Université de Montréal

Phase-I clinical trial on the effect of palatal brushing on denture stomatitis

par
Marla Kabawat

Département de dentisterie de restauration
Faculté de médecine dentaire
Université de Montréal

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Ce mémoire intitulé:

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Présenté par:
Marla Kabawat

A été évalué par un jury composé des personnes suivantes:

Dr Benoît Lalonde, président-rapporteur
Dre Elham Emami, directrice de recherche
Dr Louis de Koninck, co-directeur de recherche
Dr Jean Barbeau, co-directeur de recherche
Dr Gilles Gauthier, membre du jury

RÉSUMÉ

Introduction: La stomatite prothétique est une condition inflammatoire chronique de la muqueuse buccale recouverte par une prothèse. Cette maladie est considérée comme la lésion buccale la plus fréquente chez les porteurs de prothèses amovibles. Des études récentes sur l'étiologie de la stomatite prothétique suggèrent que des traitements basés sur la réduction de l'inflammation seraient efficaces dans le traitement de cette maladie.

Objectifs: Évaluer l'efficacité du brossage du palais dans le traitement de la stomatite prothétique.

Méthodes: Quarante-huit participants (âge moyen : 66,0 ± 11,2 ans) avec un diagnostic de stomatite prothétique, ont été sélectionnés à partir d'un examen préalable de 143 individus, afin de participer à cet essai clinique de phase I à deux centres, réalisé selon un devis de type pré-test/post-test à un seul groupe. L'intervention a consisté en un brossage du palais avec une brosse manuelle après chaque repas et avant le coucher. Des examens cliniques et microbiologiques ont été effectués avant le traitement, et à 1 mois et 3 mois de suivi. Des données supplémentaires ont été obtenues par l'utilisation d'un questionnaire validé. Les résultats primaires et secondaires étaient, respectivement, la rémission de stomatite prothétique et la diminution du nombre de colonies de *Candida*. Des tests statistiques descriptifs et non paramétriques ont été menés pour analyser les données.

Résultats: À 3 mois de suivi, 10,4 % des participants ont été guéris et 70,8 % ont eu une amélioration clinique de la stomatite prothétique grâce au brossage du palais. Une

réduction statistiquement significative de la surface et de l'intensité de l'inflammation après 3 mois de brossage du palais a été démontrée ($p < 0,0001$). L'ampleur de l'effet a varié d'un effet modéré à important (0,34 à 0,54) selon la classification utilisée pour le diagnostique de la stomatite prothétique. De plus, le nombre de colonies de *Candida*, recueillies par sonication des prothèses et par échantillonnage du palais, a diminué de manière statistiquement significative après 3 mois de brossage ($p \leq 0,05$).

Conclusion: Les résultats de cette étude suggèrent que le brossage du palais est efficace comme traitement de la stomatite prothétique.

Mots-clés: Stomatite prothétique, brossage du palais, prothèse complète, *Candida*, étude de phase I.

ABSTRACT

Introduction: Denture-related erythematous stomatitis (denture stomatitis) is a chronic inflammation of the oral mucosa covered by a removable prosthesis. This disease is considered the most prevalent mucosal lesion associated with prosthesis use. Recent research on the etiology of denture stomatitis suggests that treatments based on the reduction of the inflammation are effective in the management of this disease.

Objectives: To assess the efficacy of palatal brushing in the treatment of denture stomatitis.

Methods: After screening 143 individuals with a potential diagnosis of denture stomatitis, 48 (mean age: 66.0 ± 11.2 years) were enrolled in a phase-I two-center clinical trial with one-group pre-test/post-test design. The intervention of interest was manual palatal brushing after each meal and before bedtime. Clinical and microbiological examinations were performed at baseline, 1 month and 3 months post-intervention. Additional data were obtained by the use of a validated questionnaire. The primary and secondary outcomes were the remission of denture stomatitis and the diminution of *Candida* Colony-Forming Units (CFUs), respectively. Descriptive and non-parametric statistical tests were conducted to analyze the data.

Results: At 3-month follow-up, denture stomatitis was completely cured in 10.4 % of the study participants, and 70.8 % of denture wearers showed improvement in the clinical signs of denture stomatitis. There was a significant reduction in the area and severity of the palatal inflammation at 3-month follow-up ($p < 0.0001$). The effect size

ranged from medium to large (0.34 to 0.54), depending on the classification used for the diagnosis of denture stomatitis. Furthermore, a significant reduction in the number of *Candida* CFUs isolated from the palatal mucosa and dentures was observed ($p \leq 0.05$).

Conclusion: The results of this study suggest that palatal brushing is effective in the treatment of denture stomatitis.

Keywords: Denture stomatitis, palatal brushing, complete denture, *Candida*, phase I trial

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LIST OF SYMBOLS AND ABBREVIATIONS

CFUs	Colony-Forming Units
%	Percentage
OR	Odds Ratio
CI	Confidence Interval
F	Female
WHO	World health Organization
NHANES	National Health and Nutrition Examination Survey
RCT	Randomized Controlled Trial
IL	Interleukin
TNF	Tumor Necrosis Factor
C.	*Candida*
RR	Relative Risk
PDT	Photodynamic Therapy
VAS	Visual Analogue Scale

DEDICATION

To my beloved parents and sister,

To the love of my life,

Thank you Rizkallah, Lina, Nai and Nidal for being a source of love and encouragement, and for believing in me.

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There are a number of people without whom this thesis might not have been written, and to whom I am deeply grateful.

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Finally, I am thankful for my parents, my sister and my fiancé for their endless love and support and for giving me the opportunity to pursue my studies.

CHAPTER I

LITERATURE REVIEW

1.1 INTRODUCTION

Over the last few decades, there has been substantial progress in understanding the role of oral inflammation in systemic health. Oral inflammation is a protective, non-specific response of the immune system to a pathogenic or traumatic injury [1-3]. Although this defensive inflammatory mechanism is necessary for the protection of the oral cavity, it can be potentially deleterious when it becomes long-lasting and persistent.

Denture-related erythematous stomatitis (denture stomatitis) is the most common mucosal disease associated with the wear of removable prostheses, and is characterized by a chronic inflammation of the palatal mucosa [4-6]. The treatment of this recurrent condition has challenged clinicians because of its resistant and refractory nature. Although its recalcitrance has been related to *Candida* biofilms and their attachment to prosthetic surfaces, the direct role of *Candida* in the injury to the adjacent mucosa has been questioned. The new evidence suggests that trauma initiates the inflammatory reaction in denture stomatitis [7]. Subsequently, the complex structured microbiological communities play an intermediary role in the process of denture stomatitis [7]. Based on this hypothesis, the treatment of denture stomatitis should focus on the resolution of the inflammation.

The first chapter of this thesis will review the literature to discover the rationale behind this hypothesis.

1.2 ORAL INFLAMMATION

1.2.1 Definition of oral inflammation

The oral cavity is a very complex system that is vulnerable to inflammatory diseases due to the exposure of the oral environment to different pathogenic stimuli. Although the primary role of an inflammatory response is to protect oral tissues from a deleterious injury [1, 3], this defensive mechanism could affect different sites of the oral cavity and manifest as a primary sign of oral diseases such as periodontitis, pulpitis, mucositis, and stomatitis [8].

Inflammation is defined as a nonspecific response of the body in reaction to a mechanical, chemical or microbial stimulus [9]. Its etymology comes from the Latin *inflammare*, "to set on fire". Cornelius Celsus [10], a Roman encyclopaedist, was the first person who introduced the cardinal signs of inflammation. These include redness, swelling, heat and pain, and represent the clinical manifestation of increased local vascularity, exudation of tissue fluid, increased blood flow and the release of inflammatory mediators, as well as the stimulation of pain receptors [1, 3]. In 1858, Rudolf Virchow added loss of function to the four signs of inflammation. Loss of function is caused by the combination of pathophysiological events that occur during inflammation [11].

1.2.2 Physiology of oral inflammation

An oral inflammatory process is similar to any other inflammation in the human body and consists of complex interactions between inflammatory mediators and different types of cells [1, 3]. Inflammatory mediators are soluble molecules that represent the physiological messengers of the inflammation and can positively or negatively influence the inflammatory process [7, 12]. Their role is to induce and maintain a host response. Inflammatory mediators include vasoactive amines (histamine, serotonin), arachadonic acids (prostaglandins, leukotrienes) and cytokines (tumor necrosis factor, interleukins, interferons, and colony stimulating factors). Those mediators are released from different types of cells, including mast cells, dendritic cells, platelets, neutrophils and monocytes [1, 9].

Inflammatory mediators initiate numerous physiological processes including vasodilatation, increased microvascular permeability, cellular activation, cellular adhesion, and coagulation. Vasodilatation and increased microvascular permeability at the site of injury increase the available oxygen and nutrients, generate heat, and provoke tissue oedema. This increased permeability leads to the infiltration of plasma proteins and leucocytes from the circulation. The leucocytes, which consist principally of polymorphonuclear leukocytes (neutrophils) and macrophages, are attracted by inflammatory mediators, become activated, and aggregate at the site of the injury. They also become engaged in the production of cytokines and other inflammatory mediators [3, 13]. Endothelial cells also become active and secrete additional cytokines and secondary

inflammatory mediators. These processes result in the activation of coagulation cascades and lead to local thrombosis and isolating of the inflamed areas [9].

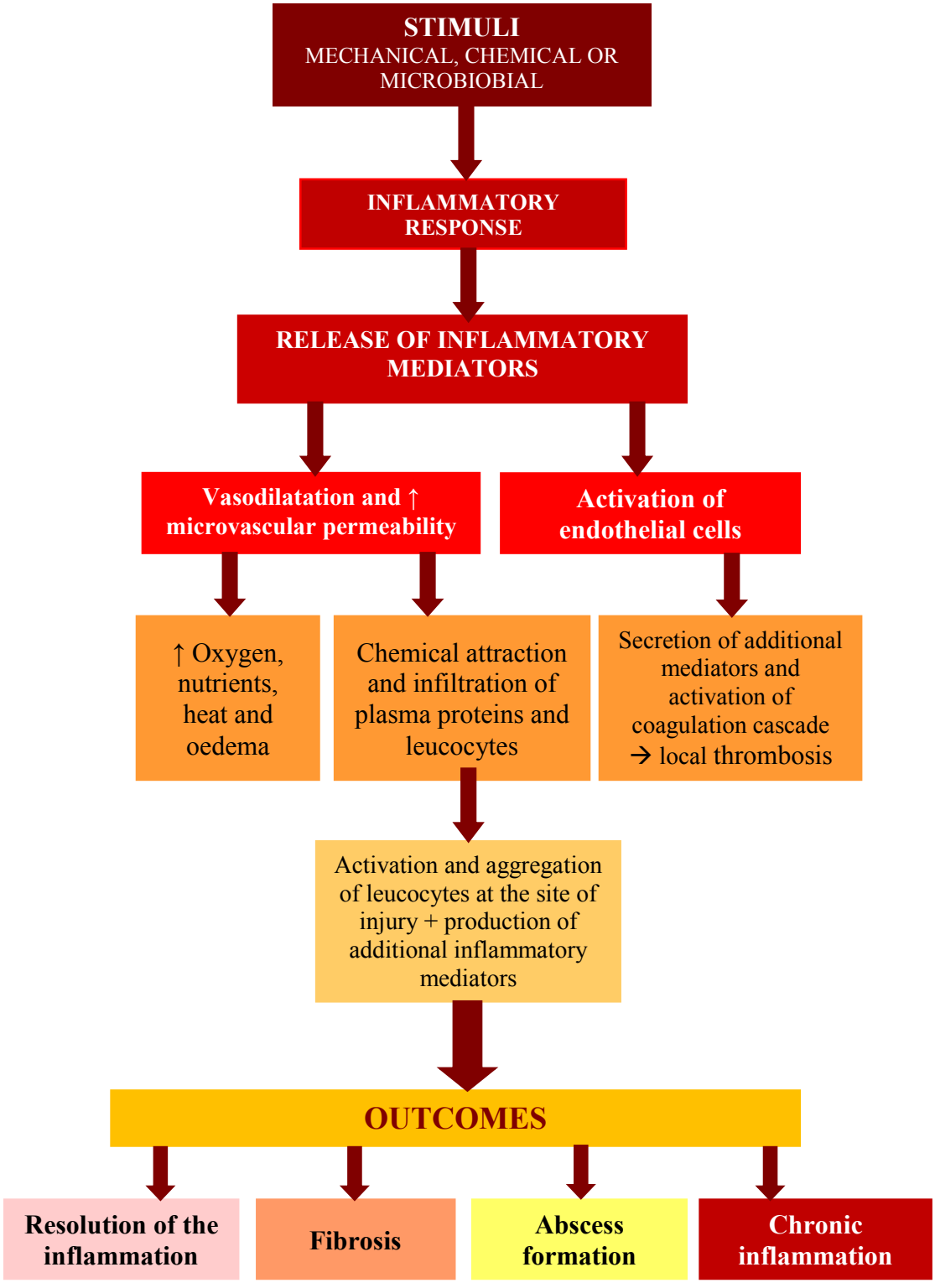


Figure 1.1: The inflammatory process

1.2.3 Types and etiology of oral inflammation

An oral inflammatory response can be classified into two main types: acute and chronic inflammation. An acute inflammatory response is a process characterized by a rapid onset, usually appearing within a few minutes or hours after the injury. This prompt response is also of short-term duration and ceases after the removal of the stimulus [3]. Acute inflammation is marked by the exudation of fluid and plasma proteins and by the migration of leukocytes, most particularly neutrophils, to the site of injury [1]. Conversely, a chronic inflammatory response is of prolonged duration and is characterized by the presence of lymphocytes and macrophages. Chronic inflammation could result from failure to eliminate the injurious stimulus, an autoimmune response, or from a chronic low-intensity irritant that persists for an extensive amount of time. A low-intensity irritation could cause deleterious changes in tissues, such as fibrosis and necrosis [1, 14].

Oral inflammation can also be described as being localized or generalized/systemic. Localized inflammation is generally confined to the site of injury. In contrast, when the local control of the inflammation is lost, an exaggerated response with systemic activation of the inflammatory response occurs [9].

The etiology of oral inflammatory reactions is multifactorial. Oral inflammation could be caused by infections (bacterial, viral, fungal), oral biofilms [14], trauma, neoplasia, chemotherapy and radiation therapy [15], as well as immune-mediated disorders [16] and systemic conditions [1].

1.3 DENTURE-RELATED ERYTHEMATOUS STOMATITIS

1.3.1 Definition, diagnosis and classification

Denture-related erythematous stomatitis, or denture stomatitis, was first described in the medical literature in 1936 by Cahn [17] under the name "denture sore mouth".

Denture stomatitis is a localized chronic inflammation of the oral mucosa covered by a removable prosthesis [4-6]. It usually affects the palatal mucosa under a complete upper prosthesis. The mandibular mucosa is rarely involved as a result of the lesser amount of tissue coverage and the continuous contact between the saliva and the lower alveolar mucosa [6, 18].

This pathology is often diagnosed clinically by an oral healthcare professional during routine examination of denture wearers since denture stomatitis is often asymptomatic [6, 19]. However, symptoms like mucosal bleeding, burning sensation of the palate and tongue, tenderness, halitosis, xerostomia, unpleasant taste and dysphagia, could occasionally be displayed [20-22].

In research and academic settings, various methods have been used to classify denture-related erythematous stomatitis. Generally, the classifications are based on three essential criteria: the distribution and the stages of the inflammation [21, 23], the intensity of the inflammation [24] and the extent of the inflammation [25, 26].

The first classification of denture stomatitis was introduced in 1958 by Östlund [27]. He distinguished three types based on the distribution of inflammation: I. Localized inflammation; II. Diffused erythema limited by the denture margins; III. Granular

reaction. Four years later, Newton [23] presented a new classification based on Östlund's. This classification, which has been widely used in clinical practice and research, has three types:

Newton Type I: Petechia: pinpoint hyperaemia around the orifices of the ducts of the palatal mucous glands;

Newton Type II: Diffuse hyperaemia: a generalised inflammation of the denture-bearing area;

Newton Type III: Inflammatory papillary hyperplasia.

In 1970, Budtz-Jørgensen and Bertram [21] removed the pinpoint hyperaemic lesions of Newton's classification and used the terms: "simple localized inflammation", "simple diffuse inflammation" and "granular inflammation". A decade later, Bergendal and Isacsson [24] classified denture stomatitis according to the intensity of the inflammation: Grade 0 : Normal pink, pale mucosa; Grade 1 : Slightly erythematous mucosa; Grade 2 : Moderately erythematous mucosa; and Grade 3: Pronouncedly erythematous mucosa. Schwartz et al. [26] added the concept of the extent of the inflammation:

0 No inflammation

1 Inflammation of the palate extending up to 20 mm on denture-bearing tissue

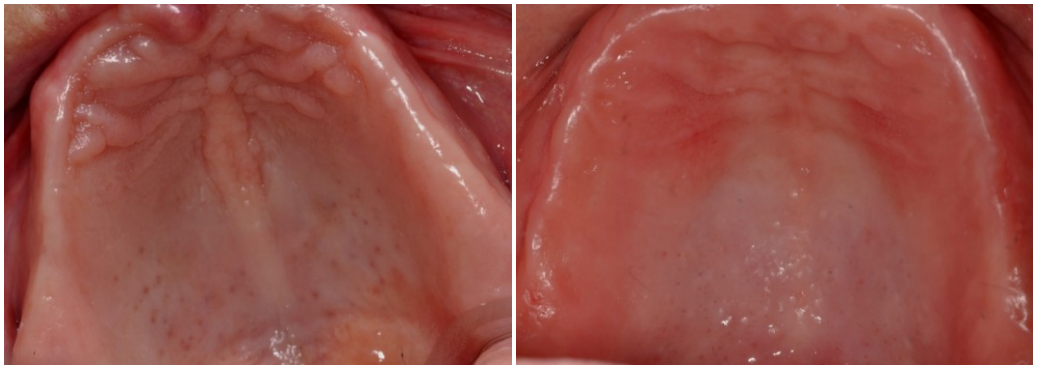
2 Inflammation of the palate extending more than 20 mm on denture-bearing tissue

3 Inflammation covering more than 50 % of the palatal denture-bearing tissue

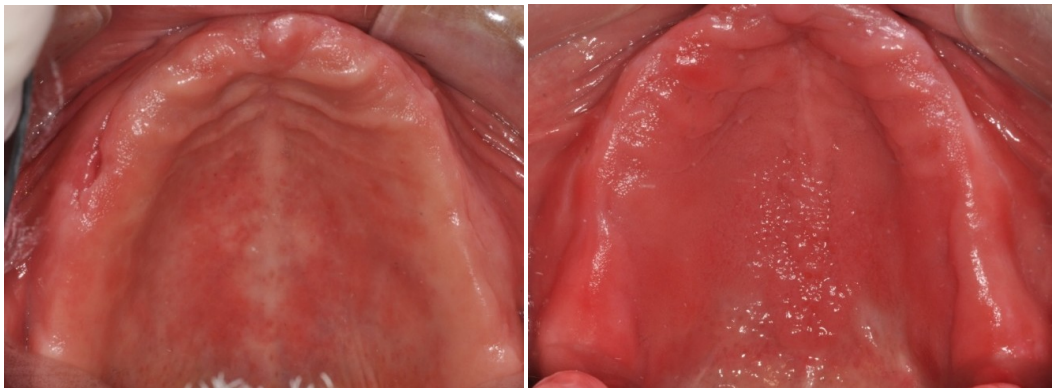
Finally in 2003, Barbeau et al. [25] modified the Newton classification to provide a more accurate evaluation of the extent of the lesion. Newton types II and III were

subclassified as A, if inflammation was present in 1 to 2 quadrants, or as B if inflammation was present in 3 to 4 quadrants.

