ADRIANA SPINOLA RIBEIRO

TRATAMENTO DA LEUCOPLASIA BUCAL COM CRIOCIRURGIA ASSOCIADA OU NÃO AO LASER DE BAIXA INTENSIDADE: UM ESTUDO PRELIMINAR.

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Dissertação apresentada ao Colegiado de Pós-graduação em Odontologia da Universidade Federal de Minas Gerais como requisito parcial à obtenção do título de Mestre em Odontologia.

Área de concentração: Estomatologia

Orientadora: Tarcília Aparecida da Silva

Co-Orientador: Ricardo Alves Mesquita

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Dissertação intitulada **"Tratamento da leucoplasia bucal com criocirurgia associada ou não ao uso do laser de baixa intensidade",** Área de Concentração em Estomatologia, apresentada pela candidata **Adriana Spinola Ribeiro**, para obtenção do grau de Mestre em Odontologia, aprovada pela banca examinadora constituída pelos seguintes professores:

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Belo Horizonte, 27 de agosto 2009.

RESUMO

A criocirurgia é um método terapêutico caracterizado pela simplicidade de técnica, seguro e efetivo. A criocirurgia pode ser utilizada no tratamento da leucoplasia bucal (LB), a lesão potencialmente maligna mais comum da cavidade bucal. Um dos principais efeitos colaterais associados ao tratamento cirúrgico é a dor pós-operatória. Neste sentido, o laser de baixa intensidade (LBI) tem sido usado para redução da dor em várias condições. O objetivo deste estudo foi investigar os efeitos da criocirurgia na resolução clínica da LB e sua associação ou não com o LBI no alívio da dor. Dezoito pacientes com LB foram randomicamente divididos em dois grupos: dez tratados com criocirurgia somente (Grupo 1) e oito tratados com criocirurgia associada com LBI (Grupo 2). Na técnica da criocirurgia foi utilizado o aparelho Cry-Ac®. O LBI foi aplicado três vezes por semana e a escala numérica de avaliação foi utilizada para mensurar a dor. O tratamento foi bem tolerado pelos pacientes e as áreas de LB tratadas se apresentam com aspecto de normalidade e sem evidência clínica de recorrência até o presente momento. Observou-se ainda, uma tendência do grupo 2 ter menos dor que o grupo 1. Nossos resultados demonstram que a LB pode ser tratada com criocirurgia e a associação com o LBI contribui para minimizar a dor pós-operatória.

Palavras chave: criocirurgia, leucoplasia, laser de baixa intensidade.

ABSTRACT

Cryosurgery is a therapeutic method characterized by safe, simple application, and effectiveness. It is used in the treatment of oral leukoplakia (OL), the most common premalignant lesion of oral cavity. One of the principal side effects associated to surgical treatment of the OL is post-operative pain. The low level laser therapy (LLLT) has been used to decrease the pain in various conditions. The objective of this study was to investigate the effect of cryosurgery in clinical resolution of OL and its association or not with LLLT on pain relief. Eighteen patients with OL were divided randomly in two groups: ten treated with cryosurgery only (Group 1) and eight treated with cryosurgery associated of the LLLT (Group 2). Cryosurgery was performed with Cry-Ac® apparatus. The LLLT was performed three times in the week and a numerical rating scale was used to measured pain. The treatment was well-tolerated, treated OL sites appeared clinically normal and without clinical evidence of recurrence until the present time. It was also observed a tendency of group 2 to have less pain than group 1. Our results demonstrate that OL may be treated by cryosurgery and the association with LLLT contributes to minimize the post-operatory pain.

Key words: cryosurgery, leukoplakia, low level laser therapy.

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1. INTRODUÇÃO

1.1. Leucoplasia bucal

A leucoplasia de boca (LB) é uma mancha ou placa, predominantemente branca, que não pode ser caracterizada clinicamente ou histologicamente como outra lesão definida (van der Waal & Axéll, 2002). A LB representa a lesão potencialmente maligna mais comum da mucosa bucal (Napier & Speight, 2008). Segundo Warnakulasuriya et al. (2007), o conceito de LB deve envolver lesões brancas com risco questionável, sendo excluída qualquer outra doença ou desordens conhecidas que não apresentam potencial de malignidade. Sendo assim, a LB deve ser separada de um grupo de outras lesões com características semelhantes, mas com etiologia bem estabelecida, tais como: líquen plano, lupus eritematoso, leucoplasia pilosa, leucoedema, *morsicatio buccae*, queratose friccional e estomatite nicotínica (Axéll et al., 1996; van der Waal et al., 1997).

A descrição etiológica identifica duas categorias de LB: aquelas com etiologia desconhecida (idiopática) e aquelas associadas com o uso do tabaco (tabaco associadas) (Axéll et al., 1996; van der Waal et al., 1997). O maior fator de risco para desenvolvimento destas lesões é o tabaco, em suas diversas formas de uso (Bánóczy et al., 2001; Dietrich et al., 2004). O uso do álcool como um fator etiológico no desenvolvimento da leucoplasia tem sido questionável (Reichart, 2001; Petti & Scully, 2006).

A LB tem sido observada mais freqüentemente em homens de meia idade e idosos, com um aumento da prevalência com o aumento da idade. Menos de 1% dos homens abaixo dos 30 anos possuem leucoplasia. A prevalência aumenta amplamente para 8% em homens após os 70 anos. Em mulheres nesta mesma faixa etária a prevalência é igual a 2% (Neville & Day, 2002).

As variantes clínicas da LB são classificadas em tipo homogêneo e não-homogêneo. As LB homogêneas são aquelas que se apresentam como uma lesão predominantemente branca, uniforme, plana, fina, que pode exibir fendas superficiais e uma

superfície homogênea franzida ou corrugada (Sciubba, 1995). As LB não-homogêneas são lesões predominantemente brancas ou branco-avermelhadas (eritroleucoplasia) que podem ser irregulares e planas, nodulares ou exofíticas (Axxél et al., 1996).

Os aspectos histopatológicos da LB podem envolver atrofia ou hiperplasia do epitélio. A displasia epitelial, se presente, pode variar de discreta, moderada a acentuada (Warnakulasuriya et al., 2008). As alterações histopatológicas das células displásicas são caracterizadas por: pleomorfismo celular e nuclear, hipercromatismo nuclear, nucléolos irregulares e proeminentes, alteração na relação núcleo-citoplasma, aumento do número de figuras de mitose, mitoses atípicas, alteração na polarização da camada basal, queratose intraepitelial, perda da estratificação e projeções epiteliais em gota (Warnakulasuriya et al., 2008).

A LB apresenta uma taxa de transformação maligna anual de 0,1 % a 17,0 % (Saito et al., 2001; Lodi & Porter, 2008). Algumas características têm sido reportadas em associação com um aumento do risco de transformação maligna da leucoplasia:

1) gênero: particularmente mulheres tendem a ter maior risco (Napier & Speight, 2008; van der Waal, 2009);

2) longa duração da lesão: LB que persistem por longo tempo após a eliminação de possíveis fatores etiológicos têm um pior prognóstico que as LB recentes (van der Waal, 2009);

3) LB em não fumantes (leucoplasia idiopática): não fumantes têm um aumento na taxa de transformação maligna em relação a pacientes não fumantes (Napier & Speight, 2008, van der Waal, 2009);

4) LB em áreas de alto risco, como assoalho da boca, lateral de língua ou palato mole, têm um alto risco de transformação maligna (Zhang et al., 2001; van der Waal, 2009);

5) tipos não homogêneos: lesões não homogêneas têm uma alteração de cores de vermelho e branco, e aspecto exofítico, papilar ou verrucoso. De acordo com o tratamento, estas lesões podem exibir uma alta taxa de recorrência e freqüentemente transformam em carcinoma de células escamosas (van der Waal et al., 1997; van der Waal, 2009);

6) presença de displasia epitelial: na presença de displasia moderada ou severa, LB têm uma grande possibilidade de transformar em carcinoma de células escamosas (van der Waal, 2009).

A excisão cirúrgica é atualmente o tratamento proposto para as LB (Al-Drouby, 1983, van der Waal, 1997, Neville & Day, 2002). Entretanto, outras modalidades de tratamento estão disponíveis, como criocirurgia, cirurgia a laser CO_2, aplicação de retinóides e outras drogas e terapia fotodinâmica (Girod & Pfahl, 1996; Fernanes, 1997; Ishii et al., 2003, 2004).

A cirurgia convencional é a mais freqüentemente usada, mas pode causar cicatriz devido à perda de tecido, sangramento transcirúrgico e dor pós-operatória. A taxa de recorrência neste tipo de método tem sido relatada em 10-35 % dos casos (Vedfote et al., 1987; Homstrup et al., 2006).

