Ana Carolina Portes Pasmadjian

Análise do perfil lipídico e dos níveis de proteína C-reativa no soro de indivíduos com periodontite crônica e diabetes mellitus tipo 2

Brasília
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Trabalho de Conclusão de Curso apresentado ao Departamento de Odontologia da Faculdade de Ciências da Saúde da Universidade de Brasília, como requisito parcial para a conclusão do curso de Graduação em Odontologia.

Orientador: Prof. Dra Maria do Carmo Machado Guimarães

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2016

Aos meus pais, por tudo que fizeram pela minha formação

Agradecimentos

À minha mãe, mulher forte e sábia, que cuidou de mim a vida toda e tanto sonhou com essa formatura que só foi possível graças à uma educação primorosa que nos permitiu saborear esse momento juntas.

Ao meu pai que é um entusiasta da ciência e um homem tão incentivador que me ensinou, por meio de seu cuidado ao longo de uma vida, o valor da cultura, do conhecimento e da educação, sem esquecer da doçura.

Ao Evandro que cuida tanto de nossa família. trouxe alegria, cuidado e amor para nossas vidas e que fez café todos os dias antes da minha aula, muitas vezes sem nem ter que sair de manhã.

Ao Lucas, homem de nobreza única que escolheu partilhar a vida comigo e o faz com tanto amor. Não tenho palavras para agradecer todos seus cuidados, desde a estatística, a revisão dos textos e a felicidade que você me traz.

A querida professora Maria do Carmo, sempre com um astral alto, por tão agradável convivência nesses dois anos de PIBIC, por ter aceitado me orientar e por sua sapiência acadêmica.

À querida Priscilla que com muita generosidade partilhou seu tempo, seus conhecimentos, seus dados, sempre com tanto carinho e atenção. Obrigada por ter aceitado o convite da banca. Você mez faz acreditar que ciência no Brasil é possível.

À Lari Sugar, a pessoa mais alegre que existe. Menina de ouro que trouxe alegria em todos os momentos que esteve presente. Obrigada pela leveza que você traz de dentro.

Às queridas professoras Valéria e Dirce que aceitaram compor a banca com alegria e prontidão.

Ao professor Tien, que me ajudou com as estatísticas e é um ortodontista tão completo e inspirador.

Às minhas amigas Karol e Watylla que partilham a vida comigo desde o primeiro dia de aula.

À Amanda por ter sido minha dupla no fim do curso e ter me ensinado tanto.

Aos professores Aline e Milki, tão queridos e dentistas exemplares.

Ao Laboratório Sabin pela parceria e possibilidade única de realização dos exames.

A todos os meus pacientes da graduação que me permitiram, com generosidade, começar aprender a ser dentista.

RESUMO

PASMADJIAN, ACP. Análise do perfil lipídico e dos níveis de proteína C-reativa no soro de indivíduos com periodontite crônica e diabetes mellitus tipo 2, 2016. Trabalho de Conclusão de Curso (Graduação em Odontologia) – Departamento de Odontologia da Faculdade de Ciências da Saúde da Universidade de Brasília.

Introdução: A doença periodontal é uma desordem inflamatória que traz implicações sistêmicas relevantes. Nos pacientes diabéticos é uma notória complicação. A proteína C-reativa (PCR) e o perfil lipídico são parâmetros laboratoriais que precisam ser analisados quanto a relação com periodontite e o diabetes. **Metodologia**: Sendo assim,o presente artigo fez um estudo transversal com coleta de sangue periférico e exame de profundidade a sondagem (PS) e nível de inserção clinico (NIC). Havia três grupos: um com (PC) periodontite crônica e diabetes (n=4); um só com PC (n=5) e um controle (n=4). **Resultados**: Cada grupo obteve p<.0001; a maior média de PCR foi no grupos PC e diabetes, 3.3168mg/l; bem como o triglicerídeo, 207.75mg/dl. O maior HDL foi no grupo controle, 56mg/dl. O LDL mais alto foi 126mg/dl, no grupo PC. Quanto aos dados clínicos, a maior PS foi a do grupo PC, 4.2mm. Os sítios com maior frequência de de PS entre 4 e 6 mm foram a mésio vestibular e mésio lingual. **Conclusão**: Esse estudo concluiu que tanto o grupo PC quanto o grupo diabetes com PC tiveram resultados alterados em relação ao grupo controle, mas é necessário aumentar a amostra, comparar dados pré e pós tratamento para ter resultados mais consistentes.

ABSTRACT

PASMADJIAN ACP. Analysis of lipid profile and C-reactive protein levels in the serum of individuals with chronic periodontitis and diabetes mellitus type 2, 2016. Undergraduate Course Final Monograph (Undergraduate Course in Dentistry) – Department of Dentistry, School of Health Sciences, University of Brasília.

Background: Periodontal disease is an inflammatory disorder that brings relevant systemic implications. In diabetic patients is a well-known complication. C- reactive protein (CRP) and lipid profile are laboratory parameters that need to be analyzed for the relationship with periodontitis and diabetes. **Methods**: Therefore, this article has a cross-sectional study of peripheral blood collection and examination of depth probing (PS) and the level of clinical integration (NIC). There were three groups: one with (CP) chronic periodontitis and diabetes (n=4); one CP (n=5) and a control (n=4). **Results**: Each group obtained p <.0001; the highest average CRP was in the CP group and diabetes, 3.3168 mg/l; as well as triglycerides, 207.75mg /dl. The higher HDL was in the control group, 56mg /dl. The highest LDL was 126mg /dl, the PC group. Regarding clinical data, most PS was the CP group, 4.2mm. The sites with greater frequency of PS between 4 and 6 mm were the mesial buccal and mesial lingual. **Conclusions**: This study found that both the PC group as diabetes CP group had results altered compared to control group, but it is necessary to increase the sample, compare data before and after treatment to have more consistent results.

