MICHEL CAMPOS RIBEIRO

AVALIAÇÃO DO TRATAMENTO DE MALFORMAÇÕES VASCULARES BENIGNAS DE BAIXO FLUXO POR MEIO DE ESCLEROTERAPIA COM OLEATO DE MONOETANOLAMINA

Universidade Federal de Minas Gerais
Faculdade de Odontologia
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Tese apresentada ao Colegiado do Programa de Pós-Graduação da Faculdade de Odontologia da Universidade Federal de Minas Gerais, como requisito parcial para obtenção do grau de Doutor em Odontologia – área de concentração em Estomatologia.

Orientador: Prof. Dr. Ricardo Alves de Mesquita

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Aos meus amores terrenos, obrigado sempre...

Minha mãe, ***Dulce***
Meu pai, ***Francisco***
Meus irmãos, ***Bruno e Denize***
Minha esposa, ***Elisa***
Meu filhinho, ***Gabriel***

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“O sucesso é ir de fracasso em fracasso sem perder entusiasmo”

Winston Churchill

LISTA DE SÍMBOLOS E SIGLAS

MVBs	Malformações Vasculares Benignas
HEMs	Hemangiomas
MFVs	Malformações Vasculares
MA	Malformação Arterial
FAV	Fístula Arteriovenosa
MAV	Malformação Arteriovenosa
MV	Malformação Venosa
ML	Malformação Linfática
MCL	Malformação Capilar Linfática
MVC	Malformação Venosa Capilar
MLV	Malformação Linfática Venosa
MAC	Malformação Arterial Capilar
MCLV	Malformação Capilar Linfática Venosa
MCAV	Malformação Capilar Arterial Venosa
MCAVL	Malformação Capilar Arterial Venosa Linfática
UFMF	Universidade Federal de Minas Gerais
TCLE	Termo de Consentimento Livre e Esclarecido
EVA	Escala Visual Analógica

RESUMO

O objetivo deste trabalho foi avaliar a eficácia e segurança do agente esclerosante oleato de monoetanolamina (OM) em concentrações de 1,25%, 2,5%, 5% e na forma de espuma em estudo clínico prospectivo descritivo, no tratamento de malformações vasculares benignas (MVBs), na região de cabeça e pescoço. Na primeira fase, tratou-se 34 pacientes portadores de 36 MVBs menores que 20mm que procuraram o serviço de Patologia da Faculdade de Odontologia da UFMG. Estes pacientes receberam protocolo de tratamento com aplicação de OM nas concentrações de 1,25% (n=10), 2,5% (n=9) descritos por Johann et al(2005) e 5% (n=19) nas doses 1ml/cm, 1ml/cm e 0,1ml/3mm respectivamente. Avaliou-se primeiramente o grupo tratado por OM 5 %, que envolveu 19 pacientes e 15 MVBs, dividindo-se em dois grupos (G1 = ≥ 6,5mm e G2= ≤6,5mm) e foram avaliados quanto a: 1) Cura clínica segundo Achauer et al., (1997) , 2) dor/ardor segundo Manionn et al., (2007), 3) edema segundo Amaral et al., (2012), 4) o uso de analgésico, 5) úlcera, 6) alterações funcionais no pós-operatório (mastigação e fonação), 7) sangramento, 8) hematoma , 9) infecção, 10) cicatriz, 11) tempo de resolução 12) satisfação segundo Penarrocha et al., (2007) e 13) recorrência. Os dados foram analisados pelo programa EPI INFO 7™ (Center for disease Control and Prevention- CDC). O local mais acometido foi o lábio inferior (n=7). Dor e edema foram relatados respectivamente por 90% e 100% dos pacientes. Não ocorreram complicações e não foi relatado uso de analgésicos. A cura clínica ocorreu em 100% das MVBs. No período de acompanhamento não houve recidiva. O índice de satisfação foi 9 em média. Na segunda parte do estudo, realizou-se comparação entre as concentrações de OM 1,25%, 2,5% e 5% quanto ao número de sessões e volume final aplicado no tratamento de escleroterapia, utilizando-se SPSS 18.0 software (SPSS Inc., Chicago, IL), observou-se diferença estatística com $p<0,003$ e $p<0,001$(Teste Kruskal-Wallis - teste Mann Whitney- correção de Bonferroni) respectivamente, evidenciando-se menor volume final aplicado na concentração de OM a 5% e consequentemente o número de sessões no tratamento também foi menor para OM a 5%, mostrando segurança equilibrada entre as 3 concentrações e eficácia superior quando OM em concentração 5%. Na terceira etapa, trataram-se 17 pacientes portadores de 34 MVBs que procuraram o ambulatório de Cirurgia Endovascular do Hospital das Clínicas da UFMG. Estes pacientes receberam protocolo de tratamento com aplicação de OM 5% em Espuma na concentração de 1ml/1cm de lesão. Os mesmos parâmetros foram avaliados. O local mais acometido foi a língua (n= 8). Dor e edema foram relatados por 100% dos pacientes. Necrose superficial ocorreu em 9 pacientes. Pacientes não relataram uso de analgésicos. A cura das lesões ocorreu em 85%. No período de acompanhamento de 6 meses não houve recidiva. O índice de satisfação foi 9 em média. Teste exato de Fisher mostrou

diferença estatística na comparação das variáveis tamanho (≥ 30mm e ≤30mm) contra dose total, número de sessões e cura clínica ($p<0,0002$; $p<0,04$; $p<0,01$respectivamente) e na comparação satisfação (≤ 9,5 e ≥9,5) com a cura clínica ($p<0,0003$). Assim, o OM em espuma mostrou-se seguro e eficaz no tratamento de MVBs.

Palavras-chave: Escleroterapia, oleato de monoetanolamina, OM, 1,25%; 2,5%; 5%, lesões vasculares benignas, espuma.

ABSTRACT

The objective of this study was to evaluate the efficacy and safety of the sclerosing agent monoethanolamine oleate (MO) in concentrations of 1.25%, 2.5%, 5% and in the form of foam descriptive prospective clinical study in the treatment of benign vascular lesions (BVLs) in the head and neck. In the first phase, we treated 34 patients with 36 smaller than 20 mm BVLs who sought the Pathology Clinical of the School of Dentistry (UFMG). These patients received treatment protocol application OM in concentrations of 1.25% (n = 10), 2.5% (n = 9) described by Johann et al (2005) and 5% (n = 19) in doses 1ml / cm,1ml / cm and 0.1 ml / 3mm respectively. Inittialy the group treated by OM 5%, which involved 19 patients and 15 LVBs, divided into two groups (G1 = ≥ 6.5 mm and G2 = ≤6,5mm) and were evaluated for: 1) Healing Clinical second Achauer et al., (1997), 2) pain / burning second Manionn et al., (2007), 3) edema according to Amaral et al., (2012), 4) the use of analgesic, 5) ulcer, 6) functional changes postoperatively (chewing and speech), 7) bleeding, 8) hematoma, 9) infection, 10) scar, 11) resolution time 12) satisfaction seconds Penarrocha et al., (2007) 13) recurrence. Data were analyzed by EPI INFO 7 ™ program (Center for disease Control and Prevention- CDC). The most frequent site was the lower lip (n = 7). Pain and swelling were reported respectively by 90% and 100% of patients. It did not occur complications and was not reported use of analgesics. The clinical healing has occurred in 100% of BVLs. At follow-up there was no recurrence. The satisfaction rate was 9 on average. In the second part of the study was performed comparing the OM concentrations 1.25%, 2.5% and 5% of the number of sessions and the final volume applied in sclerotherapy treatment, using the SPSS 18.0 Software (SPSS Inc., Chicago, IL), there was statistical difference with $p < 0.003$ and $p < 0.001$ (Kruskal-Wallis test - Mann Whitney- Bonferroni correction) respectively, demonstrating less final volume applied to the concentration of OM to 5% and consequently the number of treatment sessions for OM was lower than 5%, showing healthy and balanced between the three security levels and superior efficacy OM 5% concentration. In the third stage, treated 17 patients with 34 BVLs who sought the Endovascular Surgery Outpatient Clinic of the Clinical Hospital. These patients received treatment protocol implementation OM Foam 5% at a concentration of 1 ml / 1cm of lesion. The same parameters were evaluated. The most frequent site was the tongue (n = 8). Pain and swelling were reported by 100% of patients. Superficial necrosis occurred in 9 patients.

Patients reported no use of painkillers. Healing of the lesions occurred in 85%. At 6 months follow-up there was no recurrence. The satisfaction rate was 9 on average. Fisher's exact test showed statistical differences in the size variables (≥ 30mm and ≤30mm) against total dose, number of sessions and clinical cure ($p < 0.0002$; $p < 0.04$; $p < 0,01$respectivamente) and Compared satisfaction (≤ 9.5 and ≥9,5) with clinical cure ($p < 0.0003$). Thus, OM foam was safe and effective in treating BVLs.
Keywords: Sclerotherapy, moniethanolamine oleate (OM), 1.25%; 2.5%; 5%, benign vascular lesions (BVLs), foam.

SUMÁRIO

1. INTRODUÇÃO

As malformações vasculares benignas (MVBs) são anomalias vasculares comuns na região de cabeça e pescoço, apresentam-se de variados tamanhos, desde poucos milímetros a grandes lesões.

As anomalias vasculares são, muitas vezes, congênitas desenvolvendo-se juntamente com o indivíduo. Aquelas que involuem até os dois anos de idade denominam-se Hemangiomas, considerados os tumores mais comuns da infância. As que persistem durante a vida são consideradas como Malformações Vasculares (Mulliken e Glovacki, 1982).

As MVBs variam em relação ao componente sanguíneo presente em seu interior, podendo ser constituído de sangue arterial, arterio-venoso, venoso ou linfático. Estes componentes associados à localização da lesão e características do indivíduo portador, definirão os possíveis tratamentos (Krishna Das and Hoque, 2008). Os tratamentos mais comuns para as MVBs são: escleroterapia, cirurgia, embolização e laserterapia (Coletti et al., 2013).

Sabe-se que a presença dessas lesões repletas de sangue em face ou no interior da cavidade bucal pode predispor o indivíduo a graves hemorragias em caso de trauma, além de compressão de via aérea. Podem também comprometer o funcionamento normal do sistema estomatognático (fonação, deglutição e mastigação), e influenciar na estética do indivíduo e em seu convívio social.

Desta forma, visa-se com este trabalho avaliar parâmetros que demostrem a viabilidade da escleroterapia com oleato de monoetanolamina, que é um medicamento de custo reduzido e de fácil acesso, quanto a sua eficácia e segurança no tratamento de MVBs na região de cabeça e pescoço puro e em forma de espuma.

2. REVISÃO DE LITERATURA

As malformações vasculares benignas (MVBs) são anomalias vasculares comuns, representando-se em 50% dos casos na região de cabeça e pescoço (Zhou et al.., 2011). A classificação destas lesões sempre foi complexa e, em 1982, Mulliken e Glowacki as classificaram em: Hemangiomas (HEMs) e Malformações Vasculares (MFVs). (Gontijo et al., 2004; Arpaslan et al., 2009). Elas seriam assim categorizadas baseadas nas características celulares, aspectos clínicos e história natural da doença.

Os HEMs são os tumores mais comuns da infância, atingindo de 2 a 3% das crianças, e alcançando cerca de 10% em prematuros de baixo peso. Estas caracterizam-se por apresentar proliferação das células endoteliais, sendo considerados tumores verdadeiros. Podem estar presentes ao nascimento em apenas 40% dos casos (geralmente sob forma de lesões precursoras), apresentar crescimento rápido pós-nascimento seguido de involução espontânea lenta e mostrar uma relação de frequência entre mulheres e homens de 5:1. Podem, ainda, causar ulceração, dor, sangramento, infecção secundária e deformação tecidual (Mulliken e Glovacki, 1982, Buckmiller et al., 2010).

Os HEMs apresentam-se em três fases: a proliferativa, a de regressão e a regredido. *A fase proliferativa* corresponde ao período de maior crescimento da lesão, ocorrendo entre o nascimento e primeiro ano de vida do indivíduo. Histologicamente, observa-se atividade aumentada das células endoteliais, associada ou não ao desenvolvimento de um lúmem vascular. *A fase de regressão* ocorre do primeiro ao sétimo ano de vida. Nesta fase, observa-se dilatação do lúmem vascular e diminuição da celularidade. *A fase regredido* ocorre após regressão total da lesão, evidenciando poucos capilares finos constituídos por endotélio maduro (Mulliken e Glowacki,1982).

Os HEMs sintomáticos localizados em regiões críticas (globo ocular, por exemplo), os volumosos e os que determinam efeitos compressivos locais requerem intervenção. Estes, respondem aos corticóides, beta bloqueadores, interferon alfa e cirurgia. A escleroterapia não tem papel nestas lesões (Enermann et al., 2010; Buckmiller et al., 2010, Greene AK, 2012).

As MFVs são menos comuns, compreendendo 1,5% de todos os casos reportados das MVBs (Kohout et al.,1998; Enermann et al., 2010; Zhou et al., 2011). Acometem frequentemente os tecidos moles, sendo as lesões primárias intraósseas uma condição rara (Unni, 1971). Estas apresentam 90% das lesões reconhecidas ao

nascimento. Apresentam crescimento proporcional ao da criança e não involuem espontaneamente. A proporção entre sexo feminino/masculino é de 1:1. As MFVs relacionam-se a uma anormalidade do desenvolvimento embriogênico, sendo consideradas uma anomalia estrutural. Histologicamente os vasos sanguíneos com endotélio maduro e ciclo normal das células endoteliais podem ser observadas (Mulliken e Glowacki,1982). São categorizadas conforme a natureza dos canais vasculares: capilares, arteriais, venosos ou linfáticos. Pode-se observar a coexistência dos diferentes vasos em uma mesma lesão. Além disso, várias afecções apresentam características, padrões de distribuição e associações com outras alterações morfológicas comuns sendo referidas como síndromes, denominadas por epônimos (Gontijo et al., 2004). Podem causar alterações estéticas, funcionais, hemorragias por trauma direto, compressão, dor e trombose. São classificadas, quanto ao fluxo: em baixo fluxo (componente venoso) e alto fluxo (componente arterial ou arteriovenoso); e quanto à localização em: localizadas ou difusas (Mulliken e Glovacki, 1982; Enermann et al., 2010).

As MFVs de alto fluxo compreendem malformação arterial (MA), fístula arteriovenosa (FAV) ou malformação arteriovenosa (MAV). As de baixo fluxo incluem: malformação venosa (MV), malformação linfática (ML) e malformação capilar (MC). Temos também as malformações complexas combinadas, nas quais a maioria das síndromes com epônimos se encaixa: malformação capilar linfática (MCL), venosa capilar (MVC), linfática venosa (MLV), arterial capilar (MAC), capilar linfática venosa (MCLV), capilar arterial venosa (MCAV) e capilar arterial venosa linfática (MCAVL) (Fishman e Mulliken, 1993; Enjouras e Mulliken, 2000).

A Sociedade Internacional para o Estudo de Anomalias Vasculares em 1996 adotou a classificação em tumores (hemangioma e outros tumores) e malformações vasculares (capilar, venosa, linfática, arterial e combinada). No entanto, esta dicotomia não é absoluta, podendo haver a coexistência de tumores e malformações (Gontijo et al., 2004).

