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The efficacy of diode laser removal of leukoplakias on the tongue and in lower buccal cavity compared to other buccal cavity locations. A two-year study.

Research Article

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Abstract: Introduction. Leukoplakias of the buccal cavity are premalignant lesions with a significant 0-20% potential for malignant transformation. In addition to active follow-up screening procedures, a number of surgical interventions are recommended for their removal. One of the preferred procedures is laser ablation with consecutive histopathology using one of the many types of lasers. The efficacy of such procedure with respect to the lesion location is, however, unclear. Many studies are contradictory. Some shows laser ablations as prevention of malignisation other see it as increased risk. Aim of this is to test treatment in different locations for two years. Material and method. An outpatient ablation by a 980mm diode laser of lesions on the tongue and in the lower buccal cavity (Group A) and lesions in other parts of the buccal cavity (Group B) were performed under local anaesthesia. In total, 76 lesions were treated in 66 patients. Recurrence after 1, 3, 6, 9, 12, and 24 months were followed up. Initially, all lesions were histopathologically tested. Concurrently, the subjective tolerance of the procedure was monitored, using a 1 (ideal) to 5 (worst) scale. Results. Clearing rate of lesions was of 84.6% for Group A and of 94.7% for Group B. In two patients (3% of Group A) malignant transformation occurred which was not observed in Group B. Patient toleration in various time intervals was always higher in Group B, but generally was very high in both groups. Conclusion. Malignant transformation of leukoplakias does occur even after laser ablation, and for this reason it is necessary to subject the patients to systematic follow-ups. It is significantly higher risk of recurrences and malign transformation in tongue and oral base. Laser ablation is a simple and well-tolerated procedure with high clearing rate.

Keywords: *Leukoplakias of the buccal cavity • Leukoplakias on the tongue • Diode laser • Premalignant potential*

1. Introduction

Leukoplakia is defined by the World Health Organisation (WHO) as a white patch or coating which cannot be removed, and it is not clinically or pathologically defined as another known condition [1]. The definition has been further extended by the potential of certain leukoplakias to transform into carcinoma.

Hence it is a lesion in the buccal cavity which has a high premalignant potential. Malignant transformation is not the same for all leukoplakias; it depends on the form, characteristics – i.e. the presence of epithelial dysplasia, location of the lesion [2]. Leukoplakia with its malign potential is classified as a premalignant, precarcinogenic or potentially malignant lesion.

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Precarcinogenic lesions are defined as morphologically altered tissues with higher probability of developing into carcinoma than in the control group (healthy population) [3]. The factors which contribute to the malignant transformation from precancerous are outer environment influences, including smoking, alcohol abuse, exposure to UV radiation, viral infections, and poor dietary habits [4].

Characteristics associated with a higher risk of malignant transformation are gender (higher risk in women), time (longer presence of a leukoplakia lesion), idiopathic leukoplakia (leukoplakia in smokers), location (lower buccal cavity, tongue), non-homogeneous leukoplakia type, the presence of C. albicans (particularly on the ridge of the tongue), and the presence of dysplastic alterations [5]. Of the aforementioned, the biggest relevance is attributed to the presence of dysplastic alterations, but even lesions without dysplastic alterations bear a risk of malignant transformation, albeit in a longer period of time.

In dysplastic alterations of moderate and severe degree, the risk of malignisation is 2.3 times higher (compared to leukoplakias without dysplastic alterations or those with mild dysplastic alterations) [6]. The ratio of malignant transformation ranges from 0-20% and 1-30 years, depending on the leukoplakia lesion type [7]. In the non-homogeneous type of leukoplakias, the risk of malignisation is 7 times higher than in the homogeneous type. In lesions exceeding 200mm² the risk is 5.4 times higher [8]. The risk of transformation of leukoplakia into carcinoma is markedly higher in the older population. The incidence of carcinoma in the age group of 70-89 years is 7.5% in 5 years. In younger population, i.e. population under 50 years of age, carcinoma developed in approximately 1% [9]. It is very interesting to watch the growing risk of malignisation from the time perspective. After 10 years, as many as 6% of leukoplakias can become malignant [4], while after 20 years the risk can increase to as many as 42.2% [10].

The reported incidence of leukoplakias ranges from 1.1-2.4 per 1000 inhabitants per year in males and 0.2-1.3 in females. Prevalence ranges from 0.2-4.9%. Leukoplakias tend to develop more after the age of 30 years, with the highest proportion after 50 years of age. [5]. The occurrence of leukoplakias, however, is not exceptional in younger individuals, either.

The etiological factors of leukoplakia development are well known. Smoking and alcohol are the most influential ones [2,5]. In Northern America and Europe, smoking of tobacco prevails, while in Asia tobacco chewing plays the most important role. The decisive influence in the most important etiological factor, i.e. smoking, is the number of cigarettes smoked per day (at least 5 cigarettes per day) and the time aspect, i.e. how long (how many years) the patient has been smoking. In the case of alcohol, as another potentiating factor, the time aspect of noxa effects is also important, with more potent influence being attributed to spirits rather than beer. Candida albicans and its role has been constantly mentioned, but it is considered to be a potentiating rather than etiological factor. The role of vitamins A, B12, C, beta-carotene, and folic acid is being investigated by some studies and their exact effects are still subject of discussion. Dietary sources of vitamins C, E, A and carotenoids significantly reduce the risk of oral premalignant lesions. High doses of vitamin C are associated with the reduction of risk of development of a premalignant lesion. High doses of vitamin E and vitamin A are associated with the growing risk of premalignant lesion development. Smoking, higher doses of vitamins A and E increase this risk even more [11].