SUMÁRIO

ARTIGO CIENTÍFICO

Este trabalho de Conclusão de Curso é baseado no artigo científico:

PASMADJIAN ACP. Análise do perfil lipídico e dos níveis de proteína C-reativa no soro de indivíduos com periodontite crônica e diabetes mellitus tipo 2, 2016.

Apresentado sob as normas de publicação da Revista Jornal of Periodontology

FOLHA DE TÍTULO

Análise do perfil lipídico e dos níveis de proteina C-reativa no soro de indivíduos com periodontite crônica e diabetes mellitus tipo 2

Analysis of lipid profile and C-reactive protein levels in serum of individuals with chronic periodontitis and diabetes mellitus type 2

Ana Carolina Portes Pasmadjian[1]
Maria do Carmo Machado Guimarães[2]

[1] Aluna de Graduação em Odontologia da Universidade de Brasília.
[2] Professor Adjunto de Periodontia da Universidade de Brasília (UnB).

Correspondência: Prof. Dra. Maria do Carmo Machado Guimarães
Campus Universitário Darcy Ribeiro - UnB - Faculdade de Ciências da Saúde - Departamento de Odontologia - 70910-900 - Asa Norte - Brasília - DF
E-mail: mmgcarmo@gmail.com / Telefone: 55 (61) 31071849

RESUMO

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Resumo

Introdução: A doença periodontal é uma desordem inflamatória que traz implicações sistêmicas relevantes. Nos pacientes diabéticos é uma notória complicação. A proteina C-reativa (PCR) e o perfil lipídico são parâmetros laboratoriais que precisam ser analisados quanto a relação com periodontite e o diabetes. **Metodologia**: Sendo assim,o presente artigo fez um estudo transversal com coleta de sangue periférico e exame de profundidade a sondagem (PS) e nível de inserção clinico (NIC). Havia três grupos: um com (PC) periodontite crônica e diabetes (n=4); um só com PC (n=5) e um controle (n=4). **Resultados**: Cada grupo obteve p<.0001; a maior média de PCR foi no grupos PC e diabetes, 3.3168mg/l; bem como o triglicerídeo, 207.75mg/dl. O maior HDL foi no grupo controle, 56mg/dl. O LDL mais alto foi 126mg/dl, no grupo PC. Quanto aos dados clínicos, a maior PS foi a do grupo PC, 4.2mm. Os sítios com maior frequência de de PS entre 4 e 6 mm foram a mésio vestibular e mésio lingual. **Conclusão**: Esse estudo concluiu que tanto o grupo PC quanto o grupo diabetes com PC tiveram resultados alterados em relação ao grupo controle, mas é necessário aumentar a amostra, comparar dados pré e pós tratamento para ter resultados mais consistentes.

Palavras-chave: proteina C-reativa, periodontite crônica, perfil lipídico, diabetes mellitus tipo 2

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Analysis of lipid profile and C-reactive protein levels in serum of individuals with chronic periodontitis and diabetes mellitus type 2.

Abstract

Background: Periodontal disease is an inflammatory disorder that brings relevant systemic implications. In diabetic patients is a well-known complication. C-reactive protein CRP and lipid profile are laboratory parameters that need to be analyzed for the relationship with periodontitis and diabetes. **Methods**: Therefore, this article has a cross-sectional study of peripheral blood collection and examination of depth probing (PS) and the level of clinical integration (NIC). There were three groups: one with (CP) chronic periodontitis and diabetes (n=4); one CP (n=5) and a control (n=4). **Results**: Each group obtained p <.0001; the highest average CRP was in the CP group and diabetes, 3.3168 mg/l; as well as triglycerides, 207.75mg /dl. The higher HDL was in the control group, 56mg /dl. The highest LDL was 126mg /dl, the PC group. Regarding clinical data, most PS was the CP group, 4.2mm. The sites with greater frequency of PS between 4 and 6 mm were the mesial buccal and mesial lingual. **Conclusions**: This study found that both the PC group as diabetes CP group had results altered compared to control group, but it is necessary to increase the sample, compare data before and after treatment to have more consistent results

Keywords: chronic periodontitis, C-reactive protein, lipid profile, diabetes mellitus type 2

Introdução

As doenças periodontais são condições muito comuns de ordem inflamatória em humanos [1,3], afetando mais de 70% da população em geral [2]. Essa condição afeta os tecidos de suporte do dente, e o fenótipo mais frequente é a inflamação gengival induzida por biofilme, a gengivite. Nesse estágio, a doença não causa perda de inserção do dente, limitando-se somente à gengiva. Mediante o acúmulo do biofilme, somado à susceptibilidade biológica, a doença pode evoluir para periodontite, na qual há perdas óssea e de inserção, sangramento à sondagem e presença de bolsas periodontais[3].

Na prática clínica, são reconhecidos dois tipos mais comuns de periodonite: a crônica e a agressiva. A primeira, mais prevalente em adultos, mostra a relação entre o nível de destruição, a quantidade de biofilme e cálculo subgengival presente nos tecidos dentários[3,4]. Já a periodontite agressiva é caracterizada por perda óssea acelerada sem apresentar acúmulo de biofilme compatível com o grau de inflamação[4].

Condições sistêmicas como a diabetes possuem relação com a periodontite crônica. Diabetes tipo 2 é uma alteração metabólica associada ao sedentarismo e obesidade. Na década de 80, houve o questionamento se os níveis elevados de glicose no fluido gengival crevicular poderiam favorecer o crescimento de espécies bacterianas subgengivais, levando à periodontite[3]. Entretanto, a microbiota periodontal não parece ser alterada pela diabetes e há pouca evidência de que influencie o controle glicêmico. O papel dos neutrófilos na patogênese da periodontite em pacientes com diabetes tem sido analisado por meio de ensaios sobre funções dos neutrófilos. Apesar da teoria de que a função neutrofílica na periodontite e diabetes seja defeituosa, a evidência obtida é variável devido à dificuldade da metodologia empregada[5]. Tem sido discutido

que neutrófilos hiperativos, possivelmente ativados no periodonto, seriam uma fonte de espécies reativas de oxigênio. Estas levariam à ativação de vias pró-inflamatórias e causariam resistência insulínica em pacientes com periodontite e diabetes [5].