O diagnóstico é realizado por meio de exame clínico e manobras semiotécnicas como a diascopia ou vitropressão. Pode-se solicitar ao paciente para manter a cabeça abaixada por alguns minutos e ao levantar observa-se o enchimento da mesma por sangue (Li et al., 2010). Exames de imagem (radiografias, tomografias, ressonância magnética e exames de ultrassons) (Burrows et al., 1998; Ozaki et al., 2010) colaboram para a delimitação anatômica. Além disso, podem contribuir na

determinação de diagnósticos diferenciais, ou para detectar a presença de anomalias associadas, auxiliando na definição do tratamento. A abordagem multidisciplinar é necessária não somente para o diagnóstico, mas também para o tratamento das MFVs (Gontijo et al., 2004).

O tratamento a ser indicado para as MFVs é dependente da idade do paciente, do tamanho das lesões e das características clínicas. As opções terapêuticas são diversas e incluem: escleroterapia, uso de corticóide sistêmico ou interferon alfa, aplicação de laser ou radiação, crioterapia, embolização ou remoção cirúrgica (Muto et al., 1990; Sadeghy et al., 1991; Deams et al., 1992; Tamoyo et al., 1997; Onesty et al., 2003;Correa et al., 2007; Colleti et al., 2014).

As MFVs de alto fluxo são tratadas através da embolização seletiva por catéter dos ramos arteriais. Quando de baixo fluxo, as lesões são abordadas pela escleroterapia através de punção direta. As MFVs não respondem aos medicamentos utilizados para o tratamento dos hemangiomas (Enermann et al., 2010; Buckmiller et al., 2010, Greene AK 2012). A escleroterapia é considerada um tratamento seguro e eficaz para as MFVs de baixo fluxo, com taxa de sucesso variando de 70 a 100% (Lee et al., 2001; Johann et al., 2005; Correa et al., 2007; Enermann et al., 2010; Costa et al., 2011).

A utilização de esclerosantes químicos em lesões vasculares iniciou-se na França com Jean Charles Pravaz em 1841, que injetou percloreto de ferro para o tratamento de varizes dos membros inferiores (Zanettini et al., 2005). Estas substâncias provocam reação inflamatória na parede dos vasos sanguíneos, levando à necrose e obliteração do mesmo (Ozaki et al., 2010).

A escleroterapia consiste na punção direta da MFVs, com o auxílio de Jelco ou Scalp. Aspira-se o sangue para confirmar a punção e procede-se à injeção do agente esclerosante (Zanettini et al., 2005; Costa el al., 2011). Os agentes esclerosantes mais utilizados na atualidade são: polidocanol (1 a 3%), glicose hipertônica, álcool, salina hipertônica e oleato de monoetanolamina (5%) (Johann et al., 2005; Costa et al., 2011). A anamnese completa com investigação de possíveis antecedentes alérgicos aos medicamentos é necessária para se evitar complicações (Costa el al., 2011).

Segundo Johann et al. (2005), o tratamento com a escleroterapia em MFVs de baixo fluxo da cavidade oral consiste de aplicações de 1 ml de oleato de monoetanolamina (1,25% ou 2,5%) para cada cm^2 de lesão. A aplicação do agente esclerosante deve ser realizada de forma lenta, gradual e nunca superficial devido ao

risco de necrose local. Anti-inflamatórios ou analgésicos podem ser prescritos no pós-operatório, além de aplicação tópica de gelo (Zanettini et al., 2005; Costa et al., 2011). São realizadas de 1 a 3 sessões de aplicação do agente esclerosante, de acordo com a extensão da lesão, com intervalo mínimo de uma semana entre elas (Johann et al., 2005; Costa et al., 2011).

Costa et al. (2011) utilizaram este mesmo esclerosante - oleato de monoetanolamina - porém a 5%, na dose de 0,1ml/cm de lesão, com sucesso em 98,2% dos casos de MVBs em cavidade bucal. Na grande maioria dos casos, observou-se melhora em apenas uma sessão, apresentando reduzida taxa de complicação.

A escleroterapia para tratamento de MVBs é considerada um tratamento seguro e eficaz, minimamente invasivo, de fácil aplicação, de baixo custo e com poucas implicações pós-operatórias (Trembley et al., 1985; Johann et al., 2005; Costa et al., 2011). As complicações são dose/dependente e as mais comuns são: edema, dor, úlcera e necrose. Raras e complexas complicações também podem ser observadas tais como: choque anafilático e alterações renais (hemólise intravascular e hemoglobinúria) (Choi et al., 2002; Hiodoh et al., 2008). Desta forma, alguns autores (Matsumoto et al., 2003) indicam o uso de oleato de monetanolamina (5%) em doses menores que 1ml/sessão. A dose máxima em humanos descrita na bula do medicamento é de 20ml ou 0,4ml/kg em paciente de 50 Kg (Anvisa-2009).

Para tratamento de lesões vasculares maiores desenvolveu-se uma variação do tratamento convencional – a escleroterapia em espuma. Esta técnica foi desenvolvida e descrita por Orbach em 1944 e consiste em misturar ar ao agente esclerosante, formando-se uma espuma. Esta aumenta a área de contato do agente esclerosante com a parede do vaso sanguíneo, potencializando seu efeito. O agente esclerosante mais comumente utilizado na forma de espuma é o polidocanol entre 1 e 3% (Tan e Tan, 2009; Tessari, 2000; Tessari, 2001). Atualmente diversos autores a utilizam, variando-se o agente esclerosante e o ar misturado (ar, oxigênio, gás carbônico) (Rehman et al., 2009).

A técnica da obtenção de espuma foi modificada por TESSARI em 2000. Duas seringas de 10 ml são acopladas a uma torneira de três vias, uma com ar e a outra com o agente esclerosante O líquido é enviado de uma seringa para a outra, misturando-se com o ar, em um total de 20 ciclos. Como a espuma se liquefaz com o

tempo, deve ser injetada na lesão, obrigatoriamente, em até dois minutos (Rehman et al., 2009).

A técnica da espuma é utilizada para o tratamento de diversas lesões vasculares. O agente mais utilizado para a formação de espuma, o polidocanol (1 a 3%) pode estar associado ou não a outras drogas como corticosteróides (Mimura et al., 2009; Grover et al., 2010; Yilmaz et al., 2011). Este apresenta poucos efeitos colaterais, como menor risco de toxicidade sistêmica, de alergias, de dor durante injeção, além do desenvolvimento de úlceras (Grover et al., 2010).

Segundo Rehman et al. (2009), as vantagens obtidas com o tratamento de MFVs por meio da técnica de escleroterapia com espuma com tetradecilsulfato de sódio incluem a fácil manipulação da droga e a fácil execução da técnica, o baixo custo, a redução da quantidade do agente esclerosante, a reduzida morbidade, a ausência da necessidade de internação hospitalar, a possível redução do número de sessões de tratamento e os resultados mais duradouros. Dentre as desvantagens, pode-se observar dor, edema, ulceração e a possibilidade de formação de êmbolos que podem atingir a corrente sanguínea (Buckmiller et al., 2010).

O oleato de monetanolamina em forma líquida apresenta boa evidência no tratamento de lesões vasculares da cavidade oral, com excelentes resultados (Johann et al., 2005; Zanettini et al., 2005; Kaiji et al., 2009; Costa et al., 2011). No entanto, a literatura mostra a diluição deste agente esclerosante antes da aplicação sendo pouco utilizado na sua forma de oleato de monoetanolamina a 5% em concentrações maiores. Não obstante, não há dados na literatura da utilização do oleato de monoetanolamina a 5% em forma de espuma para o tratamento das MVBs na região de cabeça e pescoço.

Dessa forma, diante da maior eficácia da escleroterapia com a técnica de espuma quando comparada a escleroterapia convencional, o baixo custo e a eminente necessidade de se consolidar o uso do oleato de monoetanolamina a 5% no tratamento das MVBs, acrescido da ausência de publicações do oleato de monoetanolamina 5% em espuma, fazem-se necessários trabalhos que visam investigar a eficácia e segurança quanto ao uso da escleroterapia a 5% em concentrações maiores, realizar comparações entre algumas concentrações da droga e avaliar pioneiramente a espuma de oletao de monetanolamina (5%) para escleroterapia das MVBs na região de cabeça e pescoço.

3. JUSTIFICATIVA

A escleroterapia com oleato de monoetanolamina 5% encontra-se bem documentada na literatura no que se refere ao uso da droga em diluições e concentrações baixas, porém, faz-se pertinente avaliar a eficácia e a segurança do tratamento de MVBs na região de cabeça e pescoço por escleroterapia com oleato de monoetanolamina a 5% puro e em forma de espuma, na tentativa de se indicar uma concentração ideal da droga que proporcione melhores resultados nestes tratamentos. Certo de que, seu uso em forma de espuma não foi relatado até o momento na literatura vigente.

4. OBJETIVOS

4.1. Objetivo geral

Avaliar a eficácia e segurança do oleato de monoetanolamina, no tratamento por escleroterapia de MVBs na região de cabeça e pescoço.

4.2. Objetivos específicos

Avaliar a eficácia e segurança do oleato de monoetanolamina a 5% para o tratamento de MVBs na região de cabeça e pescoço, em lesões com tamanho de até 20mm.

Avaliar a eficácia e segurança do oleato de monoetanolamina em concentrações distintas (1,25%; 2,5%; 5%) no tratamento de MVBs na região de cabeça e pescoço, em lesões com tamanho de até 20mm.

Avaliar a eficácia e segurança do oleato de monoetanolamina a 5% em espuma para o tratamento de MVBs na região de cabeça e pescoço, em lesões com tamanho acima de 20mm.

5. HIPÓTESE

O oleato de monoetanolamina a 5% puro e em espuma para tratamento de MVBs na região de cabeça e pescoço será eficaz e seguro.

6. METODOLOGIA

6.1. Desenho do estudo

Este estudo apresenta-se em três etapas. Primeiramente, foi realizado estudo descritivo prospectivo tipo série de casos, de pacientes que tiveram lesões diagnosticadas como MVBs com até 20mm de extensão e foram tratadas com escleroterapia com oleato de monoetalonamina a 5% (Ethamolin®) na dosagem de 0,1/3mm de lesão. O estudo foi realizado na clínica de Patologia, Estomatologia e Radiologia Odontológica da Faculdade de Odontologia da Universidade Federal de Minas Gerais (UFMG), no período de 2011 a 2013. A segunda etapa do estudo desenvolveu-se por meio de estudo comparativo para se avaliar segurança e eficácia entre as concentrações de 1,25%; 2,5% (Johann et al., 2005) e 5%. Na terceira etapa, realizou-se estudo descritivo prospectivo tipo série de casos e foi conduzida em pacientes que tiveram diagnóstico de MVBs na região de cabeça e pescoço, com tamanho de superior a 20mm, estes foram tratados por escleroterapia com Ethamolin® a 5% em forma de espuma, na dose de 1ml/1cm de lesão. O estudo foi realizado no ambulatório da Cirurgia Endovascular do Hospital das Clínicas da UFMG, no período de 2011 a 2013.

Todos os pacientes incluídos no estudo procuraram o serviço Patologia e Semiologia Odontológicas da Faculdade de Odontologia da UFMG ou o ambulatório de Cirurgia Endovascular do Hospital das Clínicas da Faculdade de Medicina da UFMG.

Os critérios de inclusão no estudo consistiram em: pacientes que apresentaram diagnóstico de MVBs na região de cabeça e pescoço e apresentaram queixas funcionais e/ou estéticas relativas às lesões, além de concordarem com Termo de Consentimento Livre e Esclarecido (TCLE) apresentado. Foram excluídos os pacientes portadores de lesões vasculares de alto fluxo e que à anamnese relataram reações alérgicas aos medicamentos utilizados neste tratamento que incluiu o anestésico tópico (Xylocaína pomada 5%- Astra Zeneca, Cotia/SP), anestésico injetável (Xylestesin® a 2% sem vaso- Cristália, Itapira/SP), antisséptico (Clorexidina 0,12 ou 2 % - Rioquímica, São José do Rio Preto/SP) e o agente esclerosante (oleato de monetanolamina a 5%- Ethamolin®- Zest Farmacêutica Ltda, Rio de Janeiro/RJ), pacientes com alterações sistêmicas graves e que relatassem gravidez. Além de pacientes que não concordassem em assinar TCLE.

Este estudo foi submetido à avaliação do Comitê de Ética (Plataforma Brasil) foi apreciado e aprovado pelos Departamentos de Clínica, Patologia e Cirurgia Odontológicas da Faculdade de Odontologia e de Cirurgia da Faculdade de Medicina ambos da UFMG.

Os critérios de avaliação do estudo seguem-se com suas especificações:

1) Cura clínica da lesão, segundo escala de Achauer et al (1997), onde as lesões foram categorizadas em:

1- Excelente resposta (75-100% de cura)
2- Boa resposta (50-74% de cura)
3- Parcial resposta (25-49% de cura) e
4- Pobre resposta (0-24% de cura).

2) Avaliação do edema, segundo Amaral et al (2012), onde o paciente foi questionado sobre o desenvolvimento do edema após o tratamento das LVBs (presente ou ausente) e por quanto tempo persistiu.

3) Avaliação da dor pós-operatória no período de 7 dias após tratamento através da aplicação de escala visual analógica (EVA), segundo Manion et al. (2007) (fig 1).

Figura 1 - Avaliação da dor no período pós-operatório

Fonte: Escala visual analógica numérica proposta por Mannion et al (2007), utilizada para pacientes acima de seis anos de idade.

4) Avaliação clínica de recorrência no acompanhamento.

5) Avaliação do nível de satisfação do paciente diante do tratamento através de escala visual analógica (EVA), segundo Peñarrocha et al. (2007) (fig 2).

Figura 2 – Nível de satisfação do paciente

Fonte: Escala visual analógica proposta por Peñarrocha et al (2007), utilizada para medir a satisfação, onde 0 seria totalmente insatisfeito e 10 extremamente satisfeito.

6) Avaliação sobre complicações decorrentes do tratamento (Necrose).

6.2 Primeira etapa do estudo

Estudo descritivo prospectivo tipo série de casos.

a) Pacientes

Foram incluídos nesse estudo os pacientes que, no período de 2011 a 2013, compareceram à clínica de Patologia, Estomatologia e Radiologia da Faculdade de Odontologia da UFMG, portadores de lesões na cavidade bucal e lábios cujo diagnóstico clínico (exame e diascopia) foi de MVBs, com tamanho até 20mm e que apresentaram queixa estética e/ou funcional, referentes às lesões. Todos deveriam assinar o TCLE para início do tratamento. Foram registradas todas as informações sobre os pacientes referentes à anamnese, informações sobre alterações sistêmicas, localização da MVBs e tipo de tratamento a ser realizado.

O tratamento instituído foi escleroterapia com Ethamolin® 5% em todas as MVBs, sendo um tratamento ambulatorial. Todos os pacientes estavam em sua perfeita sanidade mental e em bom estado geral, não relataram alergia aos medicamentos utilizados: anestésico tópico Xylocaína pomada 5% e Ethamolin® 5% e todos concordaram e assinaram o TCLE.

