Adicionalmente, se ha visto que existe una correlación entre la reducción de los marcadores de inflamación sistémica (CRP y TNFα), los parámetros inflamatorios periodontales (la profundidad de las bolsas de sondeo, el número de bolsas periodontales de mayor profundidad y la hemorragia gingival) y los resultados de tipo sistémicos (control metabólico y funciones vasculares y/o renales) [10,11]. A pesar de ello, estas correlaciones no han sido encontradas para las medidas de producción de insulina y sensibilidad a la misma [10].

Adicionalmente, existen otros marcadores y factores que relacionan la periodontitis, su tratamiento y la diabetes, los resultados se muestran a continuación:

Se ha visto que el tratamiento de la periodontitis ayuda a reducir el estado inflamatorio periodontal, provocando una disminución de los niveles de las adipocinas antagonistas de la insulina y provocando aumentos en las adipocinas sensibilizantes a la insulina generando una mejora en el control glucémico en pacientes con diabetes tipo 2 y enfermedad periodontal [13].

Otro fenómeno típico de la periodontitis y la diabetes es el aumento del estrés oxidativo y la producción de radicales libres, en un estudio se probó que la reducción en la producción de estrés oxidativo mitocondrial tras el tratamiento periodontal se relaciona con una mejoría de la función endotelial y del control metabólico en los pacientes con diabetes tipo 2, convirtiendo al estrés oxidativo mitocondrial en un novedoso objetivo terapéutico de estudio[14].

En otro estudio se intentó observar una posible diferencia entre los niveles de la metaloproteinasa de matriz 9 (MMP-9) y la mieloperoxidasa (MPO) en el fluido crevicular gingival de individuos que presentaban diabetes tipo 2 controlada y descontrolada, con y sin periodontitis frente a pacientes sanos. Los resultados obtenidos no mostraron una relación aparente y hacen evidente la necesidad de seguir estudiando posibles marcadores que relacionen ambas patologías, además de realizar mejores ensayos clínicos para poder probar relaciones como la descrita [15].

En un ensayo clínico denominado “Ensayo sobre la diabetes y la terapia periodontal (DPTT)” se vio que la terapia periodontal y la severidad de la patología periodontal no se relacionan con cambios significativos en los biomarcadores séricos en los sujetos que participaban en el ensayo a lo largo de los seis meses de duración. Aun así, se muestra la necesidad de evaluar las correlaciones entre los cambios en la E-selectina, IL-6 (factores presenten en procesos inflamatorios que han sido relacionados directamente con la diabetes), y las variables

relacionadas con la diabetes ya que la diabetes puede ser el principal impulsor de la inflamación sistémica en pacientes con enfermedad periodontal [10].

Diferentes ensayos han tratado de realizar tratamientos no quirúrgicos para tratar la periodontitis en pacientes diabéticos, a continuación, se resumen los principales hallazgos:

En buena parte de los estudios se muestra que no se observa ningún beneficio adicional en la mejora de los parámetros clínicos periodontales y los resultados sistémicos con terapias periodontales en pacientes diabéticos [16,17]. Además, factores como el índice de masa corporal (IMC) influyen en la persistencia de las patologías y en la ausencia de resultados positivos concluyentes [9]. Pese a los resultados, se ha visto que el tratamiento periodontal mejora la calidad de vida de este tipo de pacientes [18] y, en varios estudios, si se muestra una mejoría usando una terapia periodontal en lo referido a la disminución de los niveles de HbA1c en sujetos diabéticos (HbA1c > 9%) independientemente del tipo de tratamiento realizado [19] y en un mejor pronóstico en la resistencia a la insulina [19–21]. Además, la terapia con metronidazol y amoxicilina ayuda a mejorar el resultado metabólico y la salud periodontal de los pacientes diabéticos que padecen periodontitis crónica [9].

Para resumir, el papel que juega la terapia periodontal en la mejora de la resistencia a la insulina y la sensibilidad se justifica a través de la relación bidireccional que hay entre la diabetes y la periodontitis [18]. En la periodontitis, tanto las endotoxinas bacterianas como los lipopolisacáridos promueven la estimulación de las células huéspedes desencadenando una serie de eventos intracelulares los cuales fomentan la liberación de marcadores proinflamatorios (IL-1b, IL-6, PGE2, TNF-a, RANKL, metaloproteinasas de matriz y quimiocinas), reduciendo así la cantidad de marcadores antiinflamatorios y de factores de crecimiento presentes [21]. Estos agentes llevan a cabo funciones sistémicas sobre las células ß del páncreas, alterando la

señalización y la respuesta a la insulina, lo que afecta negativamente al estado glucémico del paciente. El tratamiento periodontal puede mejorar, eventualmente, la sensibilidad a la insulina y disminuir la resistencia a la insulina en los pacientes con diabetes con enfermedad periodontal, aunque se requiera de una mayor investigación de calidad al respecto [10,21].

4.2. Detección de diabetes no diagnosticada por parte de odontólogos

Las personas con riesgo de desarrollar DM pasan por una larga fase asintomática que precede a la DM propiamente dicha [22,23].

La combinación de factores, como la lenta aparición de los síntomas, la escasa atención de la salud, la falta de conciencia de las personas y la amplia gama de los síntomas, hace que tanto al médico como al paciente les resulte complicado saber que la DM fue pasada por alto, conduciendo a un diagnóstico tardío de la patología [22].

Como se ha visto anteriormente, la enfermedad periodontal es una de las principales causantes de pérdida de la dentadura en personas adultas [10], y la DM representa un factor peligroso relacionado con la patología periodontal [9].

Los pacientes dentales con DM no controlada pueden desarrollar problemas periodontales de mucha gravedad lo que desencadena en tratamientos menos efectivos y más pobres en comparación con aquellos que controlan su glucosa sanguínea dentro de los límites normales [9,22]. Debido al vínculo existente entre la DM y la periodontitis, los dentistas juegan un papel muy importante en la posible detección de los problemas médicos de los pacientes, identificando los grupos de riesgo y referirlos a los médicos para una mayor evaluación y cuidado del paciente [22]. A diferencia de lo que sucede en el ámbito médico, la información sobre la detección de DM en el ámbito dental de manera no intencionada es limitada [22–25].

Con el fin de realizar una estimación fiable del riesgo de DM entre los pacientes dentales y así poder ayudar a los planificadores de salud a la hora de tomar decisiones informadas, la información sobre la prevalencia de la enfermedad y estrategias para abordar los casos no diagnosticados es muy necesaria [22].

El modelo más utilizado se basa en el uso de datos médico-dentales de un registro de salud electrónico integrado con el fin de identificar a las personas con DM no diagnosticada en entornos dentales [23–25]. Los resultados de los estudios muestran una cantidad elevada de personas con síntomas indicativos de diabetes que no han sido diagnosticados correctamente (31,3% en Estados Unidos) [23].

La aplicación de estos modelos es efectiva y la extrapolación de los datos obtenidos puede actuar como indicador para la detección de prediabetes en las visitas al dentista [23]. El incorporar una evaluación la evaluación del riesgo de prediabetes o diabetes en las visitas dentales de rutina puede ayudar a que las personas con prediabetes tomen medidas para reducir el riesgo de desarrollar diabetes y a las personas con diabetes formen parte de un tratamiento para disminuir el riesgo de complicaciones relacionadas con la diabetes [22,25].

4.3. Otros defectos de la cavidad oral relacionados con la diabetes

La hiperglucemia crónica conlleva a diferentes complicaciones en diferentes zonas del cuerpo, entre las que se destaca la cavidad bucal, por lo que el control de la glucosa en sangre es muy importante [26]. Los posibles mecanismos que están relacionados con este tipo de complicaciones orales de la diabetes incluyen: el deterioro de la función de los neutrófilos, el incremento de la actividad colagenasa y la disminución de la síntesis de colágeno, microangiopatía y neuropatía [6,26,27].

Debido a que la cavidad oral se encuentra muy vascularizada e inervada, es de esperar que ocurran complicaciones orales [6]. La relación entre la DM y las enfermedades bucodentales ha recibido una mayor cantidad de atención en las últimas décadas. A pesar de ello, la mayoría de los estudios solo se centran en la periodontitis y abordan la DM desde la perspectiva limitada de los niveles elevados de glucosa en sangre [6,26].

Entre las principales complicaciones de la cavidad oral relacionadas con la DM destacar las siguientes:

Xerostomía: Muchos estudios han relacionado la función salival alterada en adultos con la diabetes. La etiología es desconocida, pero se cree que se relaciona con poliuria, neuropatías autonómicas y cambios y alteraciones microvasculares en las membranas basales de las glándulas salivales [6,26].

Caries dental: La capacidad de limpieza reducida, el aumento de carbohidratos y el aumento del nivel de *estreptococos mutans* y lactobacilos en saliva de pacientes diabéticos pueden conllevar al incremento de la incidencia de caries [6,26].

Infecciones orales: La disminución del flujo salival y la ausencia de sus efectos antimicrobianos provocan infecciones. La candidiasis oral puede aparecer por numerosos factores como la xerostomía, estudios sobre las tasas de colonización por cándida muestran una mayor tendencia en pacientes con diabetes tipo 1 en comparación con la tipo 2 (84% y 68%, respectivamente), mientras que el porcentaje en sujetos no diabéticos ronda el 27% [6,26].

Boca ardiente: La sensación de ardor o disestesia en la cavidad oral de los pacientes diabéticos se relaciona con un mal control glucémico, alteraciones metabólicas de la mucosa oral, angiopatía, candidiasis y neuropatía [6,26].

Disfunción del gusto: Puede ocurrir en pacientes con diabetes mal controlada [6,26]. Entre los pacientes diabéticos o prediabéticos, el 5,7% padece un trastorno del gusto dulce y el 8,6% padece un trastorno del gusto salado [26].

Alteraciones de la mucosa oral: Algunas alteraciones de la mucosa oral, como la lengua fisurada, estomatitis aftosa recurrente y algunas lesiones premalignas, incluidocomo el liquen plano, se han relacionado con la diabetes [26,28,29]. Entre los principales causantes destacar el control insuficiente de la diabetes, la alteración inmunológica, los cambios microcirculatorios con reducción del riego sanguíneo, la xerostomía y la alteración del flujo y la composición salival [26,29].

Curación tardía de las heridas: Los factores desencadenantes son los siguientes: vascularización tardía, flujo sanguíneo reducido, hipoxia, reducción de la inmunidad innata, producción pobre de factores de crecimiento y estrés psicológico [6,26].

Las complicaciones orales en pacientes con DM son de vital importancia ya que afectan, en gran medida, a la calidad de vida de los pacientes [7]. La evidencia muestra que las complicaciones orales crónicas y persistentes en estos pacientes ejercen un efecto negativo sobre el control de la glucosa en sangre [6,26]. Debido a ello es necesario trabajar en la prevención y el tratamiento de las complicaciones orales originadas por la diabetes [26].

4.4. Diabetes en niños y salud oral

La diabetes mellitus, específicamente la de tipo 1 es una enfermedad metabólica típica en la infancia [4,30]. Alrededor de 1 de cada 500 niños y adolescentes padecen diabetes tipo 1, alrededor del el 75% de los casos de DM1 se diagnostican durante la infancia, siendo los más afectados

los menores de 14 años [4]. Por otro lado, la diabetes tipo 2 ocurre normalmente en adultos una vez el organismo es resistente a la insulina o no produce suficiente hormona [31].

Los principales factores ambientales que se relacionan con un incremento del riesgo de insulitis autoinmune son los siguientes: infecciones por enterovirus, exposición a proteínas de la leche de vaca, la lactancia materna, nitratos y nitritos, deficiencia de vitamina D, síndrome de Turner, síndrome de Prader-Willi, ataxia de Friedreich, síndrome de Alström y síndrome de Down, entre otros. También la pueden causar la cirugía, glucocorticoides, desnutrición, infecciones, exceso de glucagón, epinefrina y hormona del crecimiento [4,32].

En un estudio con niños entre 5 y 18 años de edad que pretendía evaluar el estado de salud e higiene bucal de los pacientes diabéticos tipo 1 frente a los no diabéticos, no se vió ninguna diferencia significativa entre dos grupos en el índice de placa, sin embargo, la diferencia del índice de gingivitis fue significativa en el grupo de diabéticos ($p = 0,001$). Los resultados son insuficientes como para establecer un efecto significativo de la diabetes en el incremento del riesgo de padecer enfermedades orales y periodontales. Sin embargo, los niños y adolescentes diabéticos deben recibir un mayor control y evaluación sobre la higiene bucal [30].

En otro estudio se evaluó la salud bucal de los jóvenes con diabetes tipo 1 controlada y no controlada, comparando los resultados con pacientes sanos. Los sujetos tenían entre entre 6 y 15 años. Los resultados significancia en la cantidad de placa presente entre los grupos, los jóvenes con control glucémico pobre presentaban más placa que los demás, por otra parte, el cálculo gingival no fue significativamente diferente entre los grupos ($p> 0.05$), los niveles de *candida albicans* no presentaban significancia entre los grupos, pero el grupo con mal control glucémico presentaba una mayor detección de la bacteria. Además, se vieron diferencias significativas en el nivel de *S. mutans* entre el grupo con mal control glucémico y el grupo de

sano (p = 0,032). Los resultados muestran que los jóvenes con diabetes tipo 1 tienen un nivel menor de higiene bucal y padecen un mayor riesgo de sufrir una enfermedad bucal en el futuro, sobre todo si el trastorno metabólico no está controlado. Sin embargo, los factores externos a la cavidad bucal también juegan un papel considerable en el inicio y la progresión de las enfermedades bucales [32].

En general, los resultados muestran que la diabetes, especialmente la tipo 1, afecta a los niños y jóvenes en su salud oral, pero los resultados tienden a ser inconsistentes y escasos, por ello, se requiere de una mayor cantidad de investigación al respecto con el fin de aclarar como afecta la diabetes a la salud oral en niños y jóvenes. La creciente prevalencia de diabetes tipo 1 en niños manifiesta la necesidad de que los profesionales de la salud oral sean conscientes de la complicación del tratamiento destinado a obtener y mantener niveles aceptables de glucosa en sangre en niños diabéticos [2,4].