Os pacientes com diabetes não-controlados têm risco aumentado de desenvolver doenças periodontais e apresentam maior destruição dos tecidos de suporte. A doença periodontal, por sua vez, pode, teoricamente, influenciar os níveis glicêmicos dos pacientes, porém ainda não há evidência científica suficiente para embasar esse efeito das doenças periodontais sobre o controle glicêmico [4].

Vários mecanismos estão envolvidos na fisiopatologia da doença periodontal associada ao diabetes melito: produção de produtos de glicosilação avançada, deficiente resposta imunológica alterações vasculares e do tecido conjuntivo[5] e polimorfismos genéticos. Tratando-se de inflamação, a resposta de fase aguda representa uma reação inicial e altamente complexa do organismo frente a uma variedade de agressões tais como infecções bacterianas, virais, parasitárias, traumas mecânicos ou térmicos, isquemia, necroses ou neoplasias. Refere-se a respostas fisiológicas e alterações metabólicas que se iniciam imediatamente após o início da infecção ou dano tecidual e tem como objetivo neutralizar ou eliminar o agente inflamatório e promover o reparo tecidual[7]. A PCR é uma proteina marcadora de inflamação, produzida no fígado, encontrada normalmente no plasma, e é aumentada drasticamente em resposta às agressões teciduais [7,8], podendo exceder 100 mg/L, representando, então, um marcador não-específico da resposta de fase aguda [7,8]. A síntese e secreção de PCR aumenta em horas após a agressão e pode atingir picos em 24 a 48 horas. Na ausência de inflamação, níveis de PCR acima de 1 mg/L indicam um baixo risco para doenças cardiovasculares e níveis de PCR acima de 3 mg/L indicam um alto risco a distúrbios cardiovasculares [8].

Além da diabetes, outro problema metabólico importante a ser analisado nesses pacientes é a dislipidemia. As infecções bacterianas crônicas da doença periodontal aumentam os níveis de citocinas pró-inflamatórias no soro e no fluido crevicular, o que pode

levar a um perfil aterogênico[9]. A habilidade do patógeno periodontal de induzir agregação plaquetária e formação de células espumosas tem sido relacionado ao desenvolvimento do ateroma[8]. As evidências mostram ao menos dois mecanismos biologicamente plausíveis: aumento de inflamação sistêmica em pacientes com periodontite e a frequente migração de bactérias Gram-negativas das bolsas periodontais para a corrente sanguínea [8,9]. Estudos recentes ilustraram a convergência entre doença periodontal e hiperlipidemia. Bacteriemia tem sido associada ao aumento na produção de citocinas como TNF alfa, IL-1beta e IL-6. Demonstrou-se que isso causa alterações no metabolismo lipídico, consequentemente levando à hiperlipidemia [8,9,10].
Sendo assim, o objetivo do trabalho é analisar, em pacientes com diabetes tipo 2, os efeitos sistêmicos da doença periodontal quanto aos níveis de PCR e perfil lipídico, ampliando-se, dessa forma, o entendimento da inter-relação entre a periodontite e diabetes melito.

Métodos

Os critérios estabelecidos para a execução deste estudo estão de acordo com as normas da Resolução 466/2012 do Conselho de Saúde do Ministério da Saúde Pública e Código de Ética Profissional Odontológico, segundo Resolução CFO 118/2012 Todos os indivíduos foram informados verbalmente e por escrito do objetivo do estudo e foram convidados a assinarem o termo de consentimento Livre e Esclarecido (TCLE). O projeto foi submetido e aprovado pelo Comitê de Ética em Pesquisa da Universidade de Brasília (UnB) pelo processo CAAE 46609515.7.0000.0030. O estudo incluiu a coleta de dados epidemiológicos e de amostras de sangue periférico, além de anamnese que descreve queixa principal, históricos familial e da doença atual, tratamentos médicos e medicações usadas, doenças articulares, cardiovasculares, alergias, infecções, alterações renais e hepáticas, vacinas e hábitos como tabaco e álcool. No exame físico, foram analisados os aspectos das

mucosas labial e jugal, palato, língua, orofaringe e região retromolar. Alguns pacientes da pesquisa faziam parte do Projeto de Extensão da universidade que trata pacientes com diabetes, outros fizeram parte de pesquisas de doutorado e mestrado e foram chamados novamente.

A amostra do estudo compreendeu 13 indivíduos entre 46 e 51 anos de idade que foram divididos em três grupos: o (1) primeiro (n = 5) com diagnóstico de periodontite crônica; o (2) segundo (n = 4) com diagnóstico de periodontite crônica e diabetes mellitus tipo 2; e o (3) controle (n=4), formado por pacientes saudáveis, sem doença sistêmica ou periodontite. Para os grupos teste foram selecionados indivíduos baseando-se nos seguintes critérios: Indivíduos com presença de 12 dentes; no mínimo 30% dos sítios periodontais com profundidade de sondagem ≥ 4 mm e, ao menos dois dentes com perda de inserção ≥ 3 mm. O grupo controle consistiu em indivíduos saudáveis, sistemicamente e com presença de, no mínimo, 20 dentes (com profundidade de sondagem clínica ≤3 mm, nível de inserção clínica ≤3 mm.

Foram excluídos do estudo os pacientes que tinham realizado tratamento periodontal até seis meses antes do início da pesquisa e que tinham alterado a medicação e/ou dieta durante o mesmo período do início da pesquisa até a data da última avaliação, além dos tabagistas, portadores de doenças crônicas e pacientes com menos de doze dentes.