Os pacientes foram acompanhados pós tratamento por 6 meses, sendo que semanalmente no primeiro mês e, após, mensalmente, até o sexto mês pós tratamento. Nos casos em que se fez necessária mais de uma sessão de tratamento, respeitou-se intervalo descrito na literatura (Johann et al., 2005; Costa el al., 2011) de 14 dias.

No retorno após a sessão de escleroterapia, o paciente foi questionado sobre dor, edema e complicações. Em relação à dor pós-operatória, foi fornecida ao paciente uma EVA para que assinalasse no período de 7 dias qual a intensidade da dor. Quanto ao edema, o paciente relatou se neste mesmo período o edema se fez presente ou ausente. Ao final do tratamento que se deu após 6 meses da última aplicação, questionou-se sobre satisfação frente ao tratamento, aplicando-se EVA para que assinalasse, sendo que o 0 equivalente a insatisfeito e o 10 extremamente satisfeito. Também se avaliou quanto à recorrência e à cura das lesões (Achauer et al, 1997).

b) Procedimento Terapêutico

Os pacientes foram preparados para o procedimento seguindo-se as normas de antissepsia com Clorexidina 0,12 ou 2% (Rioquímica- São José do Rio Preto/SP). Seguiu-se com anestesia tópica (Xylocaína pomada 5%- Astra Zeneca, Cotia/SP) durante 90 segundos friccionando anestésico com gaze sobre a lesão, no intuito de diminuir desconforto à punção no momento de injeção do agente esclerosante. Realizada a anestesia, com uma seringa ultrafina de insulina de 1ml (Becton, Dickinson, and Company, Franklin Lakes,NJ) era aspirado Ethamolin® da ampola. Em seguida, a MVB era puncionada e realizada manobra de aspiração para certificar que o centro da lesão foi atingido, assim, o sangue era observado em seu interior. Finalizando o procedimento, injetou-se 0,1ml de Ethamolin® para cada 3 milímetros de lesão. Os pacientes seguiram orientação pós-operatória para fazer uso de analgésicos se por acaso sentissem dor.

6.3. Segunda etapa do estudo

a) Pacientes

Foram incluídos neste estudo os pacientes que, no período de 2011 a 2013, compareceram à clínica de Patologia, Estomatologia e Radiologia da Faculdade de Odontologia da UFMG e ou ao ambulatório de Cirurgia Endovascular do Hospital das Clínicas da Faculdade de Medicina da UFMG, que, após exame clínico, foi diagnosticado MVB, com tamanho superior a 20mm e que apresentaram queixa

estética e/ou funcional, referentes às lesões. Todos deveriam assinar o TCLE para início do tratamento. Foram registradas todas as informações sobre os pacientes referentes à anamnese, informações sobre alterações sistêmicas, localização da MVBs e tipo de tratamento a ser realizado, seguindo a ficha de anamnese do projeto (APÊNDICE C).

O tratamento instituído foi a escleroterapia com Ethamolin® 5% com Espuma em todas as MVBs, sendo um tratamento ambulatorial. Todos pacientes estavam em sua perfeita sanidade mental e em bom estado geral, não relataram alergia aos medicamentos utilizados: antisséptico Clorexidina 0,12 ou 2% (Rioquímica- São José do Rio Preto/SP), anestésico injetável (Xylestesin® a 2% sem vaso- Cristália, Itapira/SP) e Ethamolin® 5% e todos concordaram e assinaram o TCLE.

Os pacientes foram acompanhados pós tratamento por 6 meses, sendo que semanalmente no primeiro mês e, após, mensalmente até o sexto mês pós tratamento. Nos casos que em que se fez necessária mais de uma sessão de tratamento, respeitou-se intervalo descrito na literatura de 14 dias (Johann et al., 2005; Costa el al., 2011).

No retorno após a sessão de escleroterapia em espuma, o paciente foi questionado sobre dor, edema e complicações. Em relação à dor pós-operatória, ela foi aferida aplicando-se ao paciente a EVA e isto foi feito em dois momentos: no pós-operatório imediato e no retorno, após 7 dias. Quanto ao edema, o paciente foi questionado se no pós operatório ele se fez presente ou ausente e por quanto tempo ele persistiu. Ao final do tratamento, que se deu após 6 meses da última aplicação, questionou-se sobre satisfação frente ao tratamento, aplicando-se EVA para que assinalasse, sendo que o 0 equivalente a insatisfeito e o 10 extremamente satisfeito. Também se avaliou quanto à recorrência e à cura das lesões (Achauer et al., 1997).

b) Procedimento Terapêutico

Os pacientes foram preparados para o procedimento seguindo-se as normas de assepsia e antissepsia. Seguiu-se com anestesia infiltrativa (Xylestesin® a 2% sem vasoconstritor- Cristália, Itapira/SP), sendo aplicado em todas as lesões 1ml da solução anestésica.

Em sequência, com uma seringa (Becton Dickinson, Curitiba, Paraná, Brasil) de 10ml, aspirou-se 2ml do agente esclerosante oleato de monoetanolamina a 5%

(Ethamolin ® - Zest Farmacêutica Ltda, Rio de Janeiro, Rio de Janeiro, Brasil) e em outra seringa também de 10ml, aspirou-se 8ml de ar (3:1). Assim, as duas seringas foram acopladas e interligadas por uma torneira de três vias (Embramed, São Paulo, São Paulo, Brasil). Posteriormente, para formação da Espuma, foram realizados 20 ciclos de transferência do conteúdo de uma seringa para outra, seguindo técnica de Tessari, 2001. Para a aplicação da Espuma intralesional, realizou-se punção do centro da LVB com “scalp” ou jelco 25G (Embramed, São Paulo, São Paulo, Brasil) conectando a seringa com a Espuma. Realizou-se aspiração para certificar-se do posicionamento correto e injetou-se a Espuma na lesão no tempo máximo de 2 minutos, tempo de estabilidade da Espuma.

Todas as lesões foram medidas antes da aplicação inicial por régua flexível e receberam 1ml de espuma para cada 1 centímetro de lesão, sendo que o volume máximo aplicada a cada sessão foi de 8 ml de Espuma.

Os pacientes seguiram orientação pós-operatória para fazer uso de analgésicos, se por acaso sentissem dor.

7. ANÁLISE ESTATÍSTICA DOS DADOS

Os dados foram submetidos à análise estatística utilizando o software SPSS (versão 17.0, Chicago, IL, USA). Para as variáveis categóricas, o exato de Fisher foram aplicados. Significância estatística foi alcançada quando os valores de $p \leq 0.05$.

8. RESULTADOS

ARTIGO 1[1]

EFFICACY AND SAFETY OF THE SCLEROTHERAPY WITH 5% ETHANOLAMINE OLEATE IN BENIGN ORAL VASCULAR LESIONS: EXPERIENCE WITH A CASE SERIE

INTRODUCTION

Benign anomalies of vascular origin are common in head and neck region, including oral cavity. Although their classification can be controversy, they are diagnosed as hemangioma (Hem), vascular malformation (VM) or varix, considering the clinical features, biologic behavior, and histological aspects (Mulliken and Glowacki 1982, Finn et al., 1983)

Hem, the most common tumor encountered in infancy (Torer et al 2007), is predominant in premature, low birth-weight, Caucasians, female infants, with prevalence up to 10% of population (Haggstrom et al, 2007; Drolet et al, 2008). Hem show three stages: proliferating (increase of the endothelial cellular activity - birth and first year old), regression (dilation of the vascular lumen and decreasing cellular activity - one to seven years old) and regressed (few tiny capillary-like feeding vessels and draining veins lined by flat mature endothelium) (Mulliken and Glowacki, 1982).

VM, a dysfunction of embriogenic and vasculogenesis regulator components, is present at birth in both gender and shows incidence of 1-4% (Stringel, 2000; Buckmiller, 2004). The causal factors include trauma, infection, hormonal alterations and/or progressive increase (growth) with age. Unlike Hem, VM never involutes. VM is classified as slow-flow (venous component) and high-flow (arteriovenous component) by International Society of Vascular Anomalies (Buckmiller et al., 2010; Kohout et al 1998). VM and Hem may cause cosmetic distress, pain, ulceration, bleeding, secondary infection, tissue deformation, dental asymmetry, impaired speech and

[1] Este artigo será enviado para a revista: Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology

obstruction of the upper airways (Enjouras and Mulliken, 1997; Dubois et al, 2001; Johnson et al 2002).

Varix, an acquired benign vascular lesion, asymptomatic, is characterized by an extensive and abnormal vein and presents a relative frequency of 16.2% in oral cavity (Kovac-Kovacic e Skaleric, 2000). It is more frequent in old persons (up 60 years of age) in sublingual region, but may appear on the lips and buccal mucosa (Johann et al, 2005; Correa et al, 2005).

The treatment to benign oral vascular lesions (BOVL) include sclerotherapy, surgical therapy, embolization, laser therapy, systemic corticosteroids, cryotherapy, interferon α and radiation therapy (Muto et al., 1990; Van Doorne et al., 2002; Johann et al., 2005; Yang et al., 2009; Hiraoka et al., 2012). The choice of treatment depends of the size, location, hemodynamics of the lesion, degree of invasion into anatomic structures, age of the patient and viability of the technique to be employed (Hanemann et al., 2004; Hiraoka et al., 2012). The American Academic of Dermatology described the importance and need of the treatment of vascular anomalies (Frieden, 1997)

Sclerotherapy is an important for the treatment of BOVL because it is an effective and noninvasive technique, with healing rate of 70% to 100% (Johann et al., 2005; Costa et al., 2011). Although there are many sclerosant agents as sodium morrhuate, sodium psylliate, quinine urethrone, ethanolamine oleate (EO), polidocanol, sodium tetradecil sulfate, hypertonic saline and absolute alcohol, the EO is useful due its low toxic effect compared with other sclerosis-inducing agents (Johann et al., 2005; Dilsiz et al., 2009, Costa et al., 2011).

EO is an unsaturated fatty acid that acts as a sclerosant agent when injected intravenously (Choi et al., 2002). It has been widely used in the management of the esophageal varix (Iso et al, 1988; Nishida et al, 1999) and BOVL (Johann et al, 2005; Costa et al, 2011; Hiraoka et al, 2012.). It acts primarily causing the irritation to intima by endothelial vein and produces a sterile inflammatory response (Nishida et al., 1999), resulting in fibrosis of the vessel wall or a possible vein occlusion. EO also diffuses rapidly through the vessel wall and produces an inflammatory extravascular (Kaji et al., 2009).

The possible complications can be related to dose/concentration of EO applied to the vascular lesion that vary since 1.25% to 5%. Johann et al., (2005) didn`t found difference between the concentrations and the number of sessions when compared

1.25% or 2.5% applying 1ml of EO. Costa et al., (2011) used 5% EO at 0.1ml/cm of lesion. The author's didn´t observe any complications.

In accordance to the efficacy and safety`s data yet demonstrated on previous literature, the current study aimed to verifying the efficacy and safety of sclerotherapy with 5% EO at 0.1ml/3mm of lesion to treatment of BOVL, the incidence of complications and the satisfaction´s of the patients submitted to this protocol of treatment. Additionally, it was used EO in 5% concentration with aim of the decreased number of session to total clinical healing of BOVL.

PATIENTS AND METHODS

Institutional review board

The study protocol conformed to the guidelines of the 1975 Declaration of Helsinki and the Committee of Bioethics in Research at the Universidade Federal de Minas Gerais approved the protocol of this study (551.062).

Patient's population

Fifteen patients with BOVL were included in this case serie study. All patients were recruited and treated consecutively in Oral Pathology Clinic of the Universidade Federal de Minas Gerais (UFMG) in the period from 2011 to 2013.

The diagnosis of BOVL was in accordance to the Mulliken and Glowacki (1982) criteria. The indications for treatment included pain, growth, swelling, pressure and esthetics complain. All the lesions diagnosed as BOVL were treated with 5% EO (Zest Farmacêutica, Ltda, Rio de Janeiro, RJ).

Study drug

EO is a synthetic mixture of ethanolamine and oleic acid with an empirical formula C20H41NO3. EO acts as a sclerosant drug when applied intravenously, and the oleic acid component is responsible for its ability to induce inflammation and fibrosis in the endothelium (Choi et al., 2002). It is prepared in 50 mg per ml of aqueous solution. Oleic acid also may activate coagulation by inducing the release of tissue factor and the activation of Hageman factor, although a procoagulant effect has not been noted, probably because the ethanolamine component inhibits fibrin clot formation through its propensity for chelating calcium (Masaki et al., 1990).

EO is less likely to cause allergenic reactions than sodium morrhuate or sodium tetradecyl sulfate, although pulmonary toxicity and allergenic reactions have been associated with it (Hedberg et al., 1982). According to Hyodoh et al., (2005) and Ozaki et al., (2010) the most important side effect seen when extravascular administration is hemolysis with renal failure and requires prophylactic administration of albumin (> 3.0g/dL) and treatment with haptoglobin (2000-4000 U/h). Exacerbation of heart failure, pleural effusions, and right-sided heart failure has also been reported, likely related to the broad intravascular distribution EO (Hyodoh et al., 2005) It is important too never exceed the security dose 20 ml or 0.3ml/kg EO (Ozaki et al., 2010). To avoid ulceration, necrosis or cosmetic/fibrosis problems, in this study the EO was applied in deep portion of the lesions, under light pressure and inside of vessels (Johann et al., 2005).

Protocol

All lesions were treated with intravessels injections of 0.1 mL of 5% EO per each 3 mm of lesion. This report`s treatment protocol was in accordance to the Johann et al., (2005), that used 1 mL of 1,25% or 2,5% EO in BOVL from 3 to 50mm. As in the current study it was used OE in 5% concentration, it was decreased the applied volume. This care was to avoid local or systemic adverse effects. Interval of 14-days was made between each application up the total clinical resolution of the lesions. The relevant clinical date observed were 1) total clinical healing, 2) pain/burning, 3) edema, 4) analgesic usage, 5) ulcer, 6) postoperative functional alterations, i.e: eating and speech, 7) bleeding, 8) hematoma, 9) infection, 10) scarring, 11) resolution`s time, 12) satisfaction degree of patient to the treatment and 13) recurrence.

Lesions were evaluated and measured initially to determine the volume of intralesional injection (Fig.1A). Topic anesthethic 5% Xylocaína (Lidocaine/ Astrazeneca, Cotia-SP) was applied about 60 seconds rubbing with a cotton swab in the lesion surface to minimize the puncture discomfort besides preserving the lumen of injury, and thereafter using a BD (Becton, Dickinson, and Company, Franklin Lakes, NJ) Ultra-Fine II Short Needle Insulin Syringe 1 CC, the lesion was aspirate, certified about blood and the 0.1ml of the 5% OE applied per each 3 mm of the lesion (Fig.1A). The patient returned in 7 days to evaluation (Fig.1B). The interval between each application was 14 day until the total clinical healing of lesion. A single operator (M.C.R.) conducted the treatment.

