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Research Article

Treatment of Type II Denture Stomatitis with Clotrimazole Mouth Paint and Photodynamic Therapy - A Comparative Study

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Abstract

Introduction: Recurrence rate is high in denture stomatitis patients taking antifungal treatment. Photodynamic therapy appears to be effective method for *Candida* spp. Inactivation *in vivo* and *in vitro*

Aim of the Study: The aim of the present study was to compare the efficacy of antifungal agent and photodynamic therapy for the treatment of type II denture stomatitis.

Materials and Methods: Forty clinically diagnosed patients of type II denture stomatitis were enrolled in the study. Patients were randomly divided into groups (Clotrimazole and PDT), each with 20 patients. Clotrimazole group were asked to apply mouth paint four times a day for 30 days. For PDT group, one session of methylene blue followed four sessions of low level laser therapy were carried out twice a week.

Results: Complete response was seen in 40% of the patients in PDT group whereas only 10% of patients showed complete response in clotrimazole group.

Conclusion: Methylene blue mediated photodynamic therapy provides better results than clotrimazole mouth paint for the treatment of type II denture stomatitis.

Keywords: *Clotrimazole; Denture Stomatitis; Photodynamic Therapy*

Abbreviations

DS: Denture Stomatitis; PDT: Photodynamic Therapy

Introduction

The oral condition called denture stomatitis, indicates an inflammatory response of the denture bearing mucosa. The other terms used for this condition are denture sore mouth, denture induced stomatitis, inflammatory papillary hyperplasia and chronic atrophic candidiasis. It is commonly seen in patients wearing complete or partial dentures. Most commonly it affects the palatal and gingival mucosa, which is in direct contact with denture base [1].

In 1962 newton suggested a classification for denture stomatitis, exclusively based on clinical criteria [1,2]:

1. **Type I:** A localised simple inflammation or pinpoint hyperemia.
2. **Type II**: An erythematous or generalised simple type seen as more diffuse erythema involving a part or the entire denture covered mucosa.
3. **Type III:** A granular type (inflammatory papillary hyperplasia) commonly involving the central part of the hard palate and alveolar ridges.

The known contributory factors for denture stomatitis are trauma due to ill-fitting dentures, rough denture surface, poor oral hygiene and night time wearing of dentures, all these superimposed by *Candida* infection [3]. *Candida albicans,* among other species of fungi colonizing dentures, has been proven to be one of the important factor contributing to DS [4]. Although *C. albicans* is the most prevalent and virulent species of the genus *Candida*, other non-*C. albicans* species are frequently isolated from acrylic denture base and the palatal mucosa, such as: *C. glabrata, C. tropicalis, C. parapsilosis, C. pseudotropicalis, C. krusei* and *C. guilliermondii* [5]. The emergence of other *Candida* species is important because they may exhibit higher denture surface adherence and species such as *C. glabrata, C. krusei* and *C. lusitaniae* show inherent resistance or intrinsic reduced susceptibility to antifungal agents [5,6]. It was shown that most *Candida* species are susceptible to topical antifungal drugs like Nystatin, Miconazole and Clotrimazole, being recommended as the first choice of treatment [7]. But the diluent effect of saliva and the cleansing action of the oral musculature tend to reduce the concentration of these agents to sub-therapeutic levels. That leads to prolonged treatment regimens and high recurrence rate [6]. So, the development of alternative therapies for the treatment of DS have been required. Photodynamic Therapy (PDT) has been suggested as a promising therapy for DS [8]. Since the reactive oxygen species produced in photodynamic procedure has potential to cause cell damage to both fungal and bacterial cells [5].

Aim of the Study

The aim of the present study was to compare the efficacy of methylene blue mediated photodynamic therapy and clotrimazole mouth paint for the treatment of type II denture stomatitis.

Objectives of the Study

To evaluate the efficacy of PDT and antifungal therapy (clotrimazole mouth paint) on denture stomatitis in terms of reduction in size of a lesion.

Materials and Methods

The study was conducted in the department of Oral medicine and radiology, for a period of 11 months.

Study design

This was a two group, randomized clinical trial comparing the effectiveness of PDT and clotrimazole mouth paint in the treatment of patients with DS. The ethical consent for the study was taken from ethical committee of the institution. All the participants voluntarily participated and signed the informed consent before their enrolment.