1.2. Criocirurgia

O uso da criocirurgia no tratamento da LB tem se mostrado bastante efetivo, com destaque para o custo baixo, fácil execução e a possibilidade de aplicação em lesões extensas que necessitariam de vários procedimentos cirúrgicos para sua completa remoção (Goode & Spooner, 1971; Sako et al., 1972; Chapin & Burkes, 1973; Bekke & Baart, 1979; Bernardi & Calandriello, 1979; Gongloff et al., 1980; Malmström & Leikooma, 1980; Tal et al., 1982; Al-Drouby, 1983; Gongloff & Gage, 1983; Vercelino et al., 1980; Barrellier et al,. 1992; Yeh, 2000; Yu et al., 2009). Dentre as vantagens da criocirurgia, destaca-se a utilização em pacientes com alto risco para intervenções cirúrgicas, portadores de coagulopatias e marca-passo, e idosos (Leopard, 1975; Kuflik, 1994; Farat & Savage, 2006; Ameerally & Colver, 2007). As contra indicações absolutas da criocirurgia são doenças sistêmicas, como: urticária por frio, crioglobulinemia, criofibrinogenemia, doença de Raynaud, doenças vasculares periféricas e diabetes descompensada (Leopard, 1975; Kuflik ,1994).

A criocirurgia é um método não-cirúrgico que consiste em um rápido congelamento seguido de lento descongelamento levando à destruição tecidual (Toida et al., 1993; Farat &

Savage, 2006). O nitrogênio líquido é considerado a melhor substância criogênica devido às suas propriedades físico-químicas: inerte, inodoro, não-combustível, não libera gases tóxicos, alcança uma menor temperatura (Ishida & Silva, 1998). Além disto, pode ser facilmente encontrado no mercado. Os aparelhos utilizados para sua aplicação podem ser classificados em sistemas abertos ou fechados. A utilização do sistema fechado consiste no resfriamento da lesão através do contato da sonda crioterápica onde internamente circula o nitrogênio líquido. Os sistemas fechados possuem maior controle da área a ser destruída, porém a profundidade alcançada é menor, pois o metal utilizado nas sondas age como uma resistência adicional na transferência de calor. Os sistemas abertos utilizam aplicação direta do nitrogênio sobre as lesões, na forma de névoa, *swabs* ou, ainda, na forma de discos congelantes. Os sistemas abertos possuem pontas com diâmetros variáveis que formam o diâmetro da névoa a ser aplicada. Podem ser mais indicados para lesões proliferativas e invasivas onde se deseja alcançar maior profundidade de destruição (Holden & Sanders, 1973; Ferris & Ho, 1992).

Durante o congelamento tecidual a formação de gelo inicia-se no fluído extracelular provocando um aumento acentuado da concentração iônica extracelular, resultando em uma diferença de concentração entre a membrana celular e o meio externo. A água intracelular tende a passar rapidamente pela membrana celular, aumentando a concentração tóxica de eletrólitos intracelulares em níveis fatais para a célula (Leopard & Poswillo, 1974). As células se tornam supercongeladas e adquirem uma pressão de vapor interna maior que a existente nos espaços extracelulares (Whittaker, 1973). Como resultado da diferença de pressão, eletrólitos extracelulares passam para dentro da célula no momento em que a água sai da célula através da membrana celular e a água remanescente tende a se congelar formando gelo intracelular e causando imediatamente um dano irreversível. (Leopard, 1975). A queda de temperatura nos tecidos resulta ainda em desnaturação de proteínas nas membranas celulares e nas mitocôndrias causando prejuízo ao metabolismo celular (Holden & Saunders, 1973).

Em relação ao uso da criocirurgia no tratamento da LB, taxas variáveis de recorrência têm sido reportadas. Enquanto Yeh, 2000; relatou recorrência em 32% dos casos tratados durante o período de acompanhamento de 3 a 46 meses, outros investigadores obtiveram taxas de recorrência entre 3% e 25% em avaliação clínica de até cinco anos (Goode & Spooner, 1971; Sako et al., 1972; Chapin & Burkes, 1973; Bekke & Baart, 1979; Gongloff et al., 1980; Vercelino et al., 1980; Al-Drouby, 1983; Gongloff & Gage, 1983; Barrellier et al., 1992; Yu et al., 2009).

A incidência de complicações após criocirurgia é baixa (Kuflik, 1994). Dentre as complicações mais comumente observadas estão edema ou dor; já entre as complicações raras ou pouco freqüentes podemos citar: sangramento, infecção, dor de cabeça, febre e formação de defeito tecidual e cicatriz (Kuflik, 1994).

Dentre as desvantagens mais comuns da criocirurgia, está a dor pós-operatória de intensidade leve a moderada (Sako et al., 1972; Chapin & Burkes, 1973; Gongloff et al., 1980; Yeh, 2000). Nesse sentido, este estudo pretendeu associar a criocirurgia ao Laser de Baixa Intensidade (LBI) a fim de minimizar a dor pós-operatória; uma vez que o LBI tem provado ser efetivo no tratamento e reparação de danos teciduais e redução da dor (Kreisler et al., 2004; Genot & Klastersky, 2005; Amorim et al., 2006; Castano, 2007).

1.3. Laser de baixa intensidade

O LBI é uma forma de fototerapia que envolve a aplicação de luz de baixa potência, no comprimento de onda do vermelho ou próximo ao infravermelho, a fim de tratar várias doenças e injúrias traumáticas pela estimulação da cicatrização e da regeneração (Kreisler et al., 2004; Genot & Klastersky, 2005; Amorim et al., 2006; Castano, 2007). Dentre os mecanismos de ação do laser, postula-se que fótons visíveis ou próximos ao infravermelho são absorvidos por cromóforos, contidos nas células, como o citocromo c oxidase localizado na mitocôndria. Alterações na atividade do citocromo c oxidase resultam no aumento da produção de adenosina trifosfato (ATP), o qual leva a normalização da função celular (Labbe et al., 1990; Lubart et al., 1992).

A irradiação com LBI é capaz de influenciar o comportamento de fibroblastos aumentando sua proliferação, maturação e locomoção; bem como transformá-los em miofibroblastos e aumentando a secreção de fator de crescimento de fibroblastos (Azevedo et al., 2006). O LBI pode atuar ainda nos linfócitos aumentando sua proliferação e ativação, bem como, nos macrófagos aumentando a fagocitose, a secreção de fatores de crescimento de fibroblasto e intensificando a reabsorção de fibrina (Pereira et al., 2002). O LBI pode também aumentar a motilidade de células epiteliais, a quantidade de tecido de granulação e diminuir a síntese de mediadores inflamatórios (Albertini et al., 2007).

O LBI tem provado ser efetivo no tratamento de danos nos tecidos bucais e na redução da dor (Kreisler et al., 2004; Genot & Klastersky, 2005; Amorim et al., 2006).

2. OBJETIVOS

2.1. Objetivo geral

- Avaliar a eficácia da criocirurgia no tratamento da leucoplasia bucal e da associação com o laser de baixa intensidade no controle da dor pós-operatória.

2.2. Objetivos específicos

- Verificar a resposta da terapêutica da utilização da criocirurgia quanto à resolução clínica da leucoplasia bucal e recorrências;
- Avaliar o efeito do laser de baixa intensidade no controle da dor pós-operatória associada a criocirurgia.

3. ARTIGOS

Os resultados e métodos desta dissertação serão apresentados no artigo 1. O artigo 2 descreve uma série de casos de leucoplasia bucal em gengiva tratadas com criocirurgia.

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3.1. Artigo 1

TREATMENT OF ORAL LEUKOPLAKIA WITH CRYOSURGERY ASSOCIATED OR NOT OF THE LOW LEVEL LASER THERAPY: A PRELIMINARY STUDY.

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ABSTRACT

Objective: To investigate the effect of cryosurgery in clinical resolution of oral leukoplakia (OL) and its association or not with low level laser therapy (LLLT) on pain relief. *Methods:* Eighteen patients with OL were divided randomly in two groups: ten treated with cryosurgery (Group 1) and eight treated with cryosurgery associated of the LLLT (Group 2). Cryosurgery was performed with Cry-Ac® apparatus. The LLLT was performed three times week and a numerical rating scale was used to assess pain. The relationship between the treated groups and pain parameter were assessed by Mann-Whitney test. *Results:* Treated OL sites appeared clinically normal and without evidence of recurrence until the present time. It was also observed a tendency of group 2 to have less pain than group 1. *Conclusion:* Our results demonstrate that OL may be treated by cryosurgery and the association with LLLT seems to contribute to minimize the post-operatory pain.