In this master's research project, in order to capture the difference between petechiae and localized inflammation in regard to denture stomatitis treatment, we added two subtypes to Newton's Type I denture stomatitis: Type IA: Petechiae around the orifices of the ducts of the palatal minor salivary glands; Type IB: Localized area of inflammation in denture-bearing area (Figure 1.2).



Type IA **Type IB**



Type II **Type III**

Figure 1.2: Clinical features of denture-related erythematous stomatitis

1.3.2 Epidemiology of denture stomatitis

Denture-related erythematous stomatitis is considered the most prevalent mucosal lesion associated with prosthesis use [4, 5, 28]. In a recent review of the literature by Gendreau and Loewy [29], the global prevalence of this disease has been reported to be between 15 % and 77.5 %. Table 1.1 presents the worldwide prevalence of denture stomatitis in the last decade. In Quebec, the prevalence of denture stomatitis in complete denture wearers has been reported to be up to 77.5 % [7, 30]. However, it should be mentioned that these studies were mainly university-based and their populations were not representative of Quebec's general population. Although denture stomatitis is generally seen in complete denture wearers [6, 28], a recent systematic review [31] revealed that denture stomatitis has a prevalence of 1.1 % to 36 % in partial denture wearers.

Regarding the relationship between gender and denture stomatitis, many studies found that this pathology is more prevalent in women [17, 32, 33], whereas some others did not find any gender difference [34, 35]. It could be argued that females may be more susceptible to this disease as they are more likely to wear their prosthesis continuously to avoid an unesthetic appearance [36].

It has been reported that the prevalence of denture stomatitis increases with age [34, 37]. This could be explained by long-term denture use, inadequate oral hygiene due to the lack of dexterity, presence of systemic diseases and medication use, as well as a decrease in host immunity in the elderly [38-42]. Paradoxically, several studies did not demonstrate any association between aging and denture stomatitis [7, 28, 43].

Several risk and predisposing factors have been related to the occurrence of denture stomatitis, including continuous and nocturnal wear of the prosthesis [7]; nutritional deficiencies in proteins, vitamins A and B, and iron [6]; several systemic diseases such as diabetes mellitus and immunosuppressive diseases and therapies [44, 45]; medications such as antibiotics, corticosteroids, xerogenic agents and hormone supplementation therapy [46, 47]; as well as smoking [6, 24].

Although the literature shows contradictory results in regard to the association between these risk factors and denture stomatitis [6, 7, 35, 48, 49], there is some evidence that highlights the dominant role of nocturnal wear of the prosthesis in this disease [34, 50, 51]. In the cross-sectional study by Barbeau et al. [25], participants with extensive palatal inflammation were five times more likely to wear their prosthesis at night than healthy denture wearers (OR = 5.00; 95 % CI 1.35 to 18.55; $p = 0.03$). Nocturnal and continuous prosthesis wear could reduce the protective effect of saliva, decrease the cleaning effect of the tongue, prevent proper oxygenation of the palatal mucosa, and finally, increase local trauma to the mucosa. These effects make denture wearers more prone to mucosal mechanical and microbiological injuries, and therefore increase the risk of denture stomatitis in this population [7, 30, 51-54].

The noticeable variations between studies in regard to the epidemiology of denture stomatitis is justified by the inconsistency in methodological aspects of the studies, especially in the diagnostic criteria of denture stomatitis, data collection, the choice of the study population and its underlying spatial, socio-demographic and lifestyle characteristics [6, 17, 34, 45, 55].

Table 1.1: Denture stomatitis prevalence in the last decade (2003-2013)

Study/year of study/Country	Study design and study population	Sample size (n) and population characteristics	Denture stomatitis predisposing factors	Diagnosis of denture stomatitis	Prevalence of denture stomatitis (%)
Espinoza et al. [56], 2003, Chile	• Cross-sectional study • Random sample of individuals from public and private health systems	• n = 889 • 62 % F • ≥ 65 years old	Not available	Epidemiology guide for the diagnosis of oral mucosal diseases (WHO)	**34 %**

Barbeau et al. [25], 2003, Canada	• Cross-sectional study
	• Convenience samples of 2 cohorts:
	  • Cohort 1: university-based study
	  • Cohort 2: Individuals living or working in a nursing home
		Cohort 1:
		• n = 47
		• 66 % F
		• Mean age 63.7 ± 11.6 years
		
		Cohort 2:
		• n = 21
		• 76.2 % F
		• Mean age 56.3 ± 11.0 years
			• Nocturnal denture wear
			• Smoking
				Modified version of Newton's classification.	Cohort 1: 76.6 %
					
					Cohort 2: 57.1%
					
					Combined: **70.6 %**

Marchini et al. [19], 2004, Brazil	• Cross-sectional university-based study • Convenience sample of completely edentate individuals	• n = 236 • 75 % F • Mean age: 62 ± 12.8 years	• Poor oral hygiene	Not available	**42.4 %**
Shulman et al. [6], 2005, United States	• Cross-sectional study • Edentate individuals from the NHANES III (1988–1994) survey	• n = 3450 • 42.3 % F • Mean age: 59.2 ± 0.50 years	• Vitamin A deficiency • Nocturnal denture wear • Smoking ≥15 cigarettes per day	Classification of Newton	**27.9 %**
Mumcu et al. [57], 2005, Turkey	• Cross-sectional study • Random sample of completely edentate institutionalized individuals	• n = 765, • 49 % F • Mean age: 35.6 ± 26.6 years	Not available	Classification of Newton	**20.5 %**
Emami et al. [30], 2007, Canada	• Cross-sectional university-based study • Completely edentate individuals	• n = 40, • 77.8 % F • Mean age: 64.5 years	• Nocturnal denture wear	Classification of Newton	**77.5 %**

Emami et al. [7], 2008 , Canada	• 1-year follow-up of a previous RCT. • University-based study • Completely edentate individuals	• n = 173 • 53.8 % F • Mean age: 72.13 ± 4.39 years	• Nocturnal denture wear • Type of the prosthesis (implant-supported overdenture or conventional)	Classification of Newton	**63.6 %**
Baran et al. [58], 2009, Turkey	• Cross-sectional university-based study • Completely edentate individuals	• n = 310 • 49 % F • Mean age: 65.74 ± 2.73 years	• Poor denture hygiene habits	Classification of Newton	**35.8 %**
Divaris et al. [51], 2010, Greece	• Cross-sectional university-based study • Completely edentate individuals	• n = 873 • 49.45 % F • Mean age: 72.0 ± 5 years	• Nocturnal denture wear	Classification of Newton	**6 %**
Ferreira et al. [5], 2010, Brazil	• Cross-sectional study • Random sample of completely edentate individuals from nursing homes	• n = 335 • 73.1 % F • ≥ 60 years old	Not available	Epidemiology guide for the diagnosis of oral mucosal diseases (WHO)	**15.2 %**
Jainkittivong et al. [4], 2010, Thailand	• Cross-sectional university-based study • Convenience sample of partially or completely edentate individuals	• n = 380 • 59.2 % F • Mean age 65.2 ± 9.1 years	Not available	Epidemiology guide for the diagnosis of oral mucosal diseases (WHO)	**18.1 %**
Mandali et al. [37], 2011, Turkey	• Cross-sectional study • Convenience sample of completely edentate individuals from a hospital dental clinic	• n = 153 • 50.3 % F • Mean age: 61.8 ± 9.8 years	• Age • Continuous use of the dentures	Not available	**35.3 %**
Evren et al. [34], 2011, Turkey	• Cross-sectional study • Convenience sample of institutionalized completely edentate individuals	• n = 269 • 55.8 % F • ≥ 65 years old	• Age • Education • Nocturnal denture wear • Denture hygiene	Classification of Newton	**44 %**

Kossioni [35], 2011, Greece	• Cross-sectional university-based study • Convenience sample of completely edentate individuals	• n = 106 • 64.2 % F • Mean age: 67.7 ± 9.9 years	• Continuous denture use	Classification of Newton	**39.6 %**
Da Silva et al. [49], 2011, Brazil	• Cross-sectional study • Convenience sample of institutionalized of partially of completely edentate household farmers	• n = 102 • 82 % F • Mean age: 49 years	• Female • Length of denture use	Classification of Newton	**48.2 %**
Mozafari et al. [59], 2012, Iran	• Cross-sectional study • Convenience sample of institutionalized elderly individuals	• n = 202 • 91.1 % F • Mean age: 79.59 ± 8.88	Not available	Not available	**54.6 %**
Cueto et al. [60], 2012, Chile	• Cross-sectional study • Random sample of completely edentate individuals from a list of patients attending medical routine consultations in a polyclinic.	• n = 126 • 75 % F • Mean age: 70.2 years	• Nocturnal denture wear • poor denture hygiene • Not well-fitted prosthesis	Not available	**37.1 %**
Sakar et al. [54], 2013, Turkey	• Cross-sectional study • Convenience sample of institutionalized elderly individuals	• n = 365 • 66 % F • Mean age: 70.5 ± 13.2 years	• Age of maxillary denture • Nocturnal denture wear • Reduced Vertical dimension of occlusion	Classification of Newton	**46.3 %**
Pesee et al. [43], 2013, Thailand	• Cross-sectional study • Convenience sample of partially or completely edentate individuals from a dental clinic located in a hospital.	• n = 128 • 67.2 % F • Mean age: 57.11 years	• Prosthesis quality	Classification of Newton	**52.3 %**

1.3.3 Histopathology and physiopathology of denture stomatitis

The chronic inflammatory reaction of the palatal mucosa in denture-related erythematous stomatitis is characterized by histopathological and physiopathological alterations similar to any other inflammatory reaction [61].

The epithelial changes that occur in denture stomatitis include reduced thickness of the epithelium, with areas of epithelial hyperplasia or atrophy, as well as accelerated cellular turnover of the epithelium [61-63]. Another important change that was demonstrated in several studies was the parakeratinization or absence of keratinization of the surface layers of the palatal mucosa [61-64]. Regarding connective tissue changes, Le Bars et al. [62, 65] compared biopsies of the palatal mucosa of healthy patients wearing complete upper dentures with those affected by Type II denture stomatitis. They found a moderate inflammation in the connective tissue with the presence of polymorphonuclear leucocytes and lymphocytes and the display of thin collagen and a disorganized lamina densa. Furthermore, they demonstrated disruptions in the basement membrane.

Other cytological studies of palatal mucosal smears also showed higher inflammatory infiltrates in patients with denture stomatitis than healthy patients [63, 66].

Recently, many research groups highlighted the role of salivary inflammatory mediators in denture-related erythematous stomatitis. In a case-control study by Barros et al. [67], high levels of salivary cytokines such as IL-1β and IL-8 were found in patients with Type II and III denture stomatitis. Gasparoto et al. [68] assessed patients with *Candida*-associated denture stomatitis and found that they had higher salivary levels of IL-4 and IL-10. Pesee et al. [43] found no association between the occurrence of denture stomatitis

and the salivary levels of IL-6, IL-8, IL-10, IL-17, and TNF-α. However, in this study [43], the majority of the study participants (65.7 %) had Type I denture stomatitis.

With regard to denture stomatitis and the systemic levels of inflammatory markers, the literature is still inconclusive. The findings of the longitudinal cohort study by Ajwani et al. [69] in completely edentate individuals demonstrated higher systemic levels of C-reactive protein in patients affected by denture stomatitis. In contrast, Barros et al. [67] found that the amount of C-reactive protein was similar in patients with denture stomatitis and healthy edentate, suggesting a lack of systemic inflammation associated with denture stomatitis. Pietruski et al. [70] found that denture wearers had higher serum levels of IL-6 and TNF-α, regardless of the presence of denture stomatitis, compared to dentate individuals.

Recently, Matsumoto et al. [71] evaluated the cytogenetical damage induced by denture stomatitis by means of micronucleus assay in exfoliated cells of the palatal mucosa. The findings of this study showed a lack of malignancy risk in denture stomatitis patients. However, this chronic inflammation had cytotoxic effects on the cells of the oral mucosa by inducing nuclear alterations such as nucleus pyknosis, karyorrhexis and karyolysis [71]. Finally, Kaplan et al. [72] compared palatal biopsies of patients with normal mucosa and patients with papillary hyperplasia or Type III denture stomatitis. They found no evidence of dysplasia in denture stomatitis patients. Similarly, Flanagan and Porter [73] reported no histological premalignant changes in Type III denture stomatitis.

1.3.4 Etiology of denture stomatitis

The etiology of denture-related erythematous stomatitis remains poorly understood and controversial [25, 30]. Three etiologic factors have been reported to play a major role in denture stomatitis including fungal infections (particularly *Candida*) [32, 74], denture biofilm [75] and trauma [7, 52].

Fungal Infection:

In 1936, Cahn [17] was the first to propose *Candida* infection as a main etiologic factor for denture stomatitis. Since then, a relationship between denture stomatitis and fungal infection has been widely reported in the literature [18, 74, 76]. However, several studies did not prove any statistically significant association between the presence of denture stomatitis, the severity of the inflammation, and the number of *Candida* Colony-Forming Units (CFUs) isolated from the prosthesis and the palate of patients affected by denture stomatitis [22, 25, 30, 67, 77]. Furthermore, high recurrence rates of the clinical signs of denture stomatitis and recolonization of *Candida* after the antifungal therapy have been widely reported [78-80].

Denture Biofilm:

Denture biofilm is a surface-attached, dense and complex layer consisting of microbial communities and their metabolites, which are embedded in an extracellular polysaccharide matrix [81]. It has been reported that denture biofilm contains 10^{11} microorganisms per gram [82], including aerobic and anaerobic bacteria, yeasts, and amoebae [83]. Poor hygienic habits such as continuous and nocturnal wear of the

prosthesis, in addition to inadequate denture cleaning, promote the formation and accumulation of denture biofilm. This biofilm harbours a wide array of pathogenic microorganisms which produce toxins and metabolic waste. These metabolites in turn could initiate the inflammatory process in denture stomatitis [6, 32, 34, 48, 83, 84]. Furthermore, biofilms provide a protective niche for these microorganisms and allow them to become resistant to antimicrobials [83, 85, 86].

Trauma:

The role of trauma in the onset of denture stomatitis was suggested for the first time in 1929 by Wright [87] and since then has been reported in several studies [20, 21, 52]. Recently, many studies have assessed the plausibility of this hypothesis. In the study by Pesee et al. [43], there was a statistically significantly relationship between the prevalence of denture stomatitis and the absence of adequate hygiene, fit, retention and stability of the prosthesis. Furthermore, the results of a randomized controlled trial by Emami et al. [7] suggest that a lack of stability of the lower denture can cause trauma to the palatal mucosa following the displacement of the upper denture and thus, promote the development of denture stomatitis. In fact, in this study, the risk of denture stomatitis was 4.5 times greater in patients wearing mandibular conventional dentures than in those wearing more stable and less traumatic two-implant overdentures (Adjusted OR = 4.54, 95 % CI 2.20 to 9.40).

1.3.5 Systemic effects of denture stomatitis

There is overwhelming evidence of the link between oral and general health [88, 89]. The oral mucosa constitutes the lining of ports of entry to several systems of the human body. When the mucosal defences are breached, the systemic health could be affected [90]. Although the association between denture stomatitis and systemic disease such as diabetes mellitus has been the focus of several studies [45, 91], this investigation has always been unidirectional, and the direct and indirect impact of denture stomatitis has not been examined yet mainly because of the silent nature of this disease. We can hypothesize that this disease could affect the general health through two pathways: local infection and local inflammation. Evidence regarding the role of local inflammation and infection in the development of several diseases supports this hypothesis.

Denture stomatitis favours the colonization of infectious pathogens which in turn could lead to serious disease such as oral candidiasis, bacterial endocarditis and aspiration pneumonia, especially in individuals with a compromised immune system, hospitalized patients, and elders with cognitive impairments and dementia [46, 92-98].

There is also persuasive scientific evidence on the consequences of chronic inflammation [99, 100]. The evidence of the presence of inflammatory markers such as C-reactive protein in the saliva and serum of patients affected by denture stomatitis suggests that this chronic inflammation may be involved in many seemingly unrelated diseases. As we get older, chronic inflammation can have pathological consequences throughout the body. As supported by Ajwani et al. [69], among the edentulous, chronic inflammatory lesions like denture stomatitis are important determinants of inflammatory

markers, comparable to periodontal disease in the dentate individuals. This evidence shows the need for future and novel studies on this topic.

1.4 TREATMENT OF DENTURE-RELATED ERYTHEMATOUS STOMATITIS

The history of the treatment of denture-related erythematous stomatitis demonstrates the recognition of this disease as being multifactorial. Therefore, denture stomatitis has not received a unique treatment, and a variety of different therapies have been used to treat this chronic inflammation [101-103].

The first trace of denture stomatitis treatment dates back to 1929. At that time, the etiology of this disease was considered to be trauma and treatments based on the reduction of traumatic injuries were introduced. Since 1935, the hypotheses on the role of fungal infections in denture stomatitis have convinced most of the clinicians to prescribe different kinds of antifungal medications to treat this disease. In 1952, Fisher and Rashid [104] reported that denture stomatitis is caused by a lack of denture hygiene, and recommended improving the oral hygiene of patients. In general, we can classify denture stomatitis treatments into two major categories: the conservative methods and the use of antifungal medications [94].