Evaluation measures

The efficacy of treatment was in accordance to the total clinical healing and recurrence. The safety was assess in relation to the pain/burning, edema, analgesic usage, ulcer, postoperative functional alterations, bleeding, hematoma, infection, scarring and satisfaction degree of patient to the treatment.

Total clinical healing was determined when there is extinction complete of the lesions and the presence of a tissue with normal color. If the lesions didn't present total clinical healing until five treatment`s sessions, the treatment was suspended. Pain/burning and postoperative functional alterations was measured by visual scale analogue (VSA) and ranged between zero to ten (Mannion et al., (2007). The left endpoint of the pain scale was designated as "no pain, and the right endpoint was marked as worst imaginable pain". The end-points of the scales for the degree of discomfort during eating and speech were marked as no discomfort on the left side and worst imaginable discomfort on the right side. The edema was measured as present or absent in accordance to the Amaral et al., 2012 and asked to the patient the time`s duration. All patients were instructed to use the same analgesic drug containing paracetamol (750mg, four times per day), if needed to alleviate the pain/burning. Ulcer was determined by absence of the epithelial tissue and formation of the rind, bleeding by output remains of blood, hematoma by formation of red papule, infection by local purulent exudates and scarring by local fibrous tissue. All this evaluations was performed 7 days after application. The cases that required more than one session of treatment, the new application occurred with 14 days of interval between sessions, and so was determined the resolution's time. A visual analogue scale (VAS) was applied to verify the satisfaction´s degree of the patient to the treatment: 0 = totally unsatisfied and 10 = totally satisfied (Penarrocha et al., 2007). Recurrence was determined by return of lesion in some local after 6 months of end´s treatment.

The term *number of session* was used when it was necessary more than one day for treatment, therefore after 14 days the patients could be submitted to other new application. The term *number of application* refereed to number of points chose to apply the 5% OE in the lesion and the same session.

Post-sclerotherapy care

The mainly guidelines were observed any adverse effect, avoid physic effort, if atypical bleeding would be compressing area with gauze, use analgesic (paracetamol 750mg, four times per day) only in case of severe pain. It should be expected some swelling and Ifif necessary contact the research team.

Statistical analysis

Descriptive statistical analysis was performed using EPI INFO 7™ (Center for disease Control and Prevention- CDC). Fisher exact test was applied for categorical variables. The level of significance of the statistical differences was set at $p \leq 0.05$.

RESULTS

Fifteen patients (8 women and 7 men) composed the sample, with 19 BOVL, whose age range was 45 to 86 years (mean of 65.7). The most frequently BOVL treated were varix (15 lesions - 79.0%), and site more common was lower lip (7 lesions - 38.9%). Clinical features of the patients treated; diagnosis, site and size of BOVL; number of sessions necessary to treatment; number of applications on the lesions and the final volume of 5% EO are described in table 1.

All 19 BOVL presented total clinical healing up 28 days. Pain/burning was reported by 90% (13) of patients with an slightly scale in accordance to the VSA (median= 2.5). Persisted mild edema by 48hs was observed in 100% of them. No patient used analgesic drug. Ulcer, postoperative functional alterations, bleeding, hematoma, infection or scarring did not was observed. Recurrence was not observed in follow-up of 6 months.

Pain/burning scale, satisfaction degree of patient to the clinical resolution and resolution´s time in both groups were similar. Although the number of sessions was similar in both groups, the number of applications on average were different, and the group 2 which holds the larger lesions showed a value greater than three times group 1 consequently final volume applied in group 1 comparative group 2 was three times smaller, however there was no statistical difference between them. The resolution´s time in group1 in median showed up in less time (14 days). Satisfaction to treatment in both groups was reached in maximum rate (9). (Table 2).

DISCUSSION

The classification used to nominate the BOVL was in accordance to the Mulliken and Glowacki (1982) and it has also been used by others studies (Johann et al., 2005 and Costa et al., 2011). The choice, in this study, by 5% OE is also in accordance to other authors that has demonstrated efficacy and safety results (Johann et al., 2005; Costa et al., 2011), although several other sclerosing agents may be used in this type of treatment as absolute ethanol, polidocanol, sodium tetradecyl sulphate (Hyodoh et al., 2005; Krishna Das and Hoque, 2008; Ozaki et al., 2010).

OE has been used to treat benign vascular lesions in oral cavity and others body sites, although the OE`s concentration of each study is different (Krishna Das and Hoque, 2008). Diluted (Johann et al., 2005) or undiluted EO (Costa et al., 2011) has demonstrated success in treatment of BOVL. Corroborating with this authors, the current study demonstrated success in the use of 5% EO in treatment of 19 BOVL, because it was effective (healed all cases; no recurrence) and safety (no use of analgesic drug, ulcer, postoperative functional alterations, bleeding, hematoma, infection or scarring; mild pain/burning and edema; patients satisfied). Additionally, the cost of treatment is low, because there are low number of sessions' treatment and applications. The previous study related in literature allowed in this study using 0,1ml/3mm per/each lesion.

Costa et al., (2011) used 0,1ml/cm of 5% EO to treat 66 lesions in oral and maxillofacial region, Hiraoka et al., (2012) used 0,2ml/cm of 2,5% EO diluted in anesthetic 1:1 to treat 18 oral lesions and Johann et al. (2005) used 1ml of EO diluted in distilled water (1.25% or 2.5%) applied to treat 30 oral vascular lesions. The success rate these studies showed above 94% corroborate with present study.

Differently our results, when its used diluted EO, decreasing the concentration the number of application was greater. Hiraoka et al., (2012) shows 3.22 sessions in median, Johann et al., (2005) showed 3.07 sessions in median the same can be see in study of Costa et al., (2011), on the other hand the results of present study that showed in median only 2 sessions until the final resolution of lesions, may be it can be explain due to higher concentration of drug (0,1/3mm 5% EO) in comparison to the other studies.

The fact of reducing the concentration of the drug to be applied and or even dilute it in anesthetic does not improve pain/burning reported by patients. Just evaluate the study of Johann et al (2005), Costa et al (2011) and Hiraoka et al (2012). Therefore

pain/burning slight to moderate was common aspects related by patients to sclerotherapy by EO regardless of the concentration used. Although the authors have showed efficacy of this diluted way to apply EO, the effect of these mixture of anesthetics and EO are unknown yet. Thus, it was used the topic anesthetic that it would allow better visualization of lesions because did not produce edema, preventing distortions. The other factor important relative to pain was that same using topic anesthetic the VSA number was lower (median= 2.5) and did not difficult the procedure.

Costa et al., (2011) present three cases that developed ulceration after treatment, and according the authors in five days spontaneous healing. Anaphylactic reaction, hemoglobinuria, nerve damage, cardiovascular collapse and ulcerations can be observed in this kind of treatment (Bordas et al, 1989 and Buckmiller 2004, Johann et al., 2005; Costa et al., 2011 and Hiraoka et al., 2012) although this did not occur in available patients in present study.

A hemolytic effect, visualized as red urine, occurs when the sclerosing agents leaks to the outside of the lumen. In cases in which it may be necessary to inject and overdose of EO, prophilatic haptoglobin (2.000 – 4.000 U/h) and albumin (> 3.0g/dL) should be given before injection to prevent permanent renal insufficiency then to avoid this complication its recommended by Ozaki et al (2010) never exceed safe limits EO that 20ml in adult patients or 0.3 ml/kg EO in accordance with body weight. To avoid necrosis/ulcer is important consider the concentration dosage, intravascular application of agent sclerosant and the number of application. Moreover, the professional experience of realized the adequate technique is important to avoid adverse effect of the drug.

Johann et al., (2005) reported edema maintained by 72 hours, when used the lowest concentration 1.25% or 2.5% EO in dosage 1ml/cm. In current study the edema can be observed for up to 48 hours with 5% EO to 0,1ml/3mm. The same result to edema was published by Costa et al., (2011) and Hiraoka et al., (2012) that used the respectively 5% EO to 0,1ml/cm and 2.5% EO to 0,2ml/cm. It is possible that the swelling time was longer in Johann´s study due to the applied volume (1ml) and not the concentration of the drug which by the way was less than the study of Costa et al., (2011) and the present study.

In conclusion, this study suggests that 5% OE is effective and safe to treated BOVL in higher concentration (0,1ml/3mm). No complications occurs and satisfaction

level was maximum related by the patients. It seems to induce use of smaller amount of volume of the applied substance and offers excellent results quickly and with great acceptance by the patient

Conflict of interest

None declared

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Table 1: Descriptive profile of patients and benign oral vascular lesions treated with 5% ethanolamine oleate (2011-2013).

Patient (n= 15)	Age	Sex	Race	Diagnostic (n= 19)	Site	Size (mm)	Number of sessions	Number of applications	Final volume (mL)
1	71	M	B	Varix	Alveolar mucosa	7	2	2	0.4
2	54	F	B	Varix	Lower Lip	5	1	1	0.1
3	45	F	B	Varix	Lower Lip	3	1	1	0.1
4	73	F	B	Varix	Cheek	13	1	2	0.2
5	47	M	W	VM	Palate	12	1	3	0.3
6	73	M	B	Varix	Cheek	5	1	2	0.2
7	67	M	B	VM	Cheek	14	1	4	0.4
8	86	M	W	Varix	Upper Lip	5	1	1	0.1
					Tongue	10	1	4	0.4
9	68	M	B	Varix	Cheek	8	1	2	0.2
10	59	F	B	VM	Palate	20	1	4	0.4
11	61	M	B	Varix	Lower Lip	4	1	1	0.1
					Lower Lip	6	1	1	0.1
12	58	F	W	Varix	Lower Lip	3	2	1	0.2
					Lower lip	3	1	1	0.1
13	54	F	B	VM	Cheek	12	1	3	0.3
14	79	F	W	Varix	Tongue	5	1	1	0.1
					Lower lip	5	1	1	0.1
15	70	F	W	Varix	Tongue	10	1	3	0.3

M – male; F – female; B – black; W – white; VM - vascular malformation; n – absolute sample

Table 2: Comparison between dates protocol of the 5% ethanolamine oleate and size of benign oral vascular lesions

Size of lesions*	**Group 1 (≤ 6.5mm)** (n= 10)		**Group 2 (> 6.5mm)** (n=9)	
Variables	**Range**	**Median/Mean**	**Range**	**Median/Mean**
Number of sessions	1.00-2.00	Median = 1.00	1.00-2.00	Median = 1.00
Number of applications	1.00-2.00	Median = 1.00	1.00-4.00	Median = 3.00
Final volume	0.10-0.30	Mean = 0.12	0.20-0.40	Mean = 0.32
Pain scale	0.00-7.00	Mean = 2.50	0.00-7.00	Mean = 2.30
Satisfaction	9-10	Mean = 9.00	9-10	Mean = 9.00
Resolution`s time (days)	7-28	Median=14.00	7-28	Median= 20.00

* Division of the groups (size of lesions) by the median.

Figures and Legends:

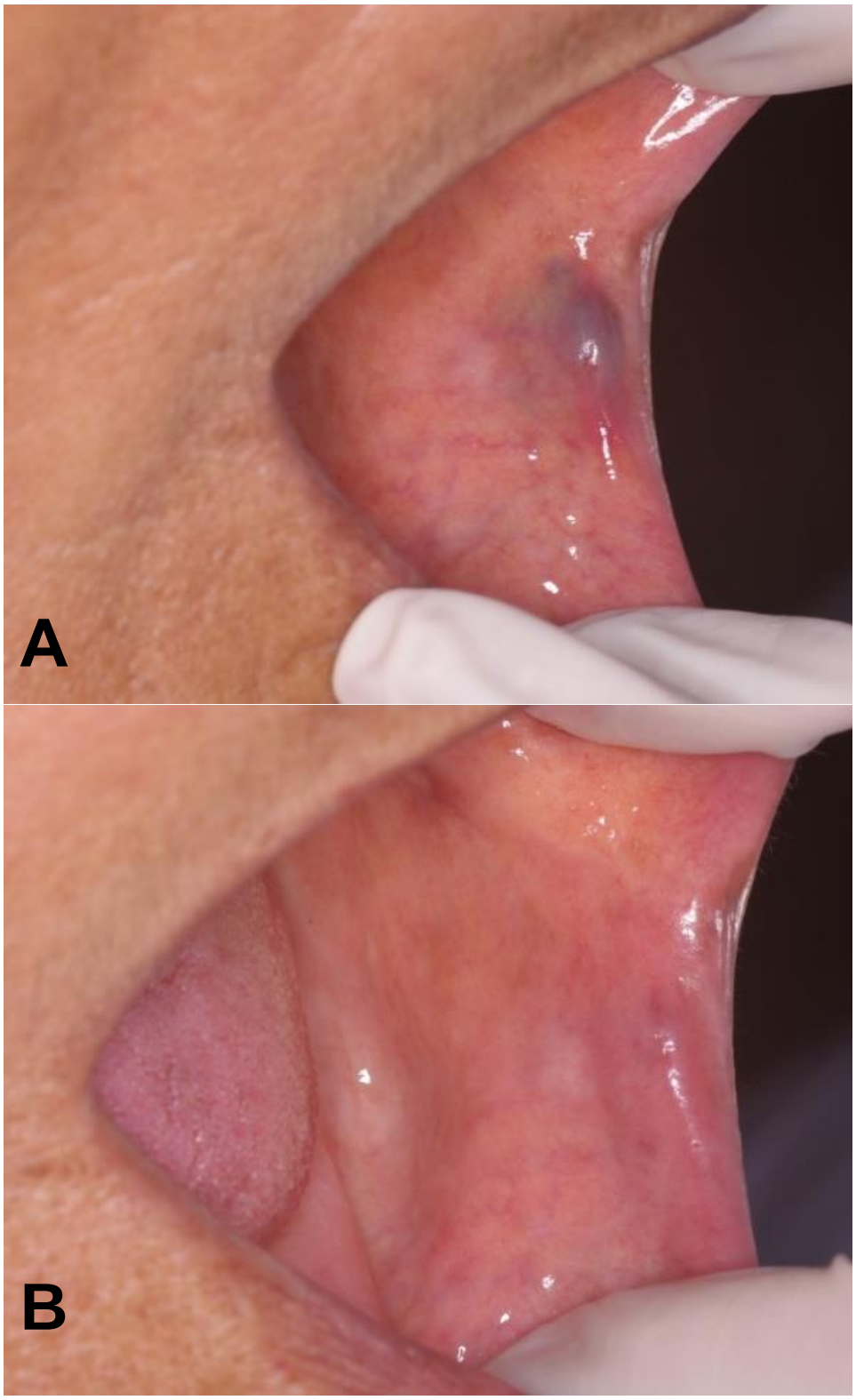

Figure 1- A, Buccal mucosa lesion (Initial clinical aspect); B, Buccal mucosa clinical resolution after 7 days 5% EO application.

ARTIGO 2[2]

SCLEROTHERAPY WITH ETHANOLAMINE OLEATE OF BENIGN ORAL VASCULAR LESIONS: WHAT IS THE IDEAL CONCENTRATION?