With a view to the malignant potential, primary prevention is important in leukoplakias, i.e. the timely diagnostics of new leukoplakia lesions on the mucosa of the buccal cavity. Annual preventive examination with a dentist should come first (although oncological orientation examination of the mouth by the general practitioner or otolaryngologist should not be neglected, either), i.e. in addition to targeted examination of the teeth always pay proper attention to potential signs of mucosal conditions. A number of diagnostic examination methods based upon various principles (electrical resistance, ultrasound, chemical surface reaction) may aid the diagnostics; the authors found auto-fluorescence with direct visualisation useful for its simplicity in screening. The system avails of different tissue auto-fluorescence, when fluorophores after excitation with light of adequate wavelength (blue light) emit light with longer wavelength (green light), which helps to detect changes in cellular, structural or metabolic activity [12]. Although the method is not sufficiently accurate and specific for final diagnostics, it may be used to simplify screening.

If a pathological lesion is present on the buccal cavity mucosa, which fails to heal within 2-4 weeks of observance, it is essential to perform a histological verification of the concerned lesion. Leukoplakias are conditioned by keratosis, hyperkeratosis, para- or hyperparakeratosis, hyperorthokeratosis [13,14]. The histopathological aspects of leukoplakias may differ from atrophic form to the hyperplastic one. Epithelial dysplasias may be of mild, moderate and severe degree [5]. Dysplasia means any epithelial differentiation disorder exhibiting at least 2 of the following signs: irregular epithelial layering, depot layer hyperplasia, droplet-like mucosal nests, mitosis multiplication (with low number of abnormal mitoses), changes in basal cell polarity, change in nucleus-plasma

ratio, nuclear polymorphia, nuclear hyperchromia, presence of larger nucleons, mono-cellular keratinisation [14].

Although most leukoplakias are asymptomatic, the objective of primary therapy is the prevention of potential malignant transformation. In the treatment of leukoplakias, the modification and elimination of the causative factors, chemo-prevention, (vitamins C, A, and E) with retinoids and carotenoids, surgical excision, laser therapy, cryotherapy, photodynamic therapy, the application of bleomycin or 5-fluorouracil are important [15].

In the case of surgical leukoplakia treatment methods, recurrence ranges from 20- 35% [5,15,16]. Surgical intervention may be used for all types of leukoplakias, the biggest advantage being the possibility to send a completely preserved sample for histopathological verification. In the case of extensive lesions, however, a defect with frequent scarring and aesthetic and functional complications which is difficult to heal often develops. In such a case it is useful to apply laser therapy. Laser intervention allows not only for the prevention of recurrences and potential malignant transformation, but also reduces post-operative dysfunctions [17]. Post-laser therapy recurrences are reported as ranging from 7.7-38.1% and malignant transformations as ranging from 2.6-9% [18]. The most often used lasers for leukoplakia therapy to date have been: the CO2 laser, Nd:YAG laser, and KTP laser [5,7,18-20].

The benefits of laser therapy include the haemostatic effect (improves the clarity of the operative field), short duration of therapeutic intervention, minimum traumatisation of adjacent tissues (reduction of acute inflammatory reaction and post-operative pain). The healing of the wound is, when a laser with optimal coagulation/ablation ratio is selected, in most cases excellent, with minimum buccal cavity dysfunctions, with limited contraction of the site. The procedure is associated with minor swelling and restriction of the usual quality of life. The disadvantage of the laser intervention is partial thermic destruction of the removed lesion, which restricts the histopathological assessment, and delayed epithelial regeneration directly in the wound compared to surgical excision with suture. The use of the laser requires observance of special rules governing the safety of work (such as the necessity to use goggles) [7,18,19]. Until recently, the key restriction for the dissemination of the method was the price of the laser. Modern apparatuses based upon any option of the diode laser are, however, compact, of small dimensions, and affordable in terms of their price. Due to other applications they have become part of many a dental surgeon's office. The issue of their importance in the treatment of leukoplakias still remains to be answered. The purpose of this work is to establish the efficacy of this therapy in various parts of the buccal cavity.

2. Methods

The prospective, monocentric study was conducted in the Centre of Photonic Medicine of the General University Hospital in Prague (Czech Republic) in 2005-2009. In total, 76 patients were observed, of which 36 were males and 40 females. These included subsequently presenting patients without any exclusion. The average age was 52.66 years in male patients and 55.85 years in female patients. 70 patients in total were treated with diode laser of the wavelength of 980nm (CeraLas D25, CeramOptec, Bonn, Germany), 4 patients opted for traditional surgical excision, and for 2 patients only regular dispensarization with autofluorescence (VELscope, LED Dental, Burnaby, Canada) was selected with a view to the scope and type of lesions. The procedures were conducted by a doctor with several years of experience with this type of procedure in order to avoid complications caused by inadequate knowledge of methodology.

The leukoplakia locations proper were monitored. The impact of leukoplakia location upon the post-laser intervention healing proper and upon recurrences was assessed. Last but not least the risk of malignant transformation of leukoplakias into carcinomas was monitored. Much emphasis was also placed upon the subjective perception of diode laser therapy by the patients themselves. The results of the therapy were assessed by an evaluator independent of the surgeon who had performed the procedure.

