PONTIFÍCIA UNIVERSIDADE CATÓLICA DO PARANÁ

ESCOLA DE CIÊNCIAS DA VIDA

PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA

ÁREA DE CONCENTRAÇÃO: ORTODONTIA

Orientador: Orlando M. Tanaka

AVALIAÇÃO DA TAXA DE DISTALIZAÇÃO DE CANINOS SUPERIORES EM ALVÉOLOS PRESERVADOS COM MEMBRANAS DE PLASMA RICO EM FIBRINA E LEUCÓCITOS (L-PRF): ESTUDO CLÍNICO RANDOMIZADO

Ariel Adriano Reyes Pacheco

Curitiba

Fevereiro 2019

ARIEL ADRIANO REYES PACHECO

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A

Dados da Catalogação na Publicação
Pontifícia Universidade Católica do Paraná
Sistema Integrado de Bibliotecas – SIBI/PUCPR
Biblioteca Central
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Pacheco, Ariel Adriano Reyes
P116a Avaliação da taxa de distalização de caninos superiores em alvéolos
2019 preservados com membranas de plasma rico em fibrina e leucócitos (L-PRF) : estudo clínico randomizado / Ariel Adriano Reyes Pacheco ; orientador, Orlando M. Tanaka. -- 2019
57 f. : il. ; 30 cm

Tese (doutorado) – Pontifícia Universidade Católica do Paraná, Curitiba, 2019.
Inclui bibliografia

1. Ortodontia. 2. Tratamento dentário. 3. Cúspide. 4. Fibrina. 5. Leucócitos. 6. Plaquetas (Sangue). I. Tanaka, Orlando Motohiro.
- II. Pontifícia Universidade Católica do Paraná. Programa de Pós-Graduação em Odontologia. III. Título.

CDD 20. ed. – 617.643

Pontifícia Universidade Católica do Paraná
Escola de Ciências da Vida
Programa de Pós-Graduação em Odontologia

TERMO DE APROVAÇÃO

ARIEL ADRIANO REYES PACHECO

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Curitiba, 21 de Fevereiro de 2019.

À minha esposa Rosanna Elizabeth Quintana de Reyes pela força e amor que me ajudaram a chegar até aqui, te amo com todo o meu coração.

Às minhas filhas Gabriela e Alejandra Reyes Quintana por serem a minha inspiração e motivação para crescer e ser melhor.

Aos meus pais Adriano Reyes Paulino e Marlene Pacheco Alvarado pela compreensão e ajuda ao longo dos anos, chegar até aqui foi um sacrifício de todos, muito obrigado.

AGRADECIMENTOS

Gostaria de agradecer aos meus colegas da 9a turma de Mestrado: Marlon Borges, Renata Marangon, Pâmela Trannin, Cyro Pellizzari II, Estephany Gordillo, Neblyssa Schneider, Adriana Rocha e Gabriela Marin. Muito obrigado por tudo o que fizeram por mim, eternamente agradecido, fico com uma enorme dívida com vocês, lembro muito de todos, saudades.

Aos colegas do Doutorado, hoje Doutores: Cláudio Sabatoski, Bruno Castilhos, Cristiano Araújo e Ariane Ximenes Graciano Parra muito obrigado pela amizade e tempo compartilhado.

Aos colegas da 10ª turma de Mestrado da PUCPR: Bruno Bertaiolli, Fernando Machuca, Wagner de Oliveira e Gustavo Vizinoni e Silva. Agradeço à sua amizade que permanece ainda.

Ao pessoal da secretaria de Pós-graduação da PUCPR, especialmente à Neide Borges por toda a ajuda oferecida desde a primeira vez que liguei para Curitiba solicitando informação sobre o curso, muito obrigado Neide.

Obrigado Nilce, da clínica de pós-graduação, pela ajuda durante os anos que estive lá.

Obrigado aos professores que fazem parte do programa da PPGO devo de agradecer enormemente tudo o que fizeram por mim durante a minha formação e permanência na PUCPR, fica minha admiração e gratidão.

Obrigado ao Prof. Dr. Sergio Vieira, Prof.ªDr.ª Renata Werneck, Prof.ª Dr.ª Evelise Machado de Souza e que foram os coordenadores do Programa de Pós-graduação em Odontologia desde que iniciei o curso de mestrado na PUCPR.

Agradeço com muita admiração e carinho ao mesmo tempo aos meus professores da O.R.T.O.D.O.N.T.I.A da PUCPR: Prof. Orlando M. Tanaka, Profa. Elisa Souza Camargo, Prof. Odilon Guariza Filho e Prof. Armando Y. Saga. Professores, muito obrigado por TUDO E TODO O QUE FIZERAM POR MIM, pelos ensinamentos, compreensão, amizade, tolerância, em fim, tudo o que me

brindaram durante os meus anos em Curitiba, dizer obrigado é muito pouco para tudo o que deveria expressar.

Agradeço ao professor Paulo Couto Souza, pela ajuda oferecida na correção desta tese e por ter participado da banca examinadora na qualificação, muito obrigado professor.

Ao Dr. Luis Rafael Serret que me levou até a PUCMM. À Dra. Susselis Ramírez pela ajuda e encaminhamento dos pacientes. Ao Dr. Marcos Peguero pela ajuda e amizade.

A todos os professores do departamento de Periodontia da Pontificia Universidad Católica Madre & Maestra- Recinto Santo Tomás de Aquino pela sua amizade e ajuda na elaboração desta tese.

Ao Dr. Dante Dotel pela amizade, parceria e compreensão.

Muito obrigado à família Quintana Vergara, por ter cuidado das minhas filhas, pelo apoio incondicional, e pela ajuda que me brindaram ao longo destes anos, vocês fizeram muito por mim, muito obrigado a todos.

AGRADECIMENTOS ESPECIAIS

Ao professor Orlando M. Tanaka. Professor eu te agradeço pelo apoio e amizade durante estes anos, por ter me motivado e incentivado a continuar, pela ajuda dentro e fora dos assuntos acadêmicos durante todos estes anos de formação. O senhor é um exemplo de dedicação e perseverança digna de admiração. Minha gratidão. Saiba que pode sempre contar comigo que farei tudo o que esteja ao meu alcance para algum dia retribuir tudo o que me foi dado, como escrevi nos agradecimentos gerais, dizer obrigado é muito pouco para tudo o que deveria expressar. Muito obrigado professor!!! Espero que possamos nos reencontrar novamente, grande abraço professor!!!.

Ao Dr. James Collins, obrigado pelo apoio e parceria durante esses anos, agradeço muito por tudo o que fez por mim durante o meu retorno à Santo Domingo. Por ter me dado a oportunidade de realizar este trabalho de tese na Pontifícia Universidad Católica Madre & Maestra (PUCMM-STA) e por acreditar no meu trabalho. Obrigado.

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PACHECO, Ariel Adriano Reyes. AVALIAÇÃO DA TAXA DE DISTALIZAÇÃO DE CANINOS SUPERIORES EM ALVÉOLOS PRESERVADOS COM MEMBRANAS DE PLASMA RICO EM FIBRINA E LEUCÓCITOS (L-PRF): ESTUDO CLÍNICO RANDOMIZADO. Orientador: Dr. Orlando Tanaka. Curitiba: PUCPR, PPGO, 2019. (Doutorado em Odontologia– Ortodontia). 39p.

RESUMO

INTRODUÇÃO: O objetivo deste estudo foi avaliar a taxa de distalização e as alterações nas inclinações dos caninos superiores em alvéolos preservados com membranas de plasma rico em fibrina e leucócitos (L-PRF), partindo da hipótese nula (H0) de não diferença. **MÉTODOS:** Dezessete pacientes adultos jovens (média 33±5,9 anos), em boas condições de saúde, com maloclusão de Classe I e II, divisão 1 de Angle, com indicação de exodontia dos primeiros pré-molares e distalização dos caninos superiores para o tratamento ortodôntico foram incluídos no estudo. Foi realizado um estudo clínico randomizado do tipo *split mouth*, no qual o lado experimental foi preservado com L-PRF e o outro lado foi o controle. A distalização foi realizada com elástico em cadeia, aplicando 150 g/força nos caninos, e arco 0,020” de aço inoxidável. A taxa de distalização foi avaliada mensalmente durante cinco meses com o uso de uma régua flexível. O grau de inclinação dos caninos foi avaliado nas imagens obtidas em tomografia de feixe cônico. Foi realizado o teste de Shapiro Wilk, e posteriormente o teste de Wilcoxon Signed Rank Test para realizar a comparação entre os grupos. **RESULTADOS:** A taxa de distalização e inclinação de caninos foi maior no lado controle quando comparado com o lado preservado com L-PRF ($p < 0,05$). **CONCLUSÕES:** A hipótese nula foi rejeitada. A preservação alveolar com membranas de L-PRF diminuiu a taxa de distalização e inclinações dos caninos superiores quando comparado com o grupo controle em pacientes adultos jovens.

Palavras-chave: Caninos, Movimentação Ortodôntica, Fibrina Rica em Leucócitos e Plaquetas.

Registro: Este estudo clínico não foi registrado.

Protocolo: O protocolo não foi publicado prévio ao início do estudo.

Financiamento: Nenhum financiamento ou conflito de interesse a ser declarado.