INTRODUCTION

Cryosurgery uses freezing temperatures to achieve specific effects on tissues. The technique of cryosurgery stresses rapid cooling, slow thawing and repetition of the freezing process to maximize tissue destruction.[1] It can be used in general surgery, dermatology and oral surgery,[2] as the treatment of choice, an alternative method, or as adjunctive for diverse benign and malignant lesions.[3] Cryosurgery can be indicated for high-risk surgical patients, such as patients with a pacemaker, the elderly, and those with a coagulopathies.[2] Furthermore, it would be the first choice in the cases of multiple and large lesions, areas of difficult surgical access and where aesthetics is important.[2]

Oral leukoplakia (OL), a pre-malignant lesion, is described as “a predominant white lesion of the oral mucosa which cannot be defined as any other known lesion”.[4] Tobacco use is the commonest pre-disposing factor for the development of OL although a certain proportion of oral white patches are idiophatic.[5] Treatment reported to OL are conventional surgery,[6,7] laser ablation[8] or cryosurgery.[9-14] Previous studies have showed the success of cryosurgery for treating OL.[14] A moderate to mild post operatory pain has been reported by patients after cryosurgery.[13,15-17]

Several studies demonstrated the beneficial effects of the low level laser therapy (LLLT) in the reduction of post operatory pain.[18-20] Laser therapy has been recommended in such clinical situations because of the well-known biological effects of the interaction between laser energy and injured tissues.[21,22] Among the possible mechanisms, they include the acceleration of the antiinflammatory and analgesic effects and process of repair.[18,20,23]

Considering the demonstrated efficiency of the cryosurgery in the treatment of the OL, that one of the most side effects of cryosurgery is post-operative pain, and the anti-inflammatory and analgesic properties of the laser, the goal of this paper was to 1) investigate the effect of cryosurgery in clinical resolution of OL and 2) its association or not to the LLLT on pain relief.

METHODOLOGY

Patients

This study was approved by Ethics Committee of the Federal University of Minas Gerais nº 36/08 and informed consent was obtained from all patients. Eighteen patients were recruited from the Oral Medicine Clinic, Dental School, Federal University of Minas Gerais, Belo Horizonte, Brazil, from October 2007 to March 2009. OL was defined as a white patch or plaque that could not be characterized clinically or pathologically as any other disease.[7] Clinical diagnosis was confirmed by a histopathological examination of biopsy specimens from all patients.[24] Age, gender, smoker status, location, size and microscopic features of OL were recorded (Table 1). It was selected patients with multiple and/or large (> 20 mm) OL, areas of difficult surgical access, where aesthetics is important or for high-risk surgical patients. Patients were randomly divided in two groups. In group 1 (n=10), the patients were treated with cryosurgery and in group 2 (n=8), they were treated with cryosurgery associated in the LLLT. Clinical evaluation and photographs of the OL were done at each visit.

Cryosurgery technique

Following local anesthesia, the treatment was performed by an application of liquid nitrogen using CryAc® apparatus (Brymill Cryogenics Systems, Ellington, CT, USA). Cryosurgery was carried out with either a spray or a closed system, depending on the surface and surgical access. In flat surfaces or areas where the contact was made easy, the probes of the closed system were used. Otherwise, in areas of difficult access or round and irregular surfaces the spray was used. In spray technique, the time was 10 seconds[25] and the closed system was 60 seconds,[16,26] for each cycle. Areas of 1 cm² of each OL lesions were delimited with the blue of methylene and exposed to two consecutive, freeze-thaw cycles, beginning at the center of the lesion, and moving out to the borders until the entire area appeared white. After the ice ball produced during freezing was completely thawed, the next freezing was performed. Thawing occurred spontaneously after 30 or 60 seconds. Lesions with a diameter larger than 1 cm were treated in two or more sessions. The second treatment was performed one month later.

Patients were examined at 1, 2, and 4 weeks; and 3 and 6 months after cryosurgery, and they were subsequently recalled every 6 months.

Laser application

In group 2 patients, LLLT was irradiated in the treated area 5 minutes before cryosurgery, after cryosurgery (until the treated area thawed out completely), 48 and 72 hours post cryosurgery.[27] The same equipment was used in all applications (Equipment model Whitening Lase II, DMC LTDA, São Carlos, Brazil). The irradiation was AsGaAl, with wavelength of 660nm, potency of 100 mW and energy density of 4J/cm². The irradiation was performed of a punctual form in an area of about 1 cm² during 39 sec. Distances of 1 cm were maintained from each point of application. Both the patients and the operator used specific protection glasses during the treatment.

Measures of pain

The pain assessment instrument used was numerical rating scale (NRS).[28] The self-reportation of pain involves asking the patients the intensity of pain from 0 to 10 scores (11 point scale) with the understanding that 0 represents no pain and 10 represents the extreme of pain intensity (unbearable pain). The NRS was verbally delivered after one week of treatment with cryosurgery. The patients were asked about the pain after the 1st session. The pain was graded on the 3 grade-scale: mild intensity (NRS 0-3); moderated (NRS 4-7) and severe (NRS 8-10). Regarding the edema, patients were asked for the presence or not.

Statistical Analysis

The statistical package SPSS version 15.0 for Windows was used for the statistical analysis. A descriptive study of each variable was made. The association between the different qualitative variables was established using Chi-Square test and Fisher's exact test. The relationship between the treated groups and pain parameter was assessed for statistical significance by a Mann-Whitney test. A p value of < 0.5 was considered statistically significant.

RESULTS

The patients consisted of 15 women and 3 men, with ages ranging from 36 to 85 years old (mean of 64.67±11.31). Four patients were smokers. The clinical features of OL were asymptomatic white plaques of the homogenous type with uniform, flat, thin, surface containing many fine cracks or fissures (Fig. 1A, 1C). The gingiva (n=6) was the most common site for OL lesions, followed by the buccal mucosa (n=5), tongue (n=5), alveolar mucosa (n=1) and hard palato (n=1). The area of the OL lesions varied from 5 to 50 mm (mean of 23.11). Histopathological examination revealed that 12 OL presented epithelial dysplasia (7 in group 1 and 5 in group 2): 7 were classified as mild epithelial dysplasia (5 in group 1 and 2 in group 2) (Fig. 2A, 2B) and 5 hyperkeratosis with moderate epithelial dysplasia (2 in group 1 and 3 in group 2) (Fig. 2C, 2D). Six patients had hyperkeratosis without epithelial dysplasia (3 in group 1 and 3 in group 2). Other clinical and microscopic findings are summarized on Table 1. There were no significant differences between the groups considering: gender, age, presence/absence of epithelial dysplasia, smoke status, location and size of OL (Chi-Square Tests, $p>0.05$).

No patient had local or systemic diseases that contra indicates for treatment with cryosurgery.

After 3-5 days of cryosurgery, necrotic tissue was observed in the treated area. The necrotic slough separated spontaneously after 1-2 weeks, leaving a fully epithelialized surface and healed mucosal tissue. Total clinical resolution of OL was observed in all patients (Fig 1B, 1D). There was no bleeding, no loss of tissue, no scarring, and no infection in the OL sites treated for both groups. In group 1 seven patients reported pain: 2 mild, 3 moderate and 2 severe. In group 2, 4 patients reported pain: 2 mild and 2 moderate. Although no significant difference was achieved, it was observed a lower rate of reported pain in group 2 (50%) than group 1 (70%). Moreover patients of group 2 showed a tendency to have less intensity of pain than group 1 (p=0.249) (Figure 3). Seven patients reported no pain, 3 in group 1 and 4 in group 2. In relation to the edema, no significant difference between the groups was observed (p=0.342). Eight patients reported edema: three in group 1 and five in group 2, within 24 hours

after treatment. At the average 9-month follow-up visit, no recurrence was noted in any of the patients. The patients were followed every 6 months.