4.5. Diabetes en pacientes mayores y salud oral

Se ha estudiado la existencia de la relación entre la enfermedad periodontal con las enfermedades sistémicas [33]. Los cambios inflamatorios sistémicos que se relacionan con la enfermedad periodontal van de la mano y son similares a los del envejecimiento, fenómeno comúnmente conocido como envejecimiento inflamatorio [33,34]. Se cree que la disminución de la capacidad para hacer frente a factores estresantes, y el incremento progresivo de la inflamación, sean características típicas del proceso de envejecimiento [35]. El proceso inflamatorio se produce por los efectos acumulativos de la carga estimulante y el estrés. En el caso de las patologías degenerativas e hiperplásicas típicas del envejecimiento, estas se generan por una respuesta de estrés celular biológica conocida como senescencia celular [33]. Las vías

comunes pueden relacionar la enfermedad periodontal y la enfermedad sistémica. Como ejemplo, en el caso de las enfermedades crónicas, como la diabetes, se muestra un incremento en la producción de endotelina 1. A pesar de ello, no se sabe con certeza si la mayor cantidad de endotelina 1 presente en el envejecimiento humano es secundaria a procesos patológicos subyacentes o inflamación. o si es un hecho causal de la progresión de la enfermedad, requiriendo de más investigación [33]. Por otra parte, la enfermedad periodontal es crónica y sus efectos se acumulan con la edad, por ello, se supone que la enfermedad periodontal no controlada a lo largo de la vida presenta mayor impacto en los pacientes mayores en comparación con los pacientes más jóvenes [36].

Existe muy poca evidencia que relacione la salud oral, la diabetes y las personas mayores. En el estudio descrito en este trabajo, un total de 500 ancianos, con diabetes tipo 2 o Sandos, respondieron a un cuestionario sobre el índice de evaluación de la salud bucal geriátrica (GOHAI) y un cuestionario de evaluación de la xerostomía. Los resultados mostraban que la prevalencia de xerostomía no era significativa entre los pacientes con diabetes tipo 2 y el control ($p < 0{,}079$). Un mayor número de pacientes con diabetes tipo 2 padeció xerostomía, pero, a pesar de ello, la correlación entre el trastorno y el índice de enfermedad periodontal (PDI), el índice de placa (IP), el índice de salud bucal simplificado (OHI-S) y el índice de evaluación de la salud bucal geriátrica (GOHAI) en los sujetos de los dos grupos de estudio no fue significativo ($p < 0{,}0001$). El estudio demostró que no había una relación significativa entre el GOHAI y los índices periodontales, lo que se puede traducir a la no existencia de diferencias en la calidad de vida relacionada con la salud de los pacientes ancianos con diabetes tipo 2 y los adultos mayores sanos [34].

A pesar de la escasa evidencia sobre el tema, se ve claro que la relación típica entre la diabetes y la edad es muy similar a la de la edad puramente dicha, a pesar de ello, la diabetes agrava los

problemas relacionados con el envejecimiento, principalmente los procesos inflamatorios bucales, por ello, con el fin de tener una correcta salud bucal, y por tanto, disminuir de manera sustancial el riesgo de enfermedades crónicas, las personas deben mantener una buena salud bucal a lo largo de toda la vida [37]. Los profesionales de la salud oral deben proporcionar la educación necesaria tanto a los pacientes como a los cuidadores [33]. Proporcionar cuidados bucales a los pacientes adultos mayores, especialmente a los que reciben cuidados a largo plazo, puede ser una acción tomada demasiado tarde en el tiempo como para generar un cambio significativo en algunos resultados médicos crónicos, como la diabetes [33,36].

Los ensayos clínicos deberían fomentar intervenciones más rigurosas e innovadoras. El tratamiento de la enfermedad periodontal en una cohorte joven o de mediana edad debería alargarse por más de un año para incluir, para evaluar factores como los siguientes: múltiples rondas de raspado y alisado radicular, eliminación de placa, administración local de antimicrobianos o cirugía [33,36].

4.6. Implantes dentales en pacientes con diabetes

La diabetes como contraindicación para la cirugía de implantes es un tema controvertido debdo al incremento del número de pacientes que padecen diabetes, hay más pacientes diabéticos que demandan procedimientos de implantes [38,39].

Un estudio cuyo objetivo era investigar el resultado de las rehabilitaciones de implantes de función inmediata en 70 pacientes diabéticos mostró que siete pacientes perdieron hasta un total de diez implantes, generando así una tasa de supervivencia acumulada global de implantes para pacientes diabéticos del 89,8% (tipo 1: 80% y tipo 2: 90,5%). La pérdida ósea marginal promedio entre uno y cinco años fue de 1,64 mm y 2,55 mm en los pacientes con diabetes tipo

1 y 0,79 mm y 1,45 mm para pacientes diabéticos tipo 2. Los resultados evidencian que las rehabilitaciones con implantes representan un tratamiento válido para los pacientes diabéticos, pese a las escasas complicaciones, con una buena relación riesgo frente al beneficio [40].

Los estudios que relacionan la pérdida ósea marginal a largo plazo (MBL) y la estabilidad de los implantes nano-modificado en pacientes con diabetes mellitus tipo 2 en comparación con un implante convencional no muestran diferencias significativas en el cociente de estabilidad del implante entre grupos. ($p > 0.05$), excepto en lo referido al tiempo en la inserción del implante ($p < 0.05$). La pérdida de hueso marginal en el grupo de implantes nanomodificados presenta un cambio decreciente al compararlo con el grupo de implantes convencionales, entre la etapa de destapamiento y carga ($p < 0.05$), mientras que no había diferencias significativas en otras etapas ($p > 0.05$) [41].

Pese a la heterogeneidad de los resultados, se puede ver que los implantes dentales son procedimientos seguros y predecibles para tartar fenómenos de rehabilitación dental en diabéticos. La tasa de supervivencia de los implantes en diabéticos no varía mucho respecto a la tasa de supervivencia en pacientes sanos dentro durante los primeros 6 años, pero, a largo plazo (20 años), se puede ver una disminución de la supervivencia de los implantes en pacientes diabéticos [38,42,43]. Los pacientes con diabetes mal controlada tienen a padecer un retraso en la osteointegración tras la implantación. Tras un año, no hay diferencia entre diabéticos y personas sanas, ni siquiera con la HbA1c mal controlada. Por ello, la mayoría de estudios recomiendan evitar la carga inmediata de los implantes [39,43].

5. Responsabilidad

Como se ha visto a lo largo del trabajo, la diabetes y la salud oral están muy relacionadas desde el principio de la vida, por ello, es responsabilidad de todos (profesionales de sector dental, familias, cuidadores y personas diabéticas) informarse y educarse sobre como tener hábitos de salud oral correcta con el fin de evitar que la patología se descontrole y incremente con los años, haciéndose incontrolable al final de la vida.

6. Conclusiones

I. La diabetes es una patología inflamatoria crónica que afecta a la salud oral del paciente, disminuyendo las defensas propias de la región, aumentando la inflamación y la hiperglucemia, principalmente, lo que se traduce en problemas bucales relacionados con estos fenómenos como la periodontitis (patología más típica), las infecciones orales, xerostomía y otros problemas derivados de las consecuencias mencionadas.

II. La diabetes tipo 1 es más típica en la juventud, siendo la tipo 2 más típica en edad adulta, pese a ello, el control correcto de la diabetes es fundamental desde la infancia para evitar problemas mayores con la edad los cuales son más difíciles de tratar.

III. Es responsabilidad de todos (profesionales de la salud oral, familia, cuidadores y pacientes) el identificar y tratar la diabetes a tiempo, ya sea por métodos de screening o a través de la detección de síntomas y signos típicos de la patología con el fin de trabajar en ella desde el principio y evitar complicaciones. Además, los implantes dentales como solución no deben ser aplicados temprano tras la detección de la diabetes ya que los resultados, pese a ser buenos, no aseguran una mejoría respecto al no usarlos.

7. Anexos

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Oral manifestations of Diabetes Mellitus. A systematic review

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Abstract

Background: Diabetes Mellitus has become a global epidemic and presents many complications, usually proportional to the degree and duration of hyperglycemia. The aim of this systematic review was to investigate the different oral manifestations associated with Diabetes Mellitus.

Material and Methods: A MEDLINE search for "Diabetes Mellitus and oral manifestations" was performed. A further search was conducted for "diabetes" and its individual oral manifestation. Inclusion criteria were as follows: human clinical studies with a minimum of 30 patients; studies published in relevant scientific journals between January 1998 and January 2016. Nineteen studies fulfilled the inclusion criteria and were analyzed, assessing the strength of scientific evidence according to recommendations made by the Centre for Evidence-Based Medicine, Oxford (OCEBM), which permits adequate assessment of prevalence studies.

Results: A total 3,712 patients (2,084 diabetics) were included in the studies reviewed. Of the 19 studies analyzed, 4 were longitudinal studies and 15 cross-sectional studies. Periodontal disease, periapical lesions, xerostomia and taste disturbance were more prevalent among diabetic patients. An association between diabetes and caries and mucosal lesions proved positive in 5 out of 10 studies.

Conclusions: Despite multiple oral manifestations associated with DM, awareness of the associations between diabetes, oral health, and general health is inadequate. It is necessary for doctors and dentists to be aware of the various oral manifestations of diabetes in order to make an early diagnosis.

Key words: *Diabetes Mellitus, oral manifestations, oral pathology.*

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RESEARCH ARTICLE Open Access

Oral health knowledge, attitudes and care practices of people with diabetes: a systematic review

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Abstract

Background: People with uncontrolled diabetes are at greater risk for several oral health problems, particularly periodontal (gum) disease. Periodontal disease also impacts diabetes control. Good oral hygiene and regular dental visits are recommended to prevent and manage oral health problems. Several studies have been conducted to assess the oral health knowledge, attitudes, and practices of people with diabetes yet a review of these findings has not yet been undertaken. The aim of this systematic review was to synthesize current evidence on the knowledge, attitudes and practices of people with diabetes in relation to their oral health care.

Methods: A systematic search of all literature was carried out in five databases using key search terms. The inclusion criteria were: 1) published in the English language; 2) from 2000 to November, 2017; 3) conducted on persons with any type of diabetes and of all ages; 4) explored at least one study outcome (knowledge or attitude or practices toward oral health care); and 5) used quantitative methods of data collection. No restrictions were placed on the quality and setting of the study.

Results: A total of 28 studies met the inclusion criteria. The studies included a total of 27,894 people with diabetes and were conducted in 14 countries. The review found that people with diabetes have inadequate oral health knowledge, poor oral health attitudes, and fewer dental visits. They rarely receive oral health education and dental referrals from their care providers. Provision of oral health education by diabetes care providers and referral to dentists when required, was associated with improved oral health behaviours among patients.

Conclusions: Overall, people with diabetes have limited oral health knowledge and poor oral health behaviours. It is therefore essential to educate patients about their increased risk for oral health problems, motivate them for good oral health behaviours and facilitate access to dental care.

Keywords: Oral health, Diabetes mellitus, Health knowledge, attitudes, practice, Review

Background

In 2014, it was estimated that 422 million adults were living with diabetes mellitus (DM) worldwide [1]. The global prevalence of diabetes in the adult population has nearly doubled since 1980, rising from 4.7% to 8.5% [1]. Diabetes mellitus (DM) is a group of metabolic disorders that leads to hyperglycaemia and is classified into four general categories: type 1, type 2, gestational diabetes and other specific types of diabetes [2].

Hyperglycaemia can cause several complications related to different organ systems especially the eyes, kidneys, nerves, heart, and blood vessels [1]. Although not commonly discussed in diabetes care, people with uncontrolled diabetes are also at increased risk of developing oral health problems, particularly periodontal (gum) disease [3]. Periodontal disease, which includes both gingivitis and periodontitis, is a common inflammatory disorder caused by pathogenic microflora in the

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Review

Understanding Type 1 Diabetes: Etiology and Models

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ABSTRACT

Type 1 diabetes is a complex disease involving a combination of factors, such as genetic susceptibility, immunologic dysregulation and exposure to environmental triggers. Animal models serve an important function both in elucidating the pathophysiology and preliminary screening of antidiabetic molecules. Hence, the development of models for type 1 diabetes can be broadly divided into 3 categories, namely: identification of spontaneously developing type 1 diabetes mellitus strains, creating diabetes-prone species through gene transfer techniques and forced destruction of islet cells through chemical or surgical means. This review discusses the models used to study type 1 diabetes with special emphasis on genetics.

RÉSUMÉ

Le diabète de type 1 est une maladie complexe se caractérisant par une combinaison de facteurs tels que la prédisposition génétique, la dysrégulation du système immunitaire et l'exposition aux facteurs environnementaux déclencheurs. Les modèles animaux jouent un rôle important tant dans l'élucidation de la physiopathologie que dans le dépistage préliminaire des molécules antidiabétiques. En conséquence, l'élaboration de modèles liés au diabète de type 1 peut généralement être divisée en 3 catégories, à savoir l'identification des souches de diabète sucré de type 1 apparaissant spontanément, la création des espèces sujettes au diabète par les techniques de transfert génétique et la destruction forcée des îlots de Langerhans par des moyens chimiques ou chirurgicaux. Cette revue discute des modèles utilisés pour étudier le diabète de type 1, en accordant une attention particulière à la génétique.

Introduction

The past few decades have seen an unprecedented increase in the occurrence of diabetes mellitus throughout the world [1,2]. Broadly, the disease can be classified into 2 major types: type 1 and type 2. Research has been able to shed light on the multifactorial nature of type 2 diabetes, which is believed to be influenced by genetic, environmental and lifestyle factors [3]. However, the etiology of type 1 diabetes mellitus has not yet been elucidated fully.

Numerous studies have been performed to identify the causative factors involved in the disease [4,5]. Although a complete picture has not yet emerged, certain genes that play a significant role have been identified and mapped. On the basis of this knowledge, type 1 diabetes mellitus is now considered an autoimmune disease involving genetic, immunologic and environmental factors. Nevertheless, the ultimate aim of diabetic research is to find a cure for diabetes or at least find moieties that would be able to prevent the symptoms of the disease. The preliminary screening for antidiabetic molecules usually is performed in animal models; however, because of the complicated etiology, finding the right animal model for type 1 diabetes mellitus remains elusive. Extensive research in this field for the past 4 decades has resulted in a number of animal models suitable for type 1 diabetes mellitus, but a perfect model has yet to be found. The development of models for type 1 diabetes mellitus is still a high-priority research area. In this article, we have explored the existing animal models used for type 1 diabetes mellitus research with special emphasis on genetic regulation of the disease.