The total number of patients who completed the diode laser therapy, and hence were included in this study was 70 (34 males and 36 females). The average age was 59 years; 55.76 in males (range 26-89), 62.06 in females (range 42-78). The total number of monitored affections was 76; a single leukoplakia lesion in 56 patients and 2 affections in 10 patients. Multiple occurrence was observed in 4 patients, and for this reason they were excluded from the study (the total patient set included in the study was hence 66 patients), as multiple lesions were reasonably expected to react differently and their number was insufficient for statistical validation. The histopathological verification was available for all patients and all lesions.

The representation of leukoplakias by location is presented in Table 1. The highest number of leukoplakias was located on the tongue (14 lesions), followed by the lower buccal cavity and cheek (12 lesions), the alveolar process (10 lesions), the retromolar area, the

Table 1. Localisation of lesions; (M: male; F: female)

Location	Number	M:F	%
Tongue	14	6:8	18.4%
Lower buccal cavity	12	12:0	15.8%
Vestibule of mouth	4	2:2	5.3%
Retromolar area	8	6:2	10.5%
Cheek	12	0:12	15.8%
Upper or lower lip	8	6:2	10.5%
Palate	8	6:2	10.5%
Alveolar process	10	6:4	13.2%
X- multilocular	———	2:2	———

upper or lower lip and the palate (8 lesions), and the vestibule of mouth (4 lesions).

Of the 76 lesions, 44 were homogenous leukoplakias (58%) and 32 non-homogeneous leukoplakias (42%) (Table 2,3).

The patient set was divided by location into two groups, Group A and Group B. Group A included leukoplakias located on the tongue or lower buccal cavity. Group B included leukoplakias which were located elsewhere than those in Group A, i.e. the vestibule of mouth, retromolar area, cheek, upper or lower lip, palate and the alveolar process. The purpose of this division was to compare the clinical aspects of leukoplakias located on the tongue and in the lower buccal cavity – Group A (i.e. the higher-risk area in respect of leukoplakia development), versus other locations included in Group B.

The therapeutic protocol was identical for both groups. All patients were treated by outpatient therapy under local anaesthesia. The treatment procedure started with the application of the local anaesthetic agent, i.e. 4% Supracaine (Zentiva, Prague, Czech Republic), or 3% Mepivastesin (3M Espe, Seefeld, Germany). As the application instrumentation, an injection syringe with a 29G thin needle was used in order to ensure maximum comfort for the patients, minimum pain and minimum bleeding. The therapy proper was performed using the aforementioned diode laser (Figure 4) with 4-8W output, depending on the location. It was possible to apply a higher output for laser vaporisation on the tongue or cheek; lower output was applied when treating e.g. the soft palate or the alveolar process, where the mucosa was extremely thin and the risk of exposing the palate or alveolar bone high (the casuistry below