1.4.1 The conservative methods

The conservative approach includes methods that improve the oral and prosthesis hygiene and that reduce the trauma to the underlying palatal mucosa.

1.4.1. I Oral hygiene measures

Oral hygiene measures include discontinuous use of the denture, use of mouthwash, palatal brushing, laser and photodynamic therapy, prosthesis hygiene, microwave disinfection of the prosthesis, and finally the use of phytomedicines.

1. Discontinuous use of dentures

As previously mentioned in section 1.3.2, continuous wear of the prosthesis represents a risk factor for denture-related erythematous stomatitis [28, 51]. Several studies show a relationship between nocturnal denture wear and the prevalence of denture stomatitis [6, 25, 34], and clinicians usually suggest to their patients to remove their prosthesis at night to prevent or improve this disease. A study by Divaris et al. [51] demonstrated that removing the prostheses during the night was associated with a decreased risk of having denture stomatitis (OR = 0.63, 95 % CI 0.44 to 0.90).

2. Mouthwash use

Mouthwashes such as chlorhexidine gluconate (Peridex™, Cordosyl™) [105], chlorine dioxide (CloySYS™) [106], and lawsone methyl ether mouthwash [107], have been widely used to remove palatal biofilm. In a clinical study by Lal et al. [105], 0.12 % chlorhexidine gluconate (Peridex™) was effective in elimination of *C. albicans* colonies isolated from the denture biofilm and led to a decrease in palatal inflammation. In a randomized controlled trial, Koray et al. [108] demonstrated that hexetidine mouthrinse was as effective as fluconazole capsules in reducing the number of *Candida albicans* Colony-Forming Units (CFUs). Similarly, in a clinical study by Uludamar et al. [106], chlorhexidine

gluconate and chlorine dioxide mouthwashes decreased the number of *C. albicans* colonies.

However, the recurrence of denture stomatitis after cessation of the use of these kinds of mouthwash has been reported [105]. In addition, mouthwashes containing chlorhexidine could cause side effects such as staining of the teeth and oral mucosa [109].

3. Palatal brushing

Oral health-care providers often suggest oral and prosthesis hygiene instructions such as palatal brushing to complete denture wearers. In a recent observational study [110], the chance of remission of denture stomatitis was 3.9 times higher in participants who brushed their palate (RR = 3.9, CI 1.0 to 15.9, p = 0.04). In addition, an association between the lack of palatal brushing and the occurrence of *C. albicans* was reported (OR = 1.8, 95 % CI 1.3 to 2.4, p = 0.03) [30]. However, there is still a paucity of research on this topic; and to our knowledge, no interventional study has examined this mode of oral hygiene.

4. Laser and photodynamic therapy

Photodynamic therapy (PDT) and Diode laser irradiation have been successfully used in the treatment of denture stomatitis [111-114]. Photodynamic therapy consists of activation of a photosensitizing agent by means of oxygen and a light source (Light-Emitting Diode) with specific wavelengths. This results in the formation of cytotoxic oxgen molecules that damage the cells of the microorganisms [115]. In a randomized controlled trial, Mima

et al. [113] evaluated the efficacy of PDT and found this therapy as effective as nystatin in the treatment of denture stomatitis.

The mechanism underlying the diode laser (low-power laser) therapy is not well understood. One hypothesis suggests that laser irradiation produces reactive oxygen, which reduces the proliferation of the microorganisms [116]. In a randomized controlled trial, Maver-biscanin et al. [112] compared the effects of diode laser irradiation with antifungal treatment regarding the reduction of *Candida* CFUs. They found no difference between the laser treatment and the antifungal medication regarding the remission of denture stomatitis.

The disadvantages of PDT and diode laser irradiation include the need for special equipment and difficulty in implementation. In addition, recurrence of denture stomatitis was noted for both treatments [112, 113].

5. Prosthesis hygiene

Chemical disinfection and mechanical cleaning of the prosthesis can be used to clean the dentures. The prostheses can be chemically disinfected by immersing them in cleaning solutions containing alkaline peroxide (Polident®, Efferdent®) [92, 106, 117], 0.12 % chlorhexidine gluconate (Peridex™) [105], or sodium hypochlorite 0.05 % (10 ml hypochlorite 1 % in 200ml water for 10 minutes) [118]. Sodium hypochlorite is considered an effective, accessible and inexpensive disinfecting agent [119], especially when used as a Milton™ solution (2 % aqueous solution of sodium hypochlorite with 16.5 % salt). This solution causes less damage to the dentures when compared to household bleach [120, 121].

Many studies have been conducted to test the effectiveness of chemical methods in denture biofilm removal [122, 123]. In a randomized crossover trial, Gornitsky et al. [123] assessed the efficacy of three commercial denture cleaners (Denture Brite®, Polident® and Efferdent®) in the removal of denture biofilm and in the reduction of the number of microorganisms. They did not find any difference between the three brands after 3 weeks of use. In an in-vitro study, Glass et al. [92] found that soaking of the dentures in Polident® was more effective in reducing microorganisms' load than microwaving. Some other findings showed that the use of denture cleaners containing chlorine dioxide and 0.2 % chlorhexidine gluconate were effective in the elimination of the biofilm [122]. Furthermore, the combination of a denture disinfectant such as chlorhexidine with an antifungal treatment was shown to improve the efficacy of the antifungals [124]. However, this combination could increase the resistance of *Candida* species over time [125].

Several studies compared the efficacy of the chemical and mechanical methods of denture cleaning in the treatment of denture stomatitis. Silva-Lovato et al. [126] compared the cleaning capacity of brushing the prosthesis to soaking in a denture cleaner containing sodium lauryl sulphate (NitrAdine™). They found that the chemical method was more effective in terms of biofilm removal ($p < 0.001$) and reduction of *Candida* colonies ($p < 0.05$) than cleaning the prosthesis with a denture brush.

Paranhos et al. [117] conducted a longitudinal study to compare the cleaning capacity of alkaline peroxide solution (Bonyplus®), mechanical brushing with toothpaste, and the combination of both methods. The findings of this study suggest that brushing the denture was more effective in biofilm removal than the use of a sodium peroxide

soaking solution. However, the most effective method for denture hygiene was the combination of mechanical and chemical methods [117, 127].

It should be noted that denture cleansing agents could be corrosive and detrimental to the prostheses in long-term use and could have some side effects such as altering the taste of denture wearers [108, 126].

6. Microwave disinfection

Microwaves have been used for disinfection of the prosthesis. The mechanism of action of microwaving is not well understood and is attributed to the thermal or non-thermal effect [128]. According to thermal theory, heat generated by the vibration of the molecules could result in the disintegration of the microorganisms. The disinfecting effect of microwaving could also be the result of non-thermal interactions between the molecules of the cell wall of microorganisms and the microwave electromagnetic field [128-130].

Although there is still no definitive guideline for microwave use [131], according to the literature, the prosthesis should be disinfected once a week by immersion in a 600 ml container with 200 ml of water, and irradiated at 650 W for 3 minutes [132, 133].

According to several studies, microwaving is as efficient as other alternatives such as sodium hypochlorite soaking [121], and miconazole and nystatin medications [80, 128, 132], in the treatment of denture stomatitis. This method is simple and user-friendly, especially for the elderly with decreased dexterity [131]. However, in most of these studies, high recurrence rates of denture stomatitis after cessation of the microwaving were demonstrated [80, 128]. In addition, microwave disinfection could lead to the shrinkage of the denture bases [134] or a decrease in the hardness of the denture teeth [135].

7. Phytomedicines

Lately, there has been a tendency toward the use of herbal and natural remedies (phytomedicines). The recent narrative review by Casaroto and Lara [136], in addition to several studies [78, 137, 138], reported that phytomedicines are effective in the treatment of denture stomatitis.

In a recent randomized double-blind clinical trial, Bakhshi et al. [137] compared the effect of nystatin and garlic aqueous extract on denture stomatitis. Both treatments produced a statistically significant decrease in the extent of the erythema caused by denture stomatitis. Although a faster effect was noted with the use of nystatin, the garlic extract had fewer side effects than the antifungal. In another randomized controlled trial, the efficacy of the essential oil of the *Z. multiflora* herb was compared to 2 % miconazole gel [78]. *Z. multiflora* exhibits antimicrobial activity and can inhibit the activity of inflammatory mediators [139], and proved to be as effective as the miconazole gel in the treatment of denture stomatitis.

The extract of *Punica granatum Linné* (pomegranate) [140] and *propolis* gel [138, 141] (a resinous substance collected by bees from plants), were also as effective as miconazole gel in the treatment of denture stomatitis. Other natural substances that were examined and were effective in the treatment of denture stomatitis include vinegar [142], *Melaleuca alternifolia* extracts (tea tree oil) [143], *Satureja hortensis* essential oil [144] and *Ricinus communis* [145]. Nonetheless, it should be noted that phytomedicines can have side effects such as bad taste, in addition to recurrence and relapse after cessation of their use [78, 137].

1.4.1. II Prosthodontic measures

Several prosthodontic procedures with the aim of improving the fit and the stability of the prosthesis can be performed in the cycle of treatments of denture stomatitis. These include the use of tissue conditioners, prosthesis adjustments, and the renewal of the prosthesis [38].

Tissue conditioners are used to manage ill-fitting dentures and inflamed tissue under the prostheses. They have a cushioning effect that improves distribution of the occlusal forces and decreases trauma to the underlying tissues [146]. Tissue conditioners have been shown to be successful in reducing palatal inflammation associated with denture stomatitis [147, 148]. However, they were not effective in the treatment of the candidiasis associated with this disease [102]. Furthermore, the resilient quality of tissue conditioners decreases with time and they become hard, stained and porous. This time-related deterioration of the material contributes to the microorganisms' colonization [149, 150].

A number of studies examined the efficacy of incorporating antifungals in denture lining materials [143, 150-152]. Geerts et al. [150] evaluated the benefit of adding an antifungal in a short-term denture liner. Their findings showed that antifungals inhibit the colonization of *Candida* species in the relining material.

Hard autopolymerising reline materials have also been examined in the treatment of denture stomatitis. These hard liners are long lasting, produce a low polymerising exothermic reaction and can be used directly in the mouth. In a randomized controlled trial by Marin Zuluaga et al. [153], treatments with hard and soft tissue conditioners were found to be equally effective in the management of denture stomatitis. However, the

time needed for remission of inflammation was longer for the soft tissue conditioners compared to the harder one.

In a one-group pre-test/post-test study, Pires et al. [18] evaluated the effect of new well-fitted complete dentures on denture stomatitis. They found a 30 % decrease in the frequency of this disease. However, there was no change in the number of *Candida* colonies. In accordance with several studies [103, 154], Arikan et al. [124] found that the making a new prosthesis for patients with denture stomatitis will improve the localized inflammation but will have no effect on generalized inflammation and colonization of *Candida*.

1.4.2 Antifungal medications

Antifungal medications are used to eliminate different fungal species, particularly *Candida* species. The antifungals used in the treatment of denture stomatitis can be applied topically or used systemically. Topical antifungals include the polyenes (nystatin or amphotericin B) used as lozenges or suspensions and the imidazoles derivatives (such as clotrimazole and miconazole), used as gel or lacquers. Ketoconazole and the triazole derivatives (fluconazole and itraconazole) could be prescribed as tablets or capsules for systemic use [21]. Recently, other triazole antifungal agents with broader spectrum activity like voriconazole, ravuconazole, and posaconazole have been used to treat oral candidiasis associated with denture stomatitis, especially in immunocompromised patients [155, 156].

Nystatin is the most widely used antifungal in the treatment of oral candidiasis and denture stomatitis. Dentures can be soaked in a solution of nystatin (100,000 U/ml). Nystatin cream (100,000 U/g) could also be applied to the inner surface of the prosthesis. Treatment should continue for a minimum of 4 weeks along with meticulous oral hygiene maintenance [157].

The use of antifungal medications to treat denture stomatitis has been studied by several research groups [24, 101, 158]. In a randomized controlled trial by Cross et al. [79], itraconazole cyclodextrin solution and itraconazole capsules were found to be similar in terms of reduction of clinical signs of denture stomatitis and reducing the colonization of the yeast. However, recolonization of *Candida* species was seen at 6-month follow-up. Similar results were found in studies comparing the systemic and topical application of antifungals such as ketoconazole, fluconazole and amphotericin [101, 159].

Some attempts have been conducted to produce a topical antifungal with long-lasting effect to avoid the side effects of systemic antifungals. For example, miconazole has been incorporated in lacquer agents. This treatment proved to have a short-term effect and recolonization of *Candida* was observed after treatment [160, 161].

As previously mentioned in section 1.4.1, several studies [26, 78, 108, 113, 128] compared antifungal treatments with different conservative methods. No significant differences between the antifungal and the conservative methods were found.

Antifungal medications have multiple disadvantages such as side effects, the emergence of resistance, and recurrence.

The excessive use of antifungals may produce some side effects, such as bitter taste, nausea, gastrointestinal disturbance, hypersensitivity, renal and liver toxicity, and interaction with other medicines [46, 47, 50]. Side effects are especially seen with the use of systemic antifungals [79, 101, 137, 162].

Furthermore, resistance, which is defined as non-resolution of an infection despite the use of an antimicrobial agent, have been demonstrated with antifungal medications [156, 163]. High recurrence rates of denture stomatitis have also been reported after cessation of the antifungal treatment [32, 78, 101, 150, 164]. The emergence of resistance may explain this extensive recurrence of denture stomatitis [86, 125, 165, 166].

CHAPTER II

METHODOLOGY

2.1 PROBLEMATIC, HYPOTHESIS, OBJECTIVES

Denture stomatitis is the most prevalent oral disease in denture wearers [35, 60]. The treatment of this disease consists of two different approaches: the use of antifungal medications and the conservative approach [94].

Antifungal therapy is the main choice of oral healthcare professionals for the treatment of this disease, based on some evidence that *Candida* is the main etiological factor in the onset of denture stomatitis. However, a direct cause-and-effect relationship has never been shown, and high recurrence rates of denture stomatitis clinical signs and recolonization of *Candida* have been reported after cessation of the antifungal treatment [78-80].

Recent research on the etiology of denture stomatitis suggests that treatments based on the reduction of the inflammation are effective in the management of this disease [7, 25]. In this regard, some new findings suggest palatal brushing as a curative method [110]. However, to our knowledge, there is still no interventional study that has evaluated the efficacy of such an alternative approach.

2.1.1 Objectives

The objectives of this master's research project were:

1. Primary objective: To assess the efficacy of palatal brushing in the treatment of denture stomatitis.
2. Secondary objectives:
    a) To assess the efficacy of palatal brushing in controlling the colonization of *Candida* species.
    b) To standardize the study procedures and to produce preliminary data for a phase-II clinical trial.

2.1.2 Hypotheses

We tested the following null hypotheses:

1. There is no difference in the extent of palatal inflammation in individuals with denture stomatitis before and 3 months after palatal brushing.
2. There is no difference in the number of Colony-Forming Units (CFUs) of *Candida* isolated from the palate and denture of patients with denture stomatitis before and 3 months after palatal brushing.

2.2 RESEARCH METHODOLOGY

2.2.1 Study design

This study was a phase-I clinical trial with a one-group pre-test/post-test design. It has been registered in clinicaltrials.gov and received the identification number NCT01643876. The project was conducted at two Faculties of Dentistry of the Université de Montréal in Canada and the University of São Paulo (Ribeirão Preto) in Brazil.

2.2.2 Study participants and inclusion criteria

Study participants were recruited from the general population of the area of Metropolitan Montreal and Ribeirão Preto via advertisements in local newspapers, through flyers placed within dental clinics of the two dental schools, or by clinicians during clinical examination at diagnostic clinics of these faculties.

All potential participants were informed about the study, and those who were willing to participate in the study were invited to a screening clinical session. During this session, the master's students explained all aspects of the study, and examined candidates for suitability for inclusion in the study.

Candidates were considered for inclusion in this study if they:

1) were 18 years old or older;
2) were wearing a complete upper denture;
3) had a clinical diagnosis of denture stomatitis;

4) had the ability to understand and sign an informed consent form.

Candidates were excluded from the study if they:

1) had any conditions known to promote *Candida* carriage such as uncontrolled diabetes, anemia, xerostomia or immunosupression;
2) received a treatment with an antibiotic, an antifungal or corticosteroids in the last four weeks prior to the study or were being treated with chemotherapy or radiotherapy;
3) included palatal brushing in their routine oral hygiene;
4) were planning to change their existing prosthesis during the trial.

Each individual meeting the eligibility criteria were invited to read and sign the consent form (Appendix I). They were given an opportunity to ask questions and to take the research consent form home for further consideration.

Finally, forty-eight consecutive participants (men = 16, women = 32) from the two study centers (Canada, n = 22; Brazil, n = 26) participated in the clinical trial.

2.2.3 Experimental procedure

The experimental procedure (intervention) consisted in brushing the palate with a soft-bristle manual brush (Oral-B® CrossAction® Pro-Health™) after each meal and before sleeping, for a period of 3 months.

In order to standardize the experimental technique, the participants were asked to keep to their usual oral and denture hygiene routine during the trial. A cast model was used to show the participants how to brush the palate. The study participants also received a

written instruction sheet (Appendix V) to remind them of the study's experimental procedure.

2.2.4 Data collection and measurement instruments

The data collection was conducted at the postgraduate prosthodontic clinics of the Faculties of Dentistry of the Université de Montréal and the University of São Paulo at baseline (T_0), 1 month (T_1), and 3 months (T_2) of the intervention, during the period extending from May 2012 to January 2013.

One master's student in each center (MK and MB) was responsible for the data collection. Data were collected by means of a self-administered questionnaire (Appendix II), a clinical examination (Appendix III) and a microbiological investigation (Appendix IV). All procedures were standardized between the two centers during research team meetings before data collection.

2.2.4. I Clinical investigation

In each center, the diagnosis of denture stomatitis was conducted by three trained, calibrated dentists (interobserver reliability 0.6 to 0.84) using a front-surface mirror and probe (XP23/QW, HuFreidy).

Furthermore, the photographs of palate were taken with a Nikon D90 camera (105mm f/2.8 D; macro flash SB-21). These photographs were used to obtain a diagnostic consensus from research team members during a workshop held at the faculty of Dentistry of the Université de Montréal from November 19th to December 7th, 2012.