INTRODUCTION

Benign vascular anomalies are commonly found in the head and neck region, including the oral cavity. Actually, hemangioma (Hem), vascular malformation (VM) or varix may be considered in this group (Mulliken and Glowacki; 1982, Finn et al, 1983). Generally, the benign oral vascular lesions (BOVL) appear clinically as a soft mass that is compressible, non pulsating and has a coloration varying from blue to bluish-red (purple). Their clinical aspects together with their evolutionary history are necessary to diagnosis and diascopy can be an additional exam for your diagnosis (Garzon et al, 2000; Buckmiller 2004; Costa et al, 2011).

BOVL may be treated by sclerotherapy, surgical therapy, embolization, laser therapy, systemic corticosteroids, cryotherapy, interferon α and radiation therapy (Muto et al., 1990; Van Doorne et. al 2002; Johann et al., 2005; Correa et al., 2007; Yang et al., 2009; Hiraoka et al., 2012). The choice to treat is in accordance to size, location, hemodynamics of the tumor, degree of invasion into anatomic structures, age of patients and the viability of the technique to be employed (Hanemann et al, 2004; Hiraoka et al, 2012).

Sclerotheray is an important kind of treatment of benign vascular anomalies because it shows success rate of 70% to 100% (Johann et al, 2005; Costa et al, 2011). Sclerosant agents as sodium morrhuate, sodium psylliate, quinine urethrone, ethanolamine oleate (EO), polidocanol, sodium tetradecil sulfate, hypertonic saline and absolute alcohol have been indicated to treat these lesions (Johann et al, 2005; Dilsiz et al, 2009; Costa et al, 2011).

EO, an unsaturated fatty acid, is injected intravenously and it acts as a sclerosant agent (Choi et al, 2002). The OE acts primarily causing the irritation to intima

[2] Este artigo será enviado para a revista: Oral Diseases

by endothelial vein and produces a sterile inflammatory response (Nishida et al, 1999). As results, it is observed a fibrosis of the vessel wall or a possible vein occlusion. The substance also diffuses rapidly through the vessel wall and produces an inflammatory extravascular (Kaji et al, 2009) and it has been, used in the management of the esophageal varix (Iso et al, 1988; Nishida et al, 1999), oral Hem, VM and varix (Johann et al, 2005; Costa et al, 2011; Hiraoka et al, 2012). EO is preferred due its low toxic effect compared with other sclerosis-inducing agents (Costa et al, 2011; Silva et al., 2013) although the ideal concentration had not been determinate yet. Previous study showed EO effective in treatment of BOVL in the 1.25%, 2.50% or 5% concentrations. The choice between concentrations of EO can be important to prevent undesirable effect as toxicity, ulceration and necrosis (Johann et al, 2005, Costa et al, 2011).

Bearing this finding in mind, the aim of this study was compare the efficacy and safety of sclerotherapy with EO to treatment of BOVL on concentrations of the 1.25%, 2.5% and 5%.

PATIENTS AND METHODS

The protocol of this clinical survey was approved by the Committee of Bioethics in Research at the Universidade Federal de Minas Gerais (551.062).

A non-randomized clinical survey was carried out during a period of 15 years on consecutive 34 patients with BOVL recruited and treated consecutively in Oral Pathology Clinic, at School of Dentistry of the Universidade Federal de Minas Gerais.

Patients with BOVL less than 20 mm were included in this study. This 20 mm size was stated to avoid higher variation and because this size represent to major number of cases Oral Pathology Clinic. Demographic information of the patients (sex, age and previous medical history), and clinic data of the lesions (type of lesions, location and size) were obtained. The diagnosis of BOVL was made based on the Mulliken and Glowacki (1982) and the indications for treatment of these lesions included pain, growth, swelling, pressure, or esthetics.

All the lesions were treated with EO (Ethamolin™, ZEST, Rio de Janeiro/RJ, Brazil) by practiced professionals (R.A.M.). The patients were treated and included for convenience in three different groups, according the concentration of OE group 1: 1.25%; group 2: 2.5%; and group 3: 5%, applied in lesion.

To treated the patients included in groups 1 and 2 following the protocol described by Johann et al. (2005), 5% EO was diluted in distilled water in proportions

equivalent to 1:4 (vol/vol) or 1:1 (vol/vol), resulting in 1.25% or 2.5% concentrations. After, 1mL of these was then applied, by one investigator, in 3 to 4 locations within the lesion. The patients of group 3 were treated with 5% OE injected into the center of lesion, being 0.1 mL per each 0.3 cm of the lesion. Patients were not informed of the concentration´s OE belonged nor of the number of applications necessary to the total clinical healing of the lesion.

Firstly, topic anesthesia (Astrazeneca, Cotia-SP) was applied about 60 seconds in the lesion surface. After, BD (Becton, Dickinson, and Company, Franklin Lakes,NJ) Ultra-Fine II Short Needle Insulin Syringe 1 CC was used to applied the drug. Preceding the application, an aspiration was performed to verify the injection of drug in the vascular lumen. After injection, the lesion was pressure about 3 minutes with gauge to avoid regress of EO. The applications were performed using light pressure and the patients returned in 7 days to evaluation.

A 14-day interval between each application was done until achieving total clinical healing of the lesion had occurred. The final results were recorded by 2 investigators who had no knowledge of the concentrations and the number of applications of the drug.

Statistical analysis

The descriptive statistical analysis to different group was performed using SPSS 18.0 software (SPSS Inc., Chicago, IL). The comparison among the different concentrations of EO, number of session and final volume used in similar lesions was done.

RESULTS

A total of 34 patients (20 women and 14 men) with BOVL were treated and evaluated in this study period. The age range was 11 to 86 years (mean of 58.0). Ten (29.4%) of the lesions were classified as Hem, 11 (32.4%) as VM and 15 (38.2%) as varix. BOVL were more prevalent in women between 51 to 70 years old. The most frequently site was lip (13 lesions - 38.3%), principally in lower lip (11 lesions – 32.4%), followed by cheek (9 lesions – 26.5%) (Table 1).

All lesions presented total resolution healing. The comparison of size, number of session and final volume necessary to heal the BOVL were described in table 2. The

5% EO showed lower final volume (p**<0.001**) and number of sessions (p=0.030) when lesions of similar size were treated with different concentrations.

DISCUSSION

The sample studied included in this study represented the group of patients more involved with BOVL observed in the literature: women (Correa et al, 2007; Hiraoka et al., 2012) with mean of age higher than 50 years (Johann et al, 2005; Costa et al 2011 and Hiraoka et al. 2012). The more common BOVL was varix (38.2%) showed prevalence higher than it found in literature (16.2%) (Kovac-Kovacic; Skaleric, 2000). The lips were the most affected site in agreement with previous reports (Buckmiller, 2004; Johan et al., 2002; Costa et la., 2011).

In this study it was used previous topic anesthetic, during one minute, as recommended by fabricant. However, Hiraoka et al, (2012) recommended intravascular application of OE with 2% licocaine and epinephrine (1:100.000). The objective of topic use in displacement of intravascular anesthetic is to avoid the possible interaction between both drugs. Moreover, the use of infiltrative anesthesia may hinder visualization of lesion because of the swelling.

The sclerosis technique consist in direct percutaneus puncture, being an easy, simple, outpatient, fast and low cost with good tolerability and low morbidity. However, this treatment can cause side effects, such as pain/burning upon injection, partial temporary scar, psychological local tension, rash, ulcerations and risk of local necrosis (Minkow et al., 1983; Hiraoka et al., 2012). Adverse reactions associated with use of EO are due to the amount of the applied dose; it is being considered the amount of (0.4 ml/kg) the maximum safe dosage per patient (Mulliken and Glowacki, 1982; Hyodoh et al., 2009; Hoque and Das, 2011). The cases treated in this study used low concentrations of EO considered safe.

Although complications as anaphylactic reaction, hemoglobinuria, nerve damage, cardiovascular collapse and ulcerations could occur when EO is used (Bordas et al, 1989 and Buckmiller 2004, Costa et al, 2011), no one occurred in this study, corroborating with other authors (Costa et al 2011 and Hiraoka et al, 2012). Some authors reports the necessity of surgical resection of the residual lesion was performed to achieve optimal results with previous treatment with EO (Mariano et al., 2011). Thus, to avoid adverse reactions and surgical intervention is important consider

concentration, final volume and intravascular application of agent sclerosant, and we recommend the use of 5% EO in lesions until 20mm of size due to adverse local effect.

All lesions evaluated were small, which was an important factor in the choice of treatment in accordance with Assis et al. (2009), principally due the possible toxic effect of EO. In addition, sclerotherapy does not present the risk of hemorrhaging, is a low invasive method, and maintains a low cost, being effective sclerosing agent for the treatment for BOVL. The use of 1.25%, 2.5% or 5% EO as a choice treatment of BOVL was considered 100% satisfactory. In additon, among different concentrations of EO evaluated, the 5% EO presented the best of them because lower final volume and number session were necessary to resolution of lesions. For this reason, it can be suggested this concentration is a more viable option for the prevention of adverse effects.

This study suggests that 5% EO undiluted is effective and safe to treated BOVL. Moreover, the applied of 5% EO reduce the number of sessions and final volume of drug in lesions smaller than 20 mm that used 2.5% or 1.25% OE. More investigations, including a larger number of patients in prospective studies, are important to establish an ideal protocol to sclerotherapy of BOVL, however this results may contribute substantially to the choice of the EO concentration to treat in these lesions.

Conflict of interest

None declared

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Table 1 Prevalence of benign oral vascular lesions in accordance to the sex and age group (n=34)

Oral benign vascular lesion	Sex		Age group								Total
	Male **n** (%)	Female *n* (%)	11-20 years *n* (%)	21-30 years *n* (%)	31-40 years *n* (%)	41-50 years *n* (%)	51-60 years *n* (%)	61-70 years *n* (%)	71-80 years *n* (%)	81+ years *n* (%)	*n* (%)
Hemangioma	4 (11.8)	6 (17.6)	2 (5.9)	3 (8.8)	0 (0.0)	0 (0.0)	2 (5.9)	2 (5.9)	**1 (2.9)**	0 (0.0)	**10 (29.4)**
Vascular malformation	4 (11.8)	7 (20.6)	**1 (2.9)**	0 (0.0)	2 (5.9)	2 (5.9)	4 (11.8)	2 (5.9)	0 (0.0)	0 (0.0)	**11 (32.4)**
Varix	6 (17.6)	7 (20.6)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (2.9)**	3 (8.8)	4 (11.8)	4 (11.8)	**1 (2.9)**	**13 (38.2)**
Total (%)	**14 (41.2)**	**20 (58.8)**	**3 (8.8)**	**3 (8.8)**	**2 (5.9)**	**3 (8.8)**	**9 (26.5)**	**8 (23.6)**	**5 (14.7)**	**1 (2.9)**	**34 (100.0)**

Legend: *n* - absolute prevalence; (%) - relative prevalence.

Table 2 Comparison to different concentrations of ethanolamine oleato to treat benign oral vascular lesions.

Groups / **Variables**	**Group 1 (1.25%)** (n=10)	**Group 2 (2.50%)** (n=9)	**Group 3 (5.00%)** (n=19)	***p***
Size (Median/mm)	**5-20** (18.5)	**3-20** (10.0)	**3-20** (8.0)	**>0.05***
Number of sessions (Median)	**1-4**[a,b] (1.0)	**1-5**[a] (2.0)	**1-2**[b] (1.0)	**0.030***
Final Volume (Mean/mL)	**1-4**[a] (1.0)	**1-5**[a] (2.0)	**0.1-0.4**[b] (0.2)	**<0.001***

*Kruskal-Wallis Test; Different letters in columns show statistical difference (p< 0.0165 – Mann Whitney Test correct by Bonferroni Test).

ARTIGO 3[3]

EFFICACY AND SAFETY OF FOAM SCLEROTHERAPY WITH 5% ETHANOLAMINE OLEATE TO TREATMENT LOW FLOW VENOUS MALFORMATIONS IN THE REGION OF HEAD AND NECK: EXPERIENCE WITH A CASE SERIE OUR EXPERIENCE.

INTRODUCTION

In 1996, the International Society for the Study of Vascular Anomalies (ISSVA) classified these disorders in capillary malformation (CM), venous malformation (VM), lymphatic malformation (LM), arteriovenous malformation (AVM), and arteriovenous fistula (AVF), according to anomalous channels and type of flow (high or low) (Enjouras and Mulliken, 1997; Enjouras, 1997; Colletti et al., 2013).

Vascular malformations (VM) are present at birth and persist throughout life, frequent in head and neck areas (Dubois et al., 2001; Neville et al., 2002; Buckmiller, 2005, Enermann et al., 2010). VM are typically solitary with preference to the cervicofacial, extremities and trunk (Boos et al., 2004). Generally, VM appear clinically as a soft mass or stain that is compressible, non pulsat (low flow), with coloration varying from blue to bluish-red (purple) and palpation may induce some tenderness, especially with acute clots, or reveal phleboliths.(Garzon et al., 2000; Burrows and Mason, 2004; Alomari and Dubois, 2011). The VM needs be treated as disrupt normal functions of stomatognatic system, pressure in vital regions, aesthetic defect or hemorrhage risk (Johann et al., 2005). Several techniques can be used to treat VM, being the sclerotherapy an efficient option of treatment to low flow VM (Spring and Bentz, 2005; Zheng et al., 2013; Górriz-Gomez et al., 2014).

Nowadays, the sclerosing agents most commonly used are 1% or 3% polidocanol , hypertonic dextrose, sodium tetradecyl, alcohol, sodium

[3] Este artigo será enviado para a revista: Journal of Vascular Surgery.

tetradecylsulphate, hypertonic saline and 5% ethanolamine oleate (EO) (Johann et al., 2005; Rehmann et al., 2009, Yun et al., 2009, Costa et al., 2011; Sato et. al, 2012; Youshimatsu et al., 2014). Among these agents, 5% EO is one of the effective, safety and most readily available in Brazil to benign oral vascular lesions (Johann et al., 2005; Costa et al., 2011; Hiraoka et al., 2012).

Wollmann (2004) publish a history of clinical use of foam sclerotherapy and related Stuard MacAusland (1939) with first to proposed use of frouth in telangiectasia. The foam was prepared was obtained by simple shaking the rubber-capped bottle that was filled with sodium morrhuate. Foam sclerotherapy technique was developed and published, in 1944, by Egmont James Orbach and improved the previous results of sclerotherapy, when it is injected a small amount of air into the venous segment targected for treatment in order to displace blood and intensify the contact between sclerosand endothelium (Orbach, 1944 and 1950).

Over the years the technique to produce foam were undergoing changes to win big projection with modifying by Tessari modified “Tourbillon Tecnique” with success in clinical trials (Tessari, 2000 and 2001). In the literature it was observed that the most used sclerosing agents foamed are tetradecylsulfate 1-3% and polidocanol 1–3% (Tessari 2001; Tan and Tan 2009; Rehmann et al., 2009; Mimura et al., 2009). Cabrera et al., (2003) demonstrated that foamed sclerosings are twice more effective than sclerosing liquid alone.

Considering the importance of choose VM’s treatment, the main of this study was evaluated the efficacy and safety of 5% EO foam to treat low flow VM, in region of head and neck, the incidence of complications and the satisfaction´s of the patients submitted to this protocol of treatment. The issue is extremely important because it seeks to assess the first time the use sclerotherapy of 5% EO foam in the treatment of VM´s in region of the head and neck.