Figure 1. Before ablation

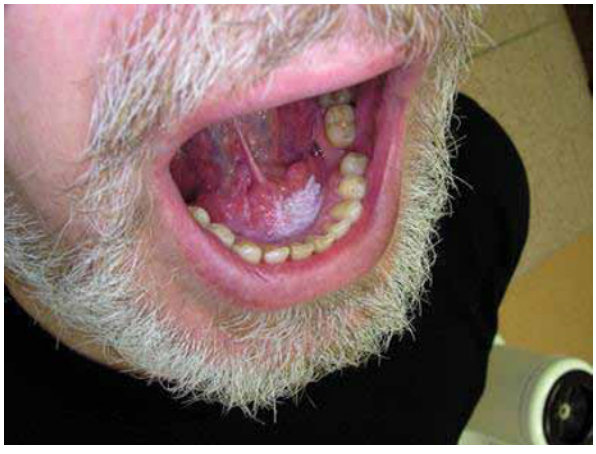


Figure 2. 4 weeks after ablation

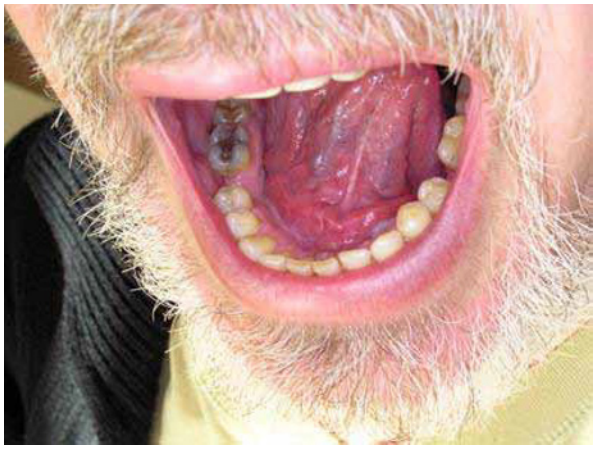


Figure 3. Before ablation

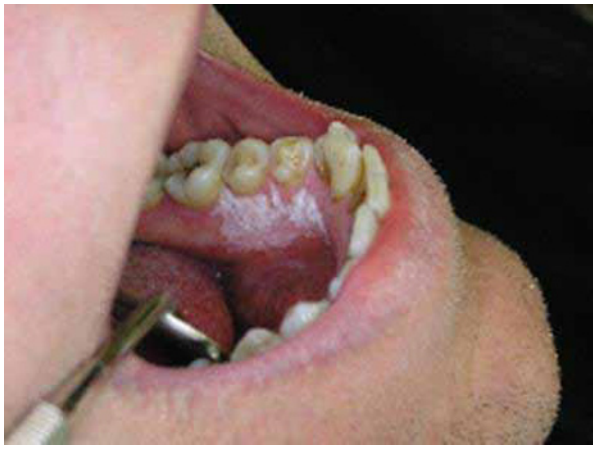
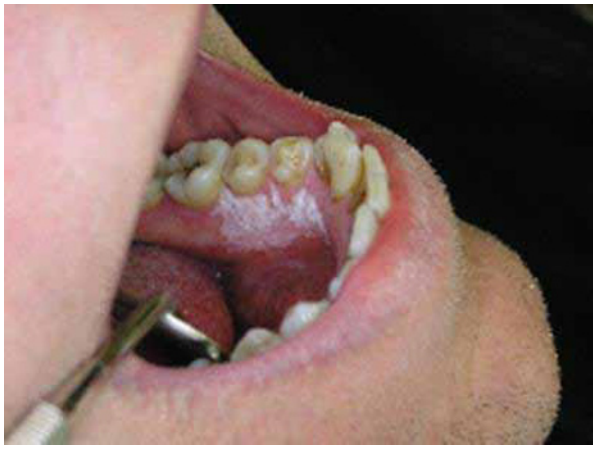


Figure 4. After visit 1



refers). The lateral margins of the selected therapy ranged from 3-5mm from the clear margin of the lesion, the depth of laser vaporisation was approximate only. The advantage of the laser vaporisation was minimal or no bleeding, which made the operative field very clear. No subsequent treatment of the wound after the laser vaporisation was necessary. In some cases, the gentian violet was applied to the wound to facilitate healing and to provide disinfection. No patient needed any analgesics immediately after the procedure. In two medically compromised patients, antibiotics as a screen were administered. These were patients who had had a heart surgery and were treated with anticoagulants. The advantage was no necessity to ensure the haematological preparation of the patient prior to the procedure proper.

It was not necessary to maintain any special treatment regimen after the patients were treated with the diode laser. Emphasis was placed only on waiting for the effects of the anaesthetic agent to subside before eating or drinking in order to avoid patient traumatisation during mastication. Patients were also recommended to use analgesics as necessary or apply ice should a bigger oedema develop.

All lesions were histopathologically verified prior to the start of the therapy. Follow-ups were conducted 1 month after laser vaporisation, and thereafter 3, 6, 9, 12 months and 2 years after therapy. In the course of the study, much emphasis was placed upon the subjective evaluation of the treatment and subsequent healing by the patient himself/herself. For this purpose a 1 to 5 scale was used, where 1 meant the best and 5 meant the worst tolerability after diode laser vaporisation. Biopsies were performed only in patients with recurrences at the time of follow-up or those where the healing process was non-standard. Much emphasis was placed upon the detection of potential malignant transformation of the leukoplakia. The final histopathological examination was conducted after two years. The results were analysed by Fisher statistical test.

Table 2. Homogenious versus non-homogenious leukoplakias

Location	Homogeneous leukoplakias	Non-homogeneous leukoplakias
Tongue	6	8
Lower buccal cavity	4	8
Vestibule of mouth	4	0
Retromolar area	6	2
Cheek	6	6
Upper or lower lip	6	2
Palate	4	4
Alveolar process	8	2

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3. Results

The study included 66 patients in total, enrolled in the study in compliance with the above-mentioned criteria; 76 leukoplakia lesions in total were treated. The treatment method was laser vaporisation by diode laser (4-8W output). All leukoplakia lesions were histologically verified.

3.1. Objective evaluation

Of the total number of 76 lesions, 44 corresponded to homogeneous leukoplakias and 36 to non-homogeneous leukoplakias. Group A included 26 lesions (34.2% of the total number of lesions), Group B included 50 lesions (65.8% of the total number of lesions). The evaluation was conducted on two various levels of observations. The objective of the first one was to establish solely the actual number of recurrences after the primary therapy of the leukoplakia lesion, and hence also the success rate of the primary therapy proper.

Follow-up at 1 month after the diode laser primary therapy evidenced recurrence in 4 patients in total (6.1% of the overall patient set; 5.3% of the total number of lesions). In Group A, recurrence was seen in 1 patient (1.5% of the overall patient set; 1.3% of the total number of lesions), and it was located in the lower buccal cavity. In Group B, recurrence was seen in 3 patients (4.6% of the overall patient set; 3.9% of the total number of lesions), with one lesion located on the alveolar process, one on the palate and one in the retromolar area.

Follow-up at 3 months evidenced recurrence after primary therapy in 1 patient from Group B (1.5% of the overall patient set; 1.3% of the total number of lesions). It concerned recurrence on the cheek. In Group A, no recurrence was seen at 3 months.

Follow-up at 6 months evidenced recurrence after primary therapy in 3 patients in total (4.6% of the overall

Table 3. The numbers and percentages of lesions in both groups; (M: male; F: female)

	Nr	%	M:F	Homogeneous leukoplakias	Non-homogeneous leukoplakias
Group A	26	34.2%	18:8	10	16
Group B	50	65.8%	26:24	34	16

patient set; 3.9% of the total number of lesions). In Group A, recurrence was seen in 3 patients (4.6% of the overall patient set; 3.9% of the total number of lesions). In two cases, the recurrence was located on the tongue, in one case in the lower buccal cavity. No new recurrence was observed in Group B during the follow-up at 6 months after the diode laser primary therapy.