INTRODUÇÃO

Os pacientes adultos procuram tratamento ortodôntico em sua maioria por motivos estéticos, sendo a correção da inclinação dos incisivos superiores o principal.[1] A correção da posição dos incisivos superiores projetados é realizada frequentemente por meio de exodontias dos primeiros pré-molares superiores.[2,3]

Vários fatores aumentam o tempo de tratamento em pacientes adultos, entre eles encontra-se a extração de primeiros pré-molares[4-7] uma vez que, a distalização de caninos pode demorar entre dez meses e um ano.[8,9] Por terem densidade óssea maior, *turnover* ósseo diminuído e ligamento periodontal com menos células do que os pacientes adolescentes, apresentam mais áreas de hialinização do ligamento periodontal e maior reabsorção radicular durante tratamento o ortodôntico,[10,11] precisando de mais tempo para superar as fases da movimentação dentária.[10,12]

Após a exodontia, o alvéolo inicia o processo de reabsorção óssea, sendo maior durante o primeiro ano. O rebordo alveolar diminui, inicialmente, em largura e posteriormente em altura. Para evitar esse colapso alveolar, a utilização de biomateriais como enxertos ósseos (autógeno, xenógeno ou aloplástico) ou o plasma rico em plaquetas, plasma rico em fibrina e derivados, vem aumentando, para a preservação das dimensões do rebordo ósseo alveolar após a exodontia.[13]

O plasma rico em fibrina e leucócitos (L-PRF) corresponde à segunda geração de biomateriais baseados no plasma sanguíneo. O L-PRF é constituído de sangue sem adição de qualquer outro componente, tendo a sua maior vantagem a facilidade para criar a membrana plasmática por centrifugação e o baixo custo.[14-16]

O L-PRF traz consigo células como proteases e antiproteases que promovem a angiogênese e remodelado vascular, citocinas e quimiocinas envolvidas na regulação da angiogênese e formação óssea. Contém ainda, fatores de crescimento que promovem a proliferação celular, angiogênese e quimiotaxia facilitando o reparo ósseo, cicatrização e angiogênese de feridas.[14-18] Essas propriedades poderiam ser benéficas para o tratamento ortodôntico, a maior quantidade de vasos sanguíneos na área de interesse e o menor tempo de reparo,

poderiam diminuir o tempo de tratamento e aumentar a taxa de movimentação dentária em adultos. Este é um dos primeiros estudos clínicos a realizar tal inter-relação. [19]

Portanto, o objetivo deste estudo foi avaliar a taxa de distalização e as alterações nas inclinações dos caninos superiores em alvéolos preservados com membranas de plasma rico em fibrina e leucócitos (L-PRF). A hipótese nula foi que não há diferenças na taxa de movimentação dos caninos entre o lado preservado, e o controle, sem preservação, somente com a manutenção do coágulo.

MATERIAL E MÉTODOS

O presente estudo foi realizado na Pontifícia Universidad Católica Madre & Maestra- Recinto Santo Tomás de Aquino (PUCMM-STA) com a aprovação do comitê de bioética (ID: COBE-FACS-M.EST-CSTA-004-2-2015-2016) (Anexo 1), entre os meses de Setembro 2016 e Dezembro 2018.

Desenho do estudo e alterações após o início

Foi realizado estudo clínico randomizado do tipo *split mouth*, no qual o lado experimental recebeu a preservação alveolar com membranas de plasma rico em fibrina e leucócitos (L-PRF) e o outro foi o controle. Foram utilizados os critérios CONSORT para reportar os resultados deste estudo.[20 21]

Participantes e critérios de elegibilidade

Os critérios de elegibilidade foram: 1) pacientes adultos, com idade mínima de 20 anos com necessidade de tratamento ortodôntico, 2) indicação de exodontia dos primeiros pré-molares superiores para o tratamento. Todos os pacientes assinaram o consentimento informado prévio ao início do tratamento (Anexo 2).

Os critérios de exclusão foram: 1) pacientes com doenças autoimunes, 2) grávidas ou lactantes, 3) utilização de medicamentos de uso prolongado nos seis meses anteriores ao início do estudo (antibióticos, anti-histamínicos, cortisona, hormônios), e outros que interferem com o processo de resposta inflamatória ou com efeito adverso diretamente no ligamento periodontal, 4) na presença de

doenças sistêmicas, estas deviam estar controladas, não contraindicando o procedimento cirúrgico da exodontia, 5) pacientes com doença periodontal foram descartados.

A amostra foi composta por 21 pacientes adultos jovens sadios, ao longo do estudo, quatro desistiram, permanecendo dezessete pacientes no total (n=17), sendo doze (12) do sexo feminino e cinco (5) do masculino. As idades foram entre os 20 e 45 anos (média de 33 anos), todos diagnosticados com maloclusão Classe I (n=14) ou II-1 de Angle (n=3). Todos com necessidade de tratamento ortodôntico com extrações de 1os pré-molares superiores. A descrição da seleção de pacientes e alocação com L-PRF está descrita na Figura 1, seguindo os critérios do CONSORT statement (Consolidated Standards of Reporting Trials).[20,21]

Aleatorização

A aleatorização dos lados foi realizada utilizando a função de geração de números aleatórios de Microsoft Excel (Microsoft Office 2016, Microsoft, Redmond, Washington, EUA). O lado que recebeu a preservação alveolar foi selecionado seguindo a ordem da sequência criada na planilha.

Cegamento

Não houve cegamento dos operadores, nem dos pacientes.

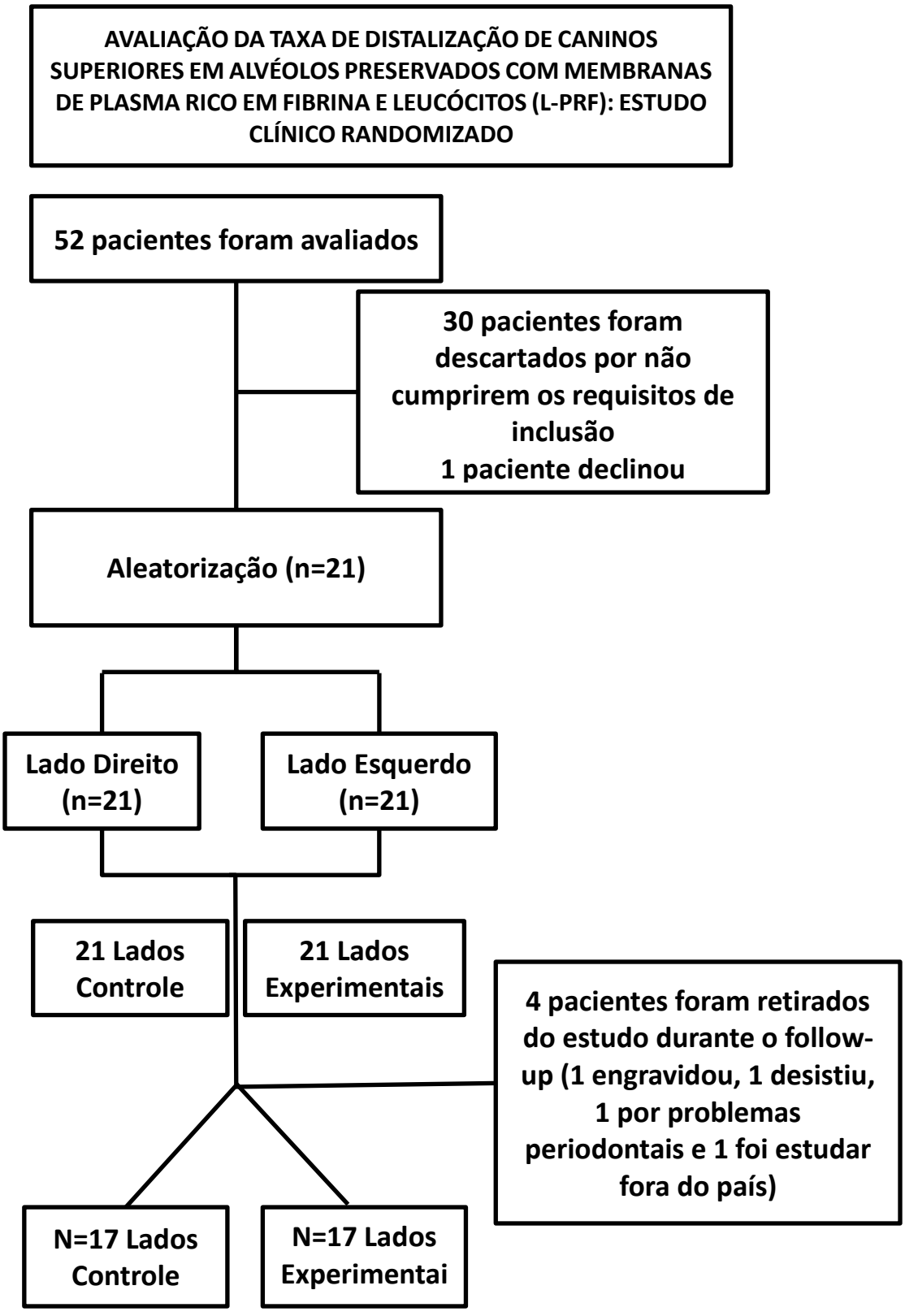


Fig 1. Diagrama CONSORT da seleção de pacientes e alocação do L-PRF.

Intervenções

Todos os pacientes foram tratados por um mesmo operador (A.A.R.P.), com bráquetes pré-ajustados prescrição MBT *slot* 0.022” (ABZIL Kirium, 3M, Brasil). Foi realizada a fase de alinhamento e nivelamento com arcos de NiTi 0.014”, 0.016” e aço inoxidável 0.018” e 0.020”. No dia da consulta de instalação do arco de aço inoxidável 0.020” na arcada superior (Fig 2) foi realizado o preenchimento do formulário solicitando a exodontia dos primeiros pré-molares superiores (14 e 24) ao departamento de Periodontia, e solicitada a primeira tomografia de feixe cônico (CBCT) (T1). O tomógrafo utilizado foi o Plan Meca ProMax 3D Max, com FOV (Field Of View) de Ø23 x 26 cm, tempo de exposição de 18-30 segundos, voxel 0.200, tempo de reconstrução de 30-150 segundos e radiação de 101-252 mSv.

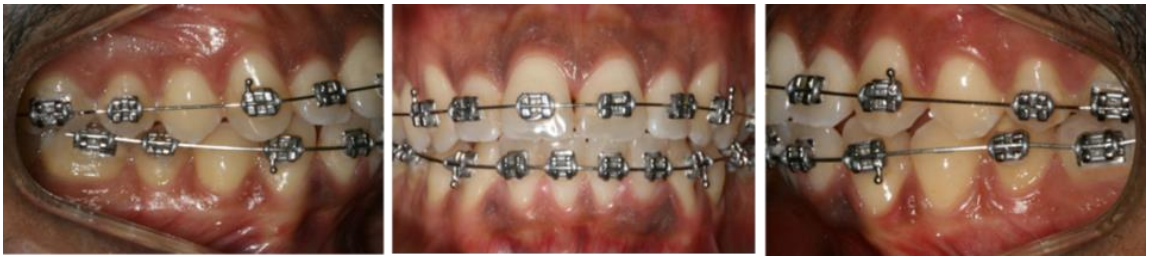


Fig 2. Imagens intra-bucais da fase de alinhamento e nivelamento.