O exame periodontal foi feito na Clínica Odontológica do HuB e consistiu em um periograma com registro em todos os dentes (seis sítios por dente) das medidas de profundidade de sondagem (PS), recessões gengivais e nível de inserção clínica (NIC). Para isto, utilizou-se sonda periodontal milimetrada do tipo “Michigan 0” com marcações de Willians, Millenium. O exame foi feito por um periodontista calibrado e experiente, PFN.

A coleta de sangue venoso ocorreu no laboratório Sabin para obtenção dos seguintes exames: hemograma completo, PCR e lipidograma completo.

Os níveis de PCR ultrassensível (PCR-us) no soro foram obtidos pelo método de Nefelometria, com limite inferior de detecção de 0,1 mg/dL. O perfil lipídico foi analisado pelo método soro/esterase – oxidase, homogêneo direto, oxidase-peroxidase e Fórmula de Friedevald, no qual o colesterol LDL teve limite inferior a 100 mg/dL, o HDL teve limite superior a 60 mg/dL e os triglicerídeos limite inferior a 150 mg/dL.

Os resultados foram calculados a partir da análise dos parâmetros clínicos bucais/periodontais, especificamente a (PS) profundidade de sondagem (≤ 3 mm; 4 a 6 mm e ≥ 7 mm, apresentados pela média ± desvio padrão). Os resultados para a variável PS em cada sítio foram expressos em porcentagem.

Os cinco dentes com maiores PS de cada paciente foram usados para obtenção da sua média de PS.

Obtidos tais dados, realizou-se teste de correlação One-Way ANOVA, segundo a normalidade das ocorrências, verificando-se a correlação e significância entre parâmetros periodontais clínicos e laboratoriais, PCR e perfil lipídico.

Resultados

O estudo envolveu três grupos. Avaliou-se cinco pacientes do grupo 1 (periodontite crônica), idade média ± 46; 80% mulheres. A média da profundidade a sondagem (PS) nesse grupo foi de ± 4,2mm, com um desvio padrão de ± 1,3038, considerando os cinco sítios com maior profundidade A média do nível de inserção clínica (NIC) foi de ±6mm e o sítio com maior frequência de PS entre 4 e 6 mm foi a mesio-lingual (ML), com 24,7%. O teste ANOVA apresentou um valor de significância (p) para cada grupo e depois analisou a relação entre cada parâmetro, que também é apresentado por “p”, sendo que, nesse grupo, o valor foi $p<0,0001$. Isso equivale a dizer que o teste tem 99,9999% de relevância. Quanto aos parâmetros laboratoriais e bioquímicos, a PCR-us apresentou a média mais elevada entre os demais grupos: ± 2,843 (risco moderado: índice

>1mg/L e <3mg/L). Ainda sobre o grupo 1 (periodontite crônica), identificou-se significância entre HDL e triglicerídeo (p<01). A PS em relação ao triglicerídeo e ao LDL apresentou p<01, cada.

O grupo 2 (diabetes com periodontite crônica) incluiu quatro indivíduos, com idade média de ± 51 anos, 50% mulheres. A média da PS foi ± 3,25 mm, com um desvio padrão de ± 0,5. Essa variável foi significativa em relação ao LDL e ao triglicerídeo, ambos com p <.01. O NIC apresentou ± 4,75 mm de média. O sítio com mais PS entre 4 e 6 mm foi a mesio-vestibular (MV), 24%. Já o LDL apresentou expressiva significância com o triglicerídeo (p<.01) e com PS (p <05). O HDL representou a menor média (± 45,75mg/dL) entre os grupos, ao passo que o triglicerídeo, nesse grupo, obteve a maior média (± 207,75mg/dL). O nível de significância do teste nesse grupo foi p <0001.

O grupo 3 (controle) foi composto por quatro pacientes saudáveis, sem periodontite e sem doenças sistêmicas, com idade média de ± 48, 100% mulheres. O NIC e PS tiveram média ± 2,75. O sítio com maior número de PS, entre 4-6mm, foi a ML (mésio-lingual), com 2%. A PCR-us foi a menor entre os grupos estudados (± 0,1489mg/L, com um desvio padrão de ± 0,11). A significância do grupo foi p <.0001. O HDL foi o mais alto, ± 56 mg/dL, e o triglicerídeo foi o mais baixo entre os grupos, ± 121 mg/dL. A PCR-us apresentou a mesma significância em relação ao LDL e ao triglicerídeo (p <01). A PS resultou em p <01 com o LDL e com triglicerídeo. Assim como nos outros grupos, PCR-us não mostrou relação com PS, nem com HDL.

Tabela 1 – Parâmetros laboratoriais

GRUPOS		PCR–us (mg/L)	HDL (mg/dl)	LDL (mg/dl)	Triglicerídeo (mg/dl)
1	Média	2.8434	55,8	126	164,2
	Desvio padrão	± 3.1942	± 7,19	± 28,03	± 94, 45
2	Média	3.3168	45,75	88,5	207,75
	Desvio padrão	± 3.6904	± 1,70	± 15,92	± 75,53
3	Média	0,14	56	107,25	121
	Desvio padrão	± 0,11	± 8,60	± 22,48	± 64,26

Tabela 2 – Dados clínicos

GRUPOS	PS (média)	NIC (média)
1	± 4,2mm	± 6mm
2	± 3,25	± 4,74
3	± 2,75	± 2,75

Tabela 3. – PS por sitio em %

GRUPO	MV		V		DV	
1	**PS**	**%**	**PS**	**%**	**PS**	**%**
	≤ 3mm	81	≤ 3mm	88	≤ 3mm	83
	4-6mm	12	4-6mm	11	4-6mm	12,8
	≥ 7mm	6,83	≥ 7mm	0,85	≥ 7mm	4,27
2	**PS**	**%**	**PS**	**%**	**PS**	**%**
	≤ 3mm	74	≤ 3mm	98,7	≤ 3mm	90
	4-6mm	24	4-6mm	1,2	4-6mm	9,6
	≥ 7mm	1	≥ 7mm	-	≥ 7mm	-
3	**PS**	**%**	**PS**	**%**	**PS**	**%**
	≤ 3mm	98	≤ 3mm	100	≤ 3mm	100
	4-6mm	1,9	4-6mm	-	4-6mm	-
	≥ 7mm	-	≥ 7mm	-	≥ 7mm	-