At the time of follow-up 9 months after the primary therapy, no new recurrence after the diode laser primary therapy was seen. The same result, i.e. no new recurrence, was also seen at the time of follow-up 12 months after the primary therapy.

At 24 months after the primary therapy, one recurrence in Group A was seen (1.5% of the overall patient set; 1.3% of the total number of lesions), which was located on the tongue.

In the second follow-up, diode laser therapy was repeated immediately upon the detection of any recurrence. The dates of follow-ups were maintained as those determined after primary therapy of leukoplakias. In this respect, the overall incidence of all recurrences as of the concerned follow-up date was monitored, i.e. not only the incidence of primary recurrence, but all recurrences (i.e. including recurring recurrences). This monitoring then served as the basis for drawing several important conclusions. It primarily showed the incidence of all recurrences, as well as the success rate of their subsequent diode laser therapy, and, last but not least, the influence of recurring recurrences upon potential malignant transformation of leukoplakias.

Follow-up at 1 month after the diode laser therapy evidenced recurrence in 4 patients in total (6.1% of the overall patient set; 5.3% of the total number of lesions). In Group A, recurrence occurred in 1 patient (1.5% of the overall patient set; 1.3% of the total number of lesions), and it was located in the lower buccal cavity. In Group B, recurrence was seen in 3 patients (4.6% of the overall patient set; 3.9% of the total number of lesions), one of them located on the alveolar process, one on the palate and one in the retromolar area.

Follow-up at 3 months evidenced recurrence in 2 patients (3% of the overall patient set; 2.6% of the total number of lesions). In Group A no recurrence was evidenced. In Group B, recurrence was seen in 2 patients (3% of the overall patient set; 2.6% of the total number of lesions), and it was located on the palate and on the cheek.

Follow-up at 6 months evidenced recurrence in 5 patients in total (7.6% of the overall patient set; 6.6% of the total number of lesions). In Group A, recurrence was seen in 4 patients (6.1% of the overall patient set; 5.3% of the total number of lesions); 2 of the recurrences were located in the lower buccal cavity and 2 on the tongue. In Group B, 1 recurrence was seen (1.5% of the overall patient set; 1.3% of the total number of lesions) located on the palate.

At the follow-up 9 months after the therapy, recurrence was detected in 3 patients (4.6% of the overall patient set; 3.9% of the total number of lesions). In Group A, recurrence was seen in 2 patients (3% of the overall patient set; 2.6% of the total number of lesions) and in both cases it affected the tongue. In Group B, 1 recurrence was detected (1.5% of the total number of patients; 1.3% of the total number of lesions), located on the cheek.

1 year after the diode laser therapy, recurrence was seen in 2 patients in total; in both cases it was in Group A (3% of the overall patient set; 2.6% of the total number of lesions), with lesions located on the tongue. Follow-up at 2 years evidenced recurrence in 4 patients in total, again only in Group A (6.1% of the overall patient set; 5.3% of the total number of lesions). In these cases, the recurrences were also located on the tongue (3) and in the lower buccal cavity (1). In Group B no recurrence was hence evidenced at follow-ups 1 year and 2 years after therapy.

The follow-up hence implies that some lesions recurred several times. Repeated recurrences were detected for 2 lesions on the tongue, 2 lesions in the lower buccal cavity, one lesion on the cheek and one lesion on the palate. This observation gained an interesting finding that the very primary diode laser therapy of buccal cavity leukoplakias was successful in 57 patients (86.4% of the total patient set) and in 67 lesions (88.2% of the total number of lesions).

Malignant transformation was seen only in Group A, in 2 patients (3% of the total patient set). In terms of location, the malignant transformation always appeared only on the tongue (2.6% of the total number of lesions). This malignant transformation was noted in repeatedly recurring leukoplakia lesions. In terms of gender, malignant transformation was equal, i.e. the M:F ratio was 1:1. The monitoring of recurrences and malignant transformation is detailed in Tables 4 and 5.

The overall therapeutic effect of diode laser application in the treatment of oral leukoplakias is provided in Table 6 (by the number of patients) and Table 7 (by the number of lesions). For the purposes of clinical application, a detailed comparison of the therapeutic effect of the diode laser in the treatment of leukoplakias in Group A and in Group B at the time of various follow-ups was more relevant (the comparison was based on the number of lesions, not the number of patients in individual groups), (Table 8 (Group A) and Table 9 (Group B) refer).

Table 4. Recurrences in the total patient set; (M: male; F: female)

Time of follow-up after diode laser therapy	Recurrences in the total patient set		Group A		Group B		M:F ratio
	Number	%	Number	%	Number	%	
1 month	4	6.1%	1	1.5%	3	4.6%	3:1
3 months	2	3.0%	———	———	2	3.0%	2:0
6 months	5	7.6%	4	6.1%	1	1.5%	3.2
9 months	3	4.6%	2	3.0%	1	1.5%	1:2
12 months	2	3.0%	2	3.0%	———	———	0:2
24 months	4	6.1%	4	6.1%	———	———	2:2

Table 5. Malignisation in the total patient set; (M: male; F: female)

	Of the total patient set		Group A		Group B		M:F ratio
	Number	%	Number	%	Number	%	
Malignisation	2	3.0%	2	3.0%	———	———	1:1

Table 6. Therapeutic effect of diode laser application in leukoplakias by patient number

Post-therapeutic follow-up time	Number of patients	Number of patients with recurrence	Number of cured patients	Number of patients with leukoplakia malignisation	Therapeutic effect
6 months	66	5	61	——	92.4%
12 months	66	2	64	——	97%
24 months	66	4	62	2	94%