Denture stomatitis was diagnosed according to the area and severity of inflammation indices [26] and a modified classification of Newton [23], as detailed below:

I. Inflammation area index:

0: No inflammation

1: Inflammation of the palate extending up to 25 % of the palatal denture-bearing tissue

2: Inflammation of the palate extending between 25 % and 50 % of the palatal denture-bearing tissue

3: Inflammation covering more than 50 % of the palatal denture-bearing tissue.

II. Inflammation severity index:

0: Normal tissue

1: Mild inflammation (slight redness, no swelling or edema)

2: Moderate inflammation (redness with some edema)

3: Severe inflammation (acutely inflamed redness, edema)

A score between 0 and 6 for total inflammation was then given, which equals the area + intensity of inflammation [26].

III. The modified classification of Newton:

0: Healthy mucosa

Type IA: Petechiae in a normal palatal tissue, which are usually found around the orifices of the ducts of the palatal mucous glands

Type IB: Localized area of inflammation of the denture-bearing area

Type II: Generalized area of inflammation of the denture-bearing area

Type III: Hyperplasic palatal surface with inflammation of the denture-bearing area.

The other assessed variables included denture cleanliness, which was evaluated by the modified Hoad-Reddick classification [167], as clean (without any soft/hard debris or stain) or dirty (with soft and hard debris or stain after washing under water).

The upper prostheses were also evaluated regarding their stability and retention. The stability was evaluated by determining the movement of the prosthesis over the supporting tissues and its resistance to rotation. The presence or absence of a noticeable rocking motion was also noted [168, 169]. The retention was evaluated by asking the participant to touch the vermillion border of their upper lip with their tongue and by opening their mouth to the maximum. If the denture dropped, it was considered non-retentive. The upper prosthesis was grasped by the thumb and index finger and a downward force was applied. The absence or presence of adequate resistance to dislodgment was noted [168, 169].

Other explanatory variables included the clinical signs of parafunctional habits, salivary flow, and the resorption and tissue resilience of the upper residual ridge [170-173], in addition to the vertical dimension of occlusion [168, 169].

Information about socio-demographic variables (age, sex, education, medical and dental histories, medication profiles), years of edentulism and age of the dentures, hygienic habits (cleaning frequency, nocturnal wear, mouthwash use) and smoking, were obtained from a validated questionnaire [30].

The level of the reported oral hygiene was estimated through questions with categorized answers (How many times per day do you clean your dentures? How do you clean your dentures?). The answers were binary summarized as cleaning of the dentures less than two times/day or 2 times and more/day; and brushing the dentures or washing without brushing.

A 100 mm visual analogue scale (VAS), with anchor words of "not at all satisfied" and "extremely satisfied" [7], was also used to assess the general satisfaction with oral condition. Furthermore, symptoms and side effects of palatal brushing, if present, were reassessed after 1 and 3 months of the intervention.

2.2.4. II Microbiological investigation

In order to evaluate the colonization of *Candida* species, microbiological investigations on the upper denture and palatal plaques were conducted. With this aim, the sonication technique [121, 174] and swabs were used to collect the upper denture biofilm and palatal biofilm, respectively.

In brief, the upper prosthesis was rinsed under tap water and placed in a Ziploc™ plastic bag with 30 ml of sterile saline water (0.85 % sodium chloride). The first bag was then put in a second bag and sonicated for 5 minutes at room temperature in an

ultrasonic bath containing distilled water (Cole Parmer 08890-21, 50/60 Hz, 1,3 Amp). The recovered plaque (sonicate) was transferred to a 50 ml sterile tube.

A sample of palatal plaque from 1 cm² of the central surface of the palate was collected by the use of a sterile swab. The swab was then placed in a sterile tube with 5ml saline and sonicated for 2 minutes. Both denture and palatal plaque sonicates were placed on ice until the microbiological examination.

Sonicates were mixed by vortex for one minute and diluted 10-fold serially with saline (dilution factors: 10^0, 10^{-1} and 10^{-2}). A volume of 100 µL of each dilution was spread-plated in duplicate on Sabouraud-Dextrose 4 % Agar (Difco™, Becton, Dickinson and Company, USA). All cultures were incubated at 37^o C for 48 hours. Colony-Forming Units (CFUs) were counted and expressed as a number of CFUs/ml, after correction for volume and dilution factor.

When a growth was observed, an imprint of colonies was obtained onto a sterile filter paper which was transferred on a *Candida* selective growth medium (CHROMagar *Candida*, Paris, France) and incubated under the same conditions. This chromogenic selective medium allows identification of the different *Candida* species [175].

2.2.5 Outcome and explanatory variables

The remission of denture stomatitis was considered as a primary outcome variable. The secondary outcome variable was the diminution of the *Candida* CFUs. The explanatory variables included socio-demographic characteristics and well-known denture stomatitis risk factors [30].

2.2.6 Statistical analysis

Assuming that the minimal practically important pre/post difference in the mean change score is 20 % and the standard deviation of the distribution of the change in score is 0.8 (based on estimates from a previous study [110]), a sample size of 44 participants is required to ensure a power of 90 % of rejecting the null hypothesis if it is indeed false. An additional number of individuals were considered to prevent the effect of potential 10 % drop-outs on the study results.

Inter-rater agreement for the diagnosis of denture stomatitis was evaluated by using Cohen's kappa (k) [176], with k value > 0.75 representing excellent agreement, 0.4–0.75 fair to good agreement and < 0.40 poor agreement.

In order to obtain frequency counts, percentages and univariate means, and to test for normality, the data was first subjected to descriptive statistical tests. Non-parametrical analyses were applied because of the deviation from a normal distribution.

Between-center differences in regard to baseline characteristics of the participants and treatment effects were analyzed by means of the Fisher's exact test, two-sample t-test and the Mann–Whitney U test.

The Wilcoxon Signed Rank Test was used to analyze the change in the classifications level, in the total score, and in the number of *Candida* colonies between T_0 and T_2. McNemar's test was used to determine if there were differences in the participants' reported symptoms between T_0 and T_2.

The Budtz-Jorgensen [177] index was used to categorize the clinical effects of treatment:

- Large effect: inflammation resolved

- Moderate effect: inflammation reduced
- No effect: no change in inflammation
- Negative effect: increased inflammation

The effect size *r* was calculated from the *Z* obtained from the Wilcoxon Signed Rank Test ($r = Z/\sqrt{N}$, where N is the number of observations over the two time points) and was defined as 0.1 = small effect, 0.3 = medium effect and 0.5 = large effect [178]. Differences were considered statistically significant at $p \leq 0.05$. All statistical analyses were performed by using SPSS version 20 (SPSS Inc., Chicago, IL, USA) and SAS 9.1 software.

2.2.7 Ethical considerations

The ethical approval for this master's research project was obtained from the Université de Montréal Research Ethics Board (CERES, certificate number 12-019-CERES-D) and the Institutional Review Board of the Ribeirão Preto Dental School (certificate number 00625912.6000.5419).

2.3 STUDY RELEVANCE

To our knowledge, this study is the first clinical trial on the effect of palatal brushing on denture stomatitis. The results of this study will provide clinicians with scientific evidence on a simple, conservative, cost/effective therapeutic and preventive approach that will contribute to the improvement of oral health in edentate individuals wearing complete dentures. The findings of this clinical trial will also assist clinicians in their

decision-making in regard to the treatment of denture stomatitis and will avoid the over-prescription of antifungal medications.

Finally, this phase-I clinical trial will allow the elaboration of a randomized clinical trial on the efficacy of palatal brushing in comparison with the use of antifungal medications.

2.4 CANDIDATE'S ROLE IN THE PROJECT

During this master's project, the candidate has fulfilled several roles. First of all, she helped in the research protocol development. She was responsible for the recruitment of the study participants, data collection and data analyses. She was in charge of the coordination of the study between the Canadian and the Brazilian centers. She also participated actively in the knowledge-transfer phase of this research project.

2.5 KNOWLEDGE TRANSFER

The candidate presented the results of this research project during several scientific meetings and conferences:

1) Oral presentation: "Séminaires de recherche en médecine dentaire" (SAB6604-A11) at the Université de Montréal;
2) Poster presentation :
    i. Kabawat M, De Souza RF, De Koninck L, Barbeau J, Rompré P, Emami E. Phase-I clinical trial on the effect of palatal brushing on denture stomatitis. Journées Dentaires Internationales du Québec (JDIQ), Montreal, Canada, May 24th to 28th 2013.

ii. Kabawat M, De Souza RF, De Koninck L, Barbeau J, Rompré P, Emami E. Phase-I clinical trial on the effect of palatal brushing on denture stomatitis. Canadian dental research student workshop, Ontario, Canada, June 10th to 11th 2013.

The candidate was also co-author of 3 articles on the topics related to the master's project:

1) Emami E, De Souza RF, Kabawat M, Feine JS. The impact of edentulism on oral and general health. *International Journal of Dentistry*; 2013:498305. doi: 10.1155/2013/498305. Epub 2013 May 8.
2) Emami E, Kabawat M, De Koninck L, Gauthier G, de Grandmont P, Barbeau J. La stomatite prothétique: nouvelle perspective. *Journal de l'Ordre des Dentistes du Québec* 2013; 50(4):7-12.
3) Emami E, Kabawat M, Rompré P, Feine JS. Linking evidence to treatment for denture stomatitis: a meta-analysis. *Journal of Dentistry* 2013; *Submitted.*

The article included in chapter III of this master's thesis was also submitted for publication in *The International Journal of Prosthodontics*.

Finally, the candidate will present the results of this study during The International Association for Dental Research (IADR) General Session in 2014.

CHAPTER III

RESULTS

3.1 MANUSCRIPT

Phase-I clinical trial on the effect of palatal brushing on denture stomatitis

Marla Kabawat[1], Raphael F. de Souza[2], Maurício M. Badaró[2], Louis de Koninck[1], Jean Barbeau[3], Pierre Rompré[3], Elham Emami[1]

[1]Département de Dentisterie de Restauration, Faculty of Dentistry, Université de Montréal, Montreal, Quebec, Canada.
[2]Department of Dental Materials and Prosthodontics, Ribeirão Preto Dental School, University of São Paulo, Ribeirao Preto, SP, Brazil.
[3]Département de stomatologie, Faculty of Dentistry, Université de Montréal, Montreal, Quebec, Canada.

Corresponding author:

Dr Elham Emami, DDS, MSc, PhD
Associate professor and Director of Oral Health and Rehabilitation Research Unit
Faculté de médecine dentaire, Université de Montréal
C.P. 6128, succ. Centre-ville
Montréal (QC), Canada H3C 3J7

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Phase-I clinical trial on the effect of palatal brushing on denture stomatitis

ABSTRACT

Objectives: To assess the efficacy of palatal brushing in the treatment of denture stomatitis.

Methods: After screening 143 individuals with a potential diagnosis of denture stomatitis, 48 (mean age: 66.0 ± 11.2 years) were enrolled in a phase-I two-center clinical trial with one-group pre-test/post-test design. The intervention of interest was manual palatal brushing after each meal and before bedtime. Clinical and microbiological examinations were performed at baseline, 1 month and 3 months post-intervention. Additional data were obtained by the use of a validated questionnaire. The primary and secondary outcomes were the remission of denture stomatitis and the diminution of *Candida* Colony-Forming Units (CFUs), respectively. Descriptive and non-parametric statistical tests were conducted to analyze the data.

Results: At 3-month follow-up, denture stomatitis was completely cured in 10.4 % of the study participants, and 70.8 % of denture wearers showed improvement in the clinical signs of denture stomatitis. There was a significant reduction in the area and severity of the palatal inflammation at 3-month follow-up ($p < 0.0001$). The effect size ranged from medium to large (0.34 to 0.54), depending on the classification used for the diagnosis of denture stomatitis. Furthermore, a significant reduction in the number of *Candida* CFUs isolated from the palatal mucosa and dentures ($p \leq 0.05$) was observed.

Conclusion: The results of this study suggest that palatal brushing is effective in the treatment of denture stomatitis.

INTRODUCTION

Denture stomatitis is a chronic inflammation of the oral mucosa covered by a removable denture. It is considered the most common mucosal lesion associated with denture use [1, 2], affecting one in every three complete denture wearers [3]. Several risk factors have been reported to be associated with denture stomatitis, including trauma [4], denture biofilm [5], bacterial and fungal infections, particularly by *Candida albicans* [6]. However, the etiology of this pathological condition remains multifactorial and controversial [7, 8]. A variety of treatments reflecting the multifactorial etiology of denture stomatitis have been used in dental practice. These treatments can be basically classified into two categories: the conservative approach and the use of antifungal medications.

Nowadays, antifungal medications are prescribed routinely by oral healthcare professionals for the treatment of denture stomatitis, based on the hypothesis that an infection by *Candida* is the main etiological factor of this disease [9-11]. However, a convincing cause-and-effect relationship between the presence of denture stomatitis and *Candida* has never been demonstrated [7, 8, 12]. Furthermore, high recurrence rates of denture stomatitis and recolonization of *Candida* have been reported after the cessation of antifungal treatment [9, 13, 14].

Recent research findings suggest that trauma from unstable dentures induces a local inflammation and creates an environment favourable to the proliferation of microorganisms [4]. Consecutively, *Candida* colonization becomes a secondary stage in the pathogenesis of denture stomatitis [7, 15]. This suggests that treatments that enable the remission of inflammation could be effective in the treatment of this disease.

Palatal brushing is a simple procedure that could reduce the extent of inflammation by different mechanisms such as the removal of denture plaque and the stimulation of the mucosal circulation and salivary flow. However, no previous clinical trial has evaluated palatal brushing as a treatment modality for denture stomatitis.

Therefore, the objective of this study was to assess the efficacy of palatal brushing in the treatment of denture stomatitis. We tested the null hypotheses that, in individuals with denture stomatitis, there are no difference in the extent of palatal inflammation and in the number of *Candida* Colony-Forming Units (CFUs), before and 3 months after palatal brushing.

MATERIALS AND METHODS

Study Design and Study Participants

A one-group pre-test/post-test research design was used to conduct a two-center phase-I clinical trial (clinicaltrials.gov ID # NCT01643876), at two Faculties of Dentistry of the Université de Montréal (Canada) and the University of São Paulo (Ribeirão Preto, Brazil). Participants were recruited from the general population of the area of Metropolitan Montreal and Ribeirão Preto via advertisements in local newspapers, through flyers placed within dental clinics of the two dental schools, or by clinicians during examination at diagnostic clinics of these faculties.

The inclusion criteria of the study were: a) being 18 years old or older, b) wearing a complete upper denture, and c) having a clinical diagnosis of denture stomatitis. Patients were excluded if they: a) had any conditions known to promote *Candida* carriage such as uncontrolled diabetes, anemia, xerostomia or immunosuppression; b) received a

treatment with an antibiotic, an antifungal or a corticosteroid or if they were under chemotherapy or radiotherapy in the last four weeks prior to the enrollment in the study; c) used palatal brushing as a routine oral hygiene procedure; and d) if they changed their existing prosthesis during the trial. The study was approved by the Université de Montréal Research Ethics Board and the Institutional Review Board of the Ribeirão Preto Dental School. Written informed consent was obtained from the participants prior to their participation in the clinical trial.

Experimental Procedures

Data collection was conducted at baseline (T_0), 1-month (T_1) and 3-month (T_2) after the intervention, by means of a self-administered questionnaire, clinical examination and microbiological investigation.

1. Intervention

The intervention consisted of brushing the palate with a soft-bristle manual toothbrush (Oral-B® CrossAction® Pro-Health™, Procter & Gamble, Iowa, IA, USA) after each meal and before sleeping, for a period of 3 months. Participants were instructed to brush their palate using horizontal, vertical and vibration movements. They were also asked to keep their usual oral and denture hygiene habits during the trial.

2. Clinical investigation

Denture stomatitis was assessed according to the modified Newton classification [16], and by means of the area and severity of the inflammation indices [17] (Table 3.1).

The clinical assessment was conducted by two trained, calibrated dentists using a front surface mirror and probe (XP23/QW, Hu-Friedy, Chicago, IL, USA). Photographs of

palate were taken with a Nikon D90 camera (105mm f/2.8 D; macro flash SB-21, Nikon Co., Tokyo, Japan). These photographs were used to obtain a diagnostic consensus from research team members. A good to excellent interobserver reliability was obtained ($\kappa = 0.6$ to 0.84).

3. Microbiological investigation

Collection of the upper denture biofilm was carried out by the sonication technique, according the protocol described by Emami et al. [8]. A sample of palatal biofilm was also collected by the use of a sterile swab [18], placed in a tube with 5ml saline and sonicated for 2 minutes. Both denture and palatal biofilm sonicates were subsequently mixed by vortex for one minute and diluted 10 fold serially with saline (dilution factors: 10^0, 10^{-1} and 10^{-2}). A volume of 100 µL of each dilution was spread-plated in duplicate on Sabouraud-Dextrose 4 % Agar (Difco™, Becton Dickinson Co., Detroit, MI, USA). All cultures were incubated at 37°C for 48 hours. Colony-Forming Units (CFUs) were counted and expressed as a number of CFUs/ml, after correction for volume and dilution factor. When a growth was observed, an imprint of colonies was obtained onto a sterile filter paper, which was transferred on a *Candida* selective growth medium (CHROMagar™, *Candida*, Paris, France) and incubated under the same conditions. This chromogenic selective medium allows identification of the *Candida* species [19]

4. Outcome measures and explanatory variables

The remission of denture stomatitis was considered as a primary outcome variable, and it was defined as decrease in the level of the modified Newton classification, decrease in

the area and the severity of the inflammation, as well as decrease in the total score of inflammation (inflammation area + severity) [17].

The Budtz-Jorgensen index [20] was used to evaluate the magnitude of the treatment effect (based on the total score of inflammation): Large effect: inflammation resolved; Moderate effect: inflammation reduced; No effect: no change in inflammation; Negative effect: increased inflammation.

The secondary outcome variable was the reduction in the number of CFUs of *Candida.*

Explanatory variables included sociodemographic variables (age, sex, education, medical and dental histories, and medication profiles), years of edentulism and age of the upper dentures, hygienic habits (cleaning frequency, nocturnal wear, mouthwash use) as well as smoking. This information was obtained from a self-administrated questionnaire [8]. General satisfaction with oral condition was assessed by a 100 mm visual analogue scale (VAS) [4]. Other independent variables included denture cleanliness, evaluated by means of the modified Hoad-Reddick classification [8, 21], and the stability and retention of upper prostheses [22, 23]. Denture stability was evaluated by determining the movement of the prosthesis over the supporting tissues and its resistance to rotational movement. The upper prosthesis was grasped in the premolar region with the thumb and index finger and a rotational force was applied in the occlusal plane. A displacement of 5 mm or more was considered as prosthesis instability. The prosthesis was considered retentive if there was a resistance to downward force when grasping the prosthesis by the thumb and index finger [22, 23].