Causes for type 1 diabetes mellitus

To understand the basis of type 1 diabetes mellitus, one needs to understand the events that lead to the development of this

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Type 1 Diabetes Mellitus (Juvenile Diabetes) – A Review for the Pediatric Oral Health Provider

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***Objective**: To describe the significance of type 1 diabetes mellitus (juvenile diabetes) to the pediatric oral health provider. **Relevance**: The oral health provider must be aware of type 1 diabetes mellitus (T1DM) characteristics, influence of on oral health, each patient pre-operative diabetic management, symptoms and treatment of hypo and hyper-glycemia, and the clinical implications before, during and after treatment of children with T1DM. **Study design**: A review of the scientific literature about the T1DM influence on dental development, caries prevalence, gingival and periodontal diseases, wound healing, salivary and taste dysfunction, oral infections, and the factors that must be taken in consideration before, during and after oral treatment of children with T1DM is presented. **Conclusion**: The increasing prevalence of T1DB in children strongly emphasizes the need for oral health providers to be aware of the complicacy of the treatment aimed to obtain and maintain acceptable blood glucose levels in diabetic children, the effect of diabetes on the oral cavity, the possible serious complications due to hypo- or hyper glycemia before, during and after oral treatments, the effect of stress on blood glucose levels, and the special behavioral interaction between the diabetic child, his/her family and the oral health providers.*

Keywords: Diabetes, pediatric dentistry, management

INTRODUCTION

Diabetes mellitus (DM) is a group of chronic, metabolic diseases characterized by elevated levels of blood glucose as the result of defects in insulin secretion, insulin action or both.[1-3] The most common type of DM is type 2 (T2DM), it occurs mostly in adults when the body becomes resistant to insulin or doesn't make enough insulin; type 1 diabetes mellitus (T1DM) also known as juvenile diabetes or insulin-dependent diabetes, is the most common type of diabetes mellitus in children and adolescents, it is a chronic condition in which the pancreas produces little or no insulin by itself, and despite of being named juvenile diabetes, this disease may develop at any age.[1-4] The decrease of insulin production and consequent hyperglycemia in T1DM is caused by β-cell destruction, including two major forms based on the presence or absence of pseudo atrophic islets: Pattern A, with all or a subset of islets lacking all insulin secreting β-cells usually in a lobular pattern; Pattern B, with islets with decreased number of β-cells.[2] The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in year 2000, this prevalence is expected to increase to 4.4% in 2030, with an increase of 21% in the prevalence of T1DM in people under age 20 years in the United states between 2001 and 2009, T1DM constituting 5% to 10% of DM cases and its incidence rate increasing from birth peaking between the ages of 10–14 years.[1,3,5]

DM has a most significant influence on oral health, and on oral treatment and its outcome. Therefore, pediatric oral health providers

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Type 2 diabetes

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415 million people live with diabetes worldwide, and an estimated 193 million people have undiagnosed diabetes. Type 2 diabetes accounts for more than 90% of patients with diabetes and leads to microvascular and macrovascular complications that cause profound psychological and physical distress to both patients and carers and put a huge burden on health-care systems. Despite increasing knowledge regarding risk factors for type 2 diabetes and evidence for successful prevention programmes, the incidence and prevalence of the disease continues to rise globally. Early detection through screening programmes and the availability of safe and effective therapies reduces morbidity and mortality by preventing or delaying complications. Increased understanding of specific diabetes phenotypes and genotypes might result in more specific and tailored management of patients with type 2 diabetes, as has been shown in patients with maturity onset diabetes of the young. In this Seminar, we describe recent developments in the diagnosis and management of type 2 diabetes, existing controversies, and future directions of care.

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Introduction

Type 2 diabetes is characterised by relative insulin deficiency caused by pancreatic β-cell dysfunction and insulin resistance in target organs. Between 1980 and 2004, the global rise in obesity, sedentary lifestyles, and an ageing population have quadrupled the incidence and prevalence of type 2 diabetes.[1] As the sixth leading cause of disability in 2015,[2] diabetes places considerable socioeconomic pressures on the individual and overwhelming costs to global health economies, estimated at US$825 billion.[3] Cardiovascular disease is the greatest cause of morbidity and mortality associated with type 2 diabetes[4] and needs intensive management of glucose and lipid concentrations as well as blood pressure to minimise risk of complications and disease progression.[5] The benefits of intensive glucose management on microvascular complications, such as retinopathy, nephropathy, and neuropathy, have been shown in several large randomised controlled trials, including the United Kingdom Prospective Diabetes Study (UKPDS),[6] Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE),[7] and Veterans Association Diabetes Trial (VADT).[8] Evidence that intensive glucose reduction reduces macrovascular outcomes such as cardiovascular disease and stroke is less well established.[9–11] Hypoglycaemia is a major barrier to optimising glucose-lowering therapy, and results of an observational study[12] showed that severe hypoglycaemia was associated with increased mortality at 12 months even in people not receiving insulin.

Quality outcomes for patients are optimised by early detection of type 2 diabetes through screening and intensive patient-centred management. Disease management should be combined with structured education and self-management programmes and psychological support based on the most recent guidelines and supported by a multidisciplinary team (figure 1).[13] As the pathophysiology and underlying mechanisms of diabetes become increasingly understood, treatment can be individualised and targeted appropriately (precision medicine).

Type 2 diabetes is especially challenging in patients younger than 25 years for whom complex phenotypes might necessitate many decades of intensive management to minimise development and progression of microvascular and macrovascular complications. Intensive management of type 2 diabetes in elderly patients (≥65 years of age or older) must be balanced against management of other comorbidities, cognitive impairment, and hypoglycaemia risk. In this Seminar, we review the existing management strategies, discuss new developments in diagnosis, treatment, and cardiovascular benefits, highlight controversies and uncertainties, and address outstanding research questions.

Epidemiology and pathophysiology

The global rising tide of obesity, physical inactivity, and energy-dense diets has resulted in an unprecedented increase in the number of patients with type 2 diabetes. In 2015, 415 million people were estimated to have diabetes, more than 90% of whom had type 2 diabetes, with a projected increase to 642 million by 2040.[4] Incidence and prevalence of type 2 diabetes vary according to geographical region, with more than 80% of patients living in low-to-middle-income countries, but the overall trend is an increase in diabetes prevalence in every country since 1980.[1] An additional 318 million people have a preclinical state of impaired glucose regulation,[14] but intensive lifestyle modification,

Search strategy and selection criteria

We searched Cochrane Library, MEDLINE, and Embase for manuscripts published between Jan 1, 2000, and Dec 31, 2016, using the terms "type 2 diabetes" and "type 2 diabetes mellitus". We largely selected articles published in the past 5 years but did not exclude commonly referenced and highly regarded, older articles. We also searched the reference lists of articles identified by this search strategy and selected those we judged relevant. Reviews are cited to provide readers with more details and more references than this Seminar could accommodate.

frontiers in Endocrinology

REVIEW
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Evaluating All Potential Oral Complications of Diabetes Mellitus

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Diabetes mellitus (DM) is associated with several microvascular and macrovascular complications, such as retinopathy, nephropathy, neuropathy, and cardiovascular diseases. The pathogenesis of these complications is complex, and involves metabolic and hemodynamic disturbances, including hyperglycemia, insulin resistance, dyslipidemia, hypertension, and immune dysfunction. These disturbances initiate several damaging processes, such as increased reactive oxygen species (ROS) production, inflammation, and ischemia. These processes mainly exert their damaging effect on endothelial and nerve cells, hence the susceptibility of densely vascularized and innervated sites, such as the eyes, kidneys, and nerves. Since the oral cavity is also highly vascularized and innervated, oral complications can be expected as well. The relationship between DM and oral diseases has received considerable attention in the past few decades. However, most studies only focus on periodontitis, and still approach DM from the limited perspective of elevated blood glucose levels only. In this review, we will assess other potential oral complications as well, including: dental caries, dry mouth, oral mucosal lesions, oral cancer, taste disturbances, temporomandibular disorders, burning mouth syndrome, apical periodontitis, and peri-implant diseases. Each oral complication will be briefly introduced, followed by an assessment of the literature studying epidemiological associations with DM. We will also elaborate on pathogenic mechanisms that might explain associations between DM and oral complications. To do so, we aim to expand our perspective of DM by not only considering elevated blood glucose levels, but also including literature about the other important pathogenic mechanisms, such as insulin resistance, dyslipidemia, hypertension, and immune dysfunction.

Keywords: diabetes mellitus, oral complications, hyperglycemia, insulin resistance, dyslipidemia, hypertension, immune dysfunction

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INTRODUCTION

Diabetes mellitus (DM) is defined as a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (1). In 2014, the global prevalence of DM was estimated to be 9% (2), and almost 1.6 million deaths worldwide were caused directly by DM in 2015 (3). DM is also associated with high morbidity due to a broad range of complications, such as retinopathy, nephropathy, neuropathy, and cardiovascular disease (4, 5). Prevention and management of these complications have become major aspects of modern diabetes care. Besides

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Review Article

Diabetes: Oral Health Related Quality of Life and Oral Alterations

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Background and Objectives. About 5% of the world's population is affected by diabetes; these patients must be further treated during medical and surgical treatments. These patients, due to the glycemic conditions, realize during their life multiorgan changes, in different body districts. Moreover, this condition obliges them to undertake hypoglycemic therapies. Diabetes is a risk factor for many diseases, including those concerning the oral district with immunological implications. *Materials and Methods.* A comprehensive review of the literature was conducted according to PRISMA guidelines accessing the NCBI PubMed database. Authors conducted the search of articles in English language. The results of the last 10 years have been considered, which present useful information regarding the oral conditions. A total of 17 relevant studies were included in the review. The study evaluated only papers with specific inclusion criteria regarding oral health. The works initially taken into consideration were 782; subsequently applying the inclusion and exclusion criteria, there were 42 works. After a careful analysis of the work obtained by two academics who have worked separately, there have been 17 studies. All data from the studies were compared and many of these confirmed alteration in the oral district. *Results.* The studies taken into consideration evaluated different factors, such as OHRQoL, QoL, and oral alterations, involving soft tissue, dental structures, and postrehabilitative complications, as well as immunological alterations. *Conclusions.* We can affirm, in conclusion, that this study has brought to light those that are complications due to diabetic pathology, from different points of view. The psychological and psychosocial alterations, certainly present in these patients, are probably due to local and systemic alterations; this is confirmed by the correlation between oral health and quality of life reported by the patients.

1. Introduction

Diabetes is a term that identifies some diseases characterized by polyuria (abundant production of urine), polydipsia (abundant ingestion of water), and polyphagia (excessive hunger). Commonly the term is used to indicate a chronic disease, which can be included in the group of diseases known as diabetes mellitus, characterized by a high concentration of glucose in the blood, which is in turn caused by a total or partial lack of insulin in the human organism, a hormone that decreases the concentration of glucose in the blood. Diabetes mellitus is a form of diabetes or a group of metabolic disorders united by the fact of persistent instability of the blood glucose level, going from conditions of hyperglycemia, more frequent, at hypoglycemia conditions. Although the term diabetes refers in the common practice to the only condition of diabetes mellitus; that is sweet, there is another pathological condition called diabetes insipidus. The percentage of affected

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Diabetes and oral disease: implications for health professionals

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Abstract

"Diabetes and Oral Disease: Implications for Health Professionals" was a one-day conference convened by the Columbia University College of Dental Medicine, the Columbia University College of Physicians and Surgeons, and the New York Academy of Sciences on May 4, 2011in New York City. The program included an examination of the bidirectional relationship between oral disease and diabetes and the inter-professional working relationships for the care of people who have diabetes. The overall goal of the conference was to promote discussion among the healthcare professions who treat people with diabetes, encourage improved communication and collaboration among them and ultimately, improve patient management of the oral and overall effects of diabetes. Attracting over 150 members of the medical and dental professions from eight different countries, the conference included speakers from academia and government and was divided into four sessions. This report summarizes the scientific presentations of the event.

Keywords

diabetes; oral disease; meeting report

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Conflicts of interest

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ORIGINAL ARTICLE

ORAL DISEASES WILEY

The effects of non-surgical periodontal therapy on glycemic control in diabetic patients: A randomized controlled trial

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Abstract

Aim: The present study aimed to monitor the clinical outcomes and the metabolic response of periodontal therapy (non-surgical) in patients with periodontitis (chronic) and uncontrolled diabetes (type 2).

Methods: Eighty-eight subjects with periodontitis (chronic) and uncontrolled diabetes (type 2) were enrolled in this controlled trial and allocated randomly to the test group (44 patients were received immediate periodontal therapy) or the control group (44 patients were received delayed periodontal therapy). The metabolic and clinical evaluations were conducted at baseline and 3 months. This included clinical attachment level, glycated hemoglobin (HbA1c), bleeding on probing, visible plaque, and pocket depth. The periodontal therapy in this study consists of one-stage scaling and root planning, a combination of systemic antibiotics (amoxicillin 500 mg and metronidazole 400 mg), and oral hygiene instructions.

Results: Regarding clinical and metabolic parameters at baseline, no statistically significant differences were displayed between the two groups. However, at 3-month follow-up period the patients within the test group demonstrated significantly better clinical and metabolic outcomes than patients in the control group.

Conclusion: The non-surgical periodontal treatment using a combination of metronidazole and amoxicillin significantly improved the metabolic outcome in addition to periodontal health in diabetic subjects with chronic periodontitis.

KEYWORDS
amoxicillin, chronic periodontitis, diabetes, glycated hemoglobin, metronidazole, periodontal medicine

1 | INTRODUCTION

Periodontitis is a chronic multifactorial infectious and inflammatory disorder manifested by the loss of structures that support teeth (Pihlstrom, Michalowicz, & Johnson, 2005). The epidemiological studies reported that the prevalence of periodontitis is 15%–30% of adult populations (König, Holtfreter, & Kocher, 2010). Clinical manifestations of periodontitis include increased clinical attachment loss or pocket depth. Periodontal therapies consist of instructions for oral hygiene, scaling, root planing, adjunctive use of antibiotics and/or chlorhexidine, surgical therapy, or a combination of these (Armitage, 2004). Miranda et al. (2014) reported that in the treatment of diabetes mellitus type 2 (T2DM) with chronic periodontitis, the adjunctive use of amoxicillin and metronidazole significantly improved the microbiological and the clinical results. The prevalence of diabetes among adults from 20 to

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Systemic Inflammatory Biomarkers and Their Association With Periodontal and Diabetes-Related Factors in the Diabetes and Periodontal Therapy Trial (DPTT), A Randomized Controlled Trial

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Background: We sought to evaluate: 1) effects of non-surgical periodontal treatment on serum biomarkers in persons with type 2 diabetes and chronic periodontitis who participated in the Diabetes and Periodontal Therapy Trial (DPTT); and 2) associations between diabetes markers, serum biomarkers, and periodontal measures in these patients.

Methods: DPTT participants who were randomized to receive immediate or delayed nonsurgical periodontal therapy were evaluated at baseline (BL) and six months. Serum samples from 475 participants with six-month data were analyzed for biomarkers [high sensitivity C-reactive protein (Hs-CRP), E-Selectin, tumor necrosis factor-alpha (TNF-α), vascular cell adhesion molecule (VCAM), interleukin-6 (IL-6), interleukin-8 (IL-8), intercellular adhesion molecule (ICAM), and interleukin-10 (IL-10)]. Changes in biomarker levels from BL and correlations between biomarker levels and clinical findings were analyzed.