No dia do ato cirúrgico, a coleta sanguínea foi realizada prévia à realização das extrações. Utilizou-se o Scalp à vácuo (borboleta) da marca BD Vacuteiner Safety-Lok™ blood collection set (New Jersey, USA) coletado diretamente no tubo de ensaio. Não foram utilizadas seringas descartáveis pela possibilidade de coagulação do sangue ou diminuição da qualidade do plasma rico em fibrina obtido, no momento da transferência da seringa para o tubo. [14,15,17,18]

A obtenção do plasma rico em fibrina e leucócitos (L-PRF) foi realizada de acordo com o protocolo da centrífuga IntraSpin (Boca Raton, FL, USA), centrifugando o sangue durante 14 minutos a 2,700 RPM. Posteriormente, o coágulo formado foi extraído do tubo de ensaio e pressionado entre duas placas de vidro cobertas com compressas impregnadas com soro fisiológico durante 30

segundos para retirar o excesso e obter uniformidade. O alvéolo experimental foi preservado com membranas de L-PRF. Os alvéolos receberam sutura com Nylon 4-0 (Mononylon- Ethicon Johnson & Johnson) para aproximar as bordas para promover a cicatrização. Esta sequência foi realizada para diminuir o tempo de exposição dos alvéolos, e colocar o L-PRF o mais rápido possível.

A luxação dos pré-molares foi realizada, durante o ato cirúrgico, com a utilização do Piezotome (Satelec Acteon, França) para a preservação das corticais alveolares, e realizar a exodontia de maneira menos traumática e diminuindo as complicações pós-operatórias[22]

Quinze dias depois de realizadas as extrações, o espaço inicial foi medido utilizando compasso de ponta seca, e posteriormente transferido à régua flexível. Na mesma consulta, iniciou-se a distalização dos caninos. Foi colocado um fio de amarrilho metálico de 0.008” do primeiro molar até o segundo pré-molar como unidade de ancoragem. Na aleta distal dos bráquetes dos caninos, outro fio de amarrilho metálico de 0.008” foi colocado para minimizar a rotação. A distalização dos caninos foi realizada sobre o arco de aço inoxidável 0.020”. Foram utilizados elásticos em cadeia (Memory Chain, American Orthodontics, Sheboygan, WI, USA), aplicando-se força de 150 g/f (Fig 3) de acordo com Burrow[8] e Mezomo *et al*.[23] Os elásticos foram colocados do segundo pré-molar até o canino. A quantidade de força foi medida com o tensiômetro CORREX (50-250 gramas) (Haag Streit, Bern, Suíça). As ativações foram realizadas uma vez por mês, a cada quatro semanas, durante cinco meses**.**

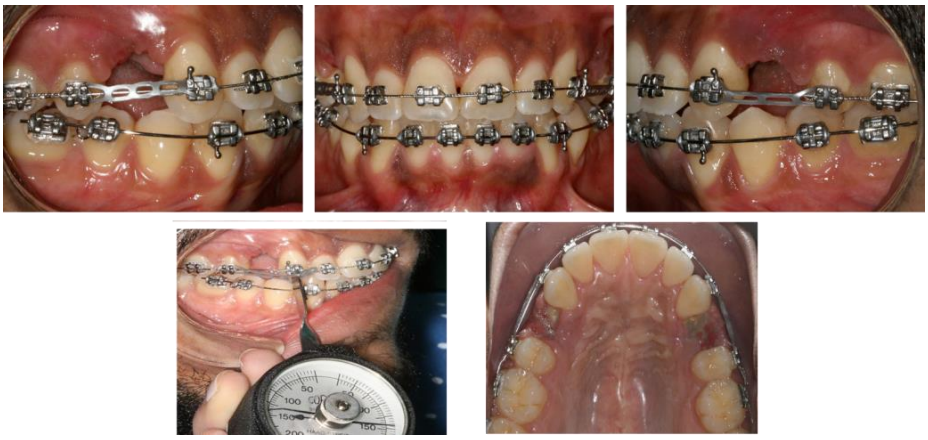


Fig 3. Utilização do tensiômetro e início da retração dos caninos superiores 15 dias após realizada a exodontia.

Resultados e alterações após o início do estudo

O objetivo principal deste estudo foi avaliar a taxa de distalização e inclinação de caninos superiores em alvéolos preservados com membranas de L-PRF quando comparados com os lados controle. O período de distalização foi de cinco meses, desde o início da fase de retração (T1) até o quinto mês (T2). Todos os meses a taxa de distalização foi medida utilizando uma régua flexível, da linha mediana dentária, entre os incisivos centrais superiores, até a mesial dos caninos. A régua era colocada por baixo dos bráquetes. As medições foram repetidas quatro vezes na mesma consulta, e a média foi registrada na planilha de dados. Posteriormente a quantidade da distância mensurada foi dividida pela quantidade de dias (28), correspondente às quatro semanas.

A inclinação dos caninos foi avaliada utilizando as imagens de tomografias de feixe cônico (CBCT) inicial (T1-pré-distalização) e final (T2-completados os cinco meses). Para medição da inclinação dos caninos, utilizou-se o corte sagital. Foi aferido o ângulo formado pelo plano do maior eixo do canino e o plano horizontal traçado desde o ápice do mesmo canino até o ponto mais proeminente e visível da espinha nasal posterior (Fig 4) utilizando o software Planmeca Romexis® Viewer (Helsinki, Finlândia).

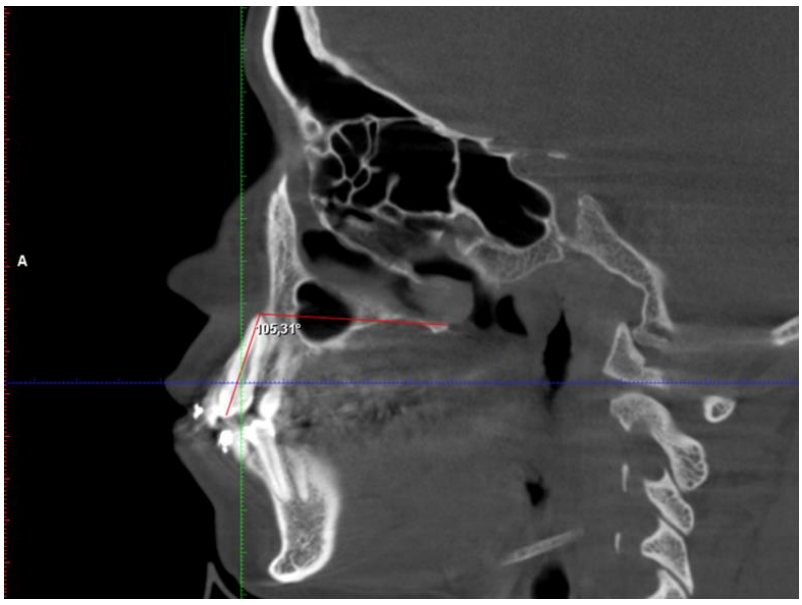


Fig 4. Avaliação da inclinação dos caninos.

Análise estatística

Para ambas as hemi-arcadas, a taxa de movimentação por mês foi avaliada em milímetros. Para avaliar a distribuição normal da amostra foi realizado o teste de Shapiro- Wilk, que mostrou uma distribuição não normal do lado controle (0,020). O lado experimental apresentou distribuição normal (0,18). O teste de Wilcoxon (signed rank test) foi utilizado para comparar as diferenças entre os lados. O nível de significância foi definido em 5% ($p < 0.05$). Foi utilizado o software IBM® SPSS® Statistics (Release 21.0.0, SPSS Inc., Chicago, Illinois, USA).

Para comparar as alterações das inclinações dos caninos, os valores foram medidos em graus (°), e as medições foram repetidas três semanas depois pelo mesmo operador (A.A.R.P), o coeficiente de correlação de Pearson foi realizado.

Posteriormente o Teste de Shapiro-Wilk foi realizado para avaliar a normalidade da amostra. A média e o desvio padrão foram calculados de forma descritiva. O teste de WILCOXON foi utilizado para comparar as diferenças entre os lados. O nível de significância foi definido em 5% ($p < 0.05$).

Para avaliar se houve correlação entre a a taxa de movimentação por mês e as alterações das inclinações dos caninos foi calculado o coeficiente de correlação de Spearman. O nível de significância foi definido em 5% ($p < 0.05$).

RESULTADOS

A média do espaço inicial foi de 7,6 mm para ambas as hemi-arcadas. Ao realizar o teste de Shapiro Wilk, o lado controle apresentou distribuição não normal. Para o lado controle, a média de distalização foi de 0,90 mm/mês, com o valor mínimo de 0,44 mm/mês e o máximo de 1,16 mm/mês.

No lado experimental a média de distalização foi de 0,67 mm/mês. O valor mínimo foi 0,40 mm/mês e o máximo de 0,88 mm/mês. O comportamento clínico está exemplificado na Figura 5.

A diferença entre ambos os lados foi de 0,24 mm/mês. O teste de Wilcoxon apresentou diferença estatisticamente significante ($p=0,004$) ($p<0,05$) entre os grupos, rejeitando a hipótese nula. A Tabela 1 apresenta a média da taxa de movimentação de cada paciente por mês para cada lado. A Tabela 2 apresenta a média da taxa de movimentação dos grupos, e Figura 5 apresenta graficamente as diferenças entre o lado controle e o experimental.