Table 7. Therapeutic effect of diode laser application in leukoplakias by lesion number

Post-therapeutic follow-up time	Number of lesions	Number of lesions with recurrence	Number of cured lesions	Number of lesions with leukoplakia malignisation	Therapeutic effect
6 months	76	5	71	——	93.4%
12 months	76	2	74	——	97.4%
24 months	76	4	72	2	94.7%

Table 8. Temporal development of the number of recurrences and malignisation in Group A

Time of follow-up after diode laser therapy	Number of lesions	Number of lesions with recurrence	Number of cured lesions	Number of lesions with leukoplakia malignisation	Therapeutic effect
1 month	26	1	25	——	96.2%
3 months	26	——	26	——	100%
6 months	26	4	22	——	84.6%
9 months	26	2	24	——	92.3%
12 months	26	2	24	——	92.3%
24 months	26	4	22	2	84.6%

Table 9. Temporal development of the number of recurrences and malignisation in Group B

Time of follow-up after diode laser therapy	Number of lesions	Number of lesions with recurrence	Number of cured lesions	Number of lesions with leukoplakia malignisation	Therapeutic effect
1 month	50	3	47	——	94%
3 months	50	2	48	——	96%
6 months	50	1	49	——	98%
9 months	50	1	49	——	98%
12 months	50	———	50	——	100%
24 months	50	———	50	——	100%

Table 10. Subjective evalution of therapy

	Location	Rating of the therapeutic procedure	Rating of healing up to 1 week of therapy	Rating of healing from 1 week to 1 month of therapy
Group A	Tongue	1.86	2.57	1.7
	Lower buccal cavity	1.5	1.85	1.5
Group B	Vestibule of mouth	1.5	1	1
	Retromolar area	1.25	1	1
	Cheek	1.33	1.16	1
	Upper or lower lip	1.5	1.25	1
	Palate	1	1.5	1.25
	Alveolar process	1	1.4	1
X–average score		1.4	1.58	1.24

Note: The follow-ups were determined upon the primary therapy of the leukoplakia lesion. Where a recurrence was established at the follow up, it was subjected to treatment, but the follow-up dates still continued to be related to the primary therapy and not to the recurrence therapy! The recurrence therapy was not taken into account during the subsequent evaluation, either, as the set would be significantly broken down and the final evaluation would not be statistically evaluable.

Tables 8 and 9 clearly show that in Group A recurrences appear later, with higher frequency after 6 months of therapy. In Group B, recurrences occurred earlier than in Group A, most often within 6 months of primary therapy. The resulting therapeutic effect of the treatment of leukoplakias in Group A was apparently lower than that in Group B.

3.2. Subjective evaluation by patients

The patients evaluated the diode laser therapeutic intervention proper, as well as the course of post-therapeutic wound healing. This was monitored in two time intervals, the first covering the period up to 1 week of the therapy, the other the period from 1 week to 1 month of the diode laser therapy. This division was intentional, as potential difficulties in healing were expected to arise most markedly in this particular interval.

In the entire study patient population, the diode laser therapeutic intervention was rated at 1.4, using a 1-5 scale. In Group A, patients rated the therapeutic procedure at 1.68. In Group B, patients rated the therapeutic procedure at 1.26. The diode laser therapeutic procedure rating is illustrated by Chart 2 (a detailed therapy evaluation by leukoplakia location is provided in Table 10). As is apparent from Chart 2, patients in Group A tolerated the therapeutic procedure much worse than those in Group B. With a view to location (Table 10 refers) the worst tolerability of all was reported by patients with leukoplakias on the tongue, while the best tolerability of therapy was reported by patients with leukoplakias on the alveolar process and palate.

Thereafter, the patient's rating of the course of wound healing after the diode laser therapy was monitored. (The rating of wound healing is also illustrated by Chart 2, with detailed evaluation by location being provided in Table 10). In the entire study patient population, wound healing within 1 week of the therapeutic procedure was rated at 1.58, using again the 1-5 scale. In Group A, patients rated wound healing within 1 week of therapy at 2.21. In Group B, patients rated wound healing within 1 week at 1.22. As illustrated by Chart 1, patients in Group A tolerated wound healing much worse. In terms of leukoplakia location, the worst tolerated wound healing was that on the tongue, and the best tolerated was in the retromolar area and the vestibule of mouth. Healing in the period from 1 week to 1 month after diode laser therapy was rated in the entire patient population at 1.24. In Group A, patients rated healing from 1 week to 1 month at 1.6. In Group B, patients rated healing from 1 week to 1 month at 1.04. Even in this period the course of healing has been evaluated much better in Group B than in Group A. With regard to location, healing in the period from 1 week to 1 month of therapy was again reported to be the worst for leukoplakias on the tongue and in the lower buccal cavity.

The worst tolerance was hence seen for both the treatment and the healing proper of leukoplakias on the tongue and in the lower buccal cavity (i.e. Group A), while the best tolerance was seen in the treatment of the palate and alveolar process, and healing progressed the best in the retromolar area and in the vestibule. The worst tolerance of healing was from day 3 to 5 post-therapy, which significantly improved after 1 week. The total time of healing usually did not exceed 4 weeks. Only in 6 patients the healing period was observed to be longer than 4 weeks. This concerned 4 lesions on the tongue and 1 lesion in the lower buccal cavity. The last lesion was located on the lingual area of the alveolar process.