Results: No differences between Treatment and Control Groups were observed for any biomarkers at BL or 6 months ($p>0.05$ for all variables). VCAM levels increased by an average (SD) of 17.9 (99.5), ng/mL ($p= 0.006$) and E-Selectin decreased by 2.33 (16.08) ng/mL ($p=0.03$) in the Treatment Group after six months. E-selectin levels were significantly correlated with diabetes-related variables [hemoglobin A1c (HbA_{1c}) and Fasting Glucose] at BL and with six-month change in both Groups; no significant correlations were found between periodontal clinical parameters and serum biomarkers or diabetes related variables. Neither HbA_{1c} or body mass index (BMI) varied during the study period in either Study Group.

Conclusions: Non-surgical periodontal therapy and periodontal disease severity were not associated with significant changes in serum biomarkers in DPTT participants over the six-month follow-up. The correlations between changes in E-selectin, IL-6, and diabetes related variables suggest that diabetes mellitus may be the primary driver of systemic inflammation in these diabetic patients.

MESH TERMS:

Periodontal Diseases, Diabetes Mellitus, Biological Markers, Periodontitis, Cytokines.

Diabetes mellitus is a group of metabolic syndromes characterized by disordered metabolism and abnormally high blood sugar (hyperglycemia) resulting from low levels of the hormone insulin with or without insulin resistance.[1] Approximately 29.1 million people in the United States (9.3%) are estimated to have diabetes with 21.0 million of those being diagnosed.[2] Approximately 1.7 million new cases were diagnosed in adults in 2012.[2] Diabetes mellitus has been linked to poor oral health and nutritional habits.[3-5] Periodontal disease is likewise a common infectious and inflammatory disease affecting nearly half of all U.S. adults.[6,7]

Inflammation has been implicated as a pathogenic mechanism in both diabetes mellitus[8] and chronic periodontitis.[9] Several pro-inflammatory cytokines including tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), and high sensitivity C-reactive protein (Hs-CRP) have been implicated in the pathogenesis of both

Systemic effects of periodontitis treatment in patients with type 2 diabetes: a 12 month, single-centre, investigator-masked, randomised trial

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See Comment page 917

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See Online for appendix

Summary

Background Chronic inflammation is believed to be a major mechanism underlying the pathophysiology of type 2 diabetes. Periodontitis is a cause of systemic inflammation. We aimed to assess the effects of periodontal treatment on glycaemic control in people with type 2 diabetes.

Methods In this 12 month, single-centre, parallel-group, investigator-masked, randomised trial, we recruited patients with type 2 diabetes, moderate-to-severe periodontitis, and at least 15 teeth from four local hospitals and 15 medical or dental practices in the UK. We randomly assigned patients (1:1) using a computer-generated table to receive intensive periodontal treatment (IPT; whole mouth subgingival scaling, surgical periodontal therapy [if the participants showed good oral hygiene practice; otherwise dental cleaning again], and supportive periodontal therapy every 3 months until completion of the study) or control periodontal treatment (CPT; supra-gingival scaling and polishing at the same timepoints as in the IPT group). Treatment allocation included a process of minimisation in terms of diabetes onset, smoking status, sex, and periodontitis severity. Allocation to treatment was concealed in an opaque envelope and revealed to the clinician on the day of first treatment. With the exception of dental staff who performed the treatment and clinical examinations, all study investigators were masked to group allocation. The primary outcome was between-group difference in HbA_{1c} at 12 months in the intention-to-treat population. This study is registered with the ISRCTN registry, number ISRCTN83229304.

Findings Between Oct 1, 2008, and Oct 31, 2012, we randomly assigned 264 patients to IPT (n=133) or CPT (n=131), all of whom were included in the intention-to-treat population. At baseline, mean HbA_{1c} was 8·1% (SD 1·7) in both groups. After 12 months, unadjusted mean HbA_{1c} was 8·3% (SE 0·2) in the CPT group and 7·8% (0·2) in the IPT group; with adjustment for baseline HbA_{1c}, age, sex, ethnicity, smoking status, duration of diabetes, and BMI, HbA_{1c} was 0·6% (95% CI 0·3–0·9; p=0·0001) lower in the IPT group than in the CPT group. At least one adverse event was reported in 30 (23%) of 133 patients in the IPT group and 23 (18%) of 131 patients in the CPT group. Serious adverse events were reported in 11 (8%) patients in the IPT group, including one (1%) death, and 11 (8%) patients in the CPT group, including three (2%) deaths.

Interpretation Compared with CPT, IPT reduced HbA_{1c} in patients with type 2 diabetes and moderate-to-severe periodontitis after 12 months. These results suggest that routine oral health assessment and treatment of periodontitis could be important for effective management of type 2 diabetes.

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Introduction

The worldwide epidemic of type 2 diabetes is a major cause of disability and premature mortality, mainly from vascular and renal complications.[1] Inflammation can affect glycaemic control in patients with diabetes and is implicated in atherosclerosis and chronic kidney disease.[2] However, whether effective control of systemic inflammation can improve glycaemic control in people with type 2 diabetes and thereby reduce their risk of diabetes complications remains unclear.

Periodontitis is a chronic inflammatory disease, which often coexists with diabetes.[3] It is caused by a dysbiosis of the oral microbiota and is associated with a dysregulated immune-inflammatory response.[4] The response induced by accumulation of bacteria on the tooth surface is not only confined to the oral cavity, but is also associated with systemic inflammation.[5] The elevated systemic inflammatory burden in people with periodontitis has been associated with increased risk of chronic and potentially life-threatening diseases including diabetes, cardiovascular disease, and end-stage renal failure.[6]

Periodontal therapy is usually delivered over three phases: an initial phase, a corrective phase, and a final supportive phase. During the initial phase, any essential dental care, oral hygiene advice, and teeth cleaning (scaling of the teeth, including subgingival root debridement) are

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Article type : Randomized Clinical Trial

The effects of periodontal treatment on diabetic patients: the DIAPERIO randomized controlled trial

Running title: Periodontitis and diabetes: DIAPERIO RCT

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Original Research
Periodontics

Glycemic control and adipokines after periodontal therapy in patients with Type 2 diabetes and chronic periodontitis

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Abstract: The mechanism by which chronic periodontitis (CP) affects type 2 diabetes (T2DM) remains unclear. Therefore, the aim of this study is to evaluate the effects of periodontal therapy (PT) on the glycemic control and adipokines of patients with T2DM and CP with the purpose of elucidating the possible mechanisms by which CP influences T2DM. Forty-four patients with T2DM and CP were randomly divided into two groups according to whether they underwent PT. Periodontal status, blood glucose, and the levels of serum tumor necrosis factor α (TNF-α), interleukin-6 (IL-6), adiponectin (APN), and fibroblast growth factor-21 (FGF-21) were measured at baseline and after 3 months. The results revealed that the probing depth (PD) and attachment loss (AL) were significantly improved, the serum levels of TNF-α and IL-6 were significantly decreased, and APN and FGF-21 exhibited substantial increases in the intervention group after 3 months ($p < 0.05$), whereas no significant changes were observed in the control group. The glycated hemoglobin (HbA1c) levels in both groups decreased significantly after 3 months compared with baseline ($p < 0.05$), but the intervention group exhibited a significantly greater change ($p < 0.05$). In conclusion, PT may relieve periodontal inflammation, which causes a reduction of insulin-antagonizing adipokines and an increase in insulin-sensitizing adipokines, thereby eliciting an improvement in glycemic control.

Keywords: Adipokines; Diabetes Mellitus; Periodontitis.

Introduction

Diabetes mellitus (DM) is a metabolic disorder that is mainly characterized by hyperglycemia due to impaired insulin action. The most common form of DM is type 2 diabetes mellitus (T2DM), which accounts for approximately 90% of all DM patients.[1,2] Due to social mobility and rapid urbanization, the global prevalence of DM has increased sharply in recent years. Globally, 415 million adults have diabetes, and by 2040, this number will rise to 642 million.[2] China now has the largest epidemic worldwide, and a recent study demonstrated that the prevalence of DM is up to 11.6% (95%CI: 11.3% –11.8%) among Chinese adults.[3]

Chronic periodontitis (CP) is one of the most common chronic infectious diseases and is characterized by destruction of the supporting structures of the teeth. According to the estimated data by Paul IE, 46% of adults in

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Mitochondrial oxidative stress, endothelial function and metabolic control in patients with type II diabetes and periodontitis: A randomised controlled clinical trial

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ABSTRACT

Background: Periodontitis (PD) and type 2 diabetes (T2D) are characterized by increased mitochondrial oxidative stress production (mtROS), which has been associated with a greater risk of cardiovascular diseases (CVD). Intensive PD treatment (IPT) can significantly improve endothelial function and metabolic control, although the mechanisms remain unclear. We explored whether, in patients with PD and T2D, changes of mtROS are associated with improvement of endothelial function and metabolic control after IPT.

Methods: 51 patients with T2D and PD were enrolled in a single-blind controlled trial and randomised to either intensive (n = 27) or standard (CPT, n = 24) PD treatment. Levels of mtROS in peripheral blood mononuclear cells (PBMC) were measured using a FACS-based assay at baseline and 24 h, 1 week, 2 and 6 months after PD treatment. Inflammatory cytokines, CVD risk factors, metabolic control and endothelial function were assessed at baseline and 6 months after intervention.

Results: After 6 months from PD treatment, the IPT group had lower mtROS (in both the whole PBMC and lymphocytes), circulating levels of HbA1c, glucose, INF-γ, TNF-α ($p < 0.05$ for all), and improved endothelial function ($p < 0.05$) compared to the CPT group. There was an association between higher mtROS and lower endothelial function at baseline ($r = -0.39$; $p = 0.01$) and, in the IPT group, changes of mtROS were associated with changes of endothelial function ($r = 0.41$; $p < 0.05$).

Conclusions: Reduced mtROS is associated with improved endothelial function and accompanied by better metabolic control in patients with T2D and PD. mtROS could represent a novel therapeutic target to prevent CVD in T2D.

1. Introduction

Chronic inflammatory diseases account for a substantial proportion of the cardiovascular disease (CVD) morbidity and mortality worldwide. Among these, type 2 diabetes (T2D) and periodontitis (PD) are highly prevalent in the general population and closely interconnected, so that people with PD are at higher risk of T2D, and vice-versa [1]. The risk of cardiorenal mortality (ischaemic heart disease and diabetic nephropathy combined) is three times higher when T2D and PD coexist than in people with T2D alone. While inflammation could account for the increased CVD risk of people with T2D and PD, we have shown that circulating levels of common inflammatory markers are unable to explain the significant improvement of endothelial function and metabolic control observed after intensive periodontal treatment [2,3]. This suggests that there might be more specific and responsive pathways associated with the activation of the inflammatory response, which could underpin

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Research Article

Levels of Myeloperoxidase and Metalloproteinase-9 in Gingival Crevicular Fluid from Diabetic Subjects with and without Stage 2, Grade B Periodontitis

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Objective. The present study aimed to compare levels of matrix metalloproteinase-9 (MMP-9) and myeloperoxidase (MPO) in gingival crevicular fluid (GCF) from subjects with controlled and noncontrolled Type 2 Diabetes Mellitus (T2D), with and without stage 2 grade B periodontitis (POD2B) versus healthy (H) subjects. *Methods.* The levels of both enzymes, from 80 GCF samples collected with PerioPaper strips, were analyzed by a Multiplex/Luminex assay. Five groups were formed, all current patients at the Institutional Dentistry Service, and distributed as follows: two groups of diabetics (one controlled and one poorly controlled); two groups with the previous conditions and diagnosed with POD2B; and one H group. *Results.* The highest concentration of MMP-9 corresponded to the H group, while the lowest corresponded to the T2D controlled group. Regarding MPO levels, the highest levels were associated with the T2D controlled with POD2B group and the lowest with the T2D controlled group. *Conclusions.* No apparent relationship between the elevation of MMP-9 and MPO levels was observed among subjects with T2D, with and without POD2B, compared to H subjects.

1. Introduction

The periodontium is a functional unit formed by a group of specialized tissues that surround the teeth. It can be classified, due to its main functions, into two categories: the attachment periodontium, which involves periodontal ligament, cementum, and alveolar bone; the protection periodontium, only formed by the gingiva which is in a close relationship with the gingival sulcus: a "V" shaped, shallow cavity that relies underneath the gingival margin. In health, the gingival sulcus maintains a depth of 0-3 millimeters (mm), measured from the gingival margin to the base of the gingival sulcus, and also contains a low amount of gingival crevicular fluid (GCF) which is an inflammatory exudate that increases its volume when inflammation occurs and also contains a variety of biomarkers that are related to inflammatory processes [1].

The oral cavity is a main source of bacterial biofilm, and the periodontium can be an ideal reservoir for oral pathogens and its proinflammatory products, such as MMP-9 and MPO, since it has an anaerobic environment inside the periodontal sulcus, a vast gingival blood stream that it is connected to the alveolar blood circulation and a rich source of collagen fibers. When bacterial invasion of the gingival sulcus occurs, a periodontal pocket is formed, increasing the depth of the

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Efficacy of adjunctive photodynamic therapy on the clinical periodontal, HbA1c and advanced glycation end product levels among mild to moderate chronic periodontal disease patients with type 2 diabetes mellitus: A randomized controlled clinical trial

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Keywords:
Advanced glycation end-products
Photodynamic therapy
Scaling and root planing
Chronic periodontitis
Diabetes mellitus

ABSTRACT

Aims: To evaluate the clinical periodontal, serum glycated haemoglobin (HbA1c) and levels of advanced glycation end-products (AGEs) in the gingival crevicular fluid (GCF) among patients with periodontitis and type 2 diabetes mellitus (DM) after photodynamic therapy (PDT) as an adjunct to full-mouth disinfection (FMD).

Materials and Methods: Thirty type 2 DM patients with mild to moderate periodontitis were divided into two main groups: Group-A receiving adjunctive PDT with FMD and Group-B receiving FMD alone. Full-mouth plaque index (PI), bleeding on probing (BOP), probing depth (PD), attachment level (AL) were recorded. Serum HbA1c was assessed among all participants using a HbA1c analyser kit. Levels of AGEs in GCF were determined using enzyme-linked immunosorbent assay. Clinical periodontal and metabolic parameters were assessed at baseline, 3 months and 6 months. Differences were compared using the Friedman test within the groups for different time points. Kruskal-Wallis test with Bonferroni correction test was applied for intragroup and multiple comparisons, respectively.