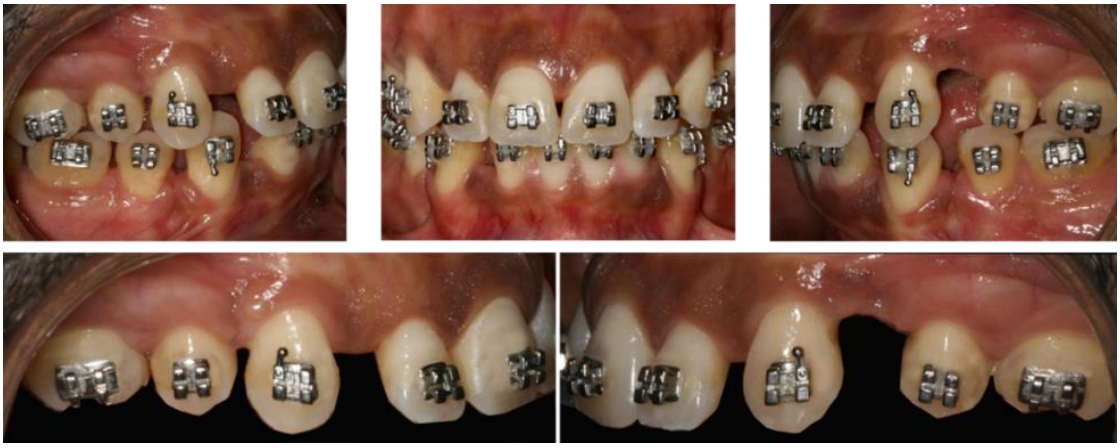


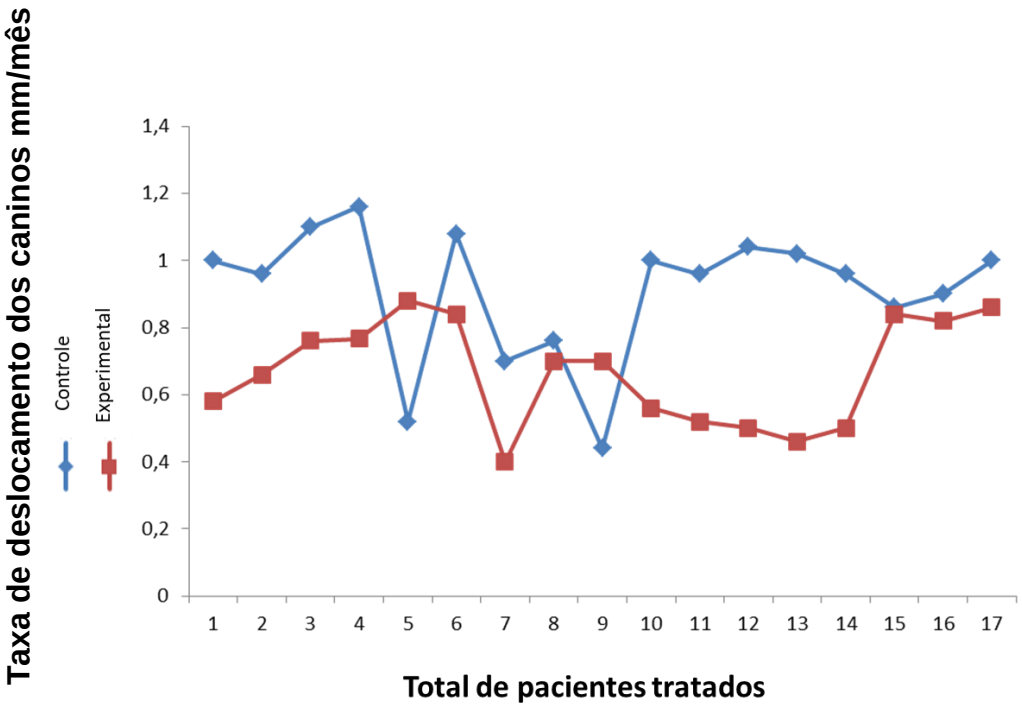
Fig 5. Fotografias intrabucais de paciente do estudo, exemplificando a maior taxa de movimentação dos caninos no lado controle (direito).

Tabela 1. Taxa de distalização por mês de cada um dos pacientes em 5 meses.

	Lado Experimental		Lado Controle	
Paciente	**Movimento Distal mm/mês**	**Amplitude, mm**	**Movimento Distal mm/mês**	**Amplitude, mm**
1	0,58	0,2	1	0,4
2	0,66	0,6	0,96	0,5
3	0,76	0,3	1,1	0,5
4	0,77	0,5	1,16	0,5
5	0,88	0,4	0,52	0,3
6	0,84	0,5	1,08	0,3
7	0,4	0,5	0,7	1,5
8	0,70	0,3	0,76	0,5
9	0,7	0,5	0,44	0,7
10	0,56	1	1	0,4
11	0,52	0,2	0,96	0,5
12	0,5	0,2	1,04	0,3
13	0,46	0,7	1,02	0,7
14	0,5	0,2	0,96	0,3
15	0,84	0,3	0,86	0,4
16	0,82	0,3	0,9	0,3
17	0,86	0,6	1	0,4

Tabela 2. Taxa de distalização do grupo controle e experimental.

	N	**Mín.**	**Máx.**	**Média**	**Wilcoxon Signed Ranked Test (valor p)**
Controle	**17**	**.44**	**1.16**	**.9094**	**.004**
Experimental	**17**	**.40**	**.88**	**.6675**	



A medição da inclinação dos caninos apresentou boa correlação intraclasse no T1 e T2, o valor do coeficiente de correlação de Pearson foi de 0,9 para ambos os lados (Tabela 3). Ao realizar o teste de Shapiro Wilk o lado com L-PRF apresentou distribuição não normal (p=0,024). No lado experimental a média de inclinação foi de 5,8°.

Tabela 3. Coeficiente de correlação intraclasse.

Medição (graus°)	T1	T2
Inclinação de caninos lado direito	0.92	0.98
Inclinação de caninos lado esquerdo	0.94	0.97

O lado controle apresentou distribuição normal (p=0.35), média de 8,5°, o valor mínimo foi 4,5° e o máximo de 15,19 °. A diferença entre ambos os lados foi de 2,7°. O teste de Wilcoxon apresentou diferença estatisticamente significante (p=0,001) entre os lados, o lado experimental apresentou menores valores (Tabela 4).

O coeficiente de correlação de Spearman para o lado controle foi de ρ= ,17 com um valor de p= ,51; e para o lado experimental o coeficiente de correlação de Spearman foi de ρ= ,11 com um valor de p= ,67 . O que representa uma correlação muito baixa entre a taxa de movimentação (mm) e a inclinação dos caninos (°) para ambos os lados.

Tabela 4. Inclinação de caninos lados controle e experimental.

	N	Min.	Max.	Média +DP	Wilcoxon Signed Rank Test (valor p)
Controle	**17**	**4.15°**	**15.19°**	**8.57° (3.07)**	**.001**
Experimental	**17**	**1.69°**	**14.53°**	**5.81° (3.09)**	

DISCUSSÃO

Na Ortodontia, estudos utilizando derivados sanguíneos são escassos. [19,24,25]. Tehranchi *et al.*[19] realizaram o primeiro estudo clínico randomizado do tipo *split mouth* utilizando o L-PRF, avaliando a taxa de movimentação de caninos superiores e inferiores, e concluíram que o uso do L-PRF poderia acelerar a movimentação dentária. A amostra consistiu de 8 pacientes, entre os 12 e 25 anos, o que pode ter afetado o resultado. Os alvéolos que receberam as membranas de L-PRF foram tanto superiores como inferiores, o que também pode ser um viés.

O presente estudo clínico randomizado foi o primeiro que avaliou a taxa de distalização em alvéolos preservados com L-PRF com uma amostrada definida e bem distribuída de pacientes adultos com uma quantidade adequada de pacientes. Esta pesquisa teve a cautela, de ter como critério de inclusão, que os pacientes fossem em sua totalidade adultos jovens, e não adolescentes e adultos jovens, evitando a variabilidade individual dos adolescentes, os quais apresentam

uma melhor resposta no ligamento periodontal às cargas ortodônticas aplicadas.[10] Neste estudo, foram avaliados e enxertados apenas os alvéolos superiores, para evitar qualquer viés referente ao local que recebeu a preservação alveolar e a densidade óssea. A amostra do presente estudo teve o dobro de pacientes, e os alvéolos superiores preservados com L-PRF também superaram a quantidade descrita por Tehranchi et al.[20]

Não existe um consenso sobre o uso dos derivados sanguíneos com finalidade de acelerar a movimentação dentária, os resultados são controversos. Existem poucos estudos em animais e um realizado em pacientes humanos.

Duas pesquisas realizadas em ratos utilizando plasma rico em plaquetas (PRP) apresentaram conclusões diferentes. Güleç et al. realizaram estudo do tipo *split mouth*, e avaliaram a mesialização de molares realizando injeções de concentrações alta e moderada de plasma. Os ratos foram sacrificados em cinco tempos diferentes (3, 7, 14, 21 e 60 dias), e mostraram o aumento na taxa de movimentação dentária quando o plasma era injetado no local de interesse, o que poderia diminuir o tempo de tratamento. [24]

O segundo estudo em ratos foi realizado por Akbulut et al., avaliaram a taxa de movimentação em cinco tempos (0,1,3,7 e 14 dias). Realizaram injeções de PRP no local de interesse, e o lado que recebeu o plasma apresentou menor taxa de movimentação do que o lado controle, concluindo que não é recomendando o uso deste biomaterial junto ao tratamento ortodôntico. [25]

Este estudo utilizou o L-PRF com maior concentração de leucócitos. Da mesma forma que o PRP, o L-PRF possui fatores de crescimento que são liberados lentamente quando colocados no lugar de interesse, entre eles: TGF-b, PDGF, EGF, IGF, PDEGF e VEGF. A presença deles pode ter alterado a regulação entre osteoblastos e osteoclastos, diminuindo o *turnover* e induzindo à neoformação óssea. [14-16]

O TGF-b presente no PRF e PRP, estimula a proliferação de osteoblastos, OPG e a síntese de colágeno, favorecendo a neoformação óssea. [26,27] O TGF-b diminui a ação dos osteoclastos, diminuindo a quantidade de reabsorção

óssea,[26,28] a qual é necessária para que ocorra a movimentação ortodôntica. Este fator pode ser uma das causas da diminuição da taxa de movimentação no lado em que a preservação alveolar com membranas de L-PRF foi realizada. Dos dezessete pacientes, somente dois pacientes apresentaram maior taxa de movimentação no lado experimental.

A média da taxa de movimentação do grupo controle foi de 0.9 mm/mês. O estudo do Burrow reportou uma média maior da taxa de movimentação (1,17mm por mês) dos caninos que foram distalizados utilizando bráquetes convencionais, porém, tratou pacientes adolescentes (média de 14,8 anos).[8] Pelo fato dos pacientes desta amostra serem exclusivamente adultos jovens, os resultados da taxa de movimentação do lado controle deste estudo apresentou valores menores do que o reportado por Burrow. Nossos valores encontram-se mais próximos dos valores reportados por Monini *et al*[9] (0.72 mm/mês) e Mezzomo *et al.* (0.84 mm/mês) para os lados tratados com bráquetes convencionais.

A força utilizada de 150 gramas foi efetiva para realizar a distalização dos caninos por deslizamento em ambos os grupos, e foi utilizada em outras pesquisas com a mesma resposta.[8,23,29] Outros estudos sobre a distalização de caninos utilizaram mecânicas sem fricção com uso de alças ou braços de distalização associando mecânicas segmentadas,[30,31] o que provocou taxas maiores de movimentação pela ausência de fricção.

Ao avaliar a inclinação distal dos caninos, os valores dos ângulos diminuíram em ambos os lados, experimental e controle. O lado controle apresentou valores de diminuição maiores do que o lado experimental, o que representa maior verticalização dos caninos. Esse resultado poderia afetar o resultado desta pesquisa, favorecendo ao lado controle, aumentando a taxa de distalização desse lado, mesmo que o coeficiente de correlação de Spearman tenha mostrado valores de correlação muito baixas entre a taxa de movimentação e a inclinação dosl caninos para ambos os grupos.A hipótese nula de não diferença entre os grupos foi rejeitada ($p<0,05$), mostrando que o lado controle

apresentou maior taxa de movimentação quando comparado com o lado experimental que recebeu a preservação alveolar com o L-PRF.