The wear of the denture teeth, the salivary flow, the resorption and the resilience of the upper residual ridge, as well as the vertical dimension of occlusion [22-27], were also evaluated.

Furthermore, symptoms of denture stomatitis and side effects of palatal brushing, if any, were documented.

Statistical Analyses

Assuming that the minimal practically important pre/post difference in the mean change score is 20 percent and the standard deviation of the distribution of the change in score is 0.8 [28], a sample size of 44 participants is required to ensure a power of 90 % of rejecting the null hypothesis if it is indeed false. An additional number of individuals were considered to address potential 10 % drop-outs on the study results.

Cohen's kappa (κ) coefficient [29] was used to evaluate the inter-rater agreement for the diagnosis of denture stomatitis, with κ value > 0.75 representing excellent agreement, 0.4–0.75 fair to good agreement and < 0.40 poor agreement.

In order to obtain frequency counts, percentages, univariate means and to test for normality, the data was first subject to descriptive statistical tests. Non-parametrical tests were applied because of the non-normal distribution of data.

Between-center differences in regard to baseline characteristics of the participants and treatment effects were analyzed by means of the Fisher's exact test, two-sample t-test and the Mann–Whitney U test.

The Wilcoxon Signed Rank test was used to compare the level of the modified Newton classification, the area and the severity of the inflammation, the total score of

inflammation as well as the number of *Candida* colonies between baseline and follow-ups. McNemar's test was used to compare nominal data on patient-reported symptoms at baseline and follow-ups. The level of significance was set at 0.05.

The Fisher's exact test and two-sample t-test were used to examine the significance of association between the explanatory variables and the treatment effect. Logistic regression was not conducted because of non-significant association ($p > 0.10$) in bivariate analyses. Statistical analyses were performed using SPSS version 20 (SPSS Inc., Chicago, IL, USA) and SAS 9.1 software (SAS Institute, Cary, NC, USA).

RESULTS

From a total of 143 individuals who participated in the screening sessions, 48 patients (16 men, 32 women; mean age: 66.0 ± 11.2 years) were enrolled in this study. Figure 3.1 illustrates the flow of participants throughout the study, indicating that there were no dropouts. Tables 3.2 and 3.3 present the socio-demographic characteristics of the participants and their profiles according to denture stomatitis risk factors at baseline, by study center.

The mean year of edentulism in the maxillary arch was 37.2 ± 14.7 years and the mean age of the current upper prostheses was 15.3 ± 13.7 years. Signs of wear facets on denture teeth were observed in 77.1 % of the participants. The majority of the patients brushed their prostheses with toothpaste (79.2 %), and 31.3 % used a denture-cleaning agent. However, only the Canadian center participants used the latter. Twenty percent of the participants had previously received denture hygiene instructions. Only one

participant used denture adhesive on his upper denture. At baseline, the most reported symptoms of denture stomatitis were halitosis (52.1 %) and a dry mouth sensation (66.7 %). The salivary flow was adequate in 83.3 % of the participants, and 91.7 % had a well-rounded ridge with sufficient height and width (Class III resorption [27]). Finally, 39.6 % of the patients had resilient tissue covering their residual ridge. There was no statistically significant difference between the two study centers regarding the demographic characteristics and risk factors associated with denture stomatitis, except for gender, income, educational level, denture cleanliness, and the mean age of the current prostheses. The Brazilian participants had more women enrolled in the trial, less income, lower education, and finally, older and less clean upper prostheses than the Canadian participants (Tables 3.2 and 3.3).

At T_0, 6.3 % of the participants had petechiae (Type IA), 16.7 % had localized inflammation (Type IB), 39.6 % had generalized palatal inflammation (Newton Type II) and finally, 37.5 % had hyperplasic inflammation (Type III). Also, 16.7 % of the participants had an inflammation extending up to 25 % of the palate, 33.3 % had an inflammation covering between 25 % and 50 % of the palate and 50 % of the participants had an inflammation covering more than 50 % of the palatal denture-bearing area (area of inflammation index). In addition, 25 % of the participants had a mild inflammation, 43.8 % had moderate inflammation and 31.3 % had a severe inflammation (severity of the inflammation index).

The microbiological analysis of the denture sonicates at T_0 revealed that 39 participants were *Candida* carriers. *Candida albicans* was the most frequent species isolated (59 % of

the cultures from the denture sonicates). Other species included *C. glabrata*, *C. krusei*, *C. tropicalis* and *C. parapsilosis.* The cultures were negative in 9 patients (18.8 %) including patients classified as Type IA, Type IB and Type II. Cultures from the palatal swab were negative in 77 % of the cultures.

There was no statistically significant difference between the two research centers according to the frequency of different types of denture stomatitis, and *Candida* carriage at baseline.

There were no statistically significant changes in results at 1-month follow-up (T_1). At 3-month follow-up (T_2), denture stomatitis was cured in 10.4 % of the participants, and 70.8 % showed substantial improvement in the clinical signs of denture stomatitis. There was a worsening of the clinical signs of denture stomatitis in only one participant (Figure 3.2). There was a significant inflammation decrease according to the modified Newton classification ($p = 0.001$), and the area ($p < 0.0001$) and severity ($p < 0.0001$) of inflammation indices at 3-month follow-up. The reduction in the total score value of the inflammation was also significant ($p < 0.0001$) (Table 3.4 and Figure 3.3). Subgroup analyses showed that there was no change in the inflammation indices for patients with Type IA. Patients with Type II and III denture stomatitis showed a significant decrease in the total inflammation score ($p < 0.0001$). However, the hyperplasic tissue remained in all patients affected by Type III denture stomatitis.

The effect size ranged from medium to large (0.34 to 0.54), depending on the classification used (Table 3.4). In addition, statistically significant improvements in the perceived oral condition of the participants ($p = 0.003$) and palatal burning sensation ($p =$

0.008) were found at 3-month follow-up. Overall, 40 % of the participants reported minor side effects of palatal brushing such as mild pain and some bleeding during the first days of treatment.

There was no statistically significant difference between the centers regarding the treatment effect. However, there was a statistically significant difference between the two centers regarding the reported side effects of palatal brushing ($p < 0.0001$), with the majority of reported side effects occurring in the Brazilian center.

Microbiological analyses showed a significant reduction in the number of CFUs of *Candida* isolated from denture plaque sonicates ($p = 0.05$) and from the palatal swabs ($p = 0.048$) at the 3-month follow-up (Table 3.5).

Bivariate analyses did not reveal any statistically significant association between explanatory variables and treatment effect.

DISCUSSION

To our knowledge, this is the first phase-I clinical trial which provided data on the efficacy of the palatal brushing on denture stomatitis. The results of this study confirmed our previous reports on the positive effect of palatal brushing. In a recent observational study [28], we demonstrated that the chance of the remission of denture stomatitis was 3.9 times higher in participants who brushed their palate (RR = 3.9, 95 % CI 1.0 to 15.9, $p = 0.04$). Furthermore, we have shown that there is an association between the lack of palatal brushing and the occurrence of *C. albicans* (OR = 1.8, 95 % CI 1.3 to 2.4, $p = 0.03$) [8].

Several mechanisms could explain the effect of palatal brushing, including mechanical stimulation and oral biofilm removal [30]. An oral biofilm is a protective niche that may harbor a wide array of pathogenic microorganisms encased in extracellular polysaccharide matrix, including aerobic and anaerobic bacteria, and yeasts [31, 32]. There is overwhelming evidence that denture and palate biofilms are important risk factors for denture stomatitis [5, 33-35]. Palatal brushing could eliminate this reservoir of pathogens and the source of irritation. This could justify the statistically significant decrease in *Candida* CFUs that was demonstrated in our study.

The results of several studies demonstrated that mechanical stimulation encourages keratinisation, reduces the infiltration of inflammatory cells and enhances the proliferation of fibroblasts and collagen synthesis [30, 36-38]. It has been shown that even in the presence of oral biofilm, brushing stimulation with techniques such as vibration motion can improve the tissue microcirculation [39]. Consequently, the effects of mechanical stimulation could counteract the effects of the inflammatory process in denture stomatitis. This resolution could lead to the re-establishment of an undamaged epithelium and basement membrane within the palatal mucosa. This healthy mucosa then serve as a mechanical barrier against microbiological colonization [40, 41].

Impaired salivary flow and xerostomia have been considered as predisposing factors in denture stomatitis [42, 43]. Palatal brushing could increase salivary flow by mechanical stimulation of the minor salivary glands of the palate. The stimulation of the salivary glands could have a mechanical cleansing effect and thus eliminate the denture biofilm [32, 40, 44]. In addition, saliva acts as an immune defence mechanism against

microorganisms [45]. In this study, patient-reported dry mouth was the most commonly reported side effect of palatal brushing. However, in accordance with several studies [46, 47], the patients' assessment did not correlate with the findings of the clinical examinations. Further research should include a more accurate assessment of unstimulated salivary flow to confirm these results [47].

There are conflicting hypotheses on whether the inflammation in denture stomatitis is associated with trauma from unstable prostheses or if it results from fungal biofilm [4, 7, 41, 46, 48]. However, there is considerable evidence demonstrating the lack of a direct cause-and-effect relationship between the presence of denture stomatitis and *Candida* [7, 8, 12]. Furthermore, several studies on the efficacy of antifungal medications in the treatment of denture stomatitis demonstrated a high recurrence rate of clinical signs of denture stomatitis and the re-colonization of the *Candida* after cessation of the antifungal treatment [13, 14]. Our study results support the previous hypothesis that trauma is a primary etiologic factor in denture stomatitis. Thus, we encourage oral healthcare professionals to use conservative approaches such as oral hygiene instructions, palatal brushing, and prosthesis adjustments rather than antifungal medications in the treatment of denture stomatitis.

In this study, we used a modified version of the Newton classification [16]. This modification introduced two subtypes for Newton's Type I denture stomatitis and allowed us to differentiate palatal petechiae (Type IA) from localized inflammation (Type IB). Our findings demonstrated a difference between these two different clinical manifestations. The microbiologic analyses of the dentures and palatal swabs of the

participants with Type IA denture stomatitis were negative for the presence of *Candida.* Furthermore, petechiae remained after palatal brushing. These results suggest that petechiae are merely the widening of the minor salivary glands ducts, which could be considered as a variation of the normal anatomy caused by trauma from the denture, and not a pathological sign of denture stomatitis [4, 49].

We also found that the use of the area and severity of the inflammation indices [17, 50] permit a better classification of the clinical signs of denture stomatitis than the Newton classification. We recommend the use of these indices in clinical and research training to ensure the standardization of the methods and comparisons between trials.

The results of this study should be interpreted with caution since a one-group pre-test/post-test design was used, and the study did not include any control group. The encouraging results of this study should be confirmed by a phase-II clinical trial.

CONCLUSION

In conclusion, the results of this study suggest that palatal brushing is effective in the treatment of denture stomatitis. We recommend the use of palatal brushing as a crucial adjunct to the routine management of this condition.

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List of Figures and Tables

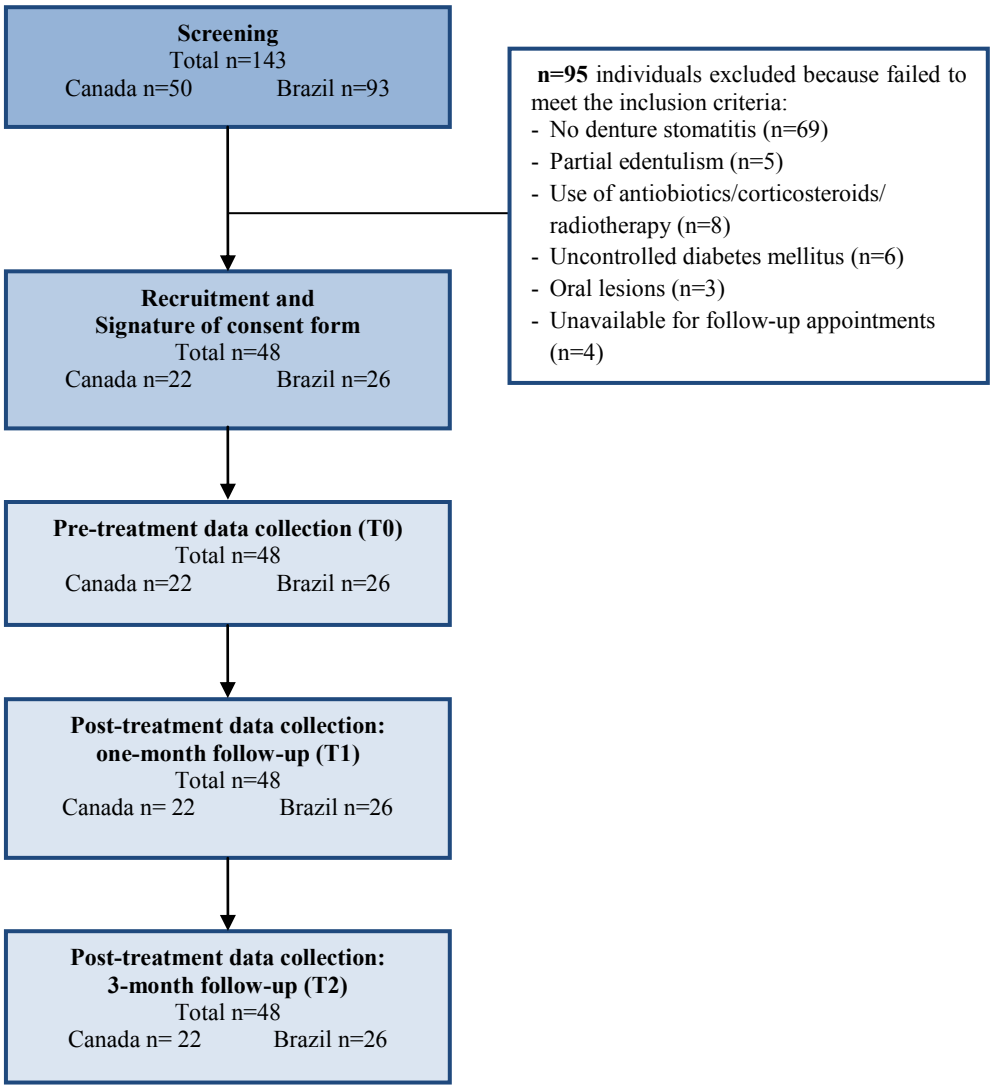

Figure 3.1: Flow chart of the study

Table 3.1: Assessments of denture stomatitis

Modified Newton classification [18]
0: Healthy mucosa **Type IA**: Petechiae in a normal palatal tissue, which are usually found around the orifices of the ducts of the palatal mucous glands **Type IB**: Localized area of inflammation of the denture-bearing area **Type II**: Generalised area of inflammation of the denture-bearing area **Type III**: Hyperplasic palatal surface with inflammation of the denture-bearing area
Inflammation area index [19]
0: No inflammation **1**: Inflammation of the palate extending up to 25 % of the palatal denture-bearing tissue **2**: Inflammation of the palate extending between 25 % and 50 % of the palatal denture-bearing tissue **3**: Inflammation covering more than 50 % of the palatal denture-bearing tissue
Inflammation severity index [19]
0: Normal tissue **1**: Mild inflammation (slight redness, no swelling or edema) **2**: Moderate inflammation (redness with some edema) **3**: Severe inflammation (acutely inflamed redness, edema)
Total score for inflammation = area+intensity (range 0 to 6) [19]

Table 3.2: Socio-demographic characteristics of the participants at baseline (T_0) by study center

Variables	Combined		Canada		Brazil		*p* value
Mean Age (years)[†]	66.0 (±11.2)		64.6 (±12.3)		67.3 (±10.2)		0.407
	N	**%**	**N**	**%**	**N**	**%**	
Gender							
➢ Male	16	33.3	12	54.5	4	15.4	0.006
➢ Female	32	66.7	10	45.5	22	84.6	
Marital status							
➢ Single/Separated/Divorced/ Widowed	23	47.9	9	41	14	53.8	0.401
➢ Married/Partnered	25	52.1	13	59	12	46.2	
Living arrangements							
➢ Alone	8	16.7	5	22.7	3	11.5	0.442
➢ With family or other adults	40	83.3	17	77.3	23	88.5	
Education							
➢ High school or less	39	81.3	13	59	26	100	<0.0001
➢ College and higher	9	18.7	9	41	0	0	
Yearly income							
➢ Less than $10,000	14	29.2	0	0	14	53.8	<0.0001
➢ $10,000 -$30,000	25	52.1	14	63.6	11	42.3	
➢ $30,000 or more	9	18.8	8	36.4	1	3.8	

[†] Mean (standard deviation)

Table 3.3: Study participants' profiles by study center at baseline (T_0) according to denture stomatitis risk factors

Variables	Combined		Canada		Brazil		*p* value
Mean years of edentulism[†]	37.2 (±14.7)		40.55 (±15.92)		34.3 (±13.3)		0.146
Mean age of current prosthesis (years)[†]	15.3 (±13.7)		9.93 (±9.53)		19.8 (±15.1)		0.011
	N	**%**	**N**	**%**	**N**	**%**	
Presence of systemic diseases	31	64.6	12	54.5	19	73.1	0.232
Medications use	36	75.0	17	77. 3	29	73.1	1.000
Unacceptable VDO	30	62.5	13	59	17	65.4	0.558
Inadequate upper retention	17	35.4	9	41	8	30.8	0.551
Unstable upper denture	22	45.8	12	54.5	10	38.5	0.384
Inadequate denture hygiene (reported by the patient)	5	10.4	4	18.2	1	3.8	0.165
Dirty denture (reported by the clinician)	39	81.3	13	59	26	100	<0,0001
No mouthwash use	35	72.9	13	59	22	84.6	0.059
Nocturnal wear (upper denture)	28	58.3	12	54.5	16	61.5	0.770
Smoking	13	27.1	6	27.3	7	26.9	1.000

[†] Mean (standard deviation)

Table 3.4: Effect of the intervention at 3-month follow-up

Diagnosis	worse		unchanged		improved/cured		*p* value (T_0-T_2)	Effect size† (T_0-T_2)
	N	%	N	%	N	%		
Modified Newton classification	1	2.1	32	66.6	15	31.3	0.001	0.34
Inflammation area index	1	2.1	18	37.5	29	60.4	<0.0001	0.49
Inflammation intensity index	1	2.1	15	31.2	32	66.7	<0.0001	0.52
Total inflammation (area+intensity)	1	2.1	8	16.7	39	81.2	<0.0001	0.54