PATIENTS AND METHODS

Institutional review board

The study protocol conformed to the guidelines of the 1975 Declaration of Helsinki and the Committee of Bioethics in Research at the Universidade Federal de Minas Gerais approved the protocol of this study (551.062).

Patient's population

This series of cases of VM´s in region head and neck study was carried out in Ambulatory of Endovascular Surgery in Hospital das Clínicas and Oral Pathology Clinic in School of Dentistry (Universidade Federal de Minas Gerais - UFMG, Belo Horizonte - Brazil) in the period from 2012 to 2014. The study was approved by the UFMG Ethical Committee for Surveys (number 551.062), and all volunteers signed informed consent form.

The diagnosis of VM´s was in accordance to the Mulliken and Glowacki (1982) criteria and it was realized clinical maneuver with position shifting test (put the head between the knees for 3 minutes) was performed in all patients (Li et al., 2010). All patients with low flow VM in region of head and neck, with size equal or superior to 20 mm, were included in this study. The indications for treatment included pain, growth, swelling, pressure and esthetics complain. All the lesions diagnosed as VM´s were treated with foam 5% EO (Zest Farmacêutica, Ltda, Rio de Janeiro, RJ). Patients with high flow lesions, uncrotolleted systemic disease, pregnancy or who reported allergy of injected anesthesic (Xylestesin® 2% without constrictor vase - Cristália, Itapira/SP), 5% EO (Ethamolin®- Zest Farmacêutica Ltda, Rio de Janeiro/RJ) and antisepsis drug (Chlorhexidine 2% Rioquímica, São José do Rio Preto/SP) were excluded of this study.

Study drug

EO is a synthetic mixture of ethanolamine and oleic acid with an empirical formula C20H41NO3. EO acts as a sclerosant drug when applied intravenously, and the oleic acid component is responsible for its ability to induce inflammation and fibrosis in the endothelium (Choi et al., 2002). It is prepared in 50 mg per ml of aqueous solution. Oleic acid also may activate coagulation by inducing the release of tissue factor and the activation of Hageman factor, although a procoagulant effect has not been noted, probably because the ethanolamine component inhibits fibrin clot formation through its propensity for chelating calcium (Masaki et al, 1990).

EO is less likely to cause allergenic reactions than sodium morrhuate or sodium tetradecyl sulfate, although pulmonary toxicity and allergenic reactions have been associated with it (Hedberg et al, 1982). According to Hyodoh et al., (2005) and Ozaki et al., (2010) the most important side effect seen when extravascular administration is hemolysis with renal failure and requires prophylactic administration of albumin (> 3.0g/dL) and treatment with haptoglobin (2000-4000 U/h). Exacerbation of heart

failure, pleural effusions, and right-sided heart failure has also been reported, likely related to the broad intravascular distribution EO (Hyodoh et al., 2005). It is important too never exceed the security dose 20 ml or 0.3ml/kg EO (Ozaki et al., 2010). To avoid ulceration, necrosis or cosmetic/fibrosis problems, in this study the EO was applied in deep portion of the lesions, under light pressure and inside of vessels (Johann et al., 2005).

Protocol

Clinical maneuver the position shifting test-putting the head between the knees for 3 minutes was performed in all patients to made to swell the injury further and facilitate hit the lumen (Li et al., 2010) in sequence all lesions were measured with a flexible ruler before start treatment

To prepare the foam sclerosing was used a syringe 10ml (Becton Dickinson, Curitiba, Paraná, Brazil) with 2ml of Ethamolin® 5% and in another similar syringe with 8ml of air (Figure 1A). Then, the two syringes were interconnected by a three-way stopcock (Embramed, São Paulo, São Paulo, Brazil). To the formation of foam, 20 cycles of transfer the contents of one syringe to another were performed, as described in literature (Tessari, 2000) (Figure 1B).

There was determined the proportion of 1mL foam/1cm lesion, being 8 mL of foam the maximum volume applied to each session (Tessari 2000, 2001). The maximum dose of injected 5% EO did not exceed 20ml for adult patient or 0.3ml/kg 5% foam EO per session (Ozaki et al., 2010)

Under strict aseptic condition and operation theatre set up the skin and or mucosa overlying the lesion was scrubbed with surgical spirit with chlorhexidine 2 % (Rioquímica, São José do Rio Preto/SP). In sequence, infiltration anesthesia Xylestesin 2% without vasoconstricter (Lidocaine / Cristalia, São Paulo/SP) was previously done in all lesions – (1ml of anesthetic in the lesion center) and waited for two minutes. The foam sclerosant was applied punctured and intralesionally in the center of VM through a scalp 25G (Embramed, São Paulo, São Paulo, Brazil) connected to the syringe with foam, after held aspiration to ensure the correct position. The foam was injected into the lesion in a maximum time of 2 minutes because the stability of foam bubbles (Peterson and Goldman, 2011; Górriz-Gómez et al., 2014)

The figure 1 showed step by step the foam sclerotherapy procedure. Initially To proceed to the sequential treatment, the lesion was measured to determine the volume

of intralesional injection and sequence it was injected 1 ml of anesthesic in center of lesion (Xylestesin® 2% without constrictor vase - Cristália, Itapira/SP). After three minutes the 5% EO foam 1ml/1cm of lesion was applied punctured and intralesionally of VM through a scalp 25G (Embramed, São Paulo, São Paulo, Brazil) connected to the syringe with foam, after held aspiration to ensure the correct position. The figure 4 (A, B) and 5 (A-D) showed VMs in initially and finally treatment with sclerotherapy by 5% EO foam.

The end of the procedure was performed in the lesion pressure with gauze for three minutes and massage for two minutes to better spread the foam with a sclerosing agent increasing the contact surface. This care was to avoid local or systemic adverse effects. Patient was asked to wait for at least 30 minutes after each session d treatment for some support if there were any complications before being released to go. The patient returned in 7 days to evaluation. The interval between each application was 14 day until the total clinical healing of lesion. A single operator (M.C.R.) conducted the treatment.

The relevant clinical date observed were 1) clinical healing, 2) pain/burning, 3) edema, 4) analgesic usage, 5) ulcer, 6) postoperative functional alterations, i.e: eating and speech, 7) bleeding, 8) hematoma, 9) infection, 10) scarring, 11) resolution`s time, 12) satisfaction degree of patient to the treatment and 13) recurrence.

Evaluation measures

The efficacy of treatment was in accordance to the total clinical healing and recurrence. The safety was assess in relation to the pain/burning, edema, analgesic usage, ulcer, postoperative functional alterations, bleeding, hematoma, infection, scarring and satisfaction degree of patient to the treatment.

Clinical healing was determined when the swelling regressed, tissue color returned to normal and the position shifting test was negative and it was considered by score: 1- Excelent response (75-100% of cure); 2- Good response (50-74% of cure); 3- Partial response (25-49% of cure); 4- Poor response (0-24% of cure), according Achauer et al., (1997).

Pain evaluation was done in period pos operative immediate and after seven days with Visual Scale Analogue (VSA), according Manion et al., (2007) (Figure 2) the left endpoint of the pain scale was designated as “no pain, and the right endpoint was marked as worst imaginable pain”. The end-points of the scales for the degree of

discomfort during eating and speech were marked as no discomfort on the left side and worst imaginable discomfort on the right side.

The edema evaluation was classified as present or absent and time of persisted (Amaral et al., 2012). The level of patient satisfaction to the treatment result was measured by Visual Scale Analogue (VSA), according Peñarrocha et al. (2007) (Figure 3) evaluated after 6 months of last application.

All patients were instructed to use the same analgesic drug containing paracetamol (750mg, four times per day), if needed to alleviate the pain/burning. Ulcer was determined by absence of the epithelial tissue and formation of the rind, bleeding by output remains of blood, hematoma by formation of red papule, infection by local purulent exudates and scarring by local fibrous tissue. All this evaluations was performed 7 days after application.

The patients were following by six months after last application of foam sclerotherapy. In the first month the follow up was weekly and after monthly. The cases that required more than one session of treatment the new application occurred with 14 days of interval between sections, as described in the literature (Johann et al., 2005; Costa et al., 2011).

A visual analogue scale (VAS) was applied to verify the satisfaction´s degree of the patient to the treatment: 0 = totally unsatisfied and 10 = totally satisfied (Penarrocha et al., 2007). Recurrence was determined by return of lesion in some local after 6 mouths of end´s treatment.

The term number of session was used when it was necessary more than one day for treatment, therefore after 14 days the patients could be submitted to other new application.

Post-sclerotherapy care

After each sessions of EO application the patients received post operative informations. The mainly guidelines were observed any adverse reactions, avoid physic effort, in case of atypical bleeding would be compressing area with gauze, use analgesic (paracetamol 750mg, four times per day) only in case of severe pain. It should be expected some swelling and If necessary contact the research team.

Statistical analysis

Descriptive statistical analysis was performed using EPI INFO 7™ (Center for disease Control and Prevention- CDC). The Fisher exact test was applied for categorical variables. The level of significance of the statistical differences was set at $p \leq 0.05$.

RESULT

A total of 19 patients and 36 lesions were evaluated. Thus, 17 patients (6 men and 11 women) with 34 low flow VM were included in this study. The age range varied since 11 to 69 years old (mean of 40 years). Most of them presented healthy (67.65%) and others remain (32.35%) reported hypertension, under medical control. Nine patients (52.90%) had only one lesion and eight patients (47.10%) had two or more lesions, not being none of these syndromic patients. None patients reported allergy to 5% EO, xylestesin 2% and chlorhexidine 2 % (Table 1).

Descriptive results of previous treatment, clinic characteristics, volume initial and final, number of session, complications, clinical resolution and satisfaction of all patients were present in table 2. The most of lesions presented as swelling (30 lesions – 88.24%) with purple color (29 lesions - 85.29%), located on tongue (8 lesions – 23.33%) and lower lip (6 lesions – 17.65%). Fifteen lesions (44.12%) never received previous treatment, four lesions (11.76%) have been treated surgically and fifteen lesions (44.12%) have been treated by polidocanol 3% foam that was not effective. All clinical data about the lesions included in this study were described in table 2.

The sizes of lesions ranged since 20 to 80 mm (median size of 30mm). Clinical healing become of Achauer´s score: 65% (1- excellent response), 20% (2- good response), 9% (3- partial response) and 6% (4- poor response). Can be seen from table 2 apparently there is a direct relationship between clinical healing and patient satisfaction, that is, when the healing was lower, satisfaction also. The same is true of the number of sessions and the final volume applied, the more sessions larger the volume of 5 % EO foam administered.

It was observed complication in 9 patients and overall they were superficial necrosis after sclerotherapy and the spontaneous cure was observed. None patient related analgesic usage, postoperative functional alterations, bleeding, hematoma, infection, scarring.

In table 3 provides important information regarding the statistical when relating the variables: size, satisfaction of patient, total dose, number of sessions and clinical

healing. It was observed that there was a direct relationship between size of VMs with volume applied to treat them, numbers of sessions and healing, with statistical significance in all aspects. To treat group of minor VMs (≤ 30mm), minor volume EO in foam was used, hence few sessions were necessary predominating one session only, and the much higher resolution index for smaller lesions. By contrast to the larger lesions (≥ 30mm) results have shown us the need for greater volume of EO foam beyond the resolution index was lower. When assessing the level of satisfaction in relation to the total volume, number of sessions and resolution, the statistical difference appears only in correlation with the resolution. For the highest satisfaction rates greater amount of lesion was completely treated.

Thus, the diagnostic lesions with smaller (≤30mm) required lesser amount of 5% foam EO to treat and results as well as for patient satisfaction and for final evaluation of research by clinical healing superior to larger diagnosed lesions (≥ 30mm). All patients, after followed up for six month, did not present recurrence.

DISCUSSION

According to 1996 version of the ISSAV classification, vascular anomalies as vascular tumors and vascular malformations are distinguished by clinical, radiological and pathological features (Kobayashi et al., 2013), being the propose treatment indicate according specific diagnosis (Górriz-Gómez et al., 2014).

The incidence of VM is approximately 1:5000-10.000; about 40.0% of them occur in the head and neck regions (Buckmiller et al., 2010; Zheng et al., 2010). All lesions included in our study were diagnosed as VM in head and neck regions, so since birth. Clinical evaluation should be done by clinic characteristics, palpation without pulsate symptom and position shifting test (Li et al., 2010) it can also be used as complementary exams: radiograph, computed tomography, magnetic resonance and doppler ultrasound (Ozaki et al., 2010). All lesions included in our study were diagnosed by clinical exam as VM characterized by low flow blood.

The treatment of all patients in this study refer complaint aesthetic disorders when VM present in face and discomfort when chewing when VM present intraoral, corroborated with Górriz-Gomez et al., 2014.

The traditional treatment of sclerotherapy involved use of pure drugs and you can achieve it with various drugs with diverse backgrounds and characteristics. The most used are polidocanol, absolute ethanol, sodium tetradecyl sulphate and oleate of

etanolamine (Ozaki et al., 2010; Górriz-Gómez et al., 2014). The mainly characteristics sought in a sclerosing agent are effective and safe.

Several different treatments to vascular lesions were reported in literature (Johann et al., 2005; Krishna Das and Hoque, 2008; Zheng et al., 2010; Costa eta al., 2011; Richter and Braswell, 2012; Zheng et al., 2013; Górriz-Gomez et al., 2013; Kobayashi et al, 2013; Colletti et al., 2014;) and this study choose the use of sclerotherapy EO due the previous experience with this medication in VM in our group (Johann et al., 2005). The choice of use to OE in foam was due its potencial of sclerosing action and minor aggressive to human organism (biologic cost) and the fact that there is no published literature with this sclerosing agent in foam. (Orbach in 1944; Tessari 2000). Jia X et al., (2007) concluded from the meta-analysis that foam sclerotherapy was more effecive than liquid sclerotherapy but less effective than surgery, at least when the full obstruction of the vessels lumen was measured. Corroborating with other authors (Correa et al., 2007; Krishna Das and Hoque, 2008; Costa et al., 2011), our patients reported symptoms of pain in minor or major grade after applications EO 5% foam, swelling immediate persisted about in mean three days posoperative. None important complication was related in present study except superficial necrosis (9) which has been reported for Costa et al., (2011) and Górriz-Gómez et al., (2014) that resolved by spontaneous cure. To avoid haemoglobinuria, that type of complication is specific to use of EO, the injection was performed intra lumen and 20 ml EO or 0.3ml/kg was respected (Ozaki et al., 2010).

Lindsey et al., (2013) draws attention the location of the lesion and the possibility of large edema should be considered possible complications difficult breathing when VM´s present in tongue. In theirs case report, the patient required oral intubation for 72 hours after the sclerotherapy procedure due exacerbated edema in the tongue obliterating airways and making breathing difficult.

There was no reports of allergy to 5 % EO in present study but there are reports of anaphylactic shock after injection sclerosis agent and even a fatal case of allergic reaction reported by Shelley in 1938 (Kiripolsky, 2010).

It was observed that quantity 5% EO foam used, in this study, demonstrated satisfactory and effective. Probably to reach the same results with foam EO when treat the large VM, the quantity of this medication could be greater if applicated pure, also increasing the possibility of severe complications. There are tendency in use minor volume to treat VM when realized sclerotherapy with EO in foam and consequently

decreasing the number of sessions and complications, becoming a more effective and safe treatment.