Results: All the clinical periodontal parameters showed significant reduction from baseline to 3 months ($P < 0.05$) and 6 months follow-up in both the groups ($P < 0.05$). Only PD showed statistically significant difference from baseline to 3 months in Group-A ($P < 0.01$). Mean percentage of HbA1c remained constant throughout the study period in both the groups. Mean level of AGEs significantly reduced in both the groups at all time-points. Mean AGEs level reduced slightly higher in Group-A compared to Group-B at 3 months follow-up. However, this difference was not statistically significant ($P > 0.05$).

Conclusion: No additional benefit was seen in the improvement of clinical periodontal parameters and systemic (HbA1c levels) outcomes with PDT except that a minor reduction in the levels of AGEs in the GCF was observed with PDT in the short term.

1. Introduction

Type 2 diabetes mellitus (DM) is a chronic metabolic condition that is comprised of derangement of blood glucose levels due to, either in the resistance of insulin action or downgrade of insulin levels [1]. Type 2 DM has surged quadrupled in the last three decades globally and is considered as major cause of death. Although research suggests that genetic tendency plays a significant role in the individual vulnerability in the cause of type 2 DM; however dietary factors are important and primary drivers in the susceptibility of type 2 DM [2,3]. Patients with type 2 DM are susceptible to have cardiovascular complications, renal and cerebral disorders later in life. There is exhaustive research in dentistry that indicates type 2 DM is a major risk factor in the development of periodontitis [4,5].

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Comparison between different D-Dimer cutoff values to assess the individual risk of recurrent venous thromboembolism: analysis of results obtained in the DULCIS study

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Keywords
D-dimer, cutoff criteria, venous thromboembolism, recurrence

SUMMARY

Introduction: D-dimer assay, generally evaluated according to cutoff points calibrated for VTE exclusion, is used to estimate the individual risk of recurrence after a first idiopathic event of venous thromboembolism (VTE).
Methods: Commercial D-dimer assays, evaluated according to predetermined cutoff levels for each assay, specific for age (lower in subjects <70 years) and gender (lower in males), were used in the recent DULCIS study. The present analysis compared the results obtained in the DULCIS with those that might have been had using the following different cutoff criteria: traditional cutoff for VTE exclusion, higher levels in subjects aged ≥60 years, or age multiplied by 10.
Results: In young subjects, the DULCIS low cutoff levels resulted in half the recurrent events that would have occurred using the other criteria. In elderly patients, the DULCIS results were similar to those calculated for the two age-adjusted criteria. The adoption of traditional VTE exclusion criteria would have led to positive results in the large majority of elderly subjects, without a significant reduction in the rate of recurrent event.
Conclusion: The results confirm the usefulness of the cutoff levels used in DULCIS.

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ORIGINAL ARTICLE

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Periodontal therapy and glycaemic control among individuals with type 2 diabetes: reflections from the PerioCardio study

Abstract: *Objectives:* Diabetes mellitus and periodontal disease are highly prevalent among Indigenous Australian adults. Untreated periodontitis impacts glycaemic control in people with diabetes. The aim of this study was to report on the effect of periodontal therapy on glycaemic control among people with obesity. *Methods:* This subgroup analysis is limited to 62 participants with diabetes from the original 273 Aboriginal Australian adults enrolled into the PerioCardio study. Intervention participants received full-mouth non-surgical periodontal scaling during a single, untimed session while controls were untreated. Endpoints of interest included change in glycated haemoglobin (HbA1c), C-reactive protein (CRP) and periodontal status at 3 months post-intervention. *Results:* There were more females randomized to the treatment group ($n = 17$) than control ($n = 10$) while the control group had a higher overall body mass index (BMI) [mean (SD)] 33.1 (9.7 kg m^{-2}) versus 29.9 (6.0 kg m^{-2}). A greater proportion of males were followed up at 3 months compared to females, $P = 0.05$. Periodontal therapy did not significantly reduce HbA1c: ANCOVA difference in means 0.22 mmol mol^{-1} (95% CI −6.25 to 6.69), CRP: ANCOVA difference in means 0.64 (95% CI −1.08, 2.37) or periodontal status at 3 months. *Conclusions:* Non-surgical periodontal therapy did not significantly reduce glycated haemoglobin in participants with type 2 diabetes. Reasons are likely to be multifactorial and may be influenced by persistent periodontal inflammation at the follow-up appointments. Alternatively, the BMI of study participants may impact glycaemic control via alternative mechanisms involving the interplay between inflammation and adiposity meaning HbA1c may not be amenable to periodontal therapy in these individuals.

Key words: diabetes mellitus, type 2; Indigenous Australian; periodontal therapy, non-surgical; randomized controlled trial

Introduction

Disparities in the health status of Indigenous Australians are well known. To illustrate, 11% of Indigenous Australians have diabetes, 60% of which is poorly controlled (1). The prevalence of type 2 diabetes is more than three times higher than in non-Indigenous Australians (2). Furthermore, it has been estimated that an additional five per cent of Indigenous Australians have impaired fasting glucose metabolism placing them at risk for diabetes (1). In terms of risk factors for other chronic conditions, almost

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RANDOMIZED CLINICAL TRIAL

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Effect of two periodontal treatment modalities in patients with uncontrolled type 2 diabetes mellitus: A randomized clinical trial

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Abstract

Aim: To evaluate the impact of two non-surgical periodontal treatment modalities on metabolic and periodontal clinical parameters in subjects with type 2 diabetes mellitus (T2DM) and poor glycaemic control and chronic periodontitis.

Material and methods: A randomized controlled clinical trial was conducted. Ninety-three T2DM subjects with glycosylated haemoglobin (HbA1c) > 7% were randomly assigned to one of two groups receiving scaling with root planing in multiple sessions quadrant-by-quadrant (Q by Q) or within 24 hr (one stage). Periodontal parameters, HbA1c, glycaemia blood levels (FPG) and C-reactive protein (CRP) values were assessed at baseline and at 3 and 6 months post-therapy.

Results: At 6 months, HbA1c had decreased by 0.48% in the Q by Q group and by 0.18% in the one-stage group ($p = 0.455$). After therapy, subjects with an initial HbA1c < 9% showed an increase of 0.31% ($p = 0.145$), compared with a decrease of 0.88% ($p = 0.006$) in those with an initial HbA1c ≥ 9%. Periodontal parameters improved significantly ($p < 0.0001$) post-therapy, with similar results for both treatment modalities.

Conclusion: Periodontal therapy had the greatest impact on HbA1c reduction on patients with an HbA1c > 9% regardless of treatment modality. Both modalities resulted in significant improvements in periodontal parameters.

KEYWORDS
C-reactive protein, glycosylated haemoglobin, periodontal treatment, periodontitis, type 2 diabetes mellitus

1 | INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a highly prevalent disease and is increasing annually (WHO, 2016). In patients diagnosed with diabetes, the glycosylated haemoglobin (HbA1c) test is commonly used to monitor glycaemic control (ADA, 2016). An association exists between increasing HbA1c levels and the development of complications. Conversely, adequate glucose control has been found to reduce the risk of complications associated with T2DM (Rohlfing et al., 2002). Chronic periodontitis (CP) is an infectious inflammatory disease characterized by the loss of both hard and soft tooth-supporting tissues (Pihlstrom, Michalowicz, & Johnson, 2005).

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ORIGINAL ARTICLE

Periodontics

Effect of non-surgical periodontal therapy on insulin resistance in patients with type II diabetes mellitus and chronic periodontitis, as assessed by C-peptide and the Homeostasis Assessment Index*

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Keywords
chronic periodontitis, C-peptide, Homeostasis Assessment Index, insulin resistance, type II diabetes mellitus.

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Abstract

Aim: A bidirectional relationship exists between diabetes and periodontitis. In the present clinical trial, we evaluated the effects of non-surgical periodontal therapy (NSPT) on insulin resistance in patients with type II diabetes mellitus (DM) and chronic periodontitis.

Methods: Forty chronic periodontitis patients with type II DM were selected and equally allocated to case and control groups. All patients were assessed for periodontal parameters and systemic parameters. The case group received NSPT, and both groups were re-evaluated after 3 months.

Results: All periodontal parameters were found to be significantly improved in the case group compared to the control group 3 months after NSPT. The mean differences in systemic parameters, such as fasting serum C-peptide, Homeostasis Assessment (HOMA) Index–insulin resistance, and HOMA–insulin sensitivity, from baseline to 3 months for the case group were 0.544 ± 0.75, 0.54 ± 0.63, and -25.44 ± 36.81, respectively; for the control group, they were significant at -1.66 ± 1.89, -1.48 ± 1.86, and 51.42 ± 38.82 respectively ($P < 0.05$). There was a significant decrease in fasting blood glucose and glycosylated hemoglobin A1c from baseline to 3 months in the case group ($P < 0.05$).

Conclusion: The present study showed that periodontal inflammation could affect glycemic control and insulin resistance. Effective periodontal therapy reduced insulin resistance and improved periodontal health status and insulin sensitivity in patients with type II DM and chronic periodontitis.

Introduction

Periodontal disease is a common, chronic immunoinflammatory disease characterized by the destruction and loss of periodontal tissue. It results in host inflammation and immune reaction. The inflammatory response is characterized by the dysregulated secretion of host-derived mediators of inflammation and tissue breakdown. It includes interleukins (IL)-1β, IL-6, prostaglandin E2 (PGE2), tumor necrosis factor-α (TNF-α), receptor activator of nuclear factor κβ ligand (RANKL), and matrix metalloproteinases. Evidence suggests that periodontal infection could significantly increase the risk of various systemic diseases, such as coronary heart disease, diabetes mellitus (DM), and rheumatoid arthritis.[1–3] DM is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both.[4] The International Diabetes Federation states that 8.3% of adults (382 million) have diabetes, and the number of people with the disease is set to rise above 592

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Effect of non-surgical periodontal therapy on insulin resistance and insulin sensitivity among individuals with borderline diabetes: A randomized controlled trial

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Borderline diabetes
Insulin resistance and sensitivity
Non-surgical periodontal therapy
Periodontitis
Randomized controlled trial

ABSTRACT

Objective: To investigate the effect of non-surgical periodontal therapy on insulin resistance and sensitivity among individuals with borderline diabetes not receiving medications.

Methods: A crossover, randomized controlled trial was conducted among participants with borderline diabetes diagnosed by a 75-g oral glucose tolerance test. Participants were randomly assigned to either an early or later intervention group. The early intervention group underwent non-surgical periodontal therapy of scaling and root planing during the first 4 months, followed by a 4-month non-intervention period. The order was reversed in the later intervention group. Primary outcomes included fasting or post-load serum glucose and insulin, body mass index (BMI), HOMA-IR, HOMA-β, and Matsuda Index.

Results: Seventy-four participants were randomized, and 71 participants completed the trial. There were no significant differences between groups in glucose and insulin concentrations during the intervention and non-intervention periods. When analyzed within groups by median-split of bleeding on probing (BOP) levels before intervention, the lower BOP group showed improved changes in BMI, HOMA-IR, HOMA-β, and Matsuda Index ($P < 0.05$). Further, we observed a positive correlation between baseline BOP and change in BMI ($P = 0.86$). Change in BMI was positively correlated with changes in HbA_{1c}, HOMA-IR, and HOMA-β ($P < 0.05$), and inversely correlated with change in Matsuda Index ($P = 0.001$).

Conclusions: Periodontal therapy had no significant effect on markers related to insulin and glucose metabolism among individuals with borderline diabetes. However, participants with a lower BOP (%) showed significant improvements in BMI, fasting serum insulin, HOMA-IR, HOMA-β and Matsuda Index.

Clinical significance: Among individuals diagnosed with borderline diabetes, those who had < 37% of a lower BOP (%) showed potential improvements in BMI, fasting serum insulin, HOMA-IR, HOMA-β and Matsuda Index following non-surgical periodontal therapy.

1. Introduction

While several observational studies have reported that periodontal disease was associated with the prevalence of diabetes mellitus [1,2], the results from clinical trials of non-surgical periodontal therapy among patients with diabetes have been inconsistent. Some studies showed an improvement in serum glucose or HbA1c [3,4] and insulin resistance [5,6] associated with non-surgical periodontal therapy, whereas other studies found no improvement in HbA1c levels [7,8]. However, previous clinical trials examined patients with type 2 diabetes that were undergoing medical treatment, so that the effect of non-surgical periodontal therapy could not be distinguished from that of the

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Review Article

Prevalence of Undiagnosed Diabetes and Prediabetes in the Dental Setting: A Systematic Review and Meta-Analysis

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Background. With the close link between diabetes mellitus (DM) and periodontal disease (PD), dentists have an unrealized opportunity to make a chance discovery of a patient's medical condition. Unlike in the medical setting, information on the point of care (PoC) and opportunistic screening for DM in the dental setting is limited. To make a reliable estimate on the prevalence of undiagnosed type 2 diabetes mellitus (T2DM) and prediabetes among dental patients in the dental setting and to assist healthcare planners in making an informed decision, information on the disease frequency and strategies employed to address this issue is of paramount importance. *Objectives.* To summarize the data on the prevalence of undiagnosed T2DM and prediabetes amongst dental patients and further explore the effectiveness of the PoC screening and its implication for use in the dental setting. *Methods.* A MEDLINE-PubMed, EMBASE, Web of Science, and Cochrane Library search was conducted with no time specification. Information on study characteristics and diagnostic parameters was retrieved for meta-analysis. All the studies were assessed for methodological quality using the QUADAS-2 tool. Proportions were presented in tables and forest plots. All statistical analysis was performed using the MedCalc software. *Results.* Nine studies met the inclusion criteria. The proportion of dental patients identified to be at a risk of hyperglycaemia with the PoC screening using random blood glucose (RBG) and HbA1 was 52.47% and 40.10%, while the estimated proportion with undiagnosed T2DM and prediabetes was identified as 11.23% and 47.38%. *Conclusion.* A significant proportion of dental patients can be identified as undiagnosed T2DM and prediabetes. Targeted opportunistic screening is a feasible approach and can help reduce the prevalence of undiagnosed T2DM and prediabetes.

1. Introduction

The World Health Organization (WHO) estimates hyperglycaemia to be the third highest risk factor for premature mortality [1–4]. Type 2 diabetes mellitus (T2DM) is the most prevalent form of diabetes mellitus (DM) and accounts for almost all cases of undiagnosed DM. Globally, 463 million (9.3% of the global population) are affected by DM. Half of those (232 million) were unaware of their disease status [2, 5, 6].

People at the risk of developing DM are in a lengthy asymptomatic phase that precedes overt DM [3, 7]. Combination of factors, including slow onset of symptoms, underperforming health care system, low awareness among people, and varied presentation of symptoms, often made the physician and the patient difficult to determine that overlooked DM as the cause, leading to late diagnosis [4, 5, 8–10].