Do ponto de vista clínico, o uso do L-PRF no tratamento ortodôntico deve ser evitado. A diminuição da taxa de distalização e de inclinação dos caninos no lado experimental acabou aumentando o tempo de movimentação. Recomenda-se que sejam realizados estudos futuros que avaliem as diferenças entre as respostas inflamatórias entre o lado controle e o lado que recebeu a preservação alveolar com membranas de L-PRF, e com amostras maiores.

CONCLUSÕES

No presente estudo a hipótese nula foi rejeitada. A preservação alveolar com membranas de L-PRF diminuiu a taxa de distalização e inclinações dos caninos superiores quando comparado com o grupo controle em pacientes adultos jovens.

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ARTIGO #1 EM INGLÊS

TITLE PAGE

DISTALIZATION RATE OF MAXILLARY CANINES IN ALVEOLUS FILLED WITH LEUCOCYTE AND PLATELET-RICH FIBRIN (L-PRF): RANDOMIZED CLINICAL STUDY

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PACHECO, Ariel Adriano Reyes. DISTALIZATION RATE OF MAXILLARY CANINES IN ALVEOLUS FILLED WITH LEUCOCYTE AND PLATELET-RICH FIBRIN (L-PRF): RANDOMIZED CLINICAL STUDY. Advisor: Dr. Orlando Tanaka. Curitiba: PUCPR, PPGO, 2019. (Doutorado em Odontologia– Ortodontia). 39p.

ABSTRACT

INTRODUCTION: The objective of this study was to evaluate the distalization rate and the changes in the inclinations of the upper canines in preserved alveolus with fibrin and leukocyte-rich plasma membranes (L-PRF).**METHODS:** Seventeen young adult patients (mean 33 ± 5.9 years), in good health, with Angle Class I and II-1 malocclusion, who had indication of the first premolar extraction, and distalization of the upper canines to the orthodontic treatment were included in the study. A randomized *split-mouth* clinical study was conducted in which the experimental side was preserved L-PRF and the other side was the control. The distalization was performed with elastic chain, applying 150 g / force to the canines, and a 0,020 "stainless steel bow was used. The distalization rate was assessed monthly for five months using a flexible ruler. The degree of inclination of the canines was evaluated by the use of cone beam tomography. Shapiro Wilk test was performed, and later the Wilcoxon Signed Rank Test to compare the groups. **RESULTS:** The distalization rate and inclination of canines was higher on the control side when compared to the side preserved with L-PRF ($p < 0.05$). **CONCLUSIONS:** In the present study, the null hypothesis was rejected. The use of L-PRF decreased the rate of distalization and changes in the inclinations of the upper canines when compared to the control group in young adult patients.

Key words: Maxillary Canines, Orthodontic tooth movement, fibrin and leukocyte-rich plasma.

Registration: This trial was not registered.

Protocol: The protocol was not published before trial commencement.

Funding: No funding or conflict of interest to be declared.

INTRODUCTION

Adult patients seek orthodontic treatment mostly for aesthetic reasons, being the correction of the inclination of the upper incisors the main.[1] Correction of proclined incisors is often performed through first maxillary premolars extraction for orthodontic purposes.[2,3,32]

Several factors increase treatment time in adult patients, among them is the extraction of first premolars [4-7] since, the distalization of canines can take between 10 months and one year.[8,9] Because of a higher bone density, decreased bone turnover and a periodontal ligament with fewer cells than younger patients, they present more areas of periodontal ligament hyalinization and greater root resorption during orthodontic treatment,[10,11] requiring more time to overcome the stages of tooth movement. [10,12]

After extraction, the alveolus begins the process of bone resorption, being greater during the first year. The alveolar ridge initially decreases in width and subsequently in height. To avoid this alveolar collapse, the use of biomaterials such as bone grafts (autogenous, xenogene or alloplastic) or platelet-rich plasma, fibrin-rich plasma and derivatives, has been increasing for the preservation of the dimensions of the alveolar bone after the exodontia.[13]

Plasma rich in fibrin and leukocytes (L-PRF) corresponds to the second generation of biomaterials based on blood plasma. L-PRF is composed of blood without addition of any other component, the greatest advantage being the facility to create the plasma membrane by centrifugation and the low cost.[14-16]

L-PRF brings with it cells such as proteases and antiproteases that promote angiogenesis and vascular remodeling, cytokines and chemokines involved in the regulation of angiogenesis and bone formation. It also contains growth factors that promote cell proliferation, angiogenesis and chemotaxis, facilitating bone repair, wound healing and angiogenesis.[14-18] These properties could be beneficial for orthodontic treatment, a greater amount of blood vessels in the area of interest and a shorter repair time could shorten treatment time and increase the rate of tooth

movement in adults. This is one of the first clinical studies to perform such interrelationship. [19]

Therefore, the objective of this study was to evaluate the distalization rate and changes in upper canine inclinations in alveoli preserved with fibrin and leukocyte-rich plasma membranes (L-PRF). The null hypothesis was that there are no differences in the canine movement rate between the preserved side, and the control, without preservation, only with the maintenance of the clot.

MATERIAL AND METHODS

The present study was conducted at the Pontificia Universidad Católica Madre & Maestra-Recinto Santo Tomás de Aquino (PUCMM-STA) with the approval of the bioethics committee (ID: COBE-FACS-M.EST-CSTA-004-2-2015-2016) (Annex 1), between the months of September 2016 and December 2018.

Trial design and any changes after trial commencement

A randomized split-mouth clinical study was conducted in which the experimental side received the alveolar preservation with fibrin-rich plasma and leukocytes (L-PRF) membranes and the other was the control. The criteria used to report the results of randomized clinical trials from CONSORT. [20 21]

Participants, eligibility criteria, and settings

Inclusion criteria were: 1) adult patients, with a minimum age of 20 years who needed orthodontic treatment, 2) indication of extraction of the first maxillary premolars for treatment. All patients signed informed consent prior to initiation of treatment (Annex 2).

Exclusion criteria were: 1) patients with autoimmune, 2) pregnant or lactating diseases, 3) use of long-term medications in the six months prior to initiation of the study (antibiotics, antihistamines, cortisone, hormones) that could interfere with the inflammatory response process or with an adverse effect directly on the periodontal ligament, 4) In the presence of systemic diseases, these should be controlled, not contraindicating the surgical procedure of the exodontia.

The sample consisted of 21 healthy young adult patients throughout the study, four of them gave up, remaining seventeen patients in total (n = 17), being twelve (12) females and five (5) males. The ages ranged from 20 to 45 years (mean 33 years), all diagnosed with Class I (n = 14) or Angle II-1 malocclusion (n = 3). All in need of orthodontic treatment with extractions of first maxillary premolars. The description of patient selection and allocation of leukocyte-rich plasma membranes is described in Figure 1 following the criteria of the CONSORT statement (Consolidated Standards of Reporting Trials).[20,21]

Randomization

Randomization of the sides was performed using the random number generation function of Microsoft Excel (Microsoft Office 2016, Microsoft, Redmond, Washington, USA). The grafted side was selected following the order of the sequence created in the worksheet.

Blinding

There was no blinding of the operators, or the patients.

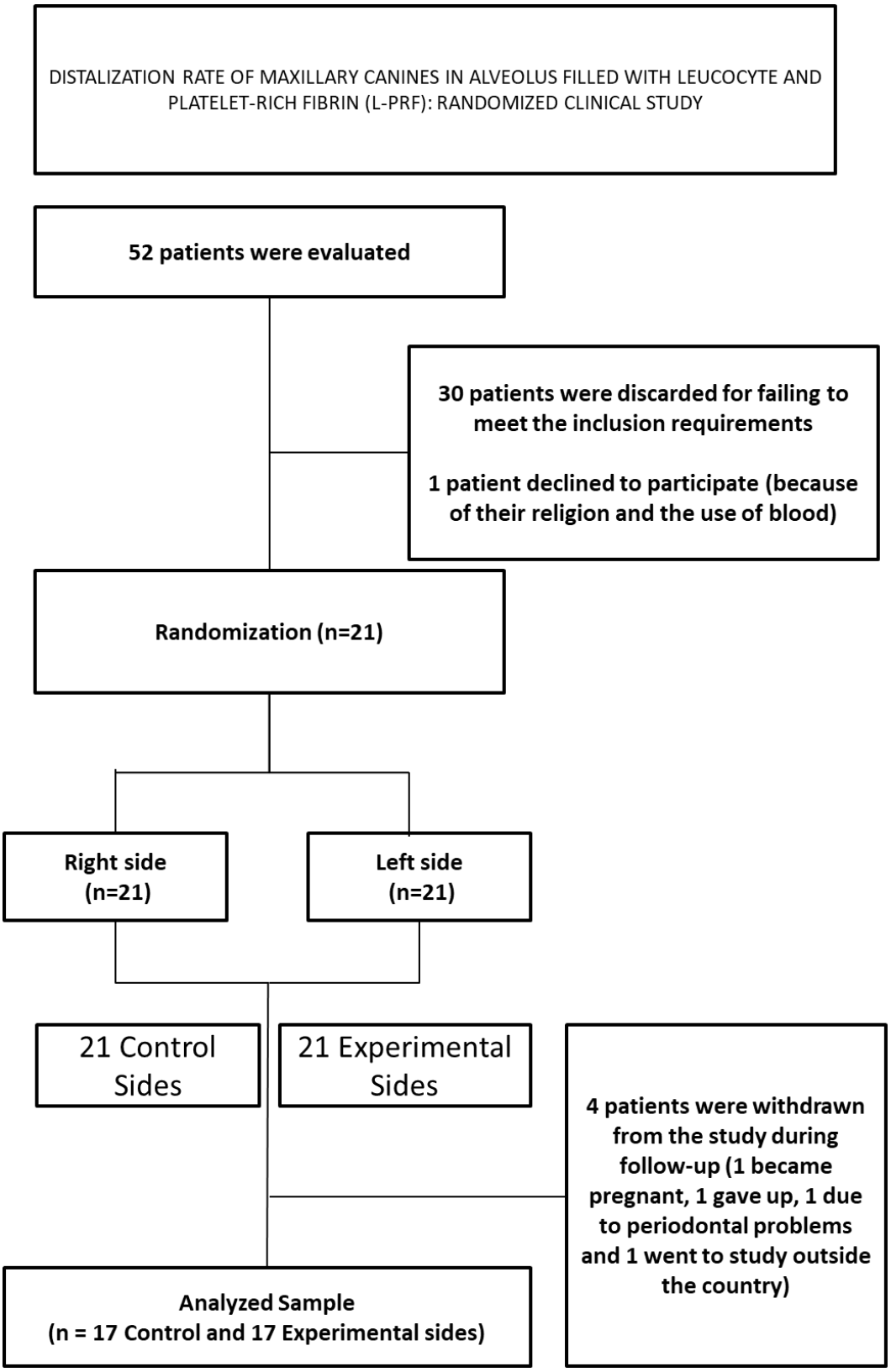


Fig 1. CONSORT diagram of patient selection and L-PRF allocation.