Note: The healing of the leukoplakia wound located here in the lingual area of the alveolar process was complicated by exposing the bone, maintaining, however, the periosteum. The final outcome was excellent,

Chart 1. Temporal efficacy of treatment

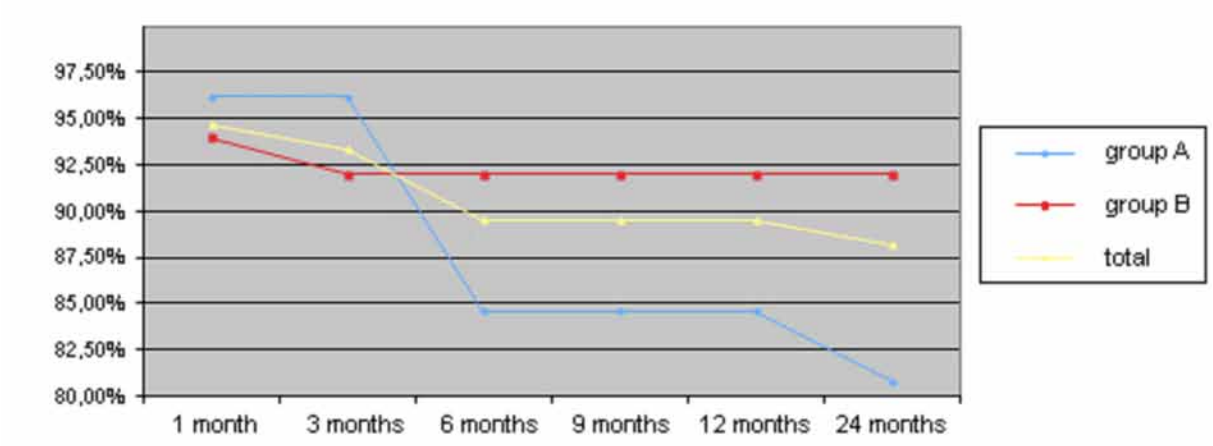
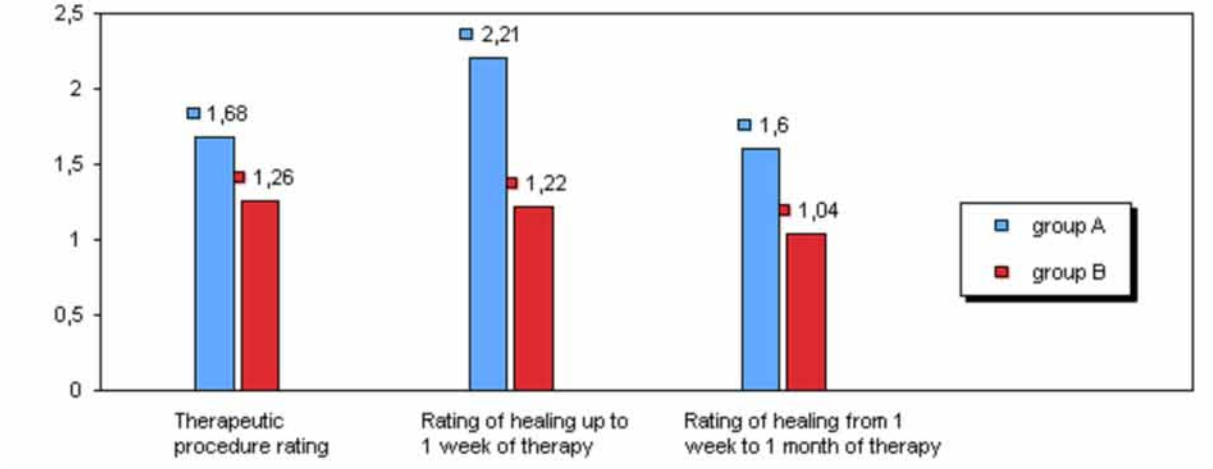


Chart 2. Subjective evaluation by patient.



because the wound healed ad integrum. It was interesting to see that the degree of pain during healing was minimal, or rather nonexistent–casuistries refer). In the course of healing 2 more pronounced oedemas in the sublingual area and the tongue were seen in a leukoplakia located in the lower buccal cavity and on the tongue, respectively.

The swelling of tissues experienced during healing after the diode laser therapy was in most patients minimal (lasting for 1-3 days) or nonexistent, not compromising the health condition of the patient at all. Where a bigger oedema was observed, it appeared after the therapy of lesions included in Group A (i.e. on the tongue or in the lower buccal cavity). In Group B, a minor oedema was observed on the lip and cheek. In the course of this study, 2 more pronounced oedemas of the sublingual area and the tongue were seen during healing, associated with leukoplakias located in the lower buccal cavity and on the tongue, respectively. In these cases, the oedema was the largest from day 3 to 5 after therapy, and subsided within 1 week, or 2 weeks of the diode laser therapy at the most.

The degree of pain after the diode laser therapy was also minimal. In most patients, if any pain was present at all, it was the most pronounced for the first 2-3 days after therapy, and subsided significantly in the following days. Even in this case, the degree of pain was perceived the most in Group A lesions, where pain was experienced from day 1 to 5 after therapy. The degree of pain in lesions included in Group B was the most severe on day 1 post-therapy and on the subsequent days was only minimal or nonexistent.

Only one major complication occurred in the course of the diode laser therapeutic procedure proper – it involved a collapse experienced by a patient with a leukoplakia in the retromolar area.