Hyperglycaemia affects nearly every organ in the body, and if left uncontrolled, complications become established in the continuum from prediabetes to DM. With no known cure, the starting point of living well with DM is early diagnosis. Hence, screening is the first stage in the care continuum [5].

Centralised laboratory testing does not represent a convenient process for the patient, often requiring more than one visit. Patient-centred healthcare is becoming a global trend and is based on the foundation that health care should be organized closer to the consumer rather than the providers [11–13]. Point of care (PoC) denotes testing done

ORIGINAL REPORT: HEALTH SERVICES RESEARCH

Prediabetes and Diabetes Screening in Dental Care Settings: NHANES 2013 to 2016

C.G. Estrich[1], M.W.B. Araujo[1], and R.D. Lipman[1]

Abstract: *Introduction:* *Early recognition of prediabetes may prevent progression to diabetes, yet not all adults are aware of their prediabetes risk. To reach all adults unaware of their risk, additional risk assessment strategies are warranted.*

Objectives: *The objective of this study was to evaluate the potential scope of benefit from prediabetes risk assessment in the dental care setting and to identify characteristics of dental patients likely to unknowingly have prediabetes or diabetes.*

Methods: *Data from 10,472 adults in the National Health and Nutrition Examination Survey from 2013 to 2014 and 2015 to 2016 were analyzed for associations among prediabetes/diabetes risk factors, health care use, and hemoglobin A1C levels according to chi-square tests and multivariate logistic regression.*

Results: *A total of 7.73% of US adults had seen a dentist but not a medical provider in the past 12 mo. The composition of this subpopulation was significantly different from that who saw a medical provider, in ways that might affect their diabetes risk. In addition, 31.27% of this subpopulation would be identified as being at high risk for prediabetes according to the CDC Prediabetes Screening Test (Centers for Disease Control and Prevention), and 15.83% had hemoglobin A1C levels indicative of undiagnosed prediabetes or diabetes. Screening in a dental setting would have the highest odds of identifying someone unaware of his or her diabetes risk among those who were non-White, obese, or ≥45 y old.*

Conclusion: *Extrapolation from this analysis indicates that screening for prediabetes at dental visits has the potential to alert an estimated 22.36 million adults of their risk for prediabetes or diabetes. Incorporating prediabetes or diabetes risk assessment into routine dental visits may enable 1) those with prediabetes to take action to decrease their risk of developing diabetes and 2) those with diabetes to engage in treatment to decrease their risk of diabetes-related complications.*

Knowledge Transfer Statement: *Screening for prediabetes and diabetes during dental visits has the potential to raise patients' awareness of diabetes risk and prevent prediabetes from progressing to diabetes. For some patients, the dental visit may be the only point of contact with the health care system, which heightens the importance of including diabetes risk assessment for patient well-being.*

Keywords: glycated hemoglobin A, nutrition surveys, hyperglycemia, asymptomatic diseases, chronic disease, dentistry

Introduction

Prediabetes is a reversible condition in which plasma glucose levels are higher than normal but below levels diagnostic of type 2 diabetes (American Medical Association and Centers for Disease Control and Prevention [CDC]

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Development of non-invasive diabetes risk prediction models as decision support tools designed for application in the dental clinical environment

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Abstract

The objective was to develop a predictive model using medical-dental data from an integrated electronic health record (iEHR) to identify individuals with undiagnosed diabetes mellitus (DM) in dental settings. Retrospective data retrieved from Marshfield Clinic Health System's data-warehouse was pre-processed prior to conducting analysis. A subset was extracted from the preprocessed dataset for external evaluation ($N_{validation}$) of derived predictive models. Further, subsets of 30%–70%, 40%–60% and 50%–50% case-to-control ratios were created for training/testing. Feature selection was performed on all datasets. Four machine learning (ML) classifiers were evaluated: logistic regression (LR), multilayer perceptron (MLP), support vector machines (SVM) and random forests (RF). Model performance was evaluated on $N_{validation}$. We retrieved a total of 5319 cases and 36,224 controls. From the initial 116 medical and dental features, 107 were used after performing feature selection. RF applied to the 50%–50% case-control ratio outperformed other predictive models over $N_{validation}$ achieving a total accuracy (94.14%), sensitivity (0.941), specificity (0.943), F-measure (0.941), Mathews-correlation-coefficient (0.885) and area under the receiver operating curve (0.972). Future directions include incorporation of this predictive model into iEHR as a clinical decision support tool to screen and detect patients at risk for DM triggering follow-ups and referrals for integrated care delivery between dentists and physicians.

Keywords

Dental informatics; Decision-support systems; Electronic health records; Evidence-based practice; Machine learning; Modeling healthcare services

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Declaration of competing interest

The authors do not have any conflict of interest.

ORIGINAL REPORT: EPIDEMIOLOGIC RESEARCH

Screening for Diabetes Risk Using Integrated Dental and Medical Electronic Health Record Data

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Abstract: *Undiagnosed diabetes and prediabetes present a serious public health challenge. We previously reported that data available in the dental setting can serve as a tool for early dysglycemia identification in a primarily Hispanic, urban population. In the present study, we sought to determine how the identification approach can be recalibrated to detect diabetes or prediabetes in a White, rural cohort and whether an integrated dental-medical electronic health record (iEHR) offers further value to the process. We analyzed iEHR data from the Marshfield Clinic, a health system providing care in rural Wisconsin, for dental patients who were ≥21 y of age, reported that they had never been told they had diabetes, had an initial periodontal examination of at least 2 quadrants, and had a glycemic assessment within 3 mo of that examination. We then assessed the performance of multiple predictive models for prediabetes/diabetes. The study outcome, glycemic status, was gleaned from the medical module of the iEHR based on American Diabetes Association blood test cutoffs. The sample size was 4,560 individuals. Multivariate logistic regression revealed that the best performance was achieved by a model that took advantage of the iEHR. Predictors included age, sex, race, ethnicity, number of missing teeth, percentage of teeth with at least 1 pocket ≥5 mm from the dental EHR, and overweight/obesity, hypertension, hyperlipidemia, and smoking status from the medical EHR. The model achieved an area under the receiver operating characteristic curve of 0.71 (95% confidence interval, 0.69–0.72), yielding a sensitivity of 0.70 and a specificity of 0.62. Across a range of populations, informed by certain patient characteristics, dental care team members can play a role in helping to identify dental patients with undiagnosed diabetes or prediabetes. The accuracy of the prediction increases when dental findings are combined with information from the medical EHR.*

Knowledge Transfer Statement: *Prediabetes and diabetes often go undiagnosed for many years. Early identification and care can lead to improved glycemic outcomes and prevent wide-ranging morbidity, including adverse oral health consequences, in affected individuals. Information available in the dental office can be used by clinicians to identify those who remain undiagnosed or are at risk; the accuracy of this prediction increases when combined with information from the medical electronic health record.*

Keywords: dentists, hyperglycemia, periodontitis, prediabetic state, prevention & control, risk

Introduction

It is estimated that almost a quarter of those with diabetes in the United States, a staggering 7.2 million individuals, are not aware of their condition (Centers for Disease Control and Prevention [CDC] 2017), and almost half of those with diagnosed diabetes do not achieve optimal glycemic control (Ali et al. 2015; Stark Casagrande et al. 2013). Prediabetes is much more prevalent than frank diabetes, affecting 84 million people in the United States, and has been described as a silent precursor; it puts

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MINIREVIEWS

Oral manifestations in patients with diabetes mellitus

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Abstract

The purpose of this article was to increase the knowledge about oral manifestations and complications associated with diabetes mellitus. An overview was performed on Google, especially in recent reliable papers in relation to diabetes mellitus and its oral manifestations (keywords were "diabetes mellitus", "oral manifestations", and "oral complications"). Data were collected and the results were declared. Diabetes mellitus is one of the most common chronic disorders characterized by hyperglycemia. This disease can have many complications in various regions of the body, including the oral cavity. The important oral manifestations and complications related to diabetes include xerostomia, dental caries, gingivitis, periodontal disease, increased tendency to oral infections, burning mouth, taste disturbance, and poor wound healing. Oral complications in diabetic patients are considered major complications and can affect patients' quality of life. There is evidence that chronic oral complications in these patients have negative effects on blood glucose control, so prevention and management of the oral complications are important.

Key words: Diabetes mellitus; Oral complications; Oral manifestations; Periodontal disease; Xerostomia

Core tip: Since diabetes mellitus is a common disease and can have some annoying manifestations in the patient's mouth, it is important for physicians to be aware of these manifestations and to treat them properly.

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The impact of type 1 diabetes on the development of the craniofacial mineralised tissues (bones and teeth): literature review

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Background: *There are many reports on the impact of diabetes on periodontium as well as the state of organs in diabetics; however, there is little research on the impact of the disease on morphological and anatomical changes in the mineralised tissues like teeth and craniofacial bones. The aim of this study was to present a review of literature on morphological and anatomical changes of mineralised tissues in the course of type 1 diabetes.*

Materials and methods: *A review of PubMed database was made using the keywords: morphological changes, anatomical changes, enamel hypoplasia, type 1 diabetes, induced diabetes and the names of individual anatomical and morphological structures of the teeth.*

Results: *The analysis of experimental studies have shown that in induced type 1 diabetes in rats there is a substantial reduction in the thickness of the enamel and dentin, compared with the control group. The changes in the content of individual minerals in the tissues of the tooth have been shown — a decrease in the concentration of calcium and fluoride ions and an increase in the concentration of magnesium. In a study conducted on embryos of rats born of diabetic dams, defects were observed in enamel organ, which can cause delayed enamel hypoplasia. Literature analysis revealed morphological disorders also in some clinical cases of patients with type 1 diabetes.*

Conclusions: *Type 1 diabetes mellitus as a metabolic disorder may affect changes in the structure of mineralised tissues, thereby increasing their susceptibility to caries development and orthognathic disorders.* [Folia Morphol 2016; 75, 3: 275–280]

Key words: diabetes type 1, tooth morphology, mineralised tissues

INTRODUCTION

Human teeth develop from ectoderm and mesoderm, and the deciduous teeth begin to develop in the 7–8th week of gestation, while the permanent teeth buds are formed between 20th week of gestation (first molars) and 5 years of age (third molars). Amelogenesis and histogenesis of deciduous teeth dentin begin in the 14–18th week of gestation, and the beginning of the formation of the enamel and dentin of the first permanent molars is in the 28–32nd week of gestation [18].

Several factors can affect the development of the dentition, including inter alia genetically determined disorders, calcium-phosphate disorders, hypo- or hy-

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PLOS ONE

RESEARCH ARTICLE

Postnatal changes in the development of rat submandibular glands in offspring of diabetic mothers: Biochemical, histological and ultrastructural study

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Abstract

Development and maturation of submandibular salivary glands are influenced by intrauterine diabetic environment. Several studies investigated the effects of diabetes on the salivary glands. However, the effects of maternal diabetes on the submandibular glands of the offspring was not properly examined. Therefore, the present study was designed to describe the changes in the development of the submandibular glands of the offspring of diabetic mothers. The submandibular glands of the offspring of Streptozotocin (STZ)-induced diabetic female rats were examined at two and four weeks after birth. Detection of mRNA demonstrated that maternal diabetes affects the level of different indicators. The reduction of expression of epidermal growth factor (EGF); a protein mitogen, cytokeratin 5 (CK5); an epithelial cell progenitor, CK7 and aquaporin 5 (AQP5); differentiation markers and B cell lymphoma 2 (Bcl2); an antiapoptotic marker were found. Increase in Bcl2-associated X protein (Bax); an apoptotic marker was detected. These changes indicate their effects on saliva secretion, glands tumorigenesis, growth of normal oral flora and oral microbes, with decreased protein synthesis and production of xerostomia and dental caries. Loss of normal glandular architecture, significant increase in fibrosis, by the detection of collagen fibers, and stagnation of secretory granules were found with atrophic changes in the acinar cells. Marked defect of polysaccharides in the acinar cells, denoting functional changes, was manifested by significant reduction of the intensity of periodic acid-Schiff (PAS) reaction. The positive immunoreactivity of caspase-3, denoting cellular apoptosis, and minimal reaction of alpha-smooth muscle actin (α SMA) and proliferating cell nuclear antigen (PCNA) were evident in the offspring of diabetic mothers. We conclude that maternal diabetes produces degenerative effects in the structure and function of the submandibular salivary glands of the offspring, reflecting possible influences on their secretory activity affecting oral and digestive health.

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Original Article

Dental Health Status and Hygiene in Children and Adolescents with Type 1 Diabetes Mellitus

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ABSTRACT

Background: There is disagreement on the effect of diabetes on oral hygiene. The purpose of this study was to assess the oral health and hygiene status of type 1 diabetic patients.

Methods: In this case control study, periodontal health and hygiene of 80 children and adolescents (5–18 yr of age) with type 1 diabetes mellitus referred to Pediatric Endocrine Clinic of Beset Hospital Hamadan Iran 2013 – 2014 and 80 non diabetic control subjects were clinically assessed. The required data such as sex, age, duration of the diabetes, type and number of insulin injections per day were obtained from self-administered questionnaire and the patient's medical records. Participants in both groups were examined for Decay-missing- filled teeth (DMFT); dmft (for primary teeth), oral hygiene using O'Leary plaque index (PI) and gingivitis index (GI). P<0.05 was considered significant.

Results: The mean age of the study and the control group was 12.5±4.05 and 12.08±3.47 yr, respectively. There were no significant difference between two groups in terms of DMFT (P=0.158) and PI indices (P=0.373). The GI index difference was statistically significant in diabetic group (P=0.001). Interestingly, a higher dmft index was observed in the control group (P=0.008). In diabetic groups, GI and DMFT index increased significantly with duration of diabetes.

Conclusions: Apart from higher scores of GI index, frequency of oral and periodontal disease was not different in diabetic patients compared with healthy subjects. Findings of present study are insufficient to support a significant effect of diabetes on increasing the risk of oral and periodontal diseases. However, diabetic children and adolescents should receive oral hygiene instructions.

Citation: Rafatjou R, Razavi Z, Tayebi S, Khalili M, Farhadian M. Dental Health Status and Hygiene in Children and Adolescents with Type 1 Diabetes Mellitus. J Res Health Sci. 2016; 16(3):122-126.

Introduction

Type 1 diabetes mellitus (T1DM) is a common metabolic disease of childhood. About 1 in every 400-600 children and adolescents has T1DM. In adults, T1DM constitutes approximately 5% of all diagnosed cases of diabetes chronic illness[1,2]. A 2011 report from the US Centers for Disease Control and Prevention (CDC) estimated that approximately one million Americans have T1DM[3]. Onset most often occurs in childhood, but the disease can also develop in adults in their late 30s and early[1].