Tabela 3.2. – PS por sitio em %

GRUPO	ML		L		DL	
1	**PS**	**%**	**PS**	**%**	**PS**	**%**
	≤ 3mm	68,3	≤ 3mm	79	≤ 3mm	76
	4-6mm	24,7	4-6mm	18,8	4-6mm	17
	≥ 7mm	6,83	≥ 7mm	1,7	≥ 7mm	5,12
2	**PS**	**%**	**PS**	**%**	**PS**	**%**
	≤ 3mm	76	≤ 3mm	89,15	≤ 3mm	90
	4-6mm	23	4-6mm	10,8	4-6mm	9,6
	≥ 7mm	1	≥ 7mm	-	≥ 7mm	-
3	**PS**	**%**	**PS**	**%**	**PS**	**%**
	≤ 3mm	98	≤ 3mm	100	≤ 3mm	99
	4-6mm	2	4-6mm	-	4-6mm	1
	≥ 7mm	-	≥ 7mm	-	≥ 7mm	-

Discussão

Para o melhor entendimento da inter-relação entre doença periodontal e parâmetros metabólicos, o presente estudo objetivou analisar os níveis de PCR associados ao perfil lipídico somado aos dados clínicos. Os critérios de exclusão visaram evitar a influência de outras desordens que também alteram PCR e perfil lipídico. O objetivo foi analisar somente a influência do diabetes tipo 2 e da periodontite crônica sobre esses dados.

Os fatores de relevância sobre a inflamação são a PCR e o diabetes, o que corrobora os achados de estudo feito na Colômbia [5] em que a média de PCR foi 5,31 mg/L em pacientes com diabetes e PC, ao passo que o grupo sem de 2,38 mg/L. No presente estudo, a maior média da PCR entre os grupos foi 3,3168 (grupo 2-periodontite e diabetes), seguida de 2,8434 (grupo 1-periodontite).

Sabe-se do fator de risco ao desenvolvimento da doença cardiovascular relacionado à PCR [8], de forma que é importante conhecer também o perfil lipídico do paciente a fim de complementar a análise de risco. Em relação aos dados do lipidograma, a PCR quando relacionada ao LDL e, depois, com triglicerídeo tiveram p<01, nos grupos 1 e 3. O grupo 2 obteve p<05 na relação PCR com LDL, um resultado pouco significativo já que esse grupo não apresentou LDL alterado.

Um estudo de caso controle conduzido no Irã[11], em 2011, analisou 45 pacientes com periodontite e comparou aos outros 45 saudáveis quanto ao colesterol total. O grupo periodontite apresentou média de 218,11, ao passo que o controle obteve 162,31mg/dL. O estudo concluiu que hiperlipidemia pode estar associada com periodontite crônica, mas que são necessários mais estudos comprovando esta relação [11,12,13]. No presente estudo, o grupo controle apresentou os níveis mais altos de HDL e no trabalho citado acima, os níveis de HDL aumentaram após a terapia. Esses achados mostram relação inversa entre HDL e inflamação sistêmica[9,14].

Outro fato importante é que o HDL apresenta uma relação inversamente proporcional aos níveis de PCR, como mostrou o trabalho de Leite Eleutério et al, em 2014[9,11,12,13]. Nesse estudo longitudinal, a terapia periodontal foi associada ao aumento do HDL e diminuição dos níveis de PCR no soro de pacientes saudáveis e com periodontite [9].

A profundidade de sondagem mostrou associação significativa somente com LDL e triglicerídeo (p <.01) no grupo 1, assim como no grupo 3 (controle). No grupo 2, LDL e PSR obtiveram p <.05; já com o triglicerídeo, o valor foi p<.01. A PS é uma informação sobre a inflamação local do paciente que induz liberação de citocinas pró inflamatórias e contribui para um perfil aterogênico. As faces que apresentaram maiores PS foram a ML e a MV, o que condiz com a prática clínica porque são as regiões proximais que representam mais dificuldade para desorganizar o biofilme.

O estudo concluiu que houve associação de PCR com LDL e triglicerídeo em todos os grupos, enfatizando o caráter inflamatório dessas condições[13,14]. Em todos os grupos houve significância entre

LDL e PS, bem como entre LDL e triglicerídeo. Os pacientes com periodontite e diabetes obtiveram os valores mais significativos quanto à PCR, PS e ao triglicerídeo. Já o HDL foi mais alto no grupo controle, em que todos eram saudáveis e não tinham fatores contribuintes para vias inflamatórias[9].

Os parâmetros analisados no presente estudo possuem relação direta com vias inflamatórias[14,15,16,]. No paciente diabético, há uma alteração metabólica consistente que pode exacerbar PC e alterar seu perfil lipídico o que, consequentemente, leva a maiores riscos cardiovasculares[5,7,9,14,17,18]. A doença periodontal é um fator agravante para a condição sistêmica dos pacientes diabéticos [6,15,17,19].

A análise seria mais completa e esclarecedora se o presente estudo fosse longitudinal, comparando os dados pré e pós terapia, o que possibilitaria um resultado mais significativo. Outra limitação do trabalho é o número da amostra, são poucos pacientes, então não é possível extrapolar os dados para a população em geral. Com uma amostra maior, haveria maior distribuição das médias e maior possibilidade de um dado se destacar.

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ANEXOS

NORMAS DA REVISTA

This update includes a general reorganization of the author guidelines as well as improved navigation. Other changes include online-only publication, conflict of interest form collection, and updates to clinical trial registration requirements.