Participants and randomization

Inclusion criteria for the study was, clinically diagnosed cases of type II denture stomatitis. Exclusion criteria for the study was, patients having history of treatment of denture stomatitis in last 3 months and Patients suffering from any systemic diseases. Total 40 patients were enrolled in the study. Randomization was carried out using chit system. Chits were made for 2 groups and kept in a box. Patients were asked to pick 1 chit and accordingly treatment was given to the patient. Here, the patients were blinded to the treatment options.

Photosensitizer and light sources

Photosensitizer used in the study was methylene blue (aqueous stain solution) (Figure 1).

Figure 1: Photosensitizer.

Laser used in the study was Biolase diode laser with 940 nm wavelength (Figure 2).

Interventions

Group A and group B: Group A patients received clotrimazole mouth paint and Group B received methylene blue mediated photodynamic therapy, as treatment for denture stomatitis. Prior to the beginning of treatment, all patients were requested to submit their dentures in the department and for both the groups measurements of the lesion were taken on day 1 [using a divider and a metal scale

Figure 2a and 2b: Diode laser (Biolase diode laser with 940 nm wavelength).

(Figure 3)] and on every follow up visit. Lastly measurements were contrasted with check for any reduction in the size of the lesion for all 40 patients. Group A patients were asked to apply clotrimazole mouth paint thrice daily and were called for follow up on 15th day. Patients were asked to continue with the mouth paint if the lesion still persist and were called for follow up on 30th day. For group B patients, PDT treatment was performed using methylene blue dye as photosensitizer agent and diode laser of 940 nm, 200 mW, in non contact mode on 1st, 4th, 8th and 12th day and patients were called for follow up on 15th day and 30th day. After the application of methylene blue dye with a cotton swab, followed by 4 sessions of laser application (Figure 4). Each session lasted for 30 seconds with a gap of 10 seconds in between covering the whole area of the lesion. After the final application, the patients we asked to gargle and then the area was cleaned using a dry cotton swab to remove the leftover dye.

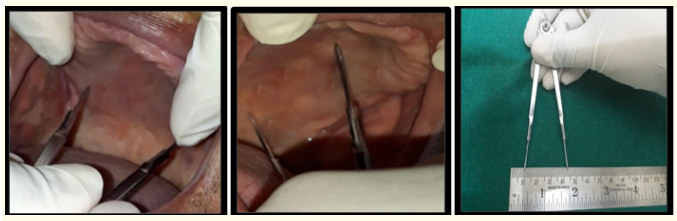


Figure 3: Measurement of lesion.

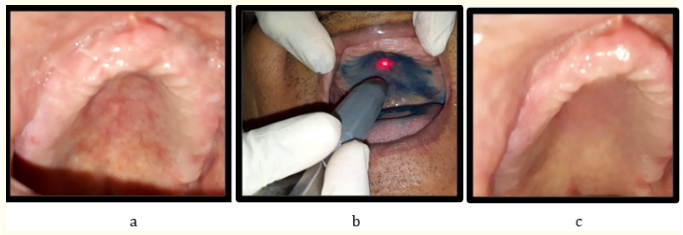


Figure 4: a) Before treatment b) Laser application c) After treatment.

Statistical analysis

Gathered data is tabulated and subjected to appropriate statistical analysis.

To find if there is any significance difference in the mean size of lesion as there were 2 treatment groups, paired 't' test is applied at 95%confidence level. The observed value F stastic 1.144 was found non-significant at 38 degrees of freedom with p value 0.2772.

Further to find, reduction in the size of lesion from baseline to follow up 1 and to follow up 2 i.e. intra group comparison, one way ANOVA is applied at 95% confidence level and at (2,57) degrees of freedom for both the groups (Group A and Group B).

Further to find, reduction in the size of lesion for group A and group B at follow up 1 i.e. inter group comparison, unpaired 't' test is applied at 95% confidence level and 38 degrees of freedom.

Further to find, reduction in the size of lesion for group A and group B at follow up 2 i.e. inter group comparison, unpaired 't' test is applied at 95% confidence level and 38 degrees of freedom.

Results

Table 1 shows the comparison of baseline mean size of the lesion between group A and group B. there is no statistical significance difference in the mean size of the lesion between 2 groups. P value of > 0.05 is considered significant.