DISCUSSION

The current results demonstrate that all of 18 cases of OL treated with cryosurgery had clinical total resolution with no evidence of loss of tissue, scarring, bleeding or infection. These results are in accordance with previous studies.[9-14,16,29-31] Moreover, the LLLT association improves the painful symptoms associated with cryosurgery. In fact, the LLLT has been proved to be effective in the treatment of damages of oral tissues and in the reduction of the pain.[18,20,23,32-34] The use of the LLLT on the control of the post-operative pain has been previously evaluated.[35-37] While some of studies showed positive outcome, others did not demonstrate satisfactory results.[38-40] These differences could be explained by variations in wavelength, power levels, irradiation method, and exposure time of LLLT. The laser light stimulates cellular activity and leads to the release of growth factors by inflammatory cells.[41-45] It also induces keratinocyte proliferation, angiogenesis, and mast cell activation and degranulation, which may accelerate wound healing.[46] This acceleration is the result of a shorter acute inflammation phase and earlier commencement of the proliferative phase of tissue repair, when granulation tissue is produced.[21,46] Among the mechanisms of action of the laser, there is postulated that photons visible or near to infrared are absorbed for cromophores, present in the cells, like the cytochrome c oxidase located in the mitochondria. Alterations in the activity of the cytochrome c oxidase in turns increase of the production of adenosin trifosfate (ATP), which leads to the normalization of the cellular function.[47,48]

In the present study, the most frequent location was the gingiva, following the tongue and buccal mucosa, alveolar mucosa and palate.The most common reported location of OL is the buccal mucosa, varying in 16.9% to 64.8%.[49-51] However, other studies demonstrated gingiva as the most frequent location.[52-55]

OL are usually treated by surgery. The more frequently method used is conventional surgery which may cause delayed cicatrization due to contraction of tissue, trans-surgical bleeding and post-surgical pain.[8,50,56] The recurrence rate of OL treated by conventional surgery is reported in 10-35% of cases.[57,58]

At the 6-month follow-up visit, no recurrence of OL was noted in any cases of current study. A recurrence rate of 20% of OL cases treated by cryosurgery has been reported considering periods of follow-up of 2 ½ to 4 ½ years.[15] However, other investigators have obtained better results in the resolution of OL with cryosurgery in clinical evaluation of five years.[9-14,16,29-31] Treatment of OL must avoid defects; especially in aesthetic areas, like gingiva, were extensive injuries with loss of tissue may occur. In the present study, in the cases of gingiva treated with cryosurgery the absence of scar and preserved function were possible. Cryosurgery is a good additional alternative to surgical excision, because destruction of the pathologically changed tissue is possible and allowed the mucosa to return to a normal clinical appearance with complete regeneration, no scar formation and consequent loss of function is avoided.[31] One of the disadvantages of the cryosurgery is the non-removal of the tissue for microscopical analysis, however, representative biopsies must be required before OL treatment.[3]

Other modality for treatment of OL may be surgical laser. Laser surgery has a hemostatic effect; it is able to remove lesions accurately with minimal damage to adjacent tissue.[8,65] It has been reported the successfully treatment of OL by CO_2 laser.[8,59-61] Various authors reported local recurrences of 10% to 40% with surgical laser.[61-65] The expense of laser systems and the relatively longer rehabilitation period of treated areas are the main disadvantages of this method.[66]

The annual malignant transformation rate of OL varies from 0.1% to 17.0%.[67,68] Some factors may contribute to increase the chance of the OL to become malignant as 1) gender; in the present study, 15 of 18 patients were women; female patients tend to present a higher risk of developing malignant transformation;[5,69] 2) epithelial dysplasia; in the present study 12 patient had hyperkeratosis with epithelial dysplasia; in the presence of moderate to severe dysplasia, OL has a greater possibility of transforming into oral squamous cell carcinomas;[69] 3) OL in lesions in the floor of mouth, ventrolateral tongue and soft palate have a high risk of malignant transformation;[69,70] our samples includes 3 sites of high risk (ventrolateral tongue); 4) OL among non-smokers (idiopathic); in the present study, 14 patients were non-smokers; non-

smokers with OL have an increased rate of malignant transformation in relation to OL in smokers.[5,69]

Potentially malignant disorders of the oral mucosa are also indicators of risk of likely future malignancies elsewhere in oral mucosa.[71]

In conclusion, our results demonstrate that OL may be successfully treated by cryosurgery and association with LLLT contributes to minimize the post-operatory pain.

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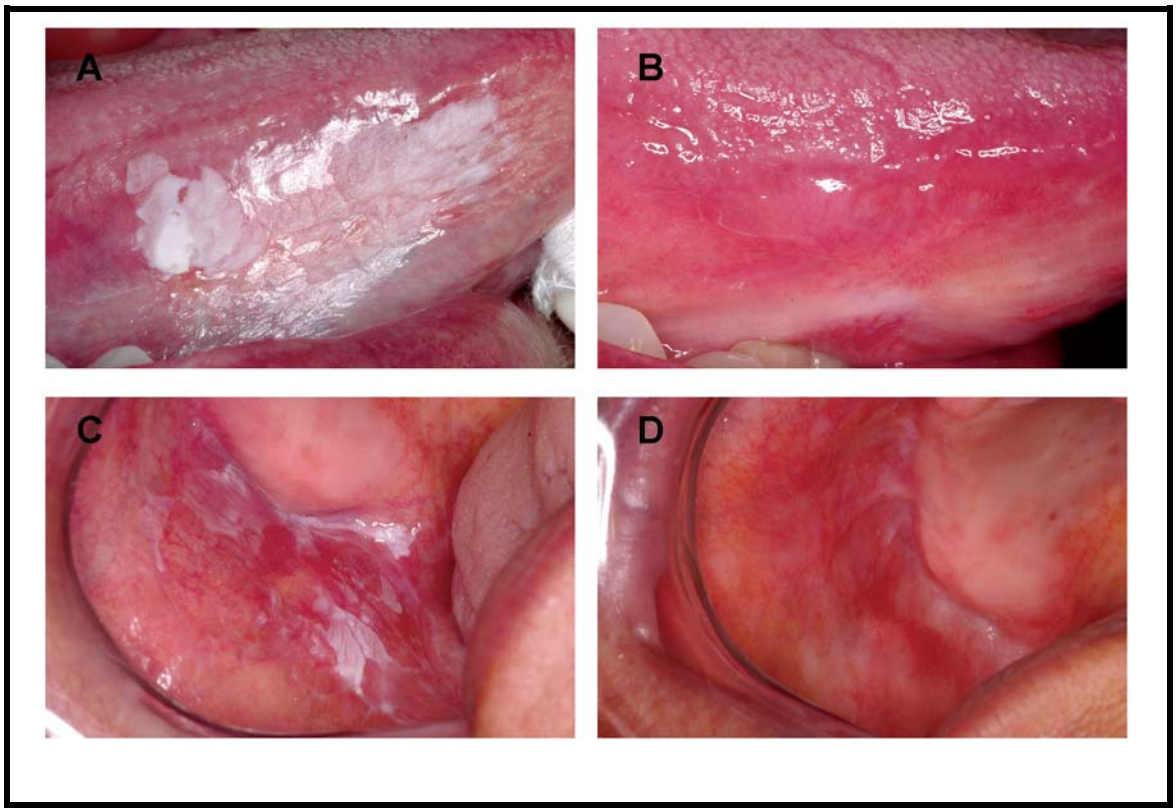

Figure 1: Clinical aspects of oral leukoplakia before (Fig. 1A, 1C) and of site mucosal normal clinically after (Fig. 1B, 1D) of treatment with cryosurgery associated or not wich low level laser therapy. Patients 1 (A, B) and 2 (C, D).

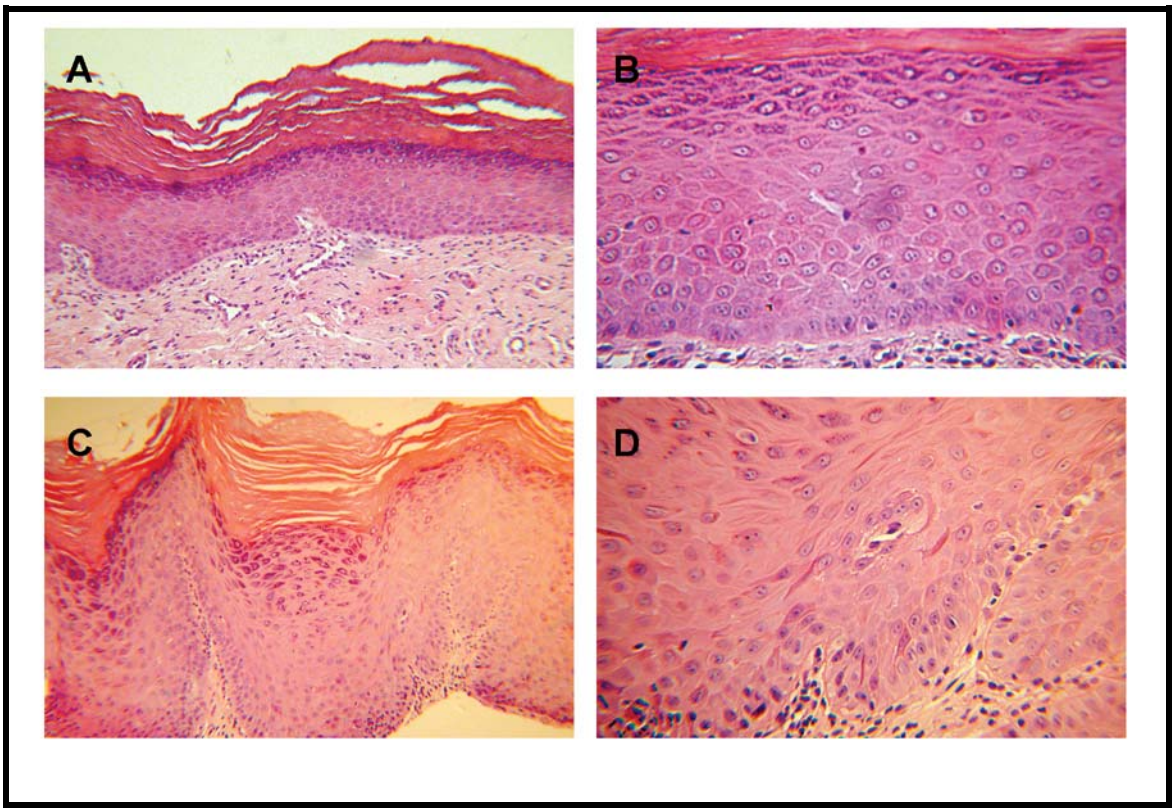

Figure 2: Histopathological aspects of oral leukoplakia in patient 1 (A, B) and patient 2 (C, D). Patient 1 presented hiperkeratosis with mild epithelial dysplasia and patient 2 hiperkeratosis with moderate epithelial dysplasia. Original magnification: x100 (A, C); x400 (B, D).