The *Journal of Periodontology* publishes articles relevant to the science and practice of periodontics and related areas. Manuscripts are accepted for consideration with the understanding that text, figures, photographs, and tables have not appeared in any other publication, except as an abstract prepared and published in conjunction with a presentation by the author(s) at a scientific meeting, and that material has been submitted only to this journal.

The *Journal of Periodontology* accepts manuscript submissions online at ScholarOne Manuscripts. To start a new submission, enter the Author Center and click "Click here to submit a new manuscript." Details regarding each submission step are located at the top of the page in ScholarOne Manuscripts. Authors should prepare manuscripts in accordance with the instructions below. Failure to do so may result in delays or manuscript unsubmission.

MANUSCRIPT CATEGORIES AND SPECIFIC FORMATS

Submissions to the *Journal of Periodontology* should be limited to one of the categories defined below. Specific information regarding length and format is provided for each category. Please also refer to the instructions provided under General Format and Style. All manuscripts will be reviewed by the Editors for novelty, potential to extend knowledge, and relevance to

clinicians and researchers in the field. Some manuscripts will be returned without review, based on the Editors' judgment of the appropriateness of the manuscript for the *Journal of Periodontology*.

ORIGINAL ARTICLES

These are papers that report significant clinical or basic research on the pathogenesis, diagnosis, and treatment of the different forms of periodontal disease. Papers dealing with design, testing, and other features of dental implants are also included.

Format

Original articles must be limited to 4,000 words (excluding the abstract, references, and figure legends). The reference list should not exceed 50 references, and the total combined number of figures and tables must be six or fewer. Multi-panel figures are acceptable.

Abstract

All original articles should be submitted with a structured abstract, consisting of no more than 250 words and the following four paragraphs:

- Background: Describes the problem being addressed.
- Methods: Describes how the study was performed.
- Results: Describes the primary results.
- Conclusion(s): Reports what authors have concluded from these results, and notes their clinical implications.

Introduction

The Introduction contains a concise review of the subject area and the rationale for the study. More detailed comparisons to previous work and conclusions of the study should appear in the Discussion section.

Materials and Methods

This section lists the methods used in the study in sufficient detail so that other investigators would be able to reproduce the

research. When established methods are used, the author need only refer to previously published reports; however, the authors should provide brief descriptions of methods that are not well known or that have been modified. Identify all drugs and chemicals used, including both generic and, if necessary, proprietary names and doses. The populations for research involving humans should be clearly defined and enrollment dates provided.

Results
Results should be presented in a logical sequence with reference to tables, figures, and supplemental material as appropriate.

Discussion
New and possible important findings of the study should be emphasized, as well as any conclusions that can be drawn. The Discussion should compare the present data to previous findings. Limitations of the experimental methods should be indicated, as should implications for future research. New hypotheses and clinical recommendations are appropriate and should be clearly identified. Recommendations, particularly clinical ones, may be included when appropriate.

Publication of Accepted Original Articles

Please note that accepted manuscripts which are classified by the Editors as "Discovery Science" will be placed on an accelerated schedule for **online-only publication**. See Online-Only Publication below.

REVIEW ARTICLES

These are focused reviews of basic and clinical science related to periodontics and implant dentistry. These reviews should be concise and address an important and timely clinical question. Authors should discuss clinical relevance and the impact on future understanding and practice. The review should be based on a critical assessment of the literature and should use the format and methods of a "systematic review." Detailed descriptions of the systematic review methodology are available

in the Cochrane Handbook for Systematic Reviews of Interventions.[1] There are many excellent published examples of systematic reviews, including "Periodontal Disease and Coronary Heart Disease Incidence: A Systematic Review and Meta-Analysis" by Humphrey et al.[2]
Authors of systematic reviews that include a meta-analysis should refer to the QUOROM statement.[3] Authors of systematic reviews without meta-analysis should refer to the papers by Cook et al.[4] and Mulrow et al.[5]

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Format
The abstract should summarize the main conclusions of the review in 350 words or less. Systematic review articles should: define a clear and clinically relevant research question; retrieve and describe the limitations of previously published reviews on this topic; and justify the need for a systematic review. The review should then define the search strategy used to identify primary articles; describe the methods used to select primary studies; specify inclusion and exclusion criteria (criteria for selecting primary studies should be based on population studied, intervention or exposure, study outcomes, and study

methodology); perform a blinded assessment of the quality of the selected articles; describe the reliability of this process in terms of agreement between two evaluators; account for all studies identified by the search and justify exclusions; state their conclusions; compare their conclusions to the literature and current standard of care; outline the limitations of the review; and suggest areas for future research.
Papers should be balanced, literature-based reviews that are concise (2,000 to 3,000 words) with about 100 key references. Tables and figures should be limited to those essential to convey the results of the review, and the total combined number of figures and tables should not exceed six. Since critical reviews require selection of reports and interpretation of data, authors should disclose financial interest in the companies making products or providing services described in the review.

COMMENTARIES

The purpose of these papers is to provide a forum for discussion of controversies and other issues as they relate to the practice of periodontics and implant dentistry. Full and balanced discussion of controversies on important issues is encouraged. This may result in several authors each presenting a relevant viewpoint. Commentaries should be concise (2,000 to 3,000 words) with no more than 50 references; however, they should be complete and balanced, which may require that the issue or controversy addressed be highly focused.

Introduction
This section should clearly state the clinical question or issues to be discussed and document their importance and timeliness.

Body
The body should present the information supporting all aspects of the issues. This portion of the Commentary may be subdivided as appropriate with headings. Figures, tables, and other illustrative materials may be incorporated. The total combined number of figures and tables should not exceed six.

Summary
The summary should place the issue in perspective and point a way for future directions in addressing the controversy.