Group	Mean	SD	SEM	P value
Group A	8.006	0.1164	0.02602	< 0.05
Group B	8.048	0.1245	0.02783	

Table 1: *SD: Standard Deviation; SEM: Standard Error of Mean.*

Table 2 and figure 5 Shows the intra group comparison between baseline, follow up 1 and follow 2 for group A. There is reduction of size of the lesion from baseline to follow up 1 and to follow up 2. P value of < 0.0001 is considered significant.

	Mean	SD	SEM	F value	P value
	8.006	0.1164	0.02602	77.791	< 0.0001
Follow up 1	Baseline	09063	0.2027		
Follow up 2	4.414	1.296	0.2898		

Table 2: *Group A: Clotrimazole group.*

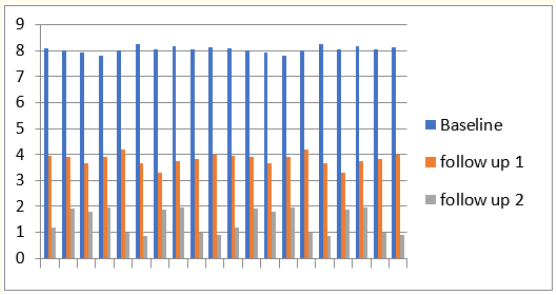


Figure 5: Group A-Intra group comparison (Baseline, follow up 1and follow up 2).

Table 3 and figure 6 shows the intra group comparison between baseline, follow up 1 and follow 2 for group B. In the present study, there is significant reduction of size of the lesion from baseline to follow up 1 and to follow up 2. P value of < 0.0001 is considered significant.

	Mean	SD	SEM	F value	P value
Baseline	8.048	0.1245	0.02783	2189.7	< 0.0001
Follow up 1	3.814	0.2416	0.05402		
Follow up 2	1.439	0.4830	0.1080		

Table 3: *Group B: Photodynamic therapy group.*

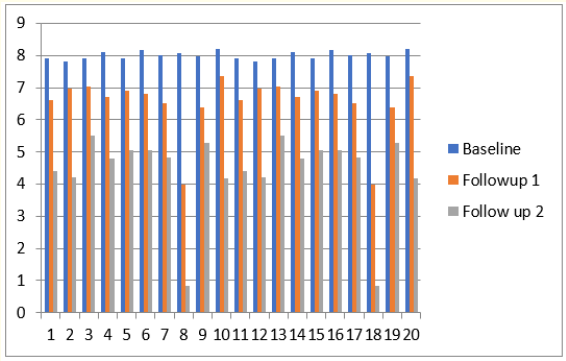


Figure 6: Group B-Intra group comparison (Baseline, follow up 1 and follow up 2).

Table 4 and figure 7 shows intergroup comparison between group A and Group B for follow up 1. There is a significant difference between the 2 at follow up 1. P value < 0.0001 is considered significant.

	Mean	SD	SEM	P value
Group A	6.529	0.9063	0.2027	< 0.0001
Group B	3.814	0.2416	0.05402	

Table 4

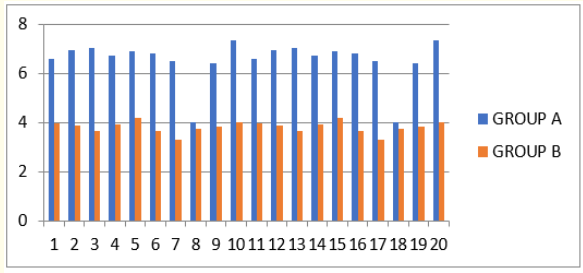


Figure 7: Inter group comparison (follow up 1 of group A and group B).

Table 5 and figure 8 shows intergroup comparison between group A and group B for follow up 2. There is a significant difference between the 2 at follow up 2. P value < 0.0001 is considered significant.

	Mean	SD	SEM	P value
Group A	4.414	1.296	0.2896	< 0.0001
Group B	1.439	0.4830	0.1080	

Table 5

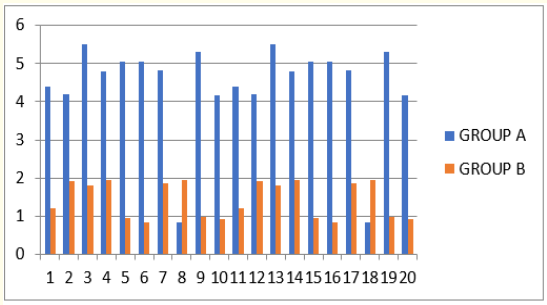