It is important emphasize the excellent results obtained in this study using 5% EO foam refered by clinical healing of lesions and satisfactory level of patients. It should be aware of the correct punction the lesion to minimized discomfort to the patient. However, this procedure can optimize the treatment with better results.

Therefore, this study showed by the first time that EO can be used safely and effectively as a FOAM form, showed no severe complications for patients, many greats results reached and remained stable for monitoring carried out in all patients. More investigations including a larger number of patients or comparing different medication are warranted to establish an ideal protocol to vascular venous malformations and comparison and it also compares a foam with pure form of drug, to evaluate clear benefits relative to each other, such as decreasing the number of sessions and applied volume final of sclerosant agent, minimizing complications.

Conflict of interest

None declared

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Table 1 Epidemiologic dates of the 17 patients with vascular malformation included in this study.

Patients	Sex	Age	Race	Comorbidities	Number of vascular malformation
1	F	37	B	Hypertension	1
2	M	23	B	Negative	1
3	F	36	W	Negative	2
4	F	69	W	Hypertension	1
5	M	65	W	Negative	1
6	F	63	B	Negative	1
7	F	16	B	Negative	1
8	F	39	B	Hypertension	2
9	F	22	W	Negative	1
10	M	56	W	Negative	2
11	F	61	W	Hypertension	1
12	F	11	B	Negative	1
13	F	64	W	Hypertension	6
14	M	44	B	Negative	3
15	M	18	B	Negative	3
16	F	43	B	Negative	3
17	M	22	B	Negative	4

Legend: F (female); M (male); B (black); W (white).

Tabel 2 Descriptive results from 34 lesions treated with 5% ethamoline oleate foam

Lesions	Previous Treatment	Color	Clinic characteristic	Site	Size (mm)	Total volume (mL)	Sessions Number	Complication	Satisfaction of patient	Clinical Healing
1	None	Red	Swelling	Lowerlip	50	5	1	1	9	2
2	None	Red	Swelling	Upperlip	30	3	1	0	9	1
3	None	Purple	Swelling	Lowerlip	20	2	1	0	10	1
4	None	Purple	Swelling	Tongue	30	6	2	0	10	1
5	None	Purple	Nodule	Buccal mucosa	20	2	1	1	10	1
6	None	Purple	Swelling	Tongue	30	6	2	0	9	1
7	None	Purple	Nodule	Buccal mucosa	30	5	2	1	9	1
8	Surgery	Skin	Swelling	Neckl	50	21	6	0	10	1
9	None	Purple	Plane	Zygomatic	30	12	8	0	6	4
10	None	Purple	Swelling	Upperlip	40	14	7	1	6	4
11	Polidocanol	Purple	Swelling	Lowerlip	50	20	5	1	6	3
12	Polidocanol	Purple	Swelling	Upperlip	40	12	4	0	10	1
13	Polidocanol	Purple	Swelling	Upperlip	30	7	3	1	10	1
14	None	Purple	Plane	Buccal mucosa	30	3	1	0	10	1
15	None	Purple	Swelling	Chin	50	39	10	1	9	2
16	Polidocanol	Purple	Swelling	Parotid	40	4	1	0	10	1
17	Polidocanol	Purple	Swelling	Chin	30	11	4	0	10	1
18	Polidocanol	Purple	Swelling	Lowerlip	30	3	1	0	9	1
19	Polidocanol	Purple	Swelling	Neck	20	6	4	0	9	2
20	Polidocanol	Purple	Swelling	Tongue	80	22	3	0	8	3
21	Polidocanol	Purple	Swelling	Tongue	60	12	2	0	8	2
22	Surgery	Skin	Swelling	Parotid	60	20	4	1	9	1
23	Surgery	Purple	Swelling	Tongue	80	29	6	0	10	1
24	Surgery	Purple	Swelling	Mouthfloor	70	9	2	0	10	1
25	Polidocanol	Purple	Swelling	Nose	70	11	2	1	8	2
26	Polidocanol	Purple	Swelling	zygomatic	30	6	2	0	7	3
27	Polidocanol	Purple	Swelling	Upperlip	20	2	1	0	10	1

Table 3 Comparison between smaller and larger lesions than 30mm.

		TOTAL VOLUME		*P*	NUMBER OF SESSIONS		*P*	HEALING		*p*
		≤ 10 ml	> 10ml		1	>1		Yes	No	
SIZE	≤ 30 mm	16 (47.0%)	2 (5.8%)	0.0002*	14 (41.1%)	4 (11.7%)	0.04*	15 (44.2%)	3 (8.8%)	0.01*
	> 30 mm	4 (11.8%)	12 (35.4%)		7 (20.6%)	9 26.6%)		7 (20.5%)	9 (26.5%)	
SATISFACTION	≤ 9.5	8 (23.5%)	9 (26.5%)	0.14	10 (29.4%)	11 (32.4%)	0.5	6 (17.6%)	16 (47.0%)	0.0003*
	> 9.5	12 (35.3%)	5 (14.7%)		7 (20.6%)	6 (17.6%)		11 (32.4%)	1 (3.0%)	

*Exact Fisher Test

Figures and Legends

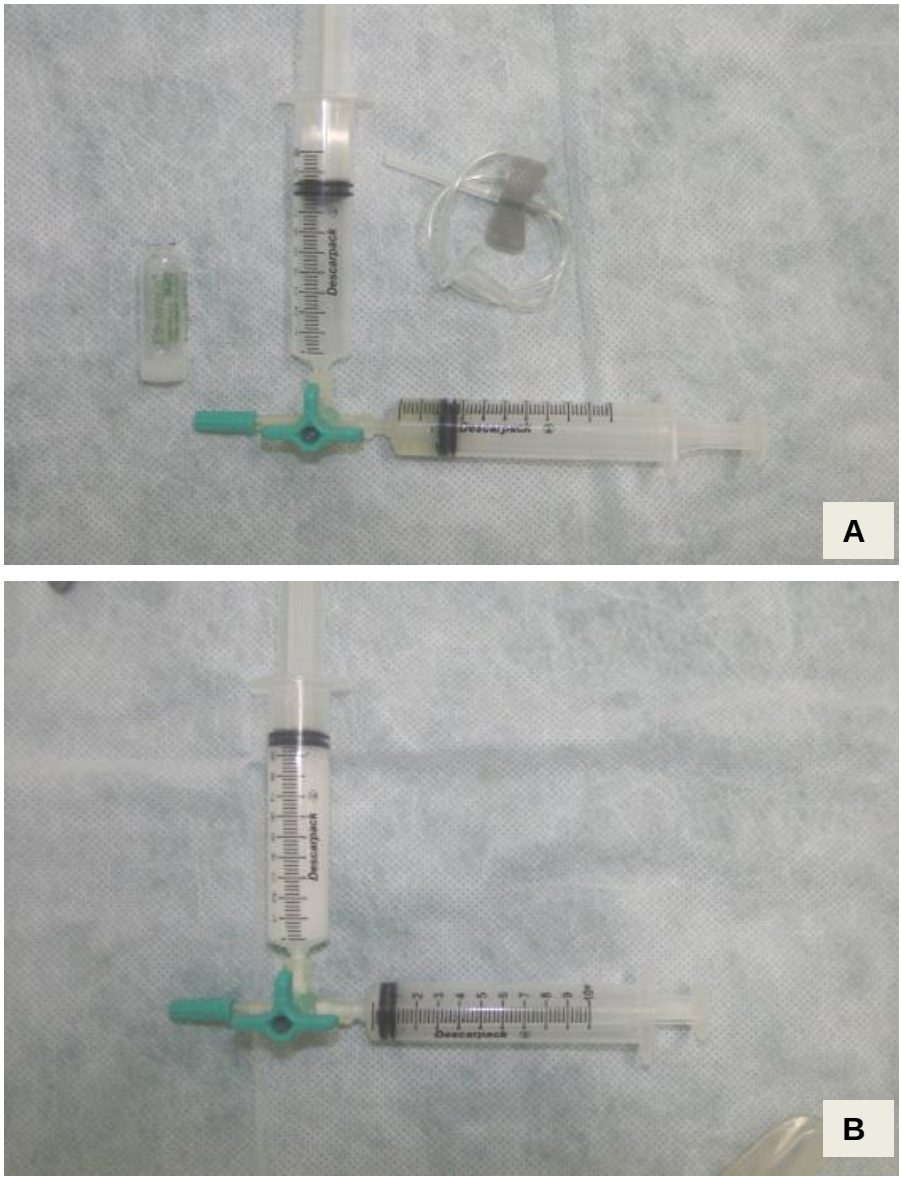

Figure 1. A, Two Syringes of 10ml, one scalp, one three way and the Ethamolin® ampoule with 8 ml of air drawn. B, Syringes after cycles showed 5% EO foam presented into one syringe with white characteristics color (Tessari technique, 2000).

Figure- 2 Example of Visual Scale Analogue (VSA) to measure pain according Mannion et al., (2007).

Figure- 3 Example of Visual Scale Analogue (VSA) to measure level of patient's satisfaction to treatment according Peñarrocha et al., (2007).

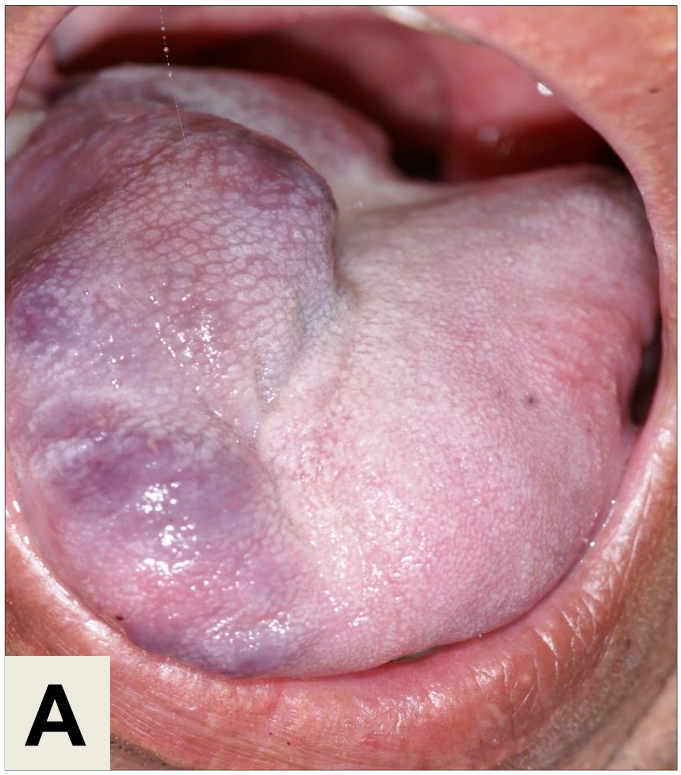

Figure 4- A, VM initial stage at tongue.

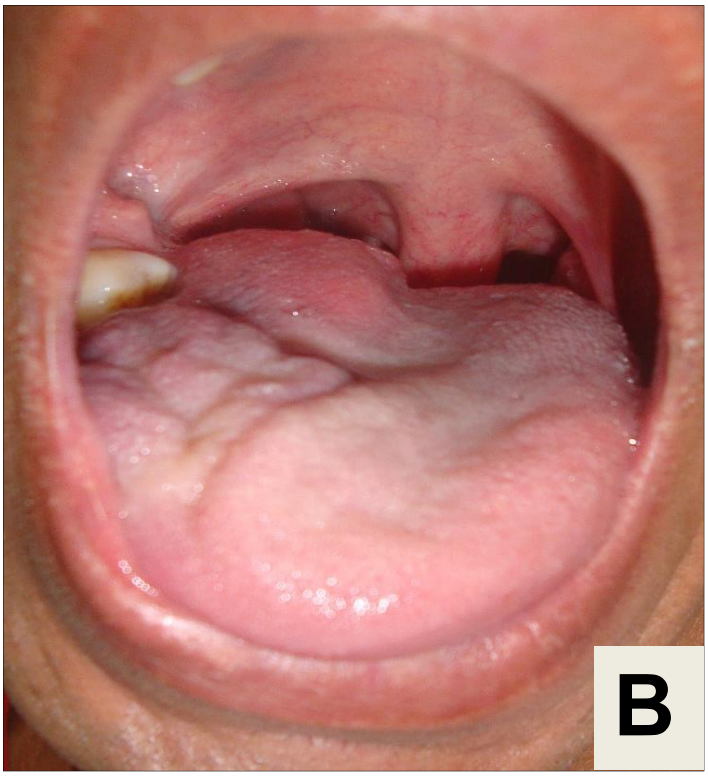

Figure4- B, VM after 3 sessions with 5% EO foam.

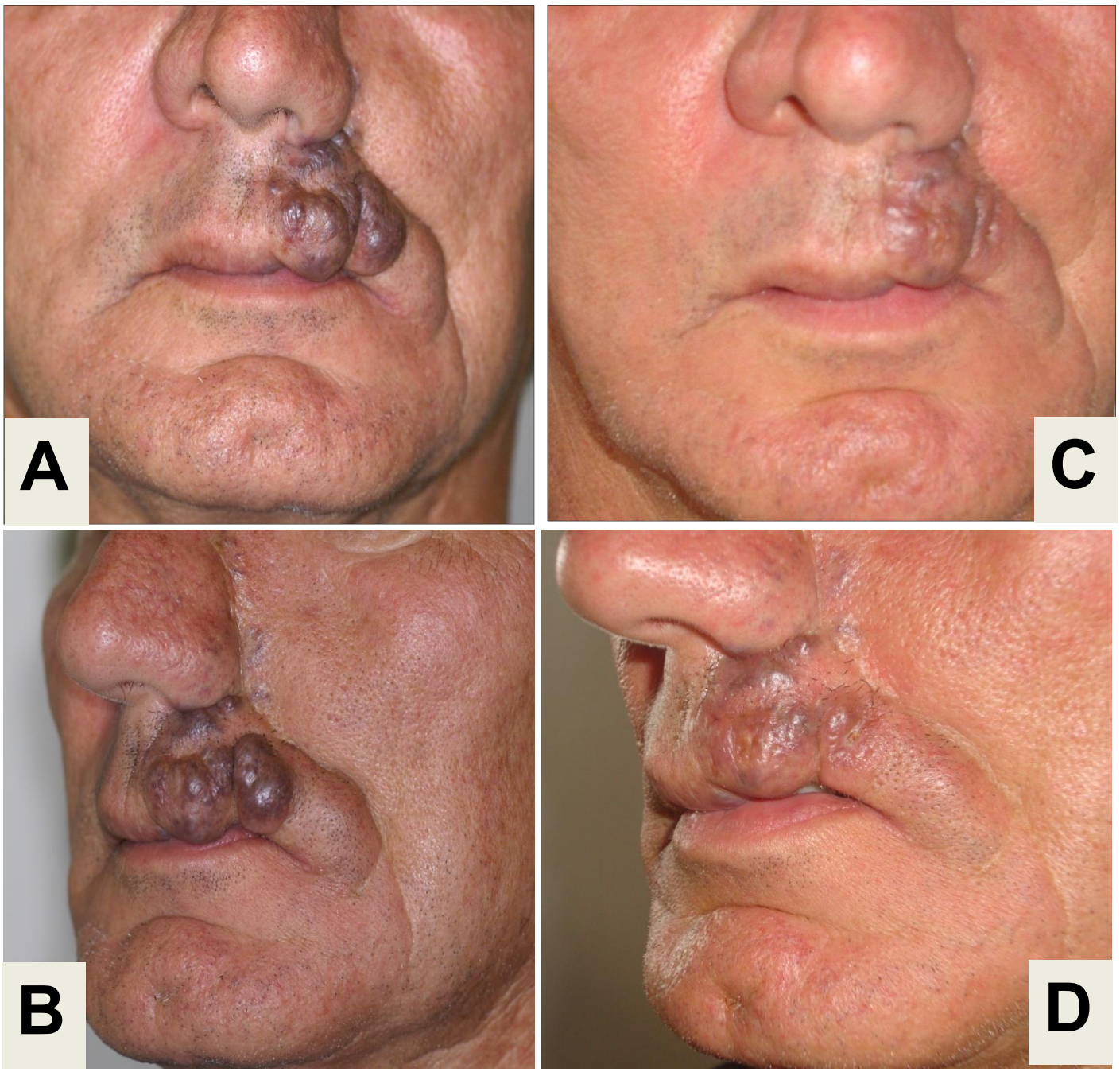

Figure 5- A, VM initial stage in upper lip in front view. B, VM initial stage in profile view. C VM finally clinical aspect after 2 sessions 5% EO foam in front view. D, VM finally clinical aspect after 2 sessions 5% EO foam in profile view.