Interventions

All patients were treated with pre-adjusted MBT brackets slot 0.022 "(ABZIL Kirium, 3M, Brazil). The alignment and leveling phase was performed with 0.014", 0.016" NiTi arches and 0.018 "and 0.020" stainless steel. On the day of installation of the 0.020 "stainless steel arch in the maxillary arch (Fig 2), the filling of the form was performed, requesting the first maxillary premolars (14-24) to be removed to the Department of Periodontics, and the first CT (CBCT) (T1) was requested. The CBCT was performed with a Plan Meca ProMax 3D Max, with FOV (Field Of View) of Ø23 x 26 cm, exposure time of 18-30 seconds, voxel 0.200, reconstruction time of 30-150 seconds and radiation of 101-252 mSv.

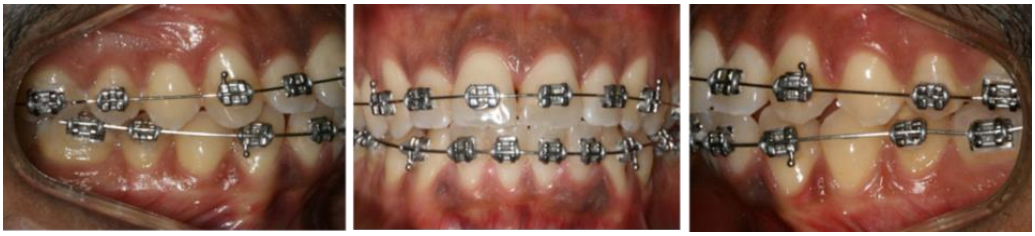


Fig 2. Intra-buccal images of the alignment and leveling phase.

On the day of the surgical procedure, the blood collection was performed prior to the extraction. The BD Vacuteiner Safety-Lok ™ blood collection set (New Jersey, USA) vacuum scalp collected directly from the test tube was used. No disposable syringes were used because they may coagulate blood or decrease the quality of the fibrin-rich plasma obtained when transferring the syringe into the tube. [14,15,17,18]

Fibrin-rich plasma and leukocytes (L-PRF) were obtained according to the IntraSpin centrifuge protocol (Boca Raton, FL, USA), centrifuging the blood for 14 minutes at 2,700 RPM (Fig. 4). Subsequently the clot formed was extracted from the test tube and pressed between two glass plates covered with saline impregnated compresses for 30 seconds to remove the excess and to obtain uniformity. The experimental alveolus was preserved with L-PRF membranes. The alveoli were sutured with 4-0 Nylon (Mononylon- Ethicon Johnson & Johnson) to approximate the edges to promote healing. This sequence was performed to

decrease the exposure time of the wells, and to place the plasma as soon as possible.

The premolar luxation was performed during the surgical procedure with the use of Piezotome (Satelec Acteon, France) for the preservation of alveolar bridge, and to perform the extraction in a less traumatic manner and to reduce postoperative complications[22] .

Fifteen days after the extractions were performed; the initial space was recorded and the distalization of the canines began. A 0.008 " ligature wire was placed from the first molar to the second premolar as an anchor unit. In the distal wing of the canine brackets, another 0.008 " ligature wire was placed to prevent rotation. The distalization of the canines was performed on the 0.020 "stainless steel arch. Elastic chains (Memory Orthodontics, American Orthodontics, Sheboygan, WI, USA) were used to apply 150 g / f (Fig 3) according to Burrow[8] and Mezomo *et al*.[23] Elastics chains were placed from the second pre- molar to the canine. The amount of force was measured with the CORREX tensiometer (50-250 grams) (Haag Streit, Bern, Switzerland). Activations were performed once a month, every four weeks, for five months.

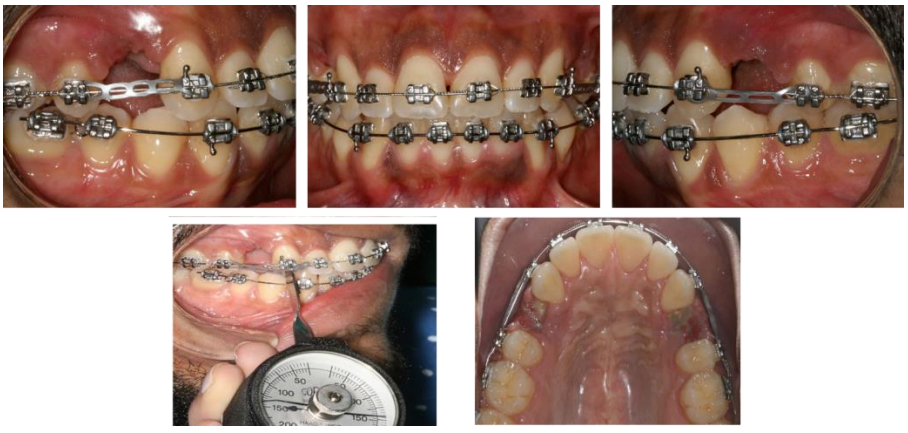


Fig 3. Use of tensiometer and beginning of retraction of maxillary canines 15 days after extractions.

Results and changes after study start

The main objective of this study was to evaluate the rate of distalization and inclination of upper canines in preserved alveolus with L-PRF membranes when compared to the control side. The distalization period was five months, from the beginning of the retraction phase (T1) to the fifth month (T2). Every month the distalization rate was measured using a flexible ruler, placed in dental midline from the maxillary central incisors to mesial of the canines. The ruler was placed under the brackets. The measurements were repeated four times in the same appointment, and the mean was recorded in the data sheet. Subsequently the amount of distance measured was divided by the number of days (28), corresponding to the four weeks.

The canine inclination was evaluated using the initial (T1-pre-distalization) and final (T2-completed five-month) cone-beam CT scans. To measure the inclination of the canines, the sagittal slice in which the angle formed by the plane of the longer axis of the canine and the horizontal plane drawn from the same canine apex to the most prominent and visible end of the posterior nasal spine, was used (Fig 4). Measurement were performed using the Planmeca Romexis® Viewer software (Helsinki,Finland).

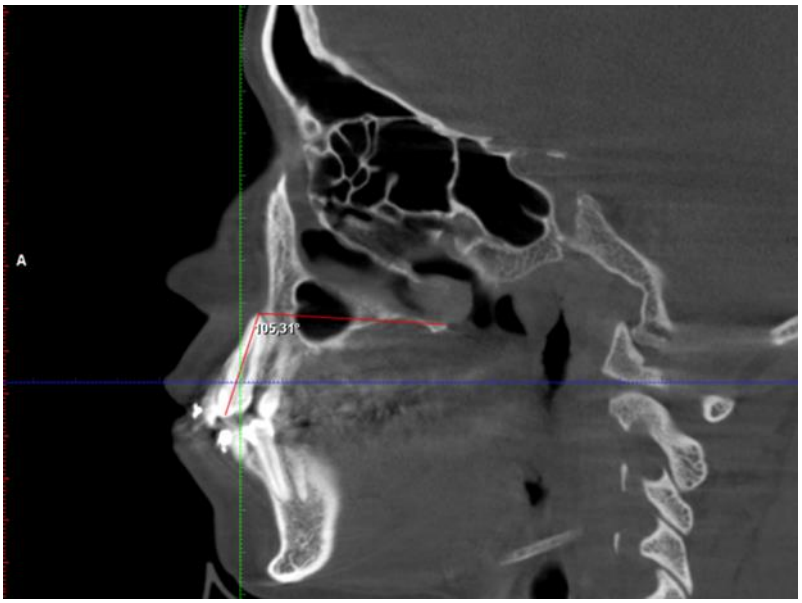


Fig 4. Assessment of canine inclination.

Statistical analysis

Descriptive statistics of patients showing the gender and type of malocclusion was performed. For both hemi-arches, the movement rate per month was evaluated in millimeters. To evaluate the normal distribution of the sample, the Shapiro-Wilk test was performed, which showed a non-normal control-side distribution (0.020). The experimental side presented a normal distribution (0.18). The Wilcoxon test (signed rank test) was used to compare the differences between the sides. The level of significance was set at 5% ($p < 0.05$). IBM® SPSS® Statistics software (Release 21.0.0, SPSS Inc., Chicago, Illinois, USA) was used.

To compare changes in canine inclination, values were measured in degrees (°), and measurements were repeated three weeks later by the same operator (A.A.R.P), Pearson's correlation coefficient was performed.

Subsequently the Shapiro-Wilk Test was performed to evaluate the normality of the sample. The mean and standard deviation were calculated descriptively. The WILCOXON test was used to compare the differences between the sides. The level of significance was set at 5% ($p < 0.05$).

To evaluate if there was a correlation between the movement rate per month and the changes in canine inclinations, the Spearman correlation coefficient was calculated. The level of significance was set at 5% ($p < 0.05$).

RESULTS

The mean initial space was 7.6 mm for both hemi-arches. When performing the Shapiro Wilk test, the control side presented a non-normal distribution. For the control side, the mean distalization was 0.90 mm / month, with a minimum value of 0.44 mm / month and a maximum of 1.16 mm / month.

On the experimental side the mean distalization was 0.67 mm / month. The minimum value was 0.40 mm / month and the maximum was 0.88 mm / month. Clinical behavior is exemplified in Figure 7.

The difference between both sides was 0.24 mm / month. The Wilcoxon test presented a statistically significant difference ($p = 0.004$) ($p < 0.05$) between the groups, rejecting the null hypothesis. Table 1 presents the mean of the movement rate of each patient per month for each side. Table 2 presents the mean of the movement rate of the groups, and Figure 5 graphically shows the differences between the control and the experimental side.