4. Casuistries

The figures illustrate leukoplakia in the lower buccal cavity before therapy (Figure 1) and after therapy (Figure 2).

The following four figures illustrate leukoplakia located on the lingual area of the alveolar process on the left (Figure 3). The treatment was divided into two visits. At visit one, the distal part of the lesion (Figure 4) was treated and subsequently, the proximal part of the lesion (Figure 5) was treated. In both cases the alveolar bone was exposed, but without compromising the periosteum. The final effect after the diode laser therapy is illustrated by Figure 6.

5. Discussion

1. The risk of malignant transformation is statistically significantly higher in leukoplakias on the tongue and in the lower buccal cavity, even after laser ablation, which is consistent with other findings regarding higher degree of risk in this location. [21]
2. Patients tolerate the procedures very well. Due to a number of different variables, the results of this study cannot be compared directly to those of another one. The authors´ own experience, however, suggests that laser therapy should be preferred. Due to recurrences following both procedures, a number of patients tried both the conventional procedure and the laser application, with laser application being preferred in the study site in approx. 90%.
3. The clearing rate (CR) proper cannot be exactly compared to other studies and it cannot be accurately predicted in general use. As any surgical technique, this method is also sensitive in terms of the experienced and exact working procedure employed by the concerned doctor. Some errors may be caused by the method, others by a mistake of the attending doctor (excision depth, excision width). Yet it may be concluded that the method is at least comparable to the conventional surgical procedure.
4. In this study, a diode laser with the wavelength of 980nm was used. This was for several reasons. This wavelength offers a relatively optimal combination of coagulation (providing haemostasis) and ablation (ensuring a gentle removal). Still, there is a number of other wavelengths providing the same, e.g. that of 1470nm. The selection of optimal wavelength should be the topic of other studies. Purely ablative lasers (CO2, Er:YAG) were intentionally left out, as these very often did not allow for sufficient depth of the operation due to the risk of bleeding. Some of these lasers, moreover, do not use fibre, which is very practical in the small space of the buccal cavity with difficult access. The CO2 and Er:YAG lasers, on the contrary, very often have an articulated arm which allows for lower precision of work, while more aggressive lasers, such as the Nd:YAG 1064nm, induce excessive coagulation, which causes longer healing.
5. The selection of laser parameters is an issue of its own. The authors use a continuous laser as it is much more practical. Pulse application would be longer, albeit with smaller thermal damage. The selection of the laser output is also given by the doctor's personal preference and the degree of risk of bleeding at the concerned location. The exact parameters hence have to be selected by the doctor himself/herself when becoming familiar with the procedure.
6. The risk of malignant transformation at two years is, in this study, lower than the aforementioned results of other studies. Nevertheless, this does not automatically imply that laser reduces this risk. This study worked with a relatively small patient sample for objective comparison, and, most importantly, it cannot be ruled out that laser ablation will only delay malignant transformation.

Figure 5. After visit 2

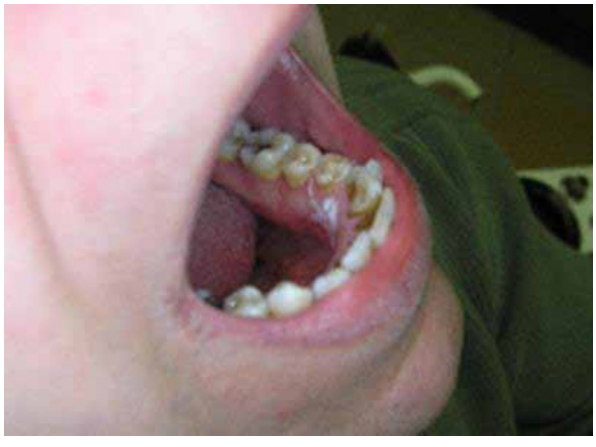
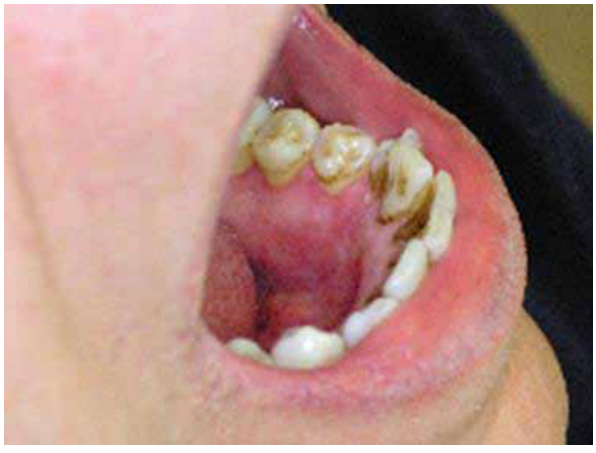


Figure 6. Final result



A better answer to this should be provided by a longer study currently conducted by the authors.

6. Conclusion

Removal of leukoplakias by diode laser is a surgical procedure well tolerated by the patient and providing significant CR even after two years. Laser ablation, however, is not an absolute prevention of malignisation of leukoplakias on the tongue and in the lower buccal cavity (the same probably applies to other parts of the buccal cavity). For this reason patient dispensarization with histopathological follow-up in the case of suspected transformation after this procedure is still necessary. The risk of malignisation, recurrences as well as worse tolerability by patients is on the tongue and in the lower buccal cavity compared to the rest of the buccal cavity.

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