9. CONSIDERAÇÕES FINAIS

O tratamento de MVBs por meio de escleroterapia está consolidado na literatura, o uso de agentes esclerosantes responsáveis pela fibrose do vaso sanguíneo e consequentemente redução/eliminação da MVB é discutido quanto ao melhor agente, concentração e dose ideal, para que o tratamento seja efetivo e seguro ao paciente. O agente esclerosante oleato de monoetanolamina a 5% demonstra ter características que permitem sucesso com seu uso para tratamento de MVBs na região de cabeça e pescoço.

O estudo prospectivo descritivo permitiu comparar de forma efetiva o uso do oleato de monoetanolamina a 5% em doses ainda não descritas na literatura evidenciando eficiência e segurança em seu uso. Observou-se ausência de complicações e efetividade em 100% dos pacientes tratados. A comparação entre as 3 doses mais utilizadas do oleato de etanolamina (1,25%; 2,5% e 5%) mostrou que a concentração de 5% é mais efetiva, tratando as LVBs em menor período, menor quantidade de medicamento e sem complicações. Por fim, o oleato de monoetanolamina a 5% em forma de espuma, para MVBs maiores, mostrou ser uma boa alternativa ao uso da droga pura, reduzindo também quantidade de medicamento aplicado, efetividade na resolução e segurança. No entanto, por ter ocorrido 9 necroses superficiais como complicação do tratamento por oleato de monoetanolamina em espuma, pode se imaginar que a diminuição da dose (1ml/1cm lesão) poderia também refletir em resultados favoráveis, reduzindo ou eliminando esta complicação. Assim, estudos com tempo de acompanhamento maior, populações distintas, comparação entre a dosagens devem ser realizados levando em consideração a escleroterapia de MVBs com oleato de etanolamina.

10. CONCLUSÕES

O tratamento por meio de escleroterapia com oleato de etanolamina de MVBs na região de cabeça e pescoço na concentração de 5% é efetivo, seguro e de melhor desempenho do que concentrações inferiores da droga (1,25% e 2,5%). A forma em espuma de tratamento da escleroterapia com oleato de monoetanolamina para estas MVBs mantém os parâmetros de segurança e eficácia já observados no uso do mesmo puro. Portanto, o estudo demonstra que o uso de oleato de etanolamina para escleroterapia de MVBs na região de cabeça e pescoço demonstra ser eficaz e seguro.

ANEXO 1

APÊNDICE A

PRODUÇÃO CIENTÍFICA:

A1- Atividades desenvolvidas relacionadas à tese (cursos, estágios, participação em eventos):

- Ao longo do doutorado fui estimulado pelo meu orientador e co-orientadora (Prof Dr Ricardo Mesquita e Profa Dra Soraya de Mattos) a realizar outras tarefas que agregassem ao curso. Assim, além do estágio docente obrigatório por 2 semestres, realizei, no ano de 2012, no segundo semestre, mais um estágio docente na clínica de Patologia e Semiologia da Faculdade de Odontologia da UFMG, de forma voluntária.

- Participei no ano de 2012, nos dias 15 a 17 de Novembro, do VII Encontro Norte e Nordeste de Cirurgia e Traumatologia Buco-Maxilo-Facial (ENNEC).

- Participei no ano de 2013, nos dias 17 a 20 de Julho, do XXI Congresso Brasileiro de Estomatologia e Patologia Oral.

A2- Produção científica (apresentação oral em eventos, resumos, trabalhos completos)

- Participei no ano de 2012, nos dias 15 a 17 de Novembro, do VII Encontro Norte e Nordeste de Cirurgia e Traumatologia Buco-Maxilo-Facial (ENNEC), sendo apresentado em forma de painel no mesmo congresso um caso clínico tratado em conjunto com o serviço de Estomatologia e Patologia (Fibroma Ossificante Juvenil: Relato de Caso).

- Participei no ano de 2013, nos dias 17 a 20 de Julho, do XXI Congresso Brasileiro de Estomatologia e Patologia Oral (Salvador/BA) sendo apresentado neste congresso dois trabalhos científicos, um de forma oral e outro painel eletrônico, referentes à Tese proposta (1-Foam sclerotherapy with 5%

Ethanolamine Oleate in Vascular Malformation e 2-Sclerotherapy with 5% Ethanolamine Oleate in oral benign vascular lesions).

- Participei no ano de 2014, do XII Encontro de Pesquisa da Faculdade de Odontologia da UFMG (Belo Horizonte/MG) que se realizou nas datas de 09 a 12 de Maio, sendo apresentado neste evento trabalho referente à Tese proposta (Uso de escleroterapia com oleato de etanolamina para tratamento de lesões vasculares bucais benignas: Qual é a concentração ideal?).

- Participei no ano de 2014 da XXI JOME (Belo Horizonte/MG) que se realizou nas datas de 20 a 22 de Agosto, sendo apresentado neste evento trabalho referente à Tese proposta (Escleroterapia com oleato de etamolin em espuma: série de casos).

- Publicação de resumo no periódico Oral Surgery, Oral Medicine, Oral Pathology Oral Radiology. February 2014; 117: 124 .(Title: Foam sclerotherapy with 5% Ethanolamine Oleate in Vascular Malformation. Authors: Michel Campos Ribeiro, Soraya de Mattos Camargo Grossmann, Wagner Henrique Castro and Ricardo Alves de Mesquita.

- Publicação de resumo no periódico Oral Surgery, Oral Medicine, Oral Pathology Oral Radiology. February 2014; 117: 222-223 (Title: Sclerotherapy with 5% Ethanolamine Oleate in oral benign vascular lesions Authors: Michel Campos Ribeiro, Soraya de Mattos Camargo Grossmann, Márcio Bruno Figueiredo do Amaral and Ricardo Alves de Mesquita.

APÊNDICE B

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Prezado paciente e/ou responsável:

Gostaríamos de convidá-lo a participar da pesquisa intitulada **“TRATAMENTO DE LESÔES VASCULARES BENIGNAS NA REGIÃO DE CABEÇA E PESCOÇO POR MEIO DE ESCLEROTERAPIA COM OLEATO DE MONOETANOLAMINA**”, com o objetivo de tratar lesões vasculares na face e cavidade oral e face. 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 tratamento de lesões vasculares da face e cavidade oral com escleroterapia com monoetanolamina em espuma.
- Todos os pacientes terão de ter diagnóstico clínico de lesão vascular da face ou cavidade.
- A técnica de escleroterapia com monoetanolamina em espuma consiste em aplicação desta espuma no centro da lesão com quantidade de espuma dependente do tamanho da lesão.
- Sua colaboração é muito importante e você não pagará nada por este tratamento. Você participa se quiser. Se você assinar concordando em participar e se arrepender, você pode desistir a qualquer momento. Se desistir, não afetará em nada o seu tratamento. 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 atendimento será feito na Faculdade de Odontologia da UFMG (clínica 4) e no Hospital das Clínicas da Faculdade de Medicina da UFMG (ambulatório Cirurgia Vascular)
- Possíveis riscos deste estudo são a possibilidade do não desaparecimento total da lesão. Alergia ao agente esclerosante. Poderá haver algum desconforto, como dor e inchaço. Não há relatos de casos com complicaçõe maiores com esta técnica. O objetivo desta pesquisa também é avaliar a dor e inchaço, 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 um procedimento e com menor quantidade de medicamento.

- Todos os examinadores são dentistas e/ou médicos e pesquisadores 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 e o convidamos a participar desta pesquisa. Os telefones dos pesquisadores para quaisquer esclarecimentos são: Michel Campos Ribeiro- 84863929; Márcio Bruno F. Amaral – 91789845, Prof. Dr. Ricardo Alves Mesquita – 3409 2499.
- **COEP/UFMG**: Campus Pampulha: Unidade Administrativa II – Prédio da FUNDEP, 2º andar. Telefone: 3409-4592.

Eu, , estou ciente de ser portador(a) de lesão vascular benigna na cavidade oral ou face. Apresentando este diagnóstico clínico, concordo em participar de um estudo que objetiva tratar estas alterações com agente esclerosante monoetanolamina puro ou em espuma.

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 novo procedimento de escleroterapia por espuma.

Tenho pleno conhecimento de que o principal objetivo é o tratamento de LBVs.

Dou pleno direito de uso dos dados para fins de pesquisa e de divulgação em jornais e/ou revistas científicas esp ecializadas 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 20 .

Assinatura do paciente ou responsável

Documento de Identidade
Contatos:
Michel Campos Ribeiro (Doutorando): tel:-8486-3929
Prof. Ricardo Alves Mesquita: tel-3409-2499

APÊNDICE C

FICHA CLÍNICA (ADMISSÃO)

PROJETO DE PESQUISA: **ESCLEROTERAPIA COM ESPUMA DE OLEATO DE MONOETANOLAMINA A 5% NO TRATAMENTO DE MALFORMAÇÕES VASCULARES DA REGIÃO DE CABEÇA E PESCOÇO: SÉRIE DE CASOS**

IDENTIFICAÇÃO DO PACIENTE

NOME:_____

DATA DE NASCIMENTO:_____ IDADE:_____ COR:_____

SEXO:_____

ENDEREÇO:_____

BAIRRO:_____

CIDADE:_____

CEP:_____

TELEFONE:_____

PROFISSÃO:_____

DATA DO ATENDIMENTO

INICIAL:_____

HISTÓRIA MÉDICA

ALERGIA:_____

TRATAMENTO MÉDICO

ANTERIOR:_____

TRATAMENTO MÉDICO

ATUAL:_____

FAZ USO CONSTANTE DE ALGUM

MEDICAMENTO?_____

_____

REVISÃO DE SISTEMAS

ENDÓCRINO:_____

CARDIOVASCULAR:_____

GASTROINTESTINAL:_____ GENITO-

URINÁRIO:_____

RESPIRATÓRIO:_____

DST:_____

HISTÓRIA FAMILIAR

PAI:_____

MÃE:_____

IRMÃOS:_____

FILHOS:_____

SINAIS E SINTOMAS:

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EXAME CLÍNICO INTRA ORAL:

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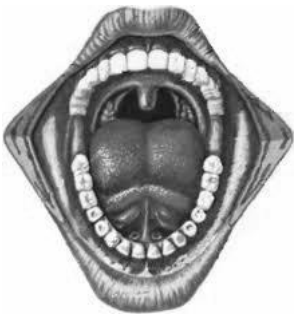

EXAME CLÍNICO EXTRA ORAL

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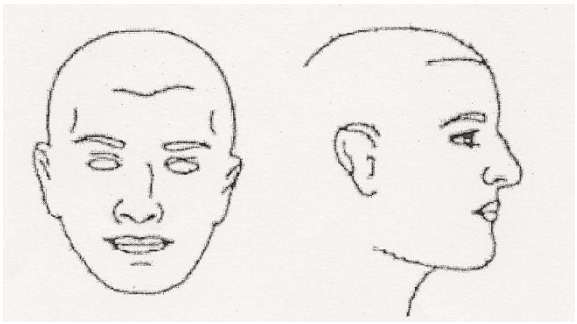

TIPO DE LESÃO

DIAGNOSTICADA:_____

CARACTERÍSTICAS DA LESÃO DIAGNOSTICADA:

_____

_____

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FICHA CLÍNICA (INTERVENÇÃO)

PROJETO DE PESQUISA: **ESCLEROTERAPIA COM ESPUMA DE OLEATO DE MONOETANOLAMINA A 5% NO TRATAMENTO DE MALFORMAÇÕES VASCULARES DA REGIÃO DE CABEÇA E PESCOÇO: SÉRIE DE CASOS**

EXAMES PRÉ OPERATÓRIOS SOLICITADOS:

_____

_____

_____

_____

TRATAMENTO PROPOSTO:

DATA

INICIAL:_____

ANESTESIA: ( ) SIM ( ) NÃO TIPO:_____

QUANTIDADE:_____

AGENTE

ESCLEROSANTE:_____

CONCENTRAÇÃO AGENTE

ESCLEROSANTE:_____

DOSE

APLICADA:_____

PURO( ) ESPUMA( )

INTERCORRÊNCIA:_____

EQUIPE:_____

REAPLICAÇÃO

(DATA):_____

ANESTESIA: ( ) SIM ( ) NÃO TIPO:_____

QUANTIDADE:_____

AGENTE

ESCLEROSANTE:_____

CONCENTRAÇÃO AGENTE

ESCLEROSANTE:_____

DOSE

APLICADA:_____

PURO( ) ESPUMA( )

INTERCORRÊNCIA:_____

EQUIPE:_____

EXAMES PÓS OPERATÓRIOS SOLICITADOS:

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MEDICAÇÃO PÓS OPERATÓRIA:

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FICHA CLÍNICA (ACOMPANHAMENTO)

PROJETO DE PESQUISA: **ESCLEROTERAPIA COM ESPUMA DE OLEATO DE MONOETANOLAMINA A 5% NO TRATAMENTO DE MALFORMAÇÕES VASCULARES DA REGIÃO DE CABEÇA E PESCOÇO: SÉRIE DE CASOS**

INTERVENÇÃO (DATA): (Nº)

DOR (ESCALA): ( ) IMEDIATO ( ) 1 SEMANA

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ANALGÉSICO/ANTIINFLATÓRIO(QUAL/DOSE) ( ) SIM ( ) NÃO

EDEMA: ( ) SIM ( ) NÃO

COMPLICAÇÕES: ( ) SIM ( ) NÃO

CURA CLÍNICA (6 MESES):

RECORRÊNCIA (6 MESES):

SATISFAÇÃO PACIENTE (6 MESES):