† Effect size: 0.1= small effect, 0.3=medium effect and 0.5=large effect

Table 3.5: Effect of the intervention on the number of *Candida* colonies at 3-month follow-up

Candida colonies counts	increased		unchanged		decreased		*p* value (T0-T2)	Effect size† (T0-T2)
	N	%	N	%	N	%		
Number of CFUs‡ from the prosthesis	13	27.1	7	14.6	28	58.3	0.050	0.19
Number of CFUs‡ from the palate	4	8.3	34	70.8	10	20.9	0.048	0.20

‡ Colony-forming units (CFUs)
† Effect size: 0.1= small effect, 0.3=medium effect and 0.5=large effect

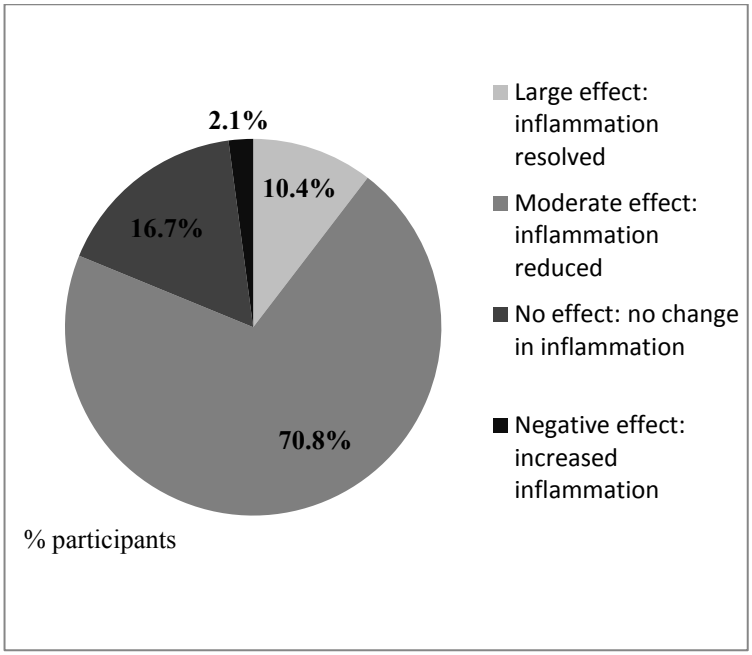

Figure 3.2: Treatment effect at 3-month follow-up (T_2)

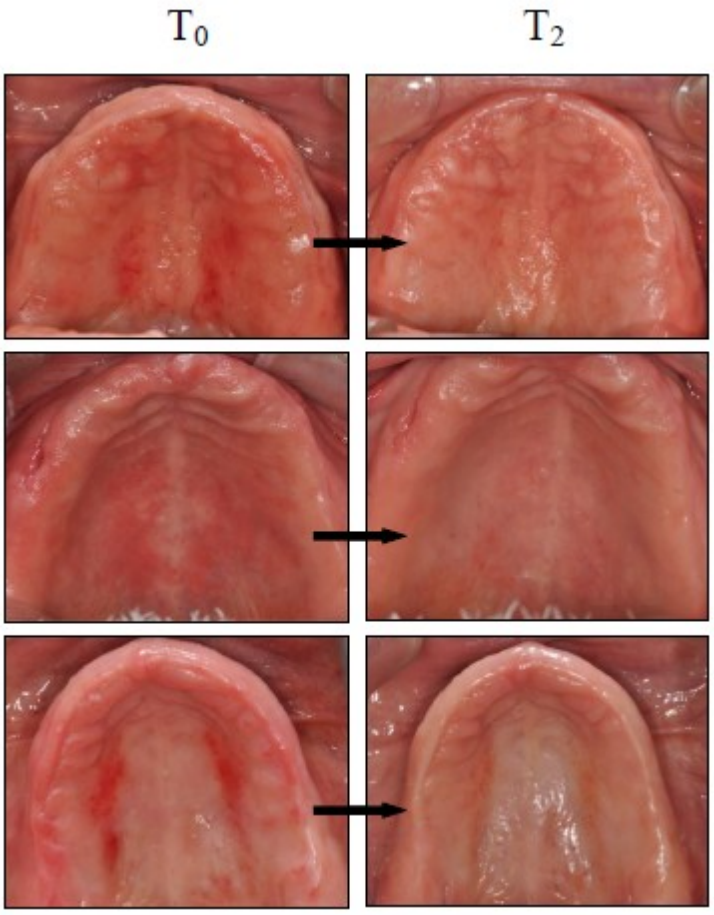

Figure 3.3: Palatal mucosa of patients at T_0 and T_2

CHAPTER IV

DISCUSSION

The results of this clinical trial demonstrated that palatal brushing can:

1. Reduce the extent of palatal inflammation in individuals affected by denture stomatitis.
2. Reduce the *Candida* colonization in the denture plaque and palate of individuals affected by denture stomatitis.

4.1 PALATAL BRUSHING EFFECTS

This master's research project is the first clinical study specifically designed to provide evidence on the efficacy of palatal brushing in the treatment of denture stomatitis.

Research on palatal brushing and its association with denture stomatitis is scarce. The only two observational studies that aimed to provide evidence on this simple hygienic measure are the previous studies of our research group [30, 110]. One of these studies consisted of a university-based cohort study [110] that assessed the evolution of denture stomatitis in term of severity and frequency and its association with potential risk factors. 135 edentate elders wearing a set of complete dentures (either with mandibular denture or mandibular implant-retained overdenture) were followed over two years. The results showed that edentate elders suffering from type II or type III denture stomatitis who brushed their palate had approximately 6 times more chance to have a decrease in

the severity of their condition (OR = 5.88, 95 % CI 1.1 to 32.2, p = 0.04). Another study by Emami et al. [30] showed a statistically significant relationship between the lack of palatal brushing and the occurrence of oral candidiasis (OR = 1.8, 95 % CI 1.3 to 2.4, p = 0.03).

The findings of this master's research project confirmed the results of these previous studies. In the present study, after 3 months of palatal brushing, denture stomatitis was cured in 10.4 % of the participants, and 70.8 % showed substantial improvement in the clinical signs of denture stomatitis. Furthermore, there was a statistically significant reduction in the number of Colony-Forming Units (CFUs) of *Candida* isolated from the palatal mucosa and from the denture biofilm. However, the effect size obtained for the microbiological data was reported to be small to medium (r = 0.19 to 0.2), which was less important than the clinical effect size (r = 0.34 to 0.54).

These promising data showed a potential success of palatal brushing in the treatment of denture stomatitis. However, in our study, one participant showed an increase in palatal inflammation. Similarly, in participants classified with Type IA denture stomatitis (the presence of petechiae in a healthy mucosa), there was no change in the level of the modified Newton classification neither in the level of area and severity of the inflammation indices. Furthermore, there was no change in the Newton classification for the patients with Type III denture stomatitis.

These negative results can be explained by three hypotheses:

1. The non-compliance to intervention. This hypothesis can be specifically attributed to the only patient with increased inflammation after palatal brushing.

2. The misconception about Type I denture stomatitis. The findings of the present study suggest that petechiae should not be considered as a type of denture stomatitis since it could be simply a variation in the normal anatomy of the minor salivary gland openings. This hypothesis can be supported by the fact that in our study, the microbiological analyses of the dentures and palatal swabs of individuals with petechiae did not show any trace of *Candida* colonization.

3. The shortcoming of conservative methods in the management of papillary hyperplasia of the palate, or Type III denture stomatitis. Hyperplasia is a reactive tissue overgrowth characterized by an inflamed mucosa with a nodular or papillary appearance in response to chronic irritation [72, 179]. The results of the present study support findings in the literature suggesting that treatment of Type III denture stomatitis should consist of the excision of the hyperplasic tissue [180, 181]. However, our findings showed that there was a statistically significant decrease in the extent and the severity of the inflammation in the individuals with Type III denture stomatitis, even though the hyperplasic tissue remained. This finding confirms the efficacy of palatal brushing in reducing the inflammation associated with denture stomatitis.

4.2 MECHANISM OF ACTION OF PALATAL BRUSHING

Palatal brushing can have two separate effects on the palatal mucosa: the effect of the mechanical stimulation and the effect of biofilm removal, both of which can lead to a reduction in the inflammation (Figure 4.1) [182].

Mechanical stimulation improves the microcirculation of an inflamed tissue by dilation of the vasculature. This action leads to an increased blood flow and oxygenation of the tissue [183]. Moreover, mechanical stimulation encourages keratinisation, reduces the infiltration of polymorphonuclear leukocytes [182] and enhances the proliferation and collagen synthesis of fibroblasts [184-186]. The process of action of the mechanical stimulus will decrease or inhibit the inflammatory reaction and will lead to the resolution of the inflammation. This resolution allows the re-establishment of undisrupted stratified squamous epithelium and basement membrane that provide an impervious mechanical barrier against microbiological colonization and permit the restitution of a healthy palatal mucosa under a removable denture [62, 65, 187, 188].

The mechanical stimulus can also increase the salivary flow by stimulating the minor salivary glands of the palate. This stimulation could have a mechanical cleansing effect and thus, contribute to the elimination of the biofilm [85, 187, 189]. Saliva also has an immune defence mechanism against microorganisms [190].

Palatal brushing also eliminates of the oral biofilm, which is considered as an etiologic factor for denture stomatitis [6, 32, 34, 48]. As previously stated in Chapter I, oral biofilm acts as a protective niche that harbours a wide array of pathogenic microorganisms [83, 85].

Those microorganisms produce toxins and metabolic waste, which can instigate the inflammatory process in denture stomatitis [6, 32, 34, 48, 83, 84].

Palatal brushing can eliminate this source of irritation and this reservoir of pathogens. This could explain the statistically significant decrease in *Candida* CFUs isolated from the palate and the dentures after 3 months of palatal brushing.

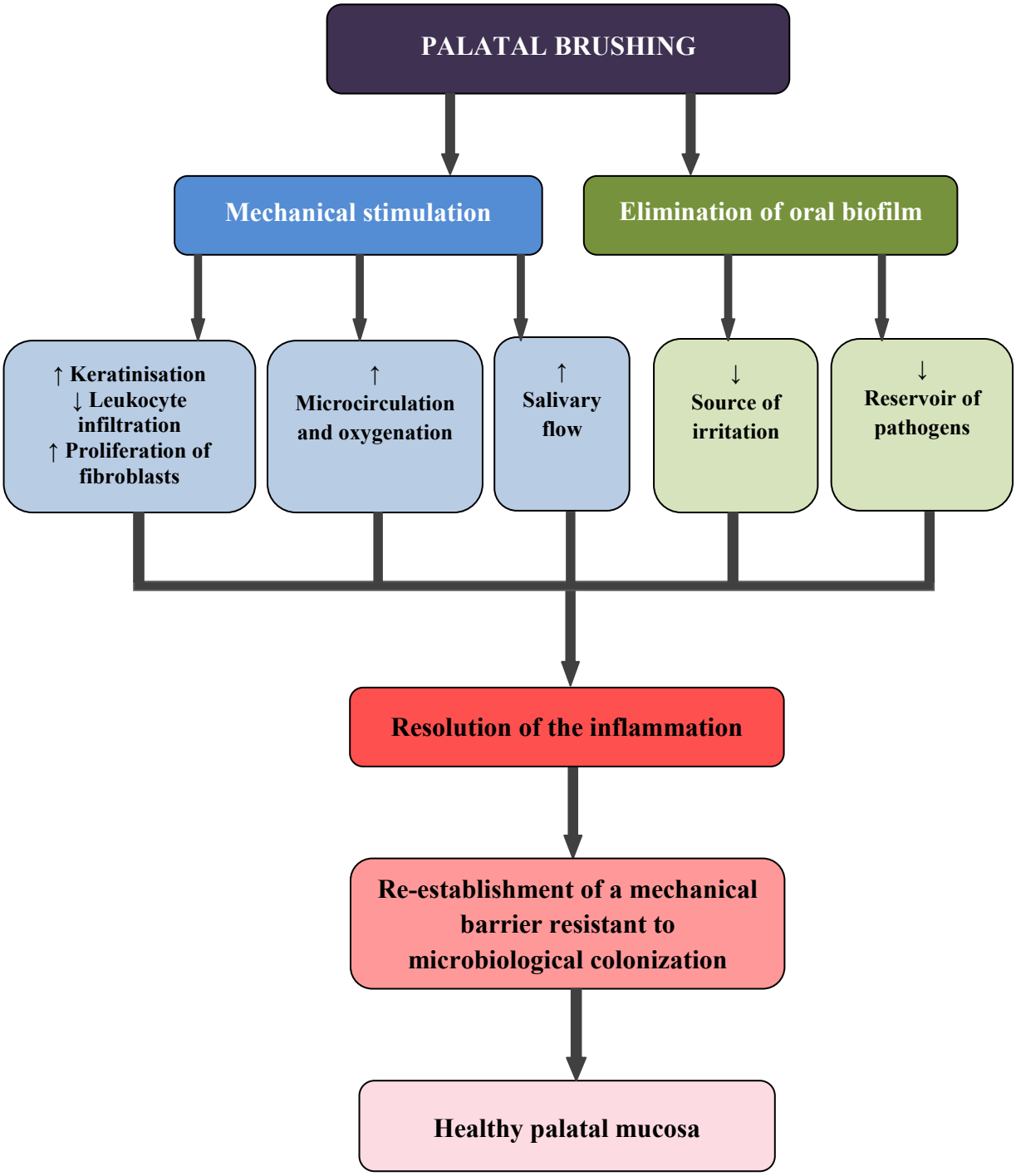

Figure 4.1: Palatal brushing effects

4.3 THE ETIOLOGY OF DENTURE-RELATED ERYTHEMATOUS STOMATITIS

The etiology of denture-related erythematous stomatitis is still controversial; the literature offers conflicting results on whether the inflammation in denture stomatitis is associated with trauma from unstable prostheses or if it results from the fungal biofilm [7, 25, 65, 191].

The lack of a direct cause-and-effect relationship between the presence of denture stomatitis and *Candida* has been demonstrated in many studies [7, 18, 30]. In addition, no difference between antifungal medications and alternative treatments of denture stomatitis were found [26, 78, 108]. Moreover, high recurrence rates of denture stomatitis and the re-establishment of the *Candida* colonization after cessation of the antifungal treatment have been frequently reported [78, 80].

There is considerable evidence supporting the hypothesis of trauma as a primary etiologic factor in denture stomatitis [7, 13, 26, 27, 29]. The histopathological changes that occur in denture stomatitis, such as incomplete or absent keratinisation, and modifications in components and structure of the epithelium and connective tissue, in addition to dissociations in the basement membrane, suggest that traumatogenic stress from unstable dentures results in an inflammatory reaction. This reaction will increase the susceptibility of the palatal mucosa to microbiological colonization [62, 63, 65].

Based on this concept we could hypothesize that *Candida* is not a primary etiologic factor of denture stomatitis [7, 18, 25] and that fungal infection contributes to the maintenance of the inflammatory reaction rather than its initiation [25, 63, 65].

4.4 MODIFICATION TO THE CLASSIFICATION OF DENTURE-RELATED ERYTHEMATOUS STOMATITIS

In the present study, we modified the Newton classification by adding two subtypes for Newton's Type I denture stomatitis. This modification allowed the differentiation between petechiae (Type IA) and localized inflammation (Type IB) in terms of the effect of treatment (as mentioned in section 4.1).

Newton classification is the most frequently used classification for the diagnosis of denture stomatitis in research and clinical settings. However, this classification does not allow an accurate representation of the clinical signs of denture stomatitis. In this clinical trial, we used the area and severity of the inflammation indices to account for this limitation. We found that this classification, which was introduced by Schwartz et al. [26], is easy to use in clinical settings and is sensitive enough to measure the effects of treatment. The inter-rater reliability results (kappa measurements) were higher with the use of those indices ($\kappa = 0.71$ to 0.86) when compared to the classification of Newton ($\kappa = 0.60$ to 0.84).

4.5 ORAL HEALTH KNOWLEDGE

Hygienic measures are essential to ensure a healthy mucosa under removable dentures. Those measures include: daily cleaning of the dentures by brushing after every meal, using a mouthwash, soaking the prosthesis in a denture-cleaning agent, and avoiding nocturnal wear of the dentures [192]. However, only one study included palatal brushing

among other hygienic instructions given to the participants [108] and there was no study assessing the effects of palatal brushing as an intervention.

In the present study, only 18.7 % of the participants had a clean prosthesis. Only 20 % of participants reported having previously received oral and denture hygiene instructions from their oral health care provider. Furthermore, half of the participants stated that they never consult a dental health care professional. There was a significant difference ($p < 0.0001$) between the two centers regarding the prosthesis hygiene of the participants. This result could be influenced by the lower level of income and education of the Brazilian participants when compared to the Canadian participants. In fact, none of the Brazilian participants were using mouthwash as a hygienic method. However, although these differences between the two centers were statistically significant, they did not have any influence on the treatment effects.

In agreement with the literature [32, 193], these findings suggest that edentate elders lack the necessary education about oral and denture hygiene. Oral health knowledge deficiency could play an important role in the prevalence of oral diseases such as denture stomatitis. It is the responsibility of the clinicians to raise awareness about oral hygiene and the necessity of periodic follow-up visits. The importance of oral health knowledge is more evident when taking into account the increase in the life expectancy and worldwide growth of the elderly population in the next decade [48, 194, 195]. This growing geriatric population is more susceptible to denture-related oral mucosal lesions due to the long-term use of removable prostheses, especially elders with systemic diseases and those who use multiple medications [38-42].

Palatal brushing could be an effective preventive measure against the development of denture stomatitis. However, it should be noted that this mode of prevention or treatment would be difficult for elderly patients with lack of manual dexterity [32, 117, 196]. Alternative hygienic methods that could be considered for this population could be the use of denture cleaners, oral mouthwashes, phytomedicines, and the microwave disinfection of the prosthesis [106, 128, 137, 197].

4.6 THE CHOICE OF STUDY DESIGN AND LESSON LEARNED FROM INTERNATIONAL COLLABORATION

Clinical trials are conducted in a series of phases and each phase is designed to achieve different objectives. Phase-I trials are conducted to test a first-time intervention or treatment in a small group of individuals in order to [198-200]:

1. Standardize the study procedures;
2. Assess the safety of the intervention;
3. Assess the recruitment strategies;
4. Collect preliminary data on the treatment effect for sample size calculations;
5. Assess the practicability of an international collaboration;
6. Guide the planning of a large-scale trial.