In this type of diabetes, an autoimmune destruction of the beta cells of the pancreatic islets leading to defects in insulin secretion. This results in persistent hyperglycemia and the clinical manifestation of the disease with dependence on exogenous insulin to prevent ketosis. The disease manifests itself in genetically predisposed individuals (polygenic genetic predisposition). Oral disease include xerostomia, periodontal disease (gingivitis and periodontitis), dental abscesses, tooth loss, soft tissue lesions, dry mouth and dental caries have been proposed as the 6th most prevalent complication of diabetes mellitus following the other diabetic complications[3,4]. The co-morbid presence of various inflammatory diseases and soft tissue pathologies in oral cavities in turn, adversely affect glycemic control and the treatment of oral complications can lead to improved metabolic control in diabetes patients[5-8]. Although patients with diabetes face a significantly higher risk for oral complications than healthy subjects[9-11], there is controversy on the impact of diabetes on oral and periodontal diseases and the mechanisms through which this occurs[12,13].

Considering the fact that some studies have reported a high prevalence of diabetes in Iran[14] and controversies about the impact of diabetes on oral health's status of T1DM and lack of public awareness in this regard further studies in this area is reasonable. Accordingly, we aimed to evaluate the oral health status of young patients with T1DM compared to healthy subjects in Hamadan west province of Iran.

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Oral Health and Type 2 Diabetes

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Abstract

Type 2 diabetes mellitus (T2DM) has been described as a new epidemic. Approximately 285 million people worldwide suffer from diabetes, and this number is predicted to increase by about 50% by year 2030.This article will review oral health manifestations of diabetes, and discuss associations between periodontal disease and diabetes. Although there is a strong body of evidence that supports the relationship between oral health and T2DM, oral health awareness is lacking among patients with diabetes and other health professionals. There is a need for the treating physician to be educated about the various oral manifestations of diabetes so that they can be diagnosed early and timely referrals to oral health specialists can be made. The established link between periodontitis and diabetes calls for an increased need to study ways to control both diseases, particularly among populations with health disparities and limited access to oral and health care.

Keywords

Periodontal health; diabetes; periodontal therapy

Hyperglycemia in diabetes has been shown to be an important risk factor for the manifestation of vascular complications. The five classic complications associated with DM include retinopathy, neuropathy, nephropathy, cardiovascular complications (coronary arterial disease, stroke and peripheral vascular disease) and delayed wound healing. Periodontal disease has recently been recognized as the "sixth complication" of DM[1].

Diabetes is a common disorder with concomitant oral manifestation that impacts dental care and there is concern about the ability of oral manifestations to profoundly affect metabolic control of the diabetes state. Physicians working to optimize the metabolic control of these patients should recognize the impact of controlling the progression of these oral complications. This warrants a comprehensive plan that involves close collaboration between physicians and oral health care providers, which will hopefully lead to better

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SCIENTIFIC RESEARCH REPORT

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Clinical and microbial oral health status in children and adolescents with type 1 diabetes mellitus†

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Objectives: To study the oral health of young individuals with controlled and uncontrolled type 1 diabetes mellitus (T1DM) and compare the results with those for healthy counterparts. **Materials and Methods:** One-hundred and forty-four youngsters (6–15 years of age) were assigned, according to glycaemic control, to three study groups: (i) diabetic patients with poor glycaemic control [glycated haemoglobin (HbA1c ≥7.5%)] (n = 35); (ii) diabetic patients with good glycaemic control (HbA1c <7.5%) (n = 35); and (iii) healthy individuals (n = 70). Plaque, gingival inflammation, calculus and decayed, missing and filled surfaces (DMFS) indices were recorded. Salivary parameters were determined, and stimulated saliva was collected to allow detection and determination of the levels of oral *Candida albicans* and *Streptococcus mutans* by real-time polymerase chain reaction (PCR). **Results:** Significantly different amounts of plaque were found among the study groups (P = 0.024): youngsters with poor glycaemic control had significantly more plaque than youngsters in the other two groups. The gingival, calculus and DMFS indices were not significantly different among groups (P > 0.05). *Candida albicans* levels were not statistically significant different among groups, but the group with poor glycemic control showed an elevated frequency of detection. *Streptococcus mutans* was isolated from the oral cavity of 96 of the 144 individuals. A statistically significant difference in the level of *S. mutans* was found between the group with poor glycaemic control and the healthy control group (P = 0.032). **Conclusions:** The results imply that youngsters with T1DM have a lower level of oral hygiene and are potentially at a higher risk of future oral disease, particularly when their metabolic disorder is uncontrolled. However, factors outside the oral cavity may also have a considerable impact on the initiation and progression of oral diseases.

Key words: Children, oral health status, Candida albicans, Streptococcus mutans, type 1 diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM), a condition whose primary characteristic is hyperglycaemia, results from defects in insulin secretion, insulin action or both. According to the classification of the American Diabetes Association, among the four types of diabetes, two are prevalent: type 1 diabetes mellitus (T1DM), which is the most common form of diabetes in children (also known as juvenile-onset diabetes); and type 2 diabetes, which is mainly observed in adults[1]. T1DM is characterised by autoimmune β-cell destruction, usually leading to absolute insulin deficiency.

Several studies have looked into the connection between T1DM and the oral health status[2–3]. There is evidence that T1DM has a significant role in the onset and evolution of oral diseases, such as periodontitis[4] and possibly dental caries, as well as in changes of the

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PERIODONTOLOGY 2000

Oral inflammation and infection, and chronic medical diseases: implications for the elderly

Frank A. Scannapieco & Albert Cantos

With the aging of our population, it is predicted that the number of older adults in the USA will double between 2010 and 2050 (45). Because of the success of preventive dental measures when these individuals were young, it is expected that more teeth will be retained into advanced age. These teeth will therefore be vulnerable to caries (particularly root caries) and periodontitis. Dental caries and periodontitis not only have local effects on the dentition and tooth-supporting tissues, but also may impact a number of systemic conditions. For example, bacteria are known to transit through carious lesions into the dental pulp and from there may enter the bloodstream. Oral organisms originating from cavitated teeth have been linked to serious systemic infections, such as endocarditis, brain abscesses, joint and bone infections and septic arthritis. Oral bacteria may also enter the blood through ulcerated periodontal pockets (117, 216) and infect organs directly or stimulate inflammatory reactions that may influence the progression of a variety of systemic diseases, such as atherosclerosis (with sequelae such as myocardial infarction and stroke), diabetes mellitus, adverse pregnancy outcomes, neurodegenerative diseases (such as Alzheimer's disease) and others. Aspiration of oropharyngeal (including periodontal) bacteria causes pneumonia, especially in hospitalized patients and in older adults (179).

The associations addressed in this paper suggest that there may be underlying mechanisms common to both periodontal disease and many systemic diseases. The systemic inflammatory changes attributed to periodontal disease are very similar to the changes seen in aging and are referred to as 'inflamm-aging' (54). It is possible that a global reduction in the capacity to cope with a variety of stressors, and a concomitant progressive increase in inflammation, are major characteristics of the aging process. 'Inflamm-aging' is provoked by the cumulative effects of stimulatory load and stress. The degenerative and hyperplastic pathologies of aging are at least partly linked by a common biological cellular stress response known as cellular senescence (23). These pathologies are linked to the systemic diseases discussed.

Common pathways may explain the connections between periodontal disease and systemic disease. For example, almost all chronic, progressive diseases show an increase in the production and/or release of endothelin 1 (11, 22, 123) (Fig. 1). It is not clear how much of the increased amount of local endothelin 1 found in human aging (44) is secondary to underlying disease processes or inflammation, or whether the concentration of local endothelin 1 is, in fact, causal for the disease progression. Endothelin may be a part of the underlying mechanism that unites periodontal disease with chronic diseases and aging (91). It has been noted that the levels of endothelin 1 are elevated in the periodontal tissues of patients with periodontitis (56) but are not elevated in the crevicular fluid of patients with periodontal disease (151). More recently, the gene expression levels of endothelin-converting enzyme in buccal mucosal tissues were found to be significantly increased in patients with advanced periodontitis compared with healthy patients and those with moderate periodontitis (94).

Periodontal disease is a chronic disease, the effects of which accumulate with age. It is therefore reasonable to assume that uncontrolled periodontal disease through life would have a greater impact on older patients compared with younger patients. This article will address the following pertinent questions related

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Original Article

Evaluation of Oral Health-Related Quality of Life in Elderly People with Type II Diabetes Mellitus

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Abstract

Background and purpose: Type 2 diabetes mellitus (T2DM) is the most common form of diabetes, and a metabolic disorder affecting patients' general health in various ways. The present study aimed to evaluate the oral health-related quality of life (OHRQoL) among older adults of Amirkola, Northern Iran.

Materials and Methods: A case-control study was conducted with a sample of 500 elderly people (250 with T2DM and 250 healthy controls) who answered geriatric oral health assessment index (GOHAI) questionnaire and a questionnaire evaluating xerostomia. Then, all participants underwent clinical dental examinations. The obtained data were then analyzed by t-test, chi-square test, and Pearson's correlation coefficient, and $p < 0.05$ was considered significant.

Results: The prevalence of xerostomia was not statistically significant between the T2DM patients and control groups ($p < 0.079$). Greater number of patients suffering T2DM reported xerostomia according to the records; however, the correlation between this disorder and periodontal disease index (PDI), Plaque index (PI), oral health index-simplified (OHI-S), and geriatric oral health assessment index (GOHAI) in the subjects of the two study groups was not significant ($p < 0.0001$).

Conclusion: In the present study, there was no significant relationship between GOHAI and periodontal indices, demonstrating no difference in the OHRQoL of elderly patients with T2DM and older healthy adults.

Keywords: Quality of Life; Diabetes Mellitus; Oral Health; Oral Health-Related Quality of Life

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Original Research
Geriatric

Association between oral health status and central obesity among Brazilian independent-living elderly

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Abstract: The aim of this study was to investigate the association between oral health status and central obesity (CO) in Brazilian independent-living elderly. A cross-sectional study was carried out in a sample of 489 elderly, who were participants of the Study on Aging and Longevity, in Londrina, state of Parana. The number of natural teeth and use of prostheses were evaluated according to the World Health Organization criteria. The presence of CO was assessed using measures of waist circumference (WC) and waist-hip ratio (WHR). Information concerning sociodemographic profile and some systemic conditions was also collected. Data were analyzed using stepwise logistic regression, α=5%. According to WC and WHR measures, the prevalence of central obesity was 79.3% and 76.1%, respectively. CO according to WC was not associated with oral status. Considering the WHR measure, the following oral conditions were associated to CO: having fewer natural teeth (OR = 2.61; 95%CI = 1.17–5.80), being edentulous and wearing both upper and lower complete dentures (OR = 2.34; 95%CI = 1.11–4.93), and being edentulous wearing only the upper complete denture (OR = 2.64; 95%CI = 1.01–6.95). Traditional risk factors for CO such as gender, dyslipidemia, hypertension and diabetes were associated with both measures. A poor oral health due to extensive tooth loss, whether partial or complete, even if rehabilitated by removable prostheses, may be considered a good predictor of CO in Brazilian independent-living elderly.

Keywords: Oral Health; Tooth Loss; Obesity, Abdominal; Aged.

Introduction

The aging of the population represents a reality throughout the world[1]. It is estimated that Brazil will be the sixth country in total population of older people by 2025[2], reaching 64 million inhabitants in 2050, about 30% of its total population[3]. The economic impact of this process in health systems has been a reason for concern for health and social policy-makers. The challenge, in addition to providing adequate health assistance, is to implement public policies that will promote general health, by controlling risk factors that are common to noncommunicable diseases (NCDs), highly prevalent among the elderly population[4].

Obesity has a multi-factorial nature, and it can be modulated by an individual's eating habits[5]. It is associated to cardiovascular diseases, such

Original Article

Evaluation of quality of life and depression levels in individuals with Type 2 diabetes

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Abstract

Introduction: Improving the quality of life in diabetic individuals is known to reduce morbidity and mortality. We aimed to investigate the quality of life and depression symptomatology situations and the related factors in patients with Type 2 diabetes mellitus (DM) in this study. **Materials and Methods:** In this study, 440 adult patients with Type 2 DM and under treatment admitted to Selcuk University Family Medicine Outpatient Diabetes Education Clinic were included in the study. A questionnaire containing sociodemographic characteristics of the participants, the Short Form 36 (SF-36) quality of life questionnaire was applied with Beck depression inventory face to face interviews. **Results:** Mean scores of females in all SF-36 subscales were statistically significantly lower than those of male patients. Physical function, physical role limitations, general health, social function, emotional role limitations, and mental health mean scores of the patients with 1–10 years duration of diabetes were found statistically significantly higher than those with 20 years and over duration of diabetes. Physical function, physical role limitations, pain, general health, and social function mean scores in patients using oral antidiabetic drug (OAD) was statistically significantly higher compared to patients using insulin + OAD. The average physical function scores of the patients with no complications were statistically significantly higher than those with two and more complications. **Conclusion:** Quality of life and depression symptomatology are worse in females, the elderly, the overweight, people with lower level of education, in the widowed or divorced, homemakers, those with low incomes, those with longer duration of diabetes, patients using insulin, and those with two or more complications. There are many medical and sociodemographic factors affecting the quality of life and depressive symptomatology in the individuals with diabetes, so both health care workers and patients should pay the necessary attention to this issue.

Keywords: Depression, diabetes, quality of life

Introduction

Diabetes mellitus (DM) is a chronic illness that requires continuing medical care and ongoing patient self-management education and support to prevent acute complications and to reduce the risk of long-term complications.[1-3] Diabetes causes morbidity and mortality with acute complications and affects adversely the quality of life with chronic complications. DM is an endocrine disease that can be seen at any age, is spreading rapidly in our country and around the world, costs too high treatment and causes so many problems due to its important complications.[3-5]

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According to the international diabetes federation (IDF-2013), it was reported that 8.3% Of adults between 20 and 79 years old had diabetes in the world. The number of diabetic patients in the world in 2030 is estimated to reach 366 million. According to TURDEP I and II conducted on a large-scale on the prevalence of diabetes in our country, while the prevalence of diabetes across the country was 7.2% Between 1997 and 1998, it was found that it increased to 13.7% According to a TURDEP II study made 12 years later (2010). According to 2013 IDF, the prevalence in turkey was reported as 14.85%. Aging population and the increase of obesity are thought to be the major causes of diabetes epidemic.[3-5]

DM affects adversely quality of life of the patients, working life, interpersonal relationships, social activities, physical and mental

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Las personas mayores y la depresión

Aprenda a reconocer las señales y buscar tratamiento.