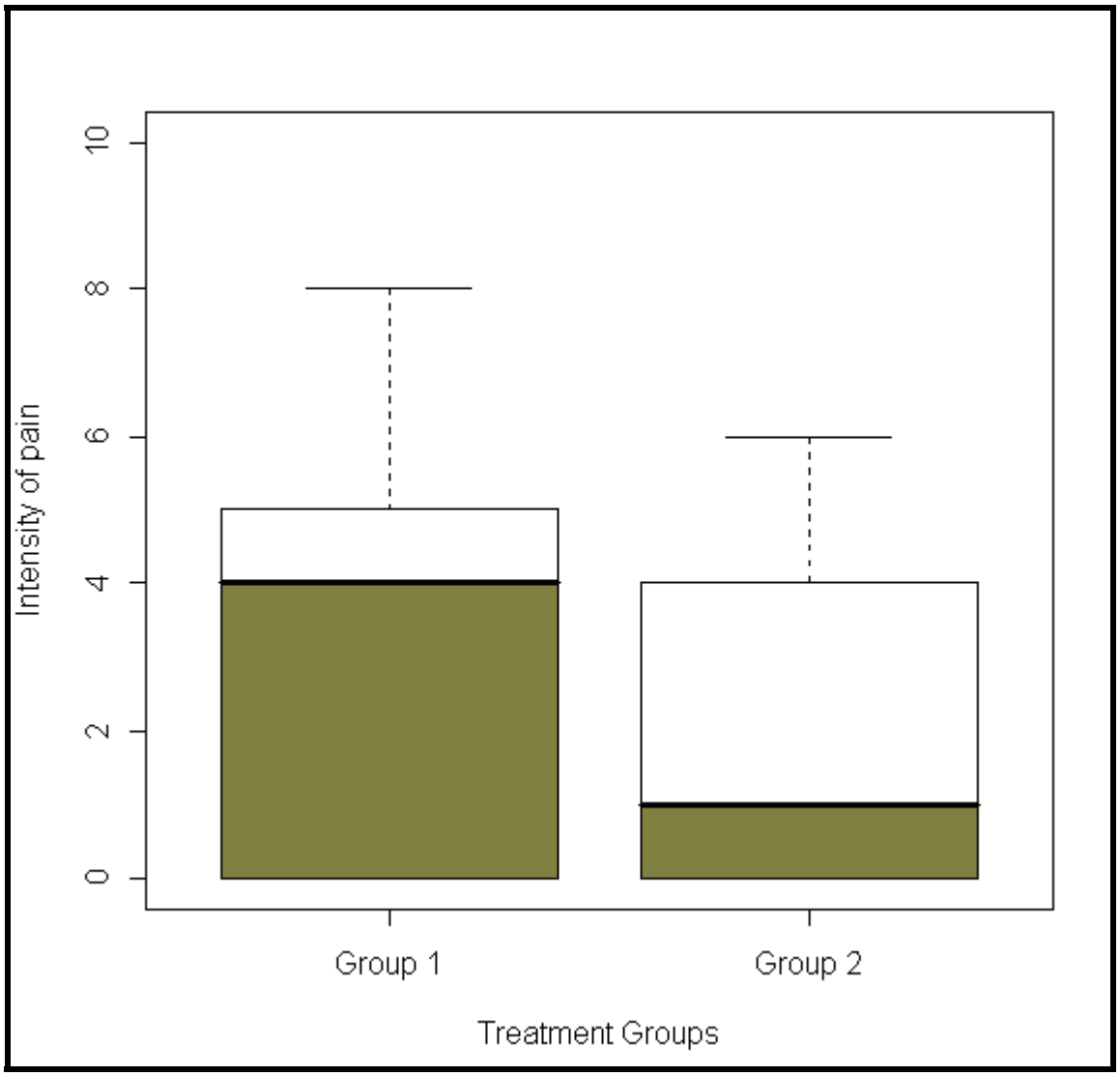

Figure 3: Intensity of pain in patients treated wit cryosurgery (Group 1, n= 10) and patients treated with cryosurgery associated to low level laser therapy (Group 2, n= 8). Pain was measured by numerical rating scale. Results represent median ± standard deviation.

Table 1- Clinical data of patients with OL treated with cryosurgery (group 1) and cryosurgery associated to LLLT (group 2).

Patients	Age	Gender	Smoke status	Histopathology	Size of OL (mm)	Location of the OL	Treatment group	Lesion	Number of sessions	Follow-up (months)
1	63	Female	Yes	H/M	10	Buccal mucosa	1	Multiple	2	12
2	45	Female	Yes	H	12	Ridge alveolar	1	Single	1	6
3	63	Female	No	H/M	18	Tongue	1	Single	2	9
4	70	Female	No	H/M	20/25	Tongue	1	Multiple	4	9
5	76	Female	No	H	50/30	Tongue and Buccal mucosa	1	Multiple	3	12
6	73	Female	No	H	6/10	Gingiva	2	Multiple	2	6
7	69	Male	No	H	25	Gingiva	2	Single	1	12
8	72	Female	No	H/Mo	20	Tongue	2	Single	2	9
9	70	Female	No	H	40	Buccal mucosa	2	Multiple	3	9
10	35	Male	Yes	H/Mo	33	Tongue	2	Multiple	2	9
11	64	Male	No	H/M	20/30	Buccal mucosa	2	Multiple	3	9
12	63	Female	No	H	Multiple	Palato	1	Multiple	5	12
13	60	Female	No	H/Mo	30	Buccal mucosa	1	Multiple	3	12
14	59	Female	No	H/M	15	Gingiva	1	Single	2	9
15	73	Female	No	H/M	25	Ridge alveolar	1	Multiple	2	12
16	55	Female	No	H/Mo	5	Gingival papilla	1	Single	1	6
17	70	Female	Yes	H/Mo	25	Buccal mucosa	2	Single	3	6
18	85	Female	No	H/M	20/15	Buccal mucosa	2	Multiple	2	6

H=hyperkeratosis; H/M= hyperkeratosis with mild epithelial dysplasia; H/Mo= hyperkeratosis with moderate epithelial dysplasia.

3.2. Artigo 2

A series of cases of gingival leukoplakia treated with cryosurgery

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Abstract

Six patients with gingival leukoplakia were treated with cryosurgery. The procedure was performed with Cry-Ac® using the spray technique for two consecutive freeze cycles of 10 seconds. Patients were examined at 1, 2, and 4 weeks; and 3 and 6 months after cryosurgery. There was no bleeding, no loss of tissue, no scarring, and no infection following treatment. The treated gingival sites appeared clinically normal and without clinical presence of leukoplakia until the present time. Cryosurgery should be considered choice of treatment when leukoplakia involves gingiva. It also has potential for use in the treatment of other gingival lesions.

Key words: leukoplakia, gingiva, cryosurgery, treatment.