The evaluation of the feasibility of the collaboration between the two study centers was an important aspect of this master research project. In order to coordinate all the methodological aspects of the study and to interpret the results, three meetings between the research groups were organized, two in Brazil and one in Canada.

During the course of this study, we found that the standardization of the methodology is a critical step in multi-center trials. This ensures the adequacy of data for combined statistical analyses.

4.7 STUDY LIMITATIONS

The results of this phase-I clinical trial should be interpreted with caution because of certain study limitations. The primary threat to the internal validity of this research project was its design as a single group pre-test/post-test quasi-experimental study. This design comprises a variety of biases:

1. History bias: the possibility that events other than the treatment could have happened between the pre-test and the post-test and could have affected the outcome;
2. Maturation bias: the natural process that leads participants to change as a function of the passage of time.

   History and maturation biases occur primarily because of the absence of a control group and lack of randomization [201].
3. Pre-test effects: the information that participants acquire during the pre-test information session could influence the outcome of the study [202]. During this project, the pre-test clinical examination could have sensitized the participants to the presence of a pathologic lesion in their oral cavity. As a result, although they were asked to keep to their routine hygiene regimen, they could have altered their behavior by improving their oral hygiene because they are taking part in an

experiment. This effect, also called the Hawthorne effect, could have led to an overestimation of the study results [201-204].

Furthermore, although this project was a two-center study with a diverse population in term of socioeconomic and educational level, and denture characteristics (denture cleanliness, the mean age of the current prostheses), the study was limited in terms of external validity and the results cannot be generalized to other populations.

In addition, we cannot generalize the study results across time because of the duration of the follow-up. In our trial, the follow-up data was collected only after 1 month and 3 months. Therefore, we couldn't assess the long-term effect of palatal brushing and the potential for the recurrence of denture stomatitis.

4.8 FUTURE RESEARCH

In order to develop clinical practice guidelines in regard to the treatment of denture stomatitis, high-quality randomized controlled trials are needed [205]. The encouraging results of this master research project will help in the development of a randomized controlled trial with valid and generalizable results.

Also, as the etiology of denture stomatitis is still subject to debate, we need well-designed long-term cohort studies to shed light on the main causal factor of this disease. Inferences about cause-effect relationships may be valid or generalized to other populations only in the presence of a strong and direct relationship between the etiological factor and denture stomatitis, based on experimental evidence [206].

Furthermore, diagnostic studies should focus on investigating the salivary or systemic biomarkers involved in denture stomatitis.

As recent studies suggest that denture-related erythematous stomatitis has cytotoxic effects on the cells of the oral mucosa and induce nuclear alterations [71], further research should be conducted to assess the cytotoxic and premalignant changes occurring in denture stomatitis.

CHAPTER V

CONCLUSIONS

The results of this phase-I clinical trial suggest that:

1. Palatal brushing is an effective method for the treatment of denture stomatitis.
2. Palatal brushing reduces the extent and severity of the palatal inflammation in individuals affected by denture stomatitis.
3. Palatal brushing reduces the number of *Candida* Colony-Forming Units (CFUs) present in the denture biofilm and palate of individuals affected by denture stomatitis.
4. The encouraging results of this phase-I clinical trial should be confirmed by a phase-II clinical trial.

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APPENDICES

APPENDIX I: CONSENT FORM

Université de Montréal

Faculté de médecine dentaire

Un essai clinique de phase I sur l'effet du brossage du palais sur la stomatite prothétique.

Support financier de la Faculté de médecine dentaire de l'Université de Montréal (Gramdent)

Hiver 2012

Étudiant responsable

Dre Marla Kabawat, DDS, candidate à la M.Sc. en Sciences Buccodentaires
Faculté de médecine dentaire, Université de Montréal
C.P.6128 succursale centre-ville
Montréal, H3C 3J7

Directeur de recherche

Dre Elham Emami, DDS, MSc, PhD
Faculté de Médecine dentaire, Université de Montréal
C.P. 6128, succursale centre-ville
Montréal, H3C 3J7

Co-directeurs de recherche

Dr Louis de Koninck, DMD, MSc, FRCD(C)
Faculté de médecine dentaire, Université de Montréal
C.P. 6128 Succursale Centre-Ville
Montréal, H3C 3J7

Dr Jean Barbeau, BSc (U laval), PhD (U laval)
Faculté de médecine dentaire, Université de Montréal
C.P. 6128 Succursale Centre-Ville
Montréal, H3C 3J7

RENSEIGNEMENTS AUX PARTICIPANTS
ET
FORMULAIRE DE CONSENTEMENT

Renseignements généraux

Vous êtes invités à prendre part à ce projet de recherche parce que vous portez une prothèse supérieure complète et que vous êtes atteints de stomatite prothétique.

Avant de décider de participer ou non à ce projet, il est important que vous compreniez le but de cette étude et son déroulement. Ce formulaire de consentement vous explique le but de cette étude, les procédures, les risques et les inconvénients, les avantages, de même que les personnes avec qui communiquer au besoin. Vous devez bien comprendre la nature du projet afin de faire un choix éclairé.

Le présent formulaire peut contenir des mots que vous ne comprenez pas. Nous vous invitons à poser toutes les questions que vous jugerez utiles au chercheur et aux autres membres du personnel impliqués dans ce projet de recherche et à leur demander de vous expliquer tout mot ou renseignement qui n'est pas clair.

S'il vous plaît veuillez lire attentivement les renseignements ci-dessous et écouter les explications données par le chercheur de l'étude. Prenez votre temps pour lire attentivement et prendre votre décision. Si vous décidez de participer à l'étude, vous devez signer et dater ce formulaire de consentement et une copie vous sera remise.

Description du projet de recherche

La stomatite prothétique est une inflammation du palais chez les porteurs de prothèses supérieures. Au cours de cette étude, nous allons déterminer l'étendue de l'inflammation de votre palais et le nombre de levures attachées à votre prothèse et à votre palais à chaque visite. Nous pourrons ainsi comparer les résultats de la première visite et ceux après 1 mois et 3 mois de brossage du palais.

La stomatite prothétique est le plus souvent traitée avec des antimicrobiens ou des désinfectants qui pourraient avoir des effets secondaires et qui, le plus souvent, ne sont plus efficaces après l'arrêt de leur utilisation. Nos études antérieures ont montré que le brossage du palais pourrait réduire l'étendue de l'inflammation, cette étude pourrait donc le confirmer, et permettre aux dentistes de traiter les patients atteints de stomatite prothétique d'une façon plus conservatrice, simple et économique.

L'objectif de cette étude, qui inclura environ 40 participants, est d'obtenir des preuves scientifiques sur l'efficacité du brossage du palais dans le traitement de la stomatite prothétique. De plus, cet essai clinique de phase I va nous permettre d'uniformiser les procédures de l'étude et de déterminer la période requise pour améliorer la stomatite prothétique par le brossage du palais. Nous pourrons aussi estimer le nombre de participants nécessaire pour un essai de phase II (essai clinique randomisé).

Conditions de la participation

- Vous serez invité à participer à cette étude si:
  1. Vous êtes âgés de 18 ans ou plus;
  2. Vous portez une prothèse complète supérieure;
  3. Et vous présentez un des différents types de stomatite prothétique.

- Vous ne pourrez pas y participer si:
  1. Vous présentez des conditions comme le diabète non-contrôlé ou la xérostomie, si vous êtes immunocompromis, ou si vous recevez un traitement de chimiothérapie ou de radiothérapie;
  2. Vous avez reçu des antibiotiques, des corticostéroïdes ou des antifongiques durant les 4 semaines précédant l'étude;
  3. Le brossage du palais fait partie de votre hygiène prothétique;
  4. Vous allez changer votre prothèse existante durant l'étude.

Nature de la participation et durée de l'étude

Si vous vous portez volontaire pour participer à cette étude, et signez le formulaire, un(e) dentiste-chercheur (euse) :

- Remplira avec vous un questionnaire au premier rendez-vous couvrant vos informations sociodémographiques, des aspects de votre style de vie ainsi qu'une courte histoire dentaire et médicale.
- Regardera l'état de santé de votre bouche et surtout de votre palais.
- Examinera l'état de vos prothèses.
- Prendra des photographies de votre palais.
- Prendra un échantillon de votre palais par frottis avec un écouvillon stérile.
- Prendra votre prothèse supérieure pour environ 15 minutes : elle sera déposée dans un sac de plastique stérile auquel on ajoutera une solution saline et sera portée au bain à ultra-sons pour 5 minutes. Votre prothèse sera donc nettoyée et nous gardons le liquide de nettoyage pour notre recherche.
- Ces procédures seront répétées après 1 et 3 mois.

Le(la) dentiste-chercheur(euse) vous remettra une brosse à dent manuelle à poils souples et vous donnera les instructions quant à son utilisation. Vous devriez brosser votre palais avec cette brosse après les repas et avant de dormir, et ce, pendant toute la durée de l'étude, c'est-à-dire pendant 3 mois.

Vous devez aussi garder vos habitudes d'hygiène buccale et prothétique inchangées.

Le tableau ci-dessous présente les étapes de l'étude :

Visite	Étapes de l'étude	Traitements/collectes de données	Durée (heure)
1	Premier examen	Consentement éclairé, questionnaire, examen buccal, photo et échantillonnage	1,5
2	Deuxième examen	Examen buccal, photo et échantillonnage	1
3	Examen de suivi	Examen buccal, photo et échantillonnage	1

Risques et inconvénients

Un examen du palais et un frotti ne provoquent en général aucun risque, douleur ou inconfort. Les prothèses seront mises dans une solution de sel et nettoyées aux ultrasons qui ne compromettent pas le matériel de la prothèse, ni sa couleur et ni sa texture.

Avantages et bénéfices

Il se peut que vous retiriez un bénéfice personnel de votre participation à ce projet comme l'amélioration de votre stomatite, mais on ne peut vous l'assurer. Par ailleurs, vous bénéficierez de nettoyages de votre prothèse aux ultra-sons.

De plus cette étude vous donne l'occasion de contribuer à l'avancement des connaissances et les résultats pourront aider à développer des mesures de traitement dans un futur proche.

Compensation financière

La participation à cette étude prévoit une compensation financière de 45$ pour vous dédommager de vos frais de déplacement. Vous recevrez 15$ à chacune des trois rencontres.

Protection de la confidentialité

Durant votre participation à ce projet, le chercheur et son équipe recueilleront dans un dossier de recherche des renseignements vous concernant nécessaires pour répondre aux objectifs scientifiques.
Toutes les données relatives à votre participation à cette étude seront strictement confidentielles et recevront un code. La clé du code reliant votre nom à votre dossier de recherche sera conservée par le chercheur responsable. Les données de recherche seront conservées au laboratoire de recherche du directeur de cette étude, Dre Emami, à l'Université de Montréal, au local D523 du pavillon Roger-Gaudry. Ces données seront gardées pendant sept ans après la fin de l'étude et seront détruites par la suite. Le CERES pourrait également accéder à ces données pour vérifier la qualité de la recherche.

Diffusion des résultats

Les résultats de cette recherche pourraient être présentées au cours de journées scientifiques et publiées dans des revues scientifiques, mais aucune information pouvant vous identifier ne sera dévoilée ni dans les présentations, ni dans les publications. Les photographies de votre palais pourraient être utilisées à des fins de recherche mais elles ne permettent pas votre identification.

Responsabilité et droit de retrait :

Votre participation est volontaire et en signant ce formulaire de consentement, vous ne renoncez à aucun de vos droits prévus par la loi. De plus, vous ne libérez pas les investigateurs et le promoteur de leur responsabilité légale et professionnelle.
Vous pouvez vous retirer de cette étude à n'importe quel moment, sans avoir à donner de raison. Vous avez simplement à aviser la personne-ressource de l'équipe de recherche et ce, par simple avis verbal. En cas de retrait ou d'exclusion, les renseignements qui auront été recueillis au moment de votre retrait ne seront pas détruits afin de ne pas mettre en péril l'intégrité de l'étude.

Personnes-ressources

Pour plus d'information concernant cette recherche ou si vous voulez vous retirer de l'étude, vous pouvez contacter le chercheur directeur de cette étude à l'université de Montréal, Dre Elham Emami, au téléphone ou par courriel.
Vous pouvez aussi contacter l'étudiante responsable, Dre Marla Kabawat.

Pour toute information d'ordre éthique concernant les conditions dans lesquelles se déroule votre participation à ce projet, vous pouvez contacter le coordonnateur du Comité d'éthique de la recherche en santé (CERES) par courriel ou par téléphone.

Pour plus d'information sur vos droits comme participants, vous pouvez consulter le portail des participants de l'Université de Montréal à l'adresse suivante : http://recherche.umontreal.ca/participants.
Toute plainte relative à votre participation à cette recherche peut être adressée à l'ombudsman de l'Université de Montréal. L'ombudsman accepte les appels à frais virés. Il s'exprime en français et en anglais et prend les appels entre 9h et 17h.

FORMULAIRE DE CONSENTEMENT

Engagement et signature du (de la) participant(e) :

Votre participation à cette étude est tout à fait volontaire. Vous êtes donc libre d'accepter ou de refuser d'y participer sans que cela n'affecte votre traitement à l'Université de Montréal.

Je, ……, déclare avoir pris connaissance des documents ci-joints, en avoir discuté avec Dre Marla Kabawat et comprendre le but, la nature, les avantages, les risques et les inconvénients de l'étude. J'affirme avoir reçu une copie de ce document.

Après réflexion et un délai raisonnable, je consens librement à prendre part à cette étude. Je sais que je peux me retirer en tout temps sans préjudice.

Je consens à ce que l'on conserve mes coordonnées et que l'on me recontacte afin de me proposer de participer à un autre projet de recherche.

☐ Oui ☐ Non

Signature du participant……..date……

Engagement et signature de l'étudiante-chercheuse :

Je, Marla Kabawat, déclare avoir expliqué le but, la nature, les avantages, les risques et les inconvénients de l'étude ainsi que d'avoir répondu à toutes les questions du participant. Je m'engage avec l'équipe de recherche à respecter ce qui a été convenu au formulaire d'information et de consentement et à en remettre une copie signée au participant.

Signature …… date……

APPENDIX II : QUESTIONNAIRE

Université de Montréal

Un essai clinique de phase I sur l'effet du brossage du palais sur la stomatite prothétique

Université de Montréal
Faculté de médecine dentaire

Hiver 2012

Questionnaire de base

Date: ☐☐ / ☐☐ / ☐☐☐☐
j j m m a a a a

Code d'identification: ☐☐

INFORMATIONS SOCIODEMOGRAPHIQUES

1. Date de naissance (année): .....

2. Sexe : ❒ Masculin ❒ Féminin

3. Quelle est votre origine ethnique ?

❒ Amérique du nord (Canadien-français, Canadien-anglais, Américain, Mexicain)

❒ Amérique du Sud (par exemple Latine / Hispano-américain)

❒ Asie de l'Est (S'il vous plaît cocher une case: ❒ Chinois, ❒ Japonais, ❒ Coréen)

❒ Asie du sud (par exemple des Indes orientales, Pakistanais, Sri lankais)

❒ Européen (par exemple Slaves, Germaniques, Anglo-saxon, Scandinave, Grecque)

❒ Asie du sud est (par exemple au Cambodge, Indonésie, Laotien, Vietnamien)

❒ Africain (Afrique /Afro-américain)

❒ Autochtones / Natif américain

❒ Moyen-Orient /Afrique du nord (par exemple Afghan, Algérien, Marocain, Égyptien, Iranien, Irakien, Israéliens, Palestinien, Syrien, Tunisien, Turc)

❒ Autre ➢ Veuillez préciser : **……..**

4. Quel est votre statut matrimonial?

❒ Célibataire (jamais marié(e) et aucun conjoint(e) de fait) ❒ Marié(e) ou vivant comme marié(e)

❒ Séparé (e) ❒ Divorcé (e) ❒ Veuf (ve)

❒ Autre : Veuillez préciser ……

5. Habitez-vous:

❒ Seul (e) ❒ Avec d'autres adultes ❒ En famille

6. Quel a été le plus haut niveau de scolarité que vous avez complété?

❒ Pas d'école ❒ École primaire
❒ École secondaire
❒ Collège (CÉGEP/Technique)
❒Université : ❒ Baccalauréat ❒ Maitrise ❒ Doctorat

7. Quel est votre revenu familial annuel?

❒ Moins que $10,000 par année ❒ $10,000 à $29,999 par année

❒ $30,000 à $49,999 par année ❒ $50,000 à $69,999 par année

❒ $70,000 à $89,999 par année ❒ $90,000 à $109,999 par année

❒ $110,000 à $139,999 par année ❒ $140,000 ou plus par an

MODE DE VIE

1. Avez-vous déjà fumé un total de 100 cigarettes ou plus durant votre vie?

❒ Oui ❒ Non (Si non, veuillez passer à la question 6)

2. Y a-t-il déjà eu une période durant laquelle vous avez fumé des cigarettes régulièrement (au moins une fois par semaine)?

❒ Oui ❒ Non

3. Quel âge aviez-vous la première fois quand vous avez commencé à fumer des cigarettes régulièrement?

_____ Ans

4. Fumez-vous encore des cigarettes?

❒ Oui ❒ Non

Si oui, combien de cigarettes fumez-vous? (généralement 1 paquet contient 20 cigarettes)

_____ # de cigarettes

❒ Par jour ❒ Par semaine ❒ Par mois

Si non, quel âge aviez-vous lorsque vous avez cessé de fumer régulièrement :

_____ Ans

Pendant les périodes où vous fumiez, combien de cigarettes aviez-vous l'habitude de fumer? (généralement 1 paquet contient 20 cigarettes)

_____ # de cigarettes

❒ Par jour ❒ Par semaine ❒ Par mois

5. Ya t-il déjà eu des périodes pendant lesquelles vous aviez arrêté de fumer pendant au moins 12 mois et aviez commencé à nouveau?

❒ Oui ❒ Non

6. Consommez-vous des boissons alcoolisées ?

❒ Souvent ❒ Fréquemment ❒ Occasionnellement

❒ Rarement ❒ Jamais (passez à l'histoire médicale)

7. À quelle fréquence consommez-vous des boissons alcoolisées?