¿Se siente muy cansado, indefenso y desesperado?
¿Ha perdido el interés en muchas de las actividades y ocupaciones que solía disfrutar?
¿Tiene dificultad para trabajar, dormir, comer y funcionar?
¿Se ha sentido así día tras día?

Si contestó que sí a estas preguntas, es posible que tenga depresión.

A medida que envejece, puede pasar por muchos cambios, tales como la muerte de seres queridos, la jubilación, acontecimientos estresantes de la vida o problemas médicos. Es normal sentirse intranquilo, estresado o triste por esos cambios, pero después de adaptarse, muchas personas mayores vuelven a sentirse bien.

La depresión es diferente. Es un problema médico que afecta la vida diaria y el funcionamiento normal. No es una parte usual del envejecimiento, ni una señal de debilidad ni un defecto de carácter. Muchas personas mayores que tienen depresión necesitan tratamiento para sentirse mejor.

Tipos de depresión

Hay varios tipos de depresión. Los más comunes incluyen los siguientes:

- **Depresión grave o mayor:** síntomas graves que interfieren con la capacidad de trabajar, dormir, concentrarse, comer y disfrutar de la vida. Algunas personas pueden tener un solo episodio en la vida, pero es más común tener varios episodios.
- **Trastorno depresivo persistente (distimia):** síntomas de depresión no tan fuertes como los de la depresión grave, pero que duran por mucho tiempo (por lo menos dos años).
- **Depresión menor:** síntomas de depresión que no son tan fuertes como los de la depresión grave o del trastorno depresivo persistente y que no duran mucho tiempo.

¿Conoce las señales?

En algunas personas mayores, la depresión puede pasar sin diagnosticarse o puede diagnosticarse erróneamente porque la tristeza no es su síntoma principal. Tal vez tengan otros síntomas de depresión menos obvios o no quieran hablar de sus sentimientos. Es importante saber cuáles son las señales y buscar ayuda si la posibilidad de tener depresión le preocupa.

La depresión tiene muchos síntomas, incluso físicos. Si usted tiene varios de los síntomas y le han

NIH National Institute of Mental Health

REVIEW

Current status of dental implants survival and peri-implant bone loss in patients with uncontrolled type-2 diabetes mellitus

Leandro Chambrone[a,b] and Luiz F. Palma[a,c]

Purpose of review
The current review summarizes recent evidence on the impact of type-2 diabetes mellitus (T2DM) on implant dentistry, highlighting the behavior of peri-implant bone.

Recent findings
There is no definitive information on the development and course of peri-implant bone loss associated with T2DM; however, poorly controlled T2DM patients present worse outcomes. Nevertheless, dental implants may be a successful therapy for these patients in a manner similar to healthy individuals, when glycemic levels and oral hygiene are strictly maintained.

Summary
The most recent literature on the impact of T2DM on peri-implant bone loss was reviewed to evaluate the feasibility of dental implant therapy over the time for these patients.

Keywords
alveolar bone loss, dental implants, peri-implantitis, type-2 diabetes mellitus

INTRODUCTION

With a global prevalence of approximately 8% in the adult population [1*], type-2 diabetes mellitus (T2DM) has been long considered a serious public health concern, mainly in developed countries [2**]. T2DM consists of a group of metabolic disorders essentially characterized by elevated serum glucose levels due to insufficient insulin secretion, defective insulin function, or both [3**]. It is associated with a greater risk of periodontal disease and tooth loss, which requires special attention of the clinician during all stages of dental care, particularly in dental implant rehabilitation cases [4].

Dental implants are an excellent choice for the replacement of missing teeth. The correct indication of this procedure should, however, consider numerous local and systemic factors of the patient [5] for osseointegration to be successful [6]. Success and survival rates of up to one hundred percentage have been reported in the literature, although complications and failures may occur in a few cases [7**]. Chronic hyperglycemia is considered to be a risk factor for peri-implant diseases [8**] and the implant rehabilitation has not historically been proposed for uncontrolled T2DM patients [9].

Despite the increasing number of clinical trials on dental implant therapy in T2DM patients, most studies have considered relatively short follow-up periods as well as different methods and sample sizes. This special commentary aims to review the most recent evidence regarding the impact of T2DM on peri-implant bone loss and dental implant survival.

PERI-IMPLANT DISEASES: CURRENT ASPECTS OF CLINICAL INTEREST

The long-term success of dental implants is determined by the maintenance of the peri-implant bone level [10**]. Nevertheless, after osseointegration,

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REVIEW Open Access

Dental implants and diabetes mellitus—a systematic review

Hendrik Naujokat*, Burkhard Kunzendorf and Jörg Wiltfang

Abstract

Dental implant surgery has developed to a widely used procedure for dental rehabilitation and is a secure and predictable procedure. Local and systemic risk factors can result in higher failure rates. Diabetes mellitus is a chronic disease that goes in with hyperglycemia and causes multifarious side effects. Diabetes as a relative contraindication for implant surgery is controversially discussed. Because the number of patients suffering from diabetes increases, there are more diabetic patients demanding implant procedures. We aimed to answer the PICO question "Do diabetic patients with dental implants have a higher complication rate in comparison to healthy controls?" by a systematic literature search based on the PRISMA statement. We identified 22 clinical studies and 20 publications of aggregated literature, which were quite heterogeneous concerning methods and results. We conclude that patients with poorly controlled diabetes suffer from impaired osseointegration, elevated risk of peri-implantitis, and higher level of implant failure. The influence of duration of the disease is not fully clear. The supportive administration of antibiotics and chlorhexidine seems to improve implant success. When diabetes is under well control, implant procedures are safe and predictable with a complication rate similar to that of healthy patients.

Keywords: Dental implants, Implant survival, Diabetes mellitus, Glycemic control, Peri-implantitis, Systemic disease, Risk factor

Review

Introduction

Today, dental implants are one of the restorative methods to replace missing teeth. Improvements in implant design, surface characteristics, and surgical protocols made implants a secure and highly predictable procedure with a mean survival rate of 94.6 % and a mean success rate of 89.7 % after more than 10 years [1]. Implant survival is initially dependent on successful osseointegration following placement. Any alteration of this biological process may adversely affect treatment outcome. Subsequently, as an implant is restored and placed into function, bone remodeling becomes a critical aspect of implant survival in responding to the functional demands placed on the implant restoration and supporting bone. The critical dependence on bone metabolism for implant survival leads us to evaluation of certain risk factors. One of the controversial discussed diseases is diabetes mellitus.

Diabetes mellitus is a chronic metabolic disorder that leads to hyperglycemia, which raises multiple complications caused by micro- and macroangiopathy. Diabetic patients have increased frequency of periodontitis and tooth loss [2], delayed wound healing [3], and impaired response to infection. In 1980, more than 150 million people worldwide were affected and that number had grown to 350 million by 2008 [4]. This trend highlights the need for better understanding of diabetes and its therapy and its impact on dental implant rehabilitation. In the past, diabetes was long time seen as a relative risk factor to dental implants. In contrast, today, there is a change in paradigm. Recent studies offer indirect evidence for diabetes patients benefiting from oral rehabilitation based on dental implant therapy. After tooth loss, patients avoid food which needs more effort to masticate which can lead to an adverse nutrition with poor metabolic control. A sufficient dental rehabilitation allows the patient to improve nutrition and the metabolic control. On the other hand, it is still unclear how quality of diabetes therapy and duration of disease influence the

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Dental implants in diabetic patients: Retrospective cohort study reporting on implant survival and risk indicators for excessive marginal bone loss at 5 years.

Running head: Multivariable analysis in diabetic patients.

Article category: Original research.

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ABSTRACT

Background: More studies evaluating the outcome of dental implant restorations in diabetics are needed.

Aim: To investigate the outcome of immediate function implant rehabilitations in diabetic patients.

Materials and methods: This retrospective cohort study included 70 diabetic patients (type 1=6 patients; type 2=64 patients; 33 females and 37 males, mean age=59 years), rehabilitated with 352 implants. Primary outcome measure was implant survival estimated at 5 years through the Kaplan-Meier product limit estimator using the patient as unit of analysis (first implant failure as reference); secondary outcome measures were marginal bone loss and biological complications. Risk indicators associated with bone loss >2.0mm were tested in a multivariate logistic regression model. The level of significance considered was 5%.

Results: Seven patients were lost to follow-up (10%). Seven patients lost ten implants rendering a global implant cumulative survival rate for diabetic patients of 89.8% (type 1=80.0%; type 2=90.5%). The average (95% confidence interval) marginal bone loss at 1- and 5-years was 1.64mm (0.00;3.32)

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Original Article

A four-year prospective study of self-assembling nano-modified dental implants in patients with type 2 diabetes mellitus

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KEYWORDS
Marginal bone loss (MBL);
Nano-modified (NM);
Resonance frequency analysis (RFA);
Type 2 diabetes mellitus

Background/purpose: Dental implantation has become an efficient and important method of replacing lost teeth. However, the success rate of dental-implant treatment in diabetics is higher than patients without diabetes. The aim of this study was to prospectively evaluate long-term marginal bone loss (MBL) and the stability of a self-assembling nano-modified implant in patients with type 2 diabetes mellitus compared with a conventional implant.
Materials and methods: Twenty-five patients with type 2 diabetes were recruited for this study. Through a random selection process, one site in each patient received a conventional implant and the other site received a nano-modified implant. The implant stability quotient was measured using resonance frequency analysis (RFA), and MBL was measured using panoramic radiography from uncovering to four-year follow-up.
Results: No significant difference in implant stability quotient was found between the two groups ($P > 0.05$), except for the time at implant insertion ($P < 0.05$). MBL in the nano-modified implant group exhibited a decreasing change compared with the conventional implant group, between the uncovering and the loading stage ($P < 0.05$), while there was no significant difference in other stages ($P > 0.05$).
Conclusion: There was potentially increased implant stability and diminished MBL around the self-assembling nano-modified implant in the uncovering-loading stage of early osseointegration in patients with type 2 diabetes.

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INFLUENCE OF DIABETES ON THE SURVIVAL RATE AND MARGINAL BONE LOSS OF DENTAL IMPLANTS: AN OVERVIEW OF SYSTEMATIC REVIEWS

--Manuscript Draft--

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Abstract:	We aimed to conduct an analysis of the systematic reviews in literature about the implant survival rate (ISR) and marginal bone loss (MBL) in diabetic and non-diabetic patients. This work was registered in The International Prospective Register of Systematic Reviews (PROSPERO) (CRD42018095314) and was developed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Cochrane Library Handbook. A search was performed on PUBMED, COCHRANE, SCOPUS, EMBASE, and LILACS. The PICO question was "Do the survival rates of dental implants and marginal bone loss differ between diabetic and non-diabetic patients?" A total of 130 articles were retrieved. After eliminating repetitions, 118 were reviewed. Finally, six systematic reviews were included, all the reviews indicated that there is no effect of diabetes on the ISR; however, a negative effect of the disease can be observed in MBL. Analysis of the quality of the studies was performed using the assessment of systematic reviews in dentistry (Glenny Scale) and Assessing the Methodological Quality of Systematic Reviews (AMSTAR 2). Glenny scale showed a moderate to high quality of the included studies. In contrast, AMSTAR 2 pointed out a critically low level for four studies, with no study fulfilling the criteria for high quality. It may be concluded that there is no effect of diabetes on the ISR; however, a negative effect of the disease can be observed on MBL.

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ARTICLE

Association between diabetes and dental implant complications: a systematic review and meta-analysis

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ABSTRACT

Objectives: The aim of this study was to explore the possible association between diabetes mellitus and dental implant complications.

Material and methods: A systematic literature review was conducted to answer the following PICO (Participants, Intervention, Comparison, and Outcome) question: Is there association between diabetes mellitus and dental implant complications? Two independent searchers performed a literature search of the PubMed/MEDLINE, Web of Science, Cochrane Library and EMBASE databases for studies published until February 2020, focussing on studies including continuous outcomes, marginal bone loss (primary outcome), probing depth, and bleeding upon probing (secondary outcomes).

Results and conclusions: A final total of 10 published studies were included in this systematic review. There were statistically significant differences between the groups with regard to marginal bone loss ($p < .00001$), probing depth ($p < .00001$) and bleeding around dental implants ($p < .00001$), and subjects without diabetes had lower complication rates. Additionally, in the subgroup analysis performed with loading time and HbA1c levels, a more evident association was found in immediate loading for probing depth. Moreover, the analysis results of bleeding around dental implants suggested that as HbA1c level increases, the bleeding of the tissues surrounding the implant will also increase. With regard to dental implant complications, there were statistically significant differences favouring patients without diabetes mellitus.

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Introduction

Diabetes mellitus comprises a group of metabolic disorders that are characterized by hyperglycaemia, which is caused by defective insulin secretion, dysfunction or both. According to the latest statistics from the International Diabetes Federation, the number of people aged 20 to 79 years with diabetes mellitus had risen to 424.9 million in 2017, roughly three times the prevalence in 2000. The number of patients with diabetes worldwide is expected to rise to 629 million by 2045 [1]. Diabetes mellitus is closely related to oral health, especially periodontal health [2], and has long been known to be a risk factor for implant failure due to susceptibility to infection, impaired healing and other complications [3]. Although diabetes mellitus has always been considered a relative contraindication to treatment with dental implants [4], dental implant restoration has been increasingly favoured by the majority of patients with tooth loss due to its advantages of reduced damage to adjacent teeth and reduced impact on alveolar bone compared to fixed bridge treatment and removable restoration, respectively [5]. A recent study surveyed a 40-year trend of tooth loss among people over the age of 25 years with and without diabetes mellitus in the United States and found that patients with diabetes lost almost twice as many teeth as patients without diabetes [6]. This observation corresponds to an increasing need for dental implant restoration among patients with diabetes.

Long-term hyperglycaemia may injure the vascular endothelium, leading to pathological changes of large vessels or microvessels, which promotes the differentiation of osteoclasts and inhibits the proliferation and differentiation of osteoblasts [7]. Hyperglycaemia also leads to excessive immune response to pathogens. Inflammatory mediators closely related to diabetes, such as interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8) and tumour necrosis factor-α (TNF-α), can all be detected in the gingiva, serum and saliva. The presence of these factors aggravates the inflammation of oral tissues and reduces collagen synthesis, thereby effecting the formation of bone matrix and effecting the healing of both hard and soft tissues [8].

Although implants have a relatively high success rate during routine procedures, dentists need to identify patients at higher risk of complications, such as peri-implantitis and peri-implant mucositis. However, for many years, the definition of peri-implant diseases has been controversial. Although these diseases were initially classified as periodontal diseases, the specificity of peri-implant bone remodelling,

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