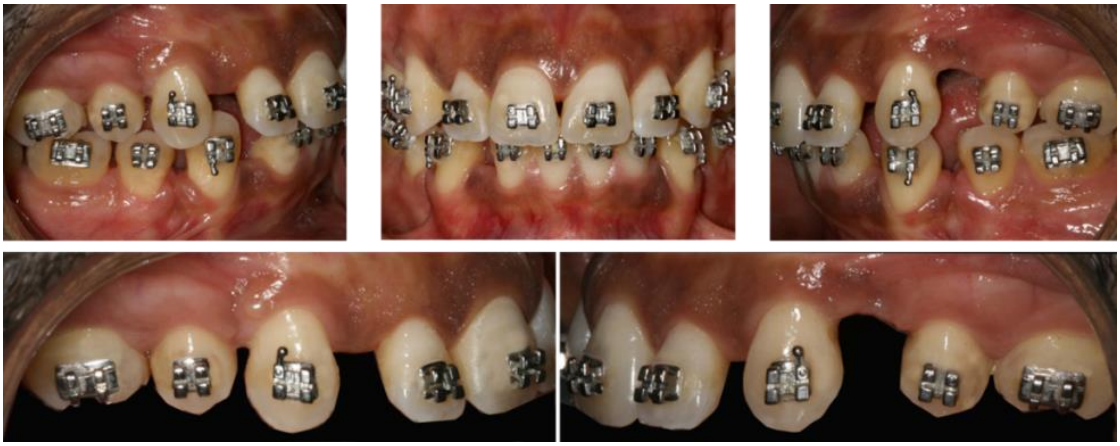


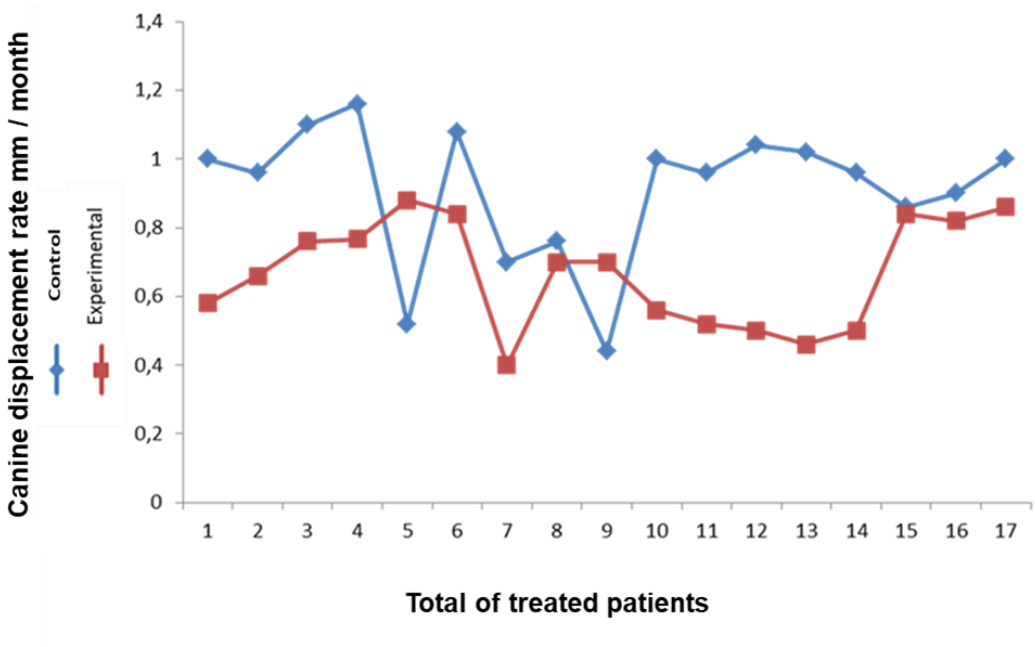
Fig. 5. Intraoral photographs of a patient, exemplifying the higher rate of movement of the canines on the control side (right).

Table 1. Distalization rate per month of each patient in 5 months.

	Experimental side		Control side	
Patient	**Distal movement mm./mo**	**Range, mm.**	**Distal movement mm./mo**	**Range, mm.**
1	0,58	0,2	1	0,4
2	0,66	0,6	0,96	0,5
3	0,76	0,3	1,1	0,5
4	0,77	0,5	1,16	0,5
5	0,88	0,4	0,52	0,3
6	0,84	0,5	1,08	0,3
7	0,4	0,5	0,7	1,5
8	0,84	0,3	0,76	0,5
9	0,7	0,5	0,44	0,7
10	0,56	1	0,94	0,4
11	0,52	0,2	0,96	0,5
12	0,5	0,2	1,04	0,3
13	0,46	0,7	1,02	0,7
14	0,5	0,2	0,96	0,3
15	0,84	0,3	0,86	0,4
16	0,82	0,3	0,9	0,3
17	0,86	0,6	1	0,4

Table 2. Rate of distalization of control and experimental group.

	N	**Min.**	**Max.**	**Mean**	**Wilcoxon Signed Ranked Test (p value)**
Control	**17**	**.44**	**1.16**	**.9094**	**.004**
Experimental	**17**	**.40**	**.88**	**.6675**	



Measurement of canine inclination showed good intraclass correlation in T1 and T2, Pearson's correlation coefficient value was 0.9 for both sides (table 3). When performing the Shapiro Wilk test, the L-PRF side showed a non-normal distribution (p = 0.024). On the experimental side the mean inclination was 5.8°.

Table 3. Intraclass correlation coefficient.

Measurement (degrees°)	T1	T2
Right side canines inclination	0.92	0.98
Left side canines inclination	0.94	0.97

The control side presented a normal distribution (p = 0.35), mean of 8.5 °, the minimum value was 4.5 ° and the maximum of 15.19 °. The difference between the two sides was 2.7 °. The Wilcoxon test presented a statistically significant difference (p = 0.001) between the sides, the experimental side presented lower values (table 4).

The Spearman correlation coefficient for the control side was ρ =, 17 with a value of p =, 51; and for the experimental side the Spearman correlation coefficient was ρ =, 11 with a value of p = 67. This represents a very low correlation between the movement rate (mm) and the inclination of the canines (°) for both sides.

Table 4. Inclination of canines control and experimental sides.

	N	Min.	Max.	Mean +DP	Wilcoxon Signed Rank Test (p value)
Control	**17**	**4.15°**	**15.19°**	**8.57° (3.07)**	**.001**
Experimental	**17**	**1.69°**	**14.53°**	**5.81° (3.09)**	

DISCUSSION

Researches looking for therapeutic options to reduce the time of orthodontic treatment have been performed (self-ligating brackets [8,9,23], corticotomies[33,34], osteoperforations[35]). In Orthodontics, studies using blood derivatives are scarce.[19,24,25] To our knowledge, this study is one of the first clinical studies evaluating the rate of distalization with the use of L-PRF during tooth movement.

The results of the use of blood derivatives to accelerate dental movement are controversial. Two studies in rats using platelet rich plasma (PRP) presented different conclusions. Güleç et al. performed a split mouth study, and evaluated molar mesialization by injecting high and moderate plasma concentrations. Rats were sacrificed at five different times (3, 7, 14, 21 and 60 days). They showed an increase in the rate of tooth movement when the plasma was injected at the site of interest at all times, except the last one. [24]

A second study in rats was performed by Akbulut et al., The times evaluated were lower (0,1,3,7 and 14 days). Injections were also performed at the site of interest, but the difference was that the side receiving the plasma moved less than

the control side, not recommending the use of this biomaterial next to the orthodontic treatment. [25]

In the present study, L-PRF was used, which has the highest concentration of leukocytes. Like PRP, L-PRF has growth factors that are released slowly when placed in the place of interest, among them: TGF-b, PDGF, EGF, IGF, PDEGF and VEGF. Their presence may have altered the regulation between osteoblasts and osteoclasts, decreasing turnover and inducing bone neo-formation. [14-16]

TGF-b is present in PRF and PR, it stimulates the proliferation of osteoblasts, OPG and collagen synthesis, favoring bone neo-formation. [26,27] TGF-b decreases the action of osteoclasts, decreasing the amount of bone resorption[26,28] which is necessary for orthodontic movement to occur. This factor may be one of the causes of the decrease in the rate of movement on the side where alveolar preservation with L-PRF membranes was performed. Of the seventeen patients, only two patients had a higher movement rate on the experimental side.

Tehranchi *et al.*[19] performed a randomized split-mouth clinical study using L-PRF, evaluating the rate of movement of upper and lower canines, and concluded that the use of L-PRF could accelerate tooth movement, but the sample consisted of 8 patients between the ages of 12 and 25, which may have affected the outcome. The alveolus that received the L-PRF membranes were both superior and inferior, which may also be a bias. The present study was cautioned to have as inclusion criterion that the patients were all young adults, not adolescents and young adults, avoiding the individual variability of the adolescents, who present a better response in the periodontal ligament to the orthodontic loads applied. [10] In this study, only the superior alveoli were evaluated and grafted, to avoid any bias regarding the site that received alveolar preservation and bone density. The sample of the present study had twice as many patients, and the upper alveoli preserved with L-PRF also surpassed the amount described by Tehranchi *et al.*

In this study, mean movement rate of the control group was 0.9 mm / month. Other studies of canine distalization reported a higher average movement rate, however, treated adult and adolescent patients in the same group. [8,23,36] Because

the sample of the present study consists exclusively of young adult patients, the results of the control side of this study showed lower values than those reported in these studies. Our values are closer to the values reported by Monini *et al*[9] who treated adult patients in their study.

The force of 150 grams was effective to perform the distalization of canines by sliding in both groups, and was used in other researches with the same response[8,23,29]. Other studies on canine distalization used frictionless mechanics with the use of segmented mechanics or power arms [30,31] which caused higher rates of movement due to the absence of friction.

When evaluating the distal inclination of the canines, the values of the angles decreased on both sides, experimental and control. The control side had higher values of decrease than the experimental side, which represents a greater verticalization of the canines. This result could affect the results of this research, favoring the control side, increasing the distalization rate on this side, even though the Spearman correlation coefficient showed very low correlation values between the movement rate and the canine inclination for both groups. The null hypothesis of non-difference between groups was rejected ($p < 0.05$), showing that the control side presented a higher movement rate when compared to the experimental side that received alveolar preservation with L-PRF.

From a clinical point of view, the use of L-PRF together with orthodontic treatment should be avoided. The decrease in the distal and canine inclination rate on the experimental side eventually increased the treatment time, which may be uncomfortable for the adult patients. It is recommended that future studies assess the differences between the inflammatory responses between the control side and the L-PRF grafted side and larger samples.

CONCLUSIONS

In the present study, the null hypothesis was rejected. The use of L-PRF decreased the rate of distalization and changes in the inclinations of the upper canines when compared to the control group in young adult patients.