Introduction

Oral leukoplakia (OL) is a pre-malignant lesion described as “a predominant white lesion of the oral mucosa which cannot be defined as any other known lesion”.[1] The concept of OL should acknowledge white lesions excluding any other lesions or known disorders which do not present potential malignant risk such as candidiasis, lupus erythematosus, lichen planus, hairy leukoplakia, frictional keratosis, nicotinic stomatitis and leukoedema.[2,3] The treatment of OL is usually performed by surgery. The surgical treatment may be done either through conventional surgery,[2] electrocautery, laser ablation[5] or cryosurgery.[6-11]

Cryosurgery is a therapeutic method characterized by simple application, effectiveness, painlessness during the procedure, and low incidence of secondary infection and hemorrhage.[12] The technique of cryosurgery stresses rapid cooling, slow thawing and repetition of the freezing process to maximize tissue destruction.[13] It can be used for high-risk surgical patients, such as patients with a pacemaker, the elderly, and those with a coagulopathies. Furthermore, it would be the first choice in the cases of multiple and large lesions, areas of difficult surgical access and where aesthetics is important. It has been used in general surgery, dermatology and oral surgery[12] Cryosurgery is considered a simple and efficient therapeutic management of OL[8,10,11,14,15] Since tissue is not removed in the cryosurgery, it is a suitable treatment for areas, such as the gingiva, where the aesthetics is an important factor. Gingival melanic pigmentation treated with cryosurgery demonstrated excellent results without aesthetic defect.[16-18] In the management of gingival leukoplakia (GL), only the study of Al-Drouby[7] presented two of three cases that disappeared completely with cryosurgery.

Increasing aesthetic demands in dentistry have created a need to maintain and restore the different parts of the gingival complex. Treatment of GL must be correctly appropriate in order to avoid defects not expected; especially extensive injuries with loss of tissue will go away and in aesthetic areas. Therefore, in accordance to the indications of the cryosurgery, in the current study we choose this modality of treatment to GL and presented a serie of six cases of GL successfully treated with cryosurgery.

Patients and methods

Patients

The protocol of this study was approved by Ethics Committee of the Federal University of Minas Gerais nº 36/08. Six patients with GL were included in the study. The clinical diagnosis criteria for GL were in accordance with Neville and Day.[4] Age, gender, smoker status, location, size and microscopic of GL were recorded. Incisional biopsy of the GL was performed in all patients. No patient had diseases that did not indicate for treatment with cryosurgery. Clinical evaluation and photographs of the GL were done at each visit.

Cryosurgery technique

Following local anesthesia, the treatment was performed by a direct application of liquid nitrogen with a spray technique using CryAc® apparatus (Brymill Cryogenics Systems, Ellington, CT, USA). Each lesion was exposed directly to two consecutive, ten second, freeze-thaw cycles, beginning at the center of the lesion, and moving out to the borders until the entire lesion appeared white. After the ice ball produced during freezing was completely thawed, the next freezing was performed. Thawing occurred spontaneously after 30-60 seconds. Patients were examined at 1, 2, and 4 weeks; and 3 and 6 months after cryosurgery, and they were subsequently recalled every 6 months. Lesions with a diameter larger than 10 mm received two treatments. The second treatment was performed one month later.

Results

The patients consisted of five women and one man, with ages ranging from 45 to 73 years old. Two of the patients were smokers. Other clinical and microscopic findings are summarized on Table 1. The clinical features of GL were asymptomatic white plaques of the homogenous type with uniform, flat, thin, surface containing many fine cracks or fissures (Figure 1A, 1C, 1E, 1G, 1I, 1K). After 3-5 days of cryosurgery, superficial necrotic tissue was observed in the treated area of the gingival tissue. The necrotic slough separated spontaneously after 1-2 weeks, leaving a fully epithelialized surface and healed gingival tissue. Three patients reported minimal edema within 24 hours after treatment. Total clinical resolution of GL was observed in all patients. There was no bleeding, no loss of tissue, no scarring, and no infection in the gingival sites treated. Two patients (33%) reported pain. For all patients, the acceptance of the treatment was excellent. At the 6-month follow-up visit, no recurrence was noted in any of the patients. The patients are followed every 6 months.

Discussion

OL has an annual malignant transformation rate of 0.1% to 17.0%.[19,20] The presence of epithelial dysplasia is generally regarded as the most important indicator of malignant potential. OL presenting low to moderate malignant risk may be either completely removed or not, and the decision should consider other factors such as gender, location, size and, in the case of smokers, the patient's engagement in smoking cessation.[2] OL located on the floor of the mouth, soft palate and tongue are considered as high-risk lesions to malignant transformation, while, in other areas, as gingiva, they are considered as low malignancy risk.[4] A predominance in the buccal mucosa and lower alveolar mucosa as a typical location of OL has been described.[21-23] However, other studies demonstrated gingiva as the most frequent location.[24-27] The frequent involvement of the gingival area has been described mostly in US studies, with a range from 23.7 to 41.8% of OL cases.[21,23] So, the GL is a frequent condition in clinical practice and their adequate management is necessary. We presented a serie of six cases of GL successfully treated with cryosurgery. In the cases of the current study the choice of treatment of GL with cryosurgery was justified because aesthetic factor. However, in general to OL must be considered: 1) epithelial dysplasia;[28] 2) smoking cessation;[28,29] and 3) gender.[28,29]

OL are usually treated by surgery. The surgery may be conventional surgery, electrocautery, cryosurgery and laser ablasion.[2,4,5,7] Conventional surgery is the more frequently used but may cause scar, loss of tissue and the recurrence has been reported in 10-35% of cases.[22,30] The results of treatment of OL with cryosurgery have been varied. While Sako et al[31] have reported recurrence in 20% of cases after cryosurgery during periods of follow-up of between 2 ½ to 4 ½ years, other investigators have reported better results in the resolution of OL in clinical evaluation of even five years.[6-11,32-35] There was not observed recurrence of GL in the cases of current study in a period of 6-month follow-up. Also, the patients will be followed.

Our results demonstrate that 100% of cases of GL treated with cryosurgery had clinical total resolution. Healed gingival tissue presented as a normally clinical appearance without leukoplakia. Lost of gingival tissue, postoperative pain, hemorrhage, infection or scarring did

not occur in any of the cases. Our results are in accordance with most of the revised studies of treatment of OL with cryosurgery in different oral mucosa location.[6-11,32-35] The uneventful healing in the present study were corroborated by previous results in which cryosurgery was used in GL[7,35] and OL in other localization.[6,8-11,32-35]

Cryosurgery, an effective method of tissue destruction by freezing, has become a firmly established surgical technique in medical and dental practice. Physical and chemical changes induced by freezing lead to cell destruction and tissue death. While most vital tissues freeze at approximately -2°C, ultralow temperatures (below -20°C) result in total cell dealth.[36] A cryogenic agent applied directly or indirectly will cause selective necrosis of tissue, which extention depends on the type of lesion and the area to be treated.[37] Liquid nitrogen is the cryogen of choice for oral surgery because it is easy obtention and coldness (-196°C).[37] The effectiveness of cryosurgical treatment is based on the formation of extracellular and intracellular ice crystals. A rapid buil-up of toxic electrolyte concentrations, alteration in pH, protein denaturation and disruption of cell membranes subsequently occur. The vascular status of the cryolesion is also regarded as the factor responsible for the completion of cell destruction in the frozen area.[37,38] The cryodose of 10 seconds was selected, in accordance to previous studies.[39,40] This dose was sufficient to remove a superficial layer of gingiva containing the diseased tissue with minimal damage to the underlying connective tissue.

Cryosurgery is useful for superficial, irregular and multiple lesions and for those on a curved surface.[37] Particularly in the treatment of large, multifocal lesions or areas of access is difficult, cryosurgery is a good alternative to surgical excision, because destruction of the pathologically changed epithelium is possible and allowed the mucosa to return to a normal clinical appearance with no scar formation. Because there is complete regeneration of epithelium from affected adjacent parts on the visible intact submucosa tissue, marked cicatrization and consequent loss of function are avoided.[35] In addition, when patients have medical problems or high-risk for surgery, and elderly it is readily accepted, as observed with the patients of this study.

The absolute contraindications of cryosurgery are systemic diseases as: cold urticaria, cryoglobulinemia, cryofibrinogenemia, coagulopathy, Raynaud's disease, vascular peripheric diseases and uncontrolled diabetes.[37] The patients of the current study did not present any of this condition.

Superficial gingival cryosurgery as well as full thickness gingival freezing in humans and animals had demonstrated healing by complete regeneration and sterile inflammatory reaction.[39-41] Studies with use of the cryosurgery in gingiva melanic pigmentation reached excellent results and without sign of recurrences in the follow-up.[11,16] Al-Drouby[7] in their series of cases, reported three GL, two of them presented complete resolution in the follow-up in two years.

In conclusion, our results suggest that cryosurgery should be considered as the treatment of choice when OL involves gingiva. It also has potential for use in the treatment of others gingival lesions.