Acknowledgment(s)
Since these papers allow authors to express their opinions on a subject, it is extremely important that authors disclose any and all affiliations, financial position, or any other information that constitutes a real or perceived conflict of interest.

CASE SERIES

The Journal of Periodontology no longer publishes Case Reports. Authors are encouraged to submit Case Reports to Clinical Advances in Periodontics. The Journal of Periodontology publishes selected Case Series that describe unusual case presentations, complex diagnoses, and novel approaches to treatment within the scope of practice of periodontology. These Case Series provide valuable information for clinicians and teachers in the field.

Case Series report a sufficient number of consecutive or randomized cases to make a persuasive argument for or against the procedure, technique, or concept under discussion. Cases should be relatively homogeneous so that a systematic evaluation of one type of disease, lesion, or condition is made for the procedure under consideration. Also, treatment and documentation should be consistent and standardized for all cases. It is recognized that definitive evidence for the safety and efficacy of any procedure, drug, or device comes primarily from well-designed, randomized, controlled trials. However, well-executed Case Series may lead to hypotheses about the usefulness of new and innovative procedures, drugs, or devices and may therefore be of value to the progress of clinical science.

The requirements for patient consent, privacy, and institutional approval are well defined for manuscripts describing research on human subjects. These basic requirements are described by the International Committee of Medical Journal Editors (ICMJE) in their Uniform Requirements for Manuscripts Submitted to Biomedical Journals (available at: www.icmje.org) and are interpreted in the instructions to authors of all peer-reviewed biomedical journals, including theJournal of Periodontology.

Due to the changing ethical and legal environment around the use of patient information, the editorial team has received multiple questions about the need for subject consent from patients described in Case Series submitted for publication.
The following applies to most Case Series. It should be noted that the Editors will determine whether specific Case Series require additional approvals beyond what is described below.

Requirement for Ethics Board Approval
Most Case Series are a retrospective description of clinical findings in cases or an observed course of events that document a new aspect of patient management during the normal course of clinical treatment. Since there is no hypothesis testing, no systematic data collection beyond that which is part of routine clinical practice, no data analysis, and the work has already been done, Case Series do not usually qualify as "research" requiring approval from ethical boards designed to protect humans involved in clinical research.
(U.S. Fed. definition: "RESEARCH is any systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.")
Example 1: Series of private practice implant cases in patients who have been taking bisphosphonates. Authors describe the findings in each case, which are collected and reported in a table format.
Example 2: Authors collect series of private practice implant cases in patients who have or have not been taking bisphosphonates. The sample size is sufficient for data analysis, and authors analyze and report the incidence of complications.
Example 1 does not qualify as "research," but example 2 does qualify and requires ethical approval.
Please see "Does My Case Series Need IRB Approval?" for more information.

Privacy in Case Series
No patient identifiers should be included in Case Series. If the authors choose to include any subject identifiers, the authors must include the patient’s informed written consent to publish the information.

Our policy conforms to the Uniform Requirements, which states: "Patients have a right to privacy that should not be violated without informed consent. Identifying information, including names, initials, or hospital numbers, should not be published in written descriptions, photographs, or pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written informed consent for publication. Informed consent for this purpose requires that an identifiable patient be shown the manuscript to be published. Authors should disclose to these patients whether any potential identifiable material might be available via the Internet as well as in print after publication."
It should be noted that patients may have given a signed "consent to treat," but that does not constitute permission to publish their case with personal identifiers unless they have explicitly approved the manuscript. Likewise, patient consent under government privacy rules, such as the Health Insurance Portability and Accountability Act (HIPAA) in the United States, does not constitute permission to publish their case with personal identifiers unless they have explicitly approved the manuscript.

Format
Case Series must be limited to 2,000 to 3,000 words (excluding the abstract, references, and figure legends). The reference list should not exceed 50 references, and the total combined number of figures and tables must be six or fewer. Multi-panel figures are acceptable.

Abstract
Case Series should be submitted with a structured abstract, consisting of no more than 250 words and the following four paragraphs:

Background: Describes the clinical situation being discussed.

Methods: Describes the clinical procedures (surgical and non-surgical) performed.

Results: Describes the clinical results.

Conclusion(s): Reports what authors have concluded, specifically clinical implications in practice situations.

Introduction
This section should include a critical review of the pertinent literature.

Case Description and Results
This section describes the cases, including all relevant data. For ease of presentation, tables describing longitudinal data in a chronological form may be useful. Carefully selected, high-quality clinical photographs in full color, as well as radiographs, are encouraged.

Discussion
This should include findings, put into perspective with respect to the field and literature. Unique arguments and new information gained should be summarized. Consideration of the clinical significance of the cases should be emphasized in all sections.

GUEST EDITORIALS

Guest Editorials may be invited or may be submitted from authorities in certain areas as a means of offering their perspective on one or more articles published in the Journal, or on other items of interest to the readership.

LETTERS TO THE EDITOR

Letters may comment on articles published in the Journal and should offer constructive criticism. If a letter comments on a published article, the author(s) will be provided 30 days to respond to the observations.
Letters to the Editor may also address any aspect of the profession, including education and training, new modes of practice, and concepts of disease and its management.
Letters should be brief (<1,000 words), focused on one or a few specific points or concerns, and can be signed by no more than

five individuals.
Citations should be handled as standard references.

GENERAL FORMAT

Manuscripts must be submitted in Microsoft Word. Margins should be at least 1" on both sides and top and bottom and all text should be double-spaced. Materials should appear in the following order:

- Title Page
- Abstract (or Introduction) and Key Words
- Text
- Footnotes
- Acknowledgment(s)
- References
- Figure Legends
- Tables

Figures should not be embedded in the manuscript. Please see the *Journal of Periodontology* Digital Art Guidelines for more information on submitting figures.
Authors should retain a copy of their manuscript for their own records.