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ANEXOS

Anexo 1: Aprovação do comité de bioética

Pontificia Universidad Católica Madre y Maestra

COBE-FACS-M.EST-CSTA-004-2-2015-2016 septiembre 20, 2016

Dr. James Collins
Asesor Oficial

Distinguido doctor Collins:

El Comité de Bioética de la Facultad de Ciencias de la Salud (COBE-FACS) en Sesión Ordinaria ha revisado y efectuado una Valoración ética de la propuesta de investigación con el titulo "Retracción de caninos superiores en alvéolos injertados con plasma rico en fibrina (PRF) post-extracción de primeros premolares durante el tratamiento Ortodóntico en adultos-estudio clínico tipo Split Mouth." Y con ID(COBE-FACS-M.EST-CSTA-004-2-2015-2016; Resuelve que dicho Proyecto se ajusta:

- A los principios generales de investigación establecidos por los diferentes códigos internacionales.
- A las normas y criterios éticos establecidos en los códigos nacionales de ética o leyes vigentes del país.
- A los principios, normas y valores sobre investigación establecidos por la PUCMM.

Y para que conste, los abajo firmantes certifican que la propuesta de investigación que se presentó a través de la Unidad de Investigación al COBE-FACS, ha sido examinada y **APROBADA.**

Por lo que dicha investigación podrá llevarse a efecto a partir de la certificación por parte de este Comité de las peticiones expresadas.

Lic. Diego Lopez Luján
Presidente

Lic. Cristobalina Betemit
En funciones de Secretaria

Copia Estudiante: Sandira Peña.

/br

COMITE DE BIOÉTICA

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Anexo 2: Consentimento Informado

Pontificia Universidad Católica Madre y Maestra (PUCMM)
Facultad de Ciencias de la Salud- Recinto Santo Tomás de Aquino (CSTA)

RETRACCIÓN DE CANINOS SUPERIORES EN ALVÉOLOS INJERTADOS CON PLASMA RICO EN FIBRINA (PRF) POST-EXTRACCIÓN DE PRIMEROS PREMOLARES DURANTE EL TRATAMIENTO ORTODÓNTICO EN ADULTOS- ESTUDIO CLÍNICO TIPO SPLIT MOUTH.

Investigadores Responsables:

Dr. James R. Collins

Dr. Ariel Adriano Reyes

Dr. Orlando Tanaka (Orientador)

El propósito de esta información es ayudarle a tomar la decisión de participar o no en una investigación médica.

1. OBJETIVOS DE LA INVESTIGACIÓN:

Evaluar si el uso del plasma rico en fibrina que es obtenido de la sangre humana disminuye el tiempo de cierre de espacios de los caninos superiores al ser comparados con el lado que no recibirá el plasma en pacientes tratados con extracciones de primeros premolares superiores.

Al mismo tiempo serán comparadas las alturas del hueso alrededor de los caninos, el grado de reabsorción o desgaste en la raíz esos dientes, y su superficie buscando la aparición de pérdida de hueso en pacientes adultos.

El presente estudio contará con la participación de 35 pacientes, con edad de 25 años en adelante, en el cual cada paciente será su propio control. Siendo así un lado el que va a recibir el plasma y el otro lado no para ver si hay diferencias en el tiempo total de cierre del

espacio. Todos los pacientes deben dar su consentimiento y aceptación con fin de poder producir el plasma rico en fibrina que será colocado.

Para poder participar en el presente estudio el paciente deberá cumplir con los siguientes requisitos:

- Criterios de inclusión: Pacientes adultos (20 años en adelante) portadores de maloclusiones de Clase I de Angle con biprotrusión dentoalveolar o Clase II-1 de Angle con indicación de extracción de primeros premolares superiores. Pacientes que presenten enfermedades sistémicas deben estar controlados y con autorización médica que no contraindique las extracciones y\o el tratamiento ortodóntico.

- Criterios de exclusión que no permiten que el paciente sea aceptado en el estudio: Pacientes que presenten enfermedad periodontal, Enfermedades del sistema inmunitário; embarazadas; lactantes dando el seno; pacientes que utilicen medicamentos de uso prolongado en los seis meses antes o al inicio del estudio (antibióticos, anti-histamínicos, cortisona, hormonas), pacientes que tomen medicamentos que puedan interferir con el proceso de respuesta inflamatoria.

2. PROCEDIMIENTOS A REALIZAR DURANTE LA INVESTIGACIÓN:

Todos los pacientes van a ser tratados con ortodoncia fija. Serán realizadas las fases de alineación y nivelación dentaria, siguiendo una secuencia de arcos hasta llegar al acero 0.020``, momento en el cual se procederá a indicar la extracción de los primeros premolares, las cuales serán realizadas por los investigadores.

El día de realizar las extracciones, se procederá a realizar la toma de 10 mililitros de sangre, una hora antes de la cirugía para poder obtener el plasma rico en fibrina, que es la sustancia que será utilizada en este estudio. La sangre colectada pasará por un proceso de centrifugación durante 40 minutos y posteriormente será colocada en los espacios de las extracciones. Los bordes serán unidos con hilo de Nylon 4-0 con el fin de promover la cicatrización de los tejidos. Es importante informar que el plasma rico en fibrina no traerá ninguna complicación al tratamiento ortodóntico ya que se trata de una sustancia creada a partir de su propia sangre. Las muestras obtenidas serán usadas únicamente para el propósito de esta investigación y no se realizarán estudios genéticos o de cualquier

otro tipo en el futuro. Las activaciones y consultas de Ortodoncia serán realizadas una vez por mes.

El tiempo total del cierre del espacio será evaluado desde el inicio de la fase de cierre (T0) hasta el canino llegar a tener contacto con el segundo premolar, cuando el espacio se haya cerrado completamente (T1). La altura del hueso del início y del final del cierre de espacios, el grado de reabsorción o desgaste de las raíces y la pérdida de hueso serán definidas utilizando radiografías periapicales, sondeo periodontal y con la tomografía cónica computarizada.

Los resultados obtenidos de esta investigación le serán informados, al igual que a su médico tratante, el que le indicará el curso de acción médico más adecuado para usted.

3. BENEFICIOS

La presente investigación está basada en los principios actuales de medicina regenerativa utilizada en otras áreas de la medicina. Además de que el participante no tendrá costo alguno del tratamiento ortodóntico, el uso del plasma rico en fibrinas podría en teoría acelerar su tratamiento ortodóntico, disminuyendo el tiempo total de tratamiento.

En caso de no existir ningún tipo de diferencia el tiempo de tratamiento será igual al de un caso tratado sin plasma rico en fibrinas, y este plasma al ser producido a partir de su propia sangre será reabsorbido y eliminado por el organismo sin ningún tipo de repercusión sobre su cuerpo.

Sin embargo, la información que se obtendrá será de utilidad para conocer más acerca de las limitaciones del uso de este plasma y si eventualmente podría beneficiar o no a otras personas con su misma condición que en un futuro necesiten de un tratamiento ortodóntico.

4. RIESGOS

Los riesgos del presente estudio son los riesgos asociados al tratamiento ortodóntico, ente los cuales podrían estar:

- Reabsorción radicular o desgaste de las raíces (especialmente en los dientes anteriores).
- Manchas blancas sobre el esmalte del diente en las regiones alrededor del bracket cuando existe falta de higiene y acúmulo de placa bacteriana en esta región.
- Fracturas de esmalte al despegar los brackets (en dientes que poseen tratamiento endodóntico y dientes rehabilitados con resinas extensas en su superficie).

Durante el proceso de retracción de los caninos aparecerá un espacio entre este diente y los dientes anteriores el cual es posteriormente cerrado cuando se retraen estos últimos.

Debido a que el tratamiento ortodóntico potencialmente puede inflamar las encías y activar el proceso inflamatorio esto puede tener efectos negativos sobre el tejido óseo de la paciente, si usted está embarazada, tiene dudas si está embarazada o planea estarlo durante la duración del estudio, no puede participar en éste.

Si en el transcurso del estudio usted cree estar embarazada, deberá comunicarse de inmediato con el investigador responsable, quien le indicará el procedimiento a seguir.

5. COSTOS:

Durante el presente estudio el costo del tratamiento ortodóntico será reducido en un 60 %, será cobrado solo el 40% restante al participante, siendo requerida su colaboración en asistencia a los controles mensuales y en los estudios radiográficos necesarios para evaluar la evolución de su tratamiento. Estos controles son los mismos en pacientes de este estudio como en todos los pacientes que son sometidos a un tratamiento ortodóntico.

Además de los estudios radiográficos, se solicitarán dos exámenes tomográficos uno al inicio del cierre de los espacios y otra al final. Estos exámenes son necesarios para poder observar los resultados de este estudio, por lo que se le pide su comprensión, ya que para esta investigación estos se hacen necesarios.

6. FUENTES DE FINANCIAMIENTO DEL ESTUDIO:

Los costos de la máquina centrífuga y tubos de ensayo para producir el Plasma Rico en Fibrina (PRF), así como todo lo que concierne a materiales de Ortodoncia de este estudio serán aportados por los investigadores. El paciente deberá costear lo referente al pago a la universidad del tratamiento ortodóntico y estudios radiográficos a realizar durante este estudio.

7. COMPENSACIONES.

En caso de brackets despegados y partes del aparato ortodóntico que se hayan perdido por el participante estos serán cubiertos y repuestos por los investigadores. En los casos de manchas blancas, las cuales son causadas por falta de higiene o por susceptibilidad específica de cada individuo estas serán tratadas con tratamientos restauradores por estudiantes de pregrado de la universidad**.**

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Si tiene preguntas acerca de esta investigación médica puede contactar o llamar al Dr. Ariel Adriano Reyes (849 763-9843) o al Dr. James Collins (809 481-0572), los cuales son los investigadores responsables del estudio.

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Al momento de la firma, se me entrega una copia firmada de este documento".

_____

Fecha

Investigadores Responsables

_____

Nombre y firma del participante

_____

Dr. Ariel Adriano Reyes

Investigador

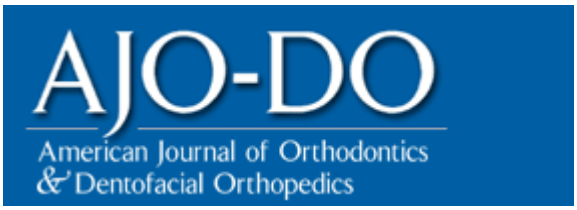
_____

Dr. James Collins

Investigador

Highlights

- The use of L-PRF decreased the rate of distalization of the maxillary canines.
- Changes in the inclinations of the upper canines were smaller compared with the control group.
- The use of L-PRF together with orthodontic treatment should be avoided.
- The decrease in the distal and canine inclination rate on the experimental side eventually increased the treatment time.
- This is one of the first clinical studies to investigate such inter-relationship.



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