Acknowledgements and Conflict of Interest

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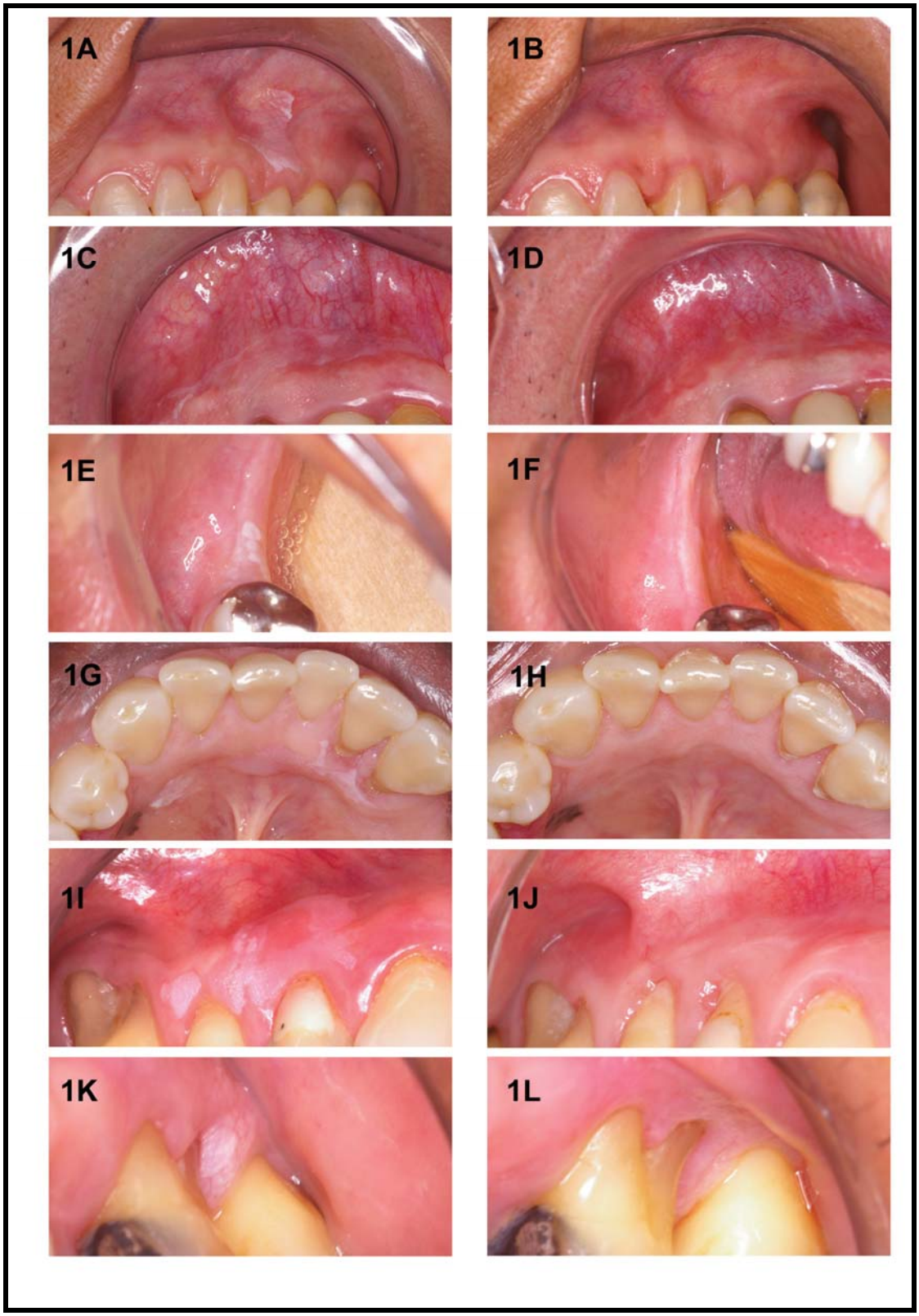

Figure 1- Clinical aspects of gingival leukoplakia before (1A, 1C, 1E, 1G, 1I, 1K) and of site gingival normal clinically after (1B, 1D, 1F, 1H, 1J, 1L) of treatment with cryosurgery. Patients 1 (A, B); 2 (C; D); 3 (E, F); 4 (G, H); 5 (I, J) and 6 (K, L).

Table 1- Clinical and microscopic data of six patients with gingival leukoplakia (GL) treated with cryosurgery.

Patients (Figures)	**Age**	**Gender**	**Smoke status**	**Histopathology**	**Size of GL (mm)**	**Location of the GL**
1 (Fig 1A, 1B)	45	Female	No	Hyperkeratosis with Mild epithelial dysplasia	18	Vestibular attached gingiva extending to vestibular oral mucosa close to 25
2 (Fig 1C, 1D)	69	Male	No	Hyperkeratosis	25	Vestibular attached gingiva close to 12-15
3 (Fig 1E, 1F)	45	Female	Yes	Hyperkeratosis	12	Ridge alveolar edentate of 46
4 (Fig 1G, 1H)	73	Female	No	Hyperkeratosis	8	Lingual attached gingiva close to 33
5 (Fig 1I, 1J)	59	Female	No	Hyperkeratosis with Mild epithelial dysplasia	15	Vestibular marginal gingiva extending to attached gingiva and oral mucosa between 14-16
6 (Fig 1K, 1L)	55	Female	No	Hyperkeratosis with Moderate epithelial dysplasia	5	Vestibular gingiva papilla between 26 - 27

4. CONSIDERAÇÕES FINAIS

O grande número de lesões de leucoplasia de boca encontradas em nossa prática diária leva-nos a buscar formas alternativas de tratamento para obter sua resolução. O tratamento para remoção da leucoplasia de boca tradicionalmente é o cirúrgico, utilizando-se para isso incisão, remoção e sutura da área tratada. Este método tem algumas desvantagens como dor, cicatrização mais demorada, contração das margens incisadas podendo gerar defeitos estéticos, dificuldade de acesso em áreas como palato e áreas extensas, além das contra-indicações em pacientes com doenças sistêmicas não-controladas.

A criocirurgia é uma modalidade terapêutica baseada em um processo físico, que provoca a dano tecidual pelo rápido e intenso resfriamento. É uma técnica efetiva e possui vantagens em comparação com outros métodos no tratamento de determinadas lesões benignas e potencialmente malignas, localizadas em pele e mucosas. Dentre as vantagens destacam-se: facilidade da técnica, baixo custo, baixa ocorrência de infecções, hemorragias e ausência de cicatrizes (Kuflik, 1994; Farat & Savage, 2006; Ameerally & Colver, 2007). Uma das desvantagens da criocirurgia é a não-remoção do tecido lesional para análise microscópia. No presente estudo, todas as lesões foram submetidas previamente à biópsia incisional e apenas foram tratados com criocirurgia os casos de LB exibindo displasia epitelial leve ou moderada. Outros fatores também devem ser considerados na escolha do método de tratamento das LB, tais como localização e extensão das lesões, uso do fumo, gênero, lesões múltiplas e pacientes com problemas sistêmicos.

No Brasil, o uso da criocirurgia se tornou bastante comum em especialidades médicas (Ishida & Silva, 1998), porém na odontologia o seu uso ainda é incipiente, possivelmente, devido a dificuldades na obtenção do equipamento adequado às condições de atendimento na clínica odontológica. Na rotina clínica de um consultório odontológico o equipamento talvez fique inoperante por muito tempo para compensar sua aquisição, mas em clínicas especializadas no tratamento de lesões bucais seu uso compensaria sua aquisição pela grande variedade indicações de lesões que poderiam ser tratadas. Neste estudo, verificou-se a efetividade da criocirurgia no tratamento das LB, de maneira similar ao

observado por outros autores (Goode & Spooner, 1971; Sako et al., 1972; Chapin & Burkes, 1973; Bekke & Baart, 1979; Gongloff et al., 1980; Vercelino et al., 1980; Al-Drouby, 1983; Gongloff & Gage, 1983; Barrellier et al., 1992; Yeh, 2000; Yu et al., 2009).

Vários estudos têm demonstrado os efeitos benéficos do LBI no tratamento de afecções bucais (Kreisler et al., 2004; Genot & Klastersky, 2005; Amorim et al., 2006). No presente trabalho, verificamos que o grupo tratado com criocirurgia associada ao LBI apresentou uma tendência à redução da frequência e intensidade de dor pós-operatória. Estes resultados podem ser explicados por observações prévias acerca dos efeitos antiinflamatórios e analgésicos do LBI, bem como na aceleração do processo de reparo (Kreisler et al., 2004; Genot & Klastersky, 2005; Amorim et al., 2006).

Os LBI têm sido utilizados na odontologia para contribuir com o processo de cicatrização tecidual. Existe ampla variação entre metodologias e protocolos (dosimetria, comprimento de onda, tempo de exposição e freqüência de tratamento) nos estudos clínicos utilizando o LBI em lesões de tecidos moles. Em termos de aplicações clínicas, existem fortes evidências que suportam a aplicação do laser em tecidos moles na prática odontológica (Bourguignon-Filho et al., 2005). Além disto, quando corretamente indicado e utilizando-se os princípios de segurança (uso de óculos de proteção) é um método efetivo não sendo descrito nenhum efeito colateral ou adverso associado ao LBI.