❒ 1 fois par mois ou moins
❒ 1 fois par semaine
❒ 1 fois par jour
❒ 2-3 fois par mois
❒ 3-4 fois par semaine
❒ 2 fois ou plus par jour

8. Chaque fois que vous buvez des boissons alcoolisées, quelle quantité en buvez-vous habituellement (nombre de verre/nombre de cannette)

❒ 1-2 ❒ 3-4 ❒ 5-6 ❒ 7 et plus

HISTOIRE MÉDICALE

1. Diriez-vous qu'en général votre santé est :

❒ Excellente ❒ Très bonne ❒ Bonne ❒ Passable ❒ Mauvaise

2. Bilan de santé : veuillez vérifier si vous avez une des maladies suivantes et pour combien de temps vous l'avez eu :

Maladie	Oui	Non	Depuis
Cancer (type) : ……..			
Anémie			
Problème de saignements			
Hyposialie (Diminution de la fabrication de salive)			
Diabète non-contrôlé			
Problème de thyroïde			
Neutropénies			
Hypoparathyroïdisme			
Maladie d'Addison			
Dépression			
Maladie hépatique (hépatite A, B, C ; cirrhose, etc.)			
Infection VIH			
SIDA			
Autre(s), précisez : ……..			

3. Veuillez vérifier si vous prenez présentement un de ces médicaments et depuis quand:

liste de médicaments	Oui	Non	Depuis
Antibiotiques (Clindamycine, l'érythromycine, amoxicilline ...)			
Corticoïdes (Prednisolone, Bétaméthasone, l'hydrocortisone ....)			

Analgésiques/Anti inflammatoires non stéroïdiens (Aspirine, Ibuprofène, la codéine, Acétaminophène, Morphine ...)			
Antifongiques (Nystatine, Fluconazole, Amphotericine B …)			
Psychotropes (Chlorpromazine, la phénothiazine, Carbonate de lithium…)			
Laxatifs			
Anti allergiques (Chlorphéniramine ...)			
Antihypertenseurs (diurétiques, bêtabloquants, la méthyldopa ...)			
Anticoagulants (Héparine, Warfarine, ...)			
Immunosuppresseurs (Méthotrexate, azathioprine, pénicillamine…)			
Hormonothérapie (œstrogène, Contraceptifs ...)			
Médicaments thyroïdiens (Synthroid, Levoxyl, Levothroid…)			
Antiépileptiques (Carbamazépine, Phénytoïne …..)			
Anti cholinergique (Bipéridène, procyclidine, dihexyvérine…)			
Autre(s) (Précisez) :……			

4. Avez-vous déjà subi une chimiothérapie ou une radiothérapie pour traiter un cancer ou une tumeur?

❒ Oui ❒ Non

Si oui, depuis quand?.....

5. Êtes-vous allergique ou bien avez-vous déjà eu des réactions secondaires à/au ?

❒ Oui ❒ Latex
❒ Acrylique de la prothèse (Méthyle méthacrylate)
❒ Adhésif pour prothèse
❒ Autre substance : ……..

❒ Non

HISTOIRE DENTAIRE

1. En général, diriez-vous que la santé de votre bouche est :

❒ Excellente ❒ Très bonne ❒ Bonne ❒ Passable ❒ Mauvaise

2. Consultez-vous souvent un professionnel dentaire?

❒ 2 fois ou plus par an pour un contrôle ou un traitement

❒ 1 à 2 fois par an pour un contrôle ou un traitement

❒ Moins d'une fois par an pour un contrôle ou un traitement

❒ Seulement pour des soins d'urgence

❒ Jamais

3. Condition buccale:
En général, êtes-vous satisfait(e) de votre condition buccale ?

Pas du tout satisfait _____ Entièrement satisfait

4. Éprouvez-vous un ou plusieurs des symptômes suivants ?

Sensation de brûlure au palais: ❒ Souvent ❒ Parfois ❒ Rarement ❒ Jamais

Sensation de brûlure à la langue : ❒ Souvent ❒ Parfois ❒ Rarement ❒ Jamais

Douleurs légères : ❒ Souvent ❒ Parfois ❒ Rarement ❒ Jamais

Mauvaise haleine : ❒ Souvent ❒ Parfois ❒ Rarement ❒ Jamais

Sécheresse buccale : ❒ Souvent ❒ Parfois ❒ Rarement ❒ Jamais

Prothèses complètes :

1. Depuis combien d'années êtes-vous édenté ?

_____ années

2. Combien de prothèses avez-vous eues depuis que vous êtes édentés (incluant celles que vous portez maintenant) ?

Prothèse du haut: _____ prothèse(s)
Prothèse du bas : _____ prothèse(s)

3. Quel est l'âge de votre ou vos prothèses actuelles ?

Prothèse du haut: _____ années
Prothèse du bas : _____ années

4. En général, comment est votre satisfaction concernant votre prothèse supérieure?

Pas du tout satisfait _____ Entièrement satisfait

En général, comment est votre satisfaction concernant votre prothèse inférieure?

Pas du tout satisfait _____ Entièrement satisfait

5. Êtes-vous satisfait(e) du confort de votre prothèse supérieure ?

Pas du tout satisfait _____ Entièrement satisfait

6. Comment est votre satisfaction concernant la rétention de votre prothèse supérieure ? (Est-ce que votre prothèse tombe?)

Pas du tout satisfait _____ Entièrement satisfait

Comment est votre satisfaction concernant la rétention de votre prothèse inférieure ? (Est-ce que votre prothèse se soulève?)

Pas du tout satisfait _____ Entièrement satisfait

7. Ressentez-vous un déplacement de la prothèse supérieure en mangeant et/ou en parlant?

❒ Souvent ❒ Fréquemment ❒ Occasionnellement ❒ Rarement

Ressentez-vous un déplacement de la prothèse inférieure en mangeant et/ou en parlant?

❒ Souvent ❒ Fréquemment ❒ Occasionnellement ❒ Rarement

8. Trouvez-vous des particules alimentaires sous vos prothèses?

❒ Souvent ❒ Fréquemment ❒ Occasionnellement ❒ Rarement

9. Utilisez-vous un adhésif pour prothèses?

Prothèse supérieure : ❒ Oui ❒ Non

Prothèse inferieure : ❒ Oui ❒ Non

Si oui, à quelle fréquence?

Prothèse supérieure :

❒ Souvent ❒ Fréquemment ❒ Occasionnellement ❒ Rarement

Prothèse inferieure :

❒ Souvent ❒ Fréquemment ❒ Occasionnellement ❒ Rarement

Habitudes d'hygiène buccale et prothétique :

1. Qui est responsable de votre hygiène buccale et prothétique?

❒ Vous-même ❒ Une autre personne (veuillez préciser) : …….

2. Si c'est vous-même, avez-vous de la difficulté à nettoyer vos prothèses?

❒Oui ❒ Non

3. Avez-vous déjà reçu des instructions quant à votre hygiène buccale et prothétique ?

❒ Oui ❒ Non

Si oui, quelles sont ces instructions? ……..
……
……

Est-ce que vous suivez ces instructions?

❒ Oui ❒ Non ❒ Pas toujours

4. Combien de fois par jour ou par semaine nettoyez-vous votre ou vos prothèses?

_____ fois par jour _____ fois par semaine

À quel moment de la journée?

❒ Avant chaque repas
❒ Après chaque repas
❒ Le matin
❒ Le soir avant de dormir
❒ Matin et soir
❒ Après les repas ainsi que le matin et le soir

5. Comment nettoyez-vous votre ou vos prothèses? (1 ou plusieurs réponses)

❒ Rinçage à l'eau sans brossage
❒ Brossage sans dentifrice
❒ Brossage avec dentifrice
❒ Utilisation d'un produit nettoyant pour prothèses
❒ Autre (précisez) : ……

6. Utilisez-vous un rince-bouche?

❒ Oui ❒ Non

Si oui, à quelle fréquence?

_____ fois par jour _____ fois par semaine

À quel moment de la journée?

❒ Avant chaque repas ❒ Après chaque repas
❒ Le matin ❒ Le soir avant de dormir
❒ Matin et soir ❒ Après les repas ainsi que le matin et le soir

7. Retirez-vous vos prothèses pendant la nuit ?

Prothèse supérieure : ❒ Oui ❒ Non ❒ Parfois

Prothèse inferieure : ❒ Oui ❒ Non ❒ Parfois

Si oui, dans quoi gardez-vous votre ou vos prothèses?

❒ À l'air libre sec
❒ Mouillée(s), à l'air libre
❒ Dans un contenant rempli d'eau seulement
❒ Dans un contenant rempli d'eau avec un agent nettoyant (type effervescent)
❒ Autre (précisez) :……

APPENDIX III: CLINICAL FORM

Université de Montréal

Un essai clinique de phase I sur l'effet du brossage du palais sur la stomatite prothétique.

Université de Montréal
Faculté de médecine dentaire

Hiver 2012

Formulaire clinique

Date :

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Code d'identification :

☐☐

Examen Oral :

Classification de la stomatite prothétique

Classification modifiée de Newton [1]:

❒ Pas de stomatite prothétique
❒ Type IA : pétéchies
❒ Type IB : inflammation localisée
❒ Type II : inflammation généralisée et diffuse
❒ Type III : inflammation avec hyperplasie papillaire du palais

Index de l'inflammation (surface) [2]:

❒ 0 Pas d'inflammation

❒ 1 Inflammation s'étendant jusqu'à 25% de la surface du palais

❒ 2 Inflammation s'étendant entre 25% et 50 % de la surface du palais

❒ 3 Inflammation couvrant plus que 50% du palais recouvert par la prothèse

Index de l'inflammation (sévérité) [2]:

❒ 0 Tissu normal (de couleur rose avec un aspect considéré comme sain)

❒ 1 Inflammation légère (une légère rougeur, pas d'œdème)

❒ 2 Inflammation modérée (rougeurs avec œdème)

❒ 3 Inflammation sévère (rougeurs et inflammation aiguë, œdème)

Total de l'inflammation = Surface + Sévérité (entre 0 et 6)

Total inflammation = …….

Autres conditions

❒ Chéilite angulaire

❒ Autres :……..

Signes cliniques d'habitudes parafonctionnelles [3-5]

1. Examination de l'articulation temporo-mandibulaire (palpation digitale des deux articulations en demandant au patient d`ouvrir et de fermer la bouche lentement)

a. sensibilité lors de la palpation :

❒ Absent ❒ Présent

b. Présence de clic ou de crépitation :

❒ Absent ❒ Présent

2. Usure des dents de la prothèse (présence de facettes d'usure)

❒ Absent ❒ Présent

Salive [3, 4]

Favorable ❒ Classe I (quantité et qualité normale de la salive)

Défavorable ❒ Classe II (salive excessive, contient beaucoup de mucus)
❒ Classe III (salive insuffisante)

Forme du palais dur

❒ En forme de U ❒ En forme de V ❒ Plat

Torus au maxillaire

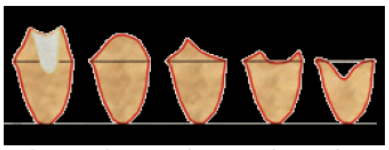
❒ Absent ❒ Présent

Résorption de l'os alvéolaire supérieur [6]

❒ Classe II : Post extraction
❒ Classe III : crête arrondie, hauteur et largeur suffisantes
❒ Classe IV : crête en lame de couteau, hauteur suffisante, largeur insuffisante
❒ Classe V : crête plate, hauteur et largeur insuffisantes
❒ Classe VI : crête concave (avec perte d'os basal)

Résorption de l'os alvéolaire inférieur

❒ Classe II : Post extraction
❒ Classe III : crête arrondie, hauteur et largeur suffisantes
❒ Classe IV : crête en lame de couteau, hauteur suffisante, largeur insuffisante
❒ Classe V : crête plate, hauteur et largeur insuffisantes
❒ Classe VI : crête concave (avec perte d'os basal)



Cl.II Cl.III Cl.IV Cl.V Cl.VI

(Adapté de la classification de Cawood et Howell)

L'élasticité des tissus au niveau de la crête résiduelle supérieure

❒ Tissus mobiles (latéralement)
❒ Tissus compressibles, résilients (verticalement)
❒ Tissus fermes

L'élasticité des tissus au niveau de la crête résiduelle inférieure

❒ Tissus mobiles (latéralement)
❒ Tissus compressibles, résilients (verticalement)
❒ Tissus fermes

Evaluation des prothèses :

Dentition inférieure:

❒ Pas de prothèse

❒ Prothèse complète

❒ Prothèse partielle

Hygiène prothétique [7]

❒ Prothèse propre (pas de débris)

❒ Prothèse sale ❒ débris légers (débris mous / débris durs légers)

❒ débris sévères (débris durs sévères)

Type d'occlusion sur la prothèse actuelle (non-squelettique)

❒ Classe I
❒ Classe II
❒ Classe III

Occlusion (Le patient est prié de se détendre et de fermer doucement sur ces dents postérieures plusieurs fois à partir d'une position légèrement ouverte) [8, 9]

❒ Stable (quand il y a un contact régulier entre les dents et un retour conforme avec la position d'intercuspidation)

❒ Glissement (quand il y a un contact irrégulier entre les dents et un retour non conforme avec la position d'intercuspidation ou un glissement supérieur à 4 mm)

Dimension verticale d'occlusion (DVO)

❒ Acceptable ❒ Réduite

❒ Excessive

Espace inter-occlusal (l'espace entre les surfaces occlusales des dents maxillaires et mandibulaires lorsque la mandibule est en position de repos physiologique)

❒ Adéquat (2-5 mm) ❒ Inadéquat (>5mm ou <2mm)

Rétention de la prothèse supérieure (Résistance à la traction verticale)[8]
L'ouverture buccale est de 20 mm. Notez si la prothèse tombe. Pendant que la bouche est encore ouverte, la prothèse est saisie par le pouce et l'index au niveau des prémolaires et une force descendante est appliquée.

❒ Rétention adéquate ❒ Pas de rétention

Stabilité de la prothèse supérieure [8]

1) Déplacement latéral : la prothèse supérieure est saisie avec le pouce et l'index dans la région des prémolaires et une force de rotation dans le plan d'occlusion est appliquée. Nous considérons le déplacement de 5 mm ou moins comme satisfaisante.

   ❒ Non (Déplacement lat≤5mm) ❒ Oui (Déplacement lat>5mm)

2) Basculement prononcé : une force légère est appliquée simultanément aux côtés droit et gauche sur les premières molaires. Tenter de faire basculer la prothèse dans la direction antéropostérieure avec le pouce et l'index placé simultanément postérieurement et antérieurement.

   ❒ Non (Basculement minimal) ❒ Oui (Basculement prononcé)

Stabilité de la prothèse inférieure

1) Déplacement: L'ouverture buccale est de 20 mm et la langue est en position de repos. L'assise de la prothèse est vérifiée.

   ❒ Non (Reste en place) ❒ Oui (Déplacement perceptible)

2) Mouvement prononcé: Le patient est invité à bouger sa langue de manière à ce que la pointe repose doucement au niveau des angles de la bouche. Vérifiez l'assise de la prothèse.

   ❒ Non (Pas de mouvement) ❒ Oui (Mouvement prononcé)

3) Le mouvement antéropostérieur: la prothèse supérieure est enlevée. La prothèse inférieure est tenue avec l'index et le pouce au niveau des incisives. Vérifier la stabilité de la prothèse dans la direction antéropostérieure.

❒ Non (Mouvement minimal) ❒ Oui (Mouvement prononcé)

Type de dents de la prothèse

❒ Acrylique

❒ Porcelaine

Autres caractéristiques des prothèses :

.....
.....
.....

1. Newton A. Denture sore mouth: a possible aetiology. Br Dent J 1962;112(9):357.
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5. Gavish A, Halachmi M, Winocur E, Gazit E. Oral habits and their association with signs and symptoms of temporomandibular disorders in adolescent girls. J Oral Rehabil 2000;27(1):22-32.
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9. Corrigan PJ, Basker RM, Farrin AJ, Mulley GP, Heath MR. The development of a method for functional assessment of dentures. Gerodontology 2002;19(1):41-5.

APPENDIX IV: MICROBIOLOGICAL FORM

Université de Montréal

Un essai clinique de phase I sur l'effet du brossage du palais sur la stomatite prothétique.

Université de Montréal
Faculté de médecine dentaire

Hiver 2012

Formulaire de microbiologie

Date :

Baseline :

☐☐ / ☐☐ / ☐☐☐☐

1 mois :

☐☐ / ☐☐ / ☐☐☐☐

3 mois :

☐☐ / ☐☐ / ☐☐☐☐

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Code d'identification :

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Sonicat de prothèse (P):

Sabouraud-Dextrose 4% Agar

	Dilution choisie	Nombre de UFCs dans 100 µL (moyenne des duplicatas)	Correction pour le facteur de dilution	Correction pour le volume inoculé (UFC/prothèse)	UFC/mL
Baseline					
1 mois					
3 mois					

CHROMagar

	Espèces trouvées	% de C. albicans
Baseline		
1 mois		
3 mois		

Swab du palais (S):

Sabouraud-Dextrose 4% Agar

	Dilution choisie	Nombre de UFCs dans 100 µL (moyenne des duplicatas)	Correction pour le facteur de dilution	Correction pour le volume inoculé (UFC/prothèse)	UFC/mL
Baseline					
1 mois					
3 mois					

CHROMagar

	Espèces trouvées	% de C. albicans
Baseline		
1 mois		
3 mois		

APPENDIX V: INSTRUCTION FORM

Université de Montréal

Instructions aux participants concernant le brossage du palais :

Quand dois-je brosser mon palais?

- Vous devez brosser votre palais après chaque repas et avant de vous coucher le soir.

Comment dois-je brosser mon palais?

- Enlevez votre dentier.
- Passez la brosse à dents qui vous a été fournie sous l'eau chaude pour assouplir ses poils.
- Ne pas utiliser de dentifrice.
- Brossez votre palais doucement avec des mouvements de va-et-vient, de gauche à droite et d'arrière vers l'avant, pour environ 1 minute.
- Brossez votre palais avec des mouvements de vibration.
- Évitez de brosser la zone située derrière la limite postérieure de votre dentier.

Y a-t-il d'autres instructions d'hygiène buccale?

- Vous devez garder vos habitudes d'hygiène buccale et d'hygiène de votre dentier inchangées pendant l'étude, sans instructions supplémentaires de notre part.

Quels sont les avantages du brossage du palais?

- Élimination de la plaque et des débris de nourriture sur votre palais.
- Prévention de la multiplication de microbes.
- Stimulation de la circulation et de la salive.
- Le brossage du palais régulier, en suivant les instructions mentionnées ci-dessus, pourrait également être bénéfique à l'état inflammatoire de votre palais.