TITLE PAGE

The title page should contain:

1. a concise but informative title;
2. first name, middle initial, and last name of each author, with the highest academic degree and the current institutional affiliation, including department, for each (please use footnote symbols in the sequence *, †, ‡, §, ‖, ¶, #, **, etc. to identify authors and their corresponding institutions);
3. disclaimers, if any;

4. the name and address (including fax number and e-mail) of the author responsible for correspondence (please indicate whether fax number and e-mail can be published);
5. word count and number of figures, tables, and references in the manuscript;
6. a short running title of no more than 60 characters, including spaces;
7. a one-sentence summary describing the key finding(s) from the study.

KEY WORDS

A maximum of six key words or short phrases, drawn from MeSH documentation, to facilitate indexing should be listed below the abstract.

ACKNOWLEDGMENT(S) AND CONFLICTS OF INTEREST

Acknowledgment(s)

Following the Discussion, acknowledgments may be made to individuals who contributed to the research or the manuscript preparation at a level that did not qualify for authorship. This may include technical help or participation in a clinical study. Authors are responsible for obtaining written permission from persons listed by name. Acknowledgments must also include a statement that includes the source of any funding for the study, and defines the commercial relationships of each author.

Conflicts of Interest

In the interest of transparency and to allow readers to form their own assessment of potential biases that may have influenced the results of research studies, the *Journal of Periodontology* requires

that all authors declare potential competing interests relating to papers accepted for publication. Conflicts of interest are defined as those influences that may potentially undermine the objectivity or integrity of the research, or create a perceived conflict of interest.

Authors are required to submit:

1. A statement in the acknowledgments section of the manuscript that includes the source of any funding for the study, and defines the commercial relationships of each author. If an author has no commercial relationships to declare, a statement to that effect should be included. This statement should include financial relationships that may pose a conflict of interest or potential conflict of interest. These may include financial support for research (salaries, equipment, supplies, travel reimbursement); employment or anticipated employment by any organization that may gain or lose financially through publication of the paper; and personal financial interests such as shares in or ownership of companies affected by publication of the research, patents or patent applications whose value may be affected by this publication, and consulting fees or royalties from organizations which may profit or lose as a result of publication. An example is shown below.
2. A conflict of interest and financial disclosure form for each author. A link to this electronic form will be e-mailed to each author after manuscript submission.

Conflict of interest information will not be used as a basis for suitability of the manuscript for publication.

Example of Conflict of Interest Statement

This study was supported by a grant from the Acme Implant Corporation, Seoul, Korea. Dr. Lee is on the scientific advisory board for Acme Implant Corporation and gives lectures sponsored by the company. Dr. Smith is a consultant and shareholder of the Brownstone Implant Corporation, Boston, Massachusetts. Dr. Wang is employed full-time as chief technical officer of the Acme Implant Corporation. Drs. Able, Kim, and Bruce report no conflicts of interest related to this study.

REFERENCES

References should be numbered consecutively in the order in which they appear in the text. A journal, magazine, or newspaper article should be given only one number; a book should be given a different number each time it is mentioned, if different page numbers are cited.

All references are identified, whether they appear in the text, tables, or legends, by Arabic numbers in superscript. Journal title abbreviations should be those used by the U.S. National Library of Medicine. If you are uncertain about the correct abbreviation for a journal title, please search for the journal athttp://www.ncbi.nlm.nih.gov/nlmcatalog.

The use of abstracts as references is strongly discouraged. Manuscripts accepted for publication may be cited and should include the manuscript's DOI, if known. Material submitted, but not yet accepted, should be cited in text as "unpublished observations." Written and oral personal communications may be referred to in text, but not cited as references. Please provide the date of the communication and indicate whether it was in a written or oral form. In addition, please identify the individual and his/her affiliation. Authors should obtain written permission and confirmation of accuracy from the source of a personal communication. Presented papers, unless they are subsequently

published in a proceedings or peer-reviewed journal, may not be cited as references. In addition, Wikipedia.org may not be cited as a reference. For most manuscripts, authors should limit references to materials published in peer-reviewed professional journals. In addition, authors should verify all references against the original documents. References should be typed double-spaced. Examples of references are given below. Authors are encouraged to consult EndNote for the Journal of Periodontology's preferred reference style.

Journals

1. Standard journal reference. Note: list all authors if six or fewer; when seven or more, list only first three and add et al. Kurita-Ochiai T, Seto S, Suzuki N, et al. Butyric acid induces apoptosis in inflamed fibroblasts. J Dent Res 2008;87:51-55.
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Electronic Citations
Note: DOIs are preferred for journal articles. If a DOI is not available, please provide a URL and access date.

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11. Web sites. Centers for Disease Control and Prevention. Periodontal Disease. Available at:http://www.cdc.gov/OralHealth/topics/periodontal_disease.htm. Accessed September 29, 2010.

TABLES

Tables should be numbered consecutively in Arabic numbers in the order of their appearance in the text. A brief descriptive title should be supplied for each. Explanations, including

abbreviations, should be listed as footnotes, not in the heading. Every column should have a heading. Statistical measures of variations such as standard deviation or standard error of the mean should be included as appropriate in the footnotes. Do not use internal horizontal or vertical rules. The submission system will easily read tables created with Word's table utility or when inserted into Word from Excel.

FIGURES

Please see the Journal of Periodontology Digital Art Guidelines for detailed instructions on submitting high-quality images.

Figure Legends
Legends should be typed double-spaced with Arabic numbers corresponding to the figure. When arrows, symbols, numbers, or letters are used, explain each clearly in the legend; also explain internal scale, original magnification, and method of staining as appropriate. Panel labels should be in capital letters. Legends should not appear on the same page as the actual figures.

FOOTNOTES

Footnotes should be used only to identify author affiliations; to explain symbols in tables and illustrations; and to identify manufacturers of equipment, medications, materials, and devices. Use the following symbols in the sequence shown: *, †, ‡, §, ‖, ¶, #, **, ††, etc.

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