Uma das limitações do presente estudo foi o pequeno número de pacientes, o que pode ter influenciado os resultados, uma vez que não foram encontradas diferenças significantes entre os grupos estudados. Com relação ao edema, a forma de avaliação foi subjetiva e somente questionada sua presença ou ausência. Verificamos ainda que as localizações da LB onde foram relatadas presenças de edema foram gengiva e mucosa jugal, áreas onde a percepção deste sinal pode ser mais evidente.

A criocirurgia foi apresentada neste estudo como uma modalidade para o tratamento da LB com resultados positivos. Apesar da efetividade de alguns tratamentos na resolução das LB, é importante ressaltar que ainda não se demonstrou capacidade destas terapias na prevenção de recorrências e transformações malignas (Lodi et al., 2002). Por estas razões,

as LB devem ser regularmente acompanhadas clinicamente, independentemente da resposta e do tipo de terapia empregada.

5. CONCLUSÕES

Diante dos resultados do trabalho apresentado, podemos concluir que:

- A criocirurgia é um método efetivo na resolução da leucoplasia bucal;
- A associação do laser de baixa intensidade contribui para minimizar a dor pós-operatória associada ao tratamento com criocirurgia.

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7. ANEXOS

ANEXO 1

UNIVERSIDADE FEDERAL DE MINAS GERAIS
COMITÊ DE ÉTICA EM PESQUISA - COEP

Parecer nº. ETIC 36/08

Interessado(a): Profa. Tarcília Aparecida da Silva
DCPCO
Faculdade de Odontologia - UFMG

DECISÃO

O Comitê de Ética em Pesquisa da UFMG – COEP aprovou, no dia 9 de abril de 2008, após atendidas as solicitações de diligência, o projeto de pesquisa intitulado **"Ensaio Clínico do tratamento da leucoplasia bucal com crioterapia associada ou não ao laser de baixa intensidade"** bem como o Termo de Consentimento Livre e Esclarecido.

O relatório final ou parcial deverá ser encaminhado ao COEP um ano após o início do projeto.

Profa. Maria Teresa Marques Amaral
Coordenadora do COEP-UFMG

Av. Pres. Antonio Carlos, 6627 – Unidade Administrativa II - 2º andar – Sala 2005 – Cep:31270-901 – BH-MG
Telefax: (031) 3409-4592 - e-mail: coep@prpq.ufmg.br

ANEXO 2

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Prezado paciente e/ou responsável:

Estamos realizando uma pesquisa intitulada “Ensaio clínico do tratamento da leucoplasia bucal com criocirurgia associada ou não ao laser de baixa intensidade”, com o objetivo de tratar a leucoplasia bucal, que é uma lesão presente na boca em diferentes localizações e muito comum. Este documento tem como finalidade propor sua participação nesta pesquisa. Gostaríamos de contar com sua colaboração, esclarecendo:

- A pesquisa consiste em preenchimento de ficha clínica própria e condução da criocirurgia, somente para os pacientes portadores da leucoplasia, fumantes ou não-fumantes.
- Todos os pacientes terão de ter diagnóstico clínico de leucoplasia e histopatológico de hiperqueratose (com ou sem atipia), para isto, têm de terem feito a biópsia;
- A criocirurgia consiste em um método que congela e “queima” a superfície onde a lesão se encontra. Para isto, anestesiamos e encostamos uma ponta congelada no local da sua lesão;
- Sua colaboração é muito importante e você não pagará nada por este exame nem pelo tratamento. Você participa se quiser. Se você assinar concordando em participar e se arrepender, você pode desistir a qualquer momento. Se você tiver alguma dúvida, pode perguntar que esclarecemos sempre que for necessário;
- Este tratamento é feito em 1 ou mais sessões, com retornos periódicos para avaliação clínica da lesão;
- O critério para a escolha da terapia (criocirurgia somente ou criocirurgia associada ao laser de baixa intensidade) para cada paciente será a ordem de atendimento;
- O atendimento será feito na Faculdade de Odontologia da UFMG, na Clínica 04.
- Os possíveis riscos deste estudo são a possibilidade do não desaparecimento total da lesão. Poderá haver algum desconforto, como uma dor de intensidade leve a moderada. O objetivo desta pesquisa também é avaliar a quantificação da dor, por isso, pedimos para prestar bastante atenção aos sintomas, se vier a desenvolver.
- Já o possível benefício é o desaparecimento total da lesão com apenas uma sessão de criocirurgia;
- O método convencional de remoção desta lesão é o cirúrgico.
- Todos os examinadores são dentistas e pesquisadores e estão aptos a fazer este exame e tratamento;

- Todos os seus dados serão confidenciais, sua identidade não será revelada publicamente, em hipótese alguma, e somente os pesquisadores envolvidos neste projeto terão acesso a estas informações, que serão utilizadas para fins de pesquisa;
- Desde já agradecemos sua colaboração. Os telefones dos pesquisadores para quaisquer esclarecimentos são: Adriana Spinola Ribeiro – 99536204 e Profª.Drª. Tarcília Aparecida Silva – 3409 2478.
- **COEP/UFMG**: Campus Pampulha: Unidade Administrativa II – Prédio da FUNDEP, 2º andar. Telefone: 3409-4592.

Eu, , estou ciente de ser portador(a) de leucoplasia bucal. Apresentando este diagnóstico clínico, concordo em participar de um estudo que objetiva tratar a leucoplasia bucal.

Após entender os objetivos e métodos da pesquisa descritos anteriormente, voluntariamente autorizo e aceito participar desta pesquisa. Comprometo-me também a fazer os retornos para avaliação e/ou necessidade de nova sessão de criocirurgia e do laser.

Tenho pleno conhecimento de que o principal objetivo é o tratamento da leucoplasia, com a possível remissão da lesão.

Dou pleno direito de uso dos dados para fins de pesquisa e de divulgação em jornais e/ou revistas científicas especializadas no País e no Exterior.

Declaro que li e entendi as informações fornecidas acima. Tive a oportunidade de fazer perguntas e todas as minhas dúvidas foram esclarecidas.

Belo Horizonte, de de 200 .

Assinatura do paciente ou responsável

Documento de Identidade

ANEXO 3

FICHA CLÍNICA

IDENTIFICAÇÃO DO PACIENTE

NOME

DATA DE NASCIMENTO COR SEXO

ENDEREÇO TELEFONE

CIDADE CEP

HÁBITOS

FUMANTE : SIM NÃO QUANTIDADE/DIA QUANTO TEMPO

SE PAROU, HÁ QUANTO TEMPO BEBIDA ALCOÓLICA:

CONDIÇÕES SISTÊMICAS

DIABETES

DISTÚRBIOS CARDIOVASCULARES

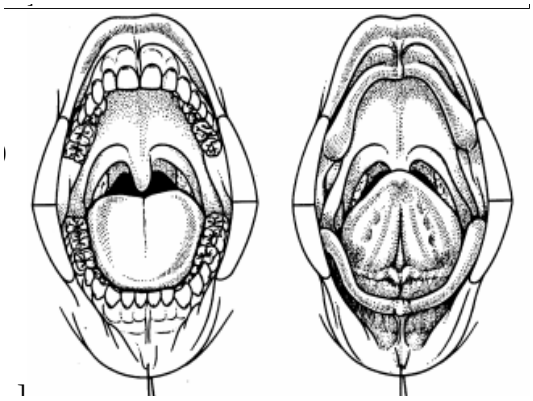
DISTÚRBIOS GASTROINTESTINAIS

AIDS

DOENÇA INFECTOCONTAGIOSA (HEPATITE,HERPES)

GRAVIDEZ

FAZ USO CONSTANTE DE ALGUM MEDICAMENTO?



EXAME INTRA-ORAL

ASPECTO CLÍNICO

TAMANHO

LOCALIZAÇÃO: BAIXO GRAU ALTO GRAU

LESÃO ÚNICA MÚLTIPLAS

BIÓPSIA INCISIONAL EXCISIONAL

RESULTADO HISTOPATOLÓGICO

HIPERQUERATOSE SEM ATIPIA

ATIPIA LEVE MODERADA SEVERA

GRUPOS

1.**Criocirurgia**

- Ciclos
- Sessão adicional
- Outras informações

2.**Criocirurgia/LBI**

- Ciclos
- Sessão adicional
- Uso do LBI:

    Antes

    Após

    48 horas

    72 horas

INÍCIO DA TERAPIA:

AVALIAÇÃO DA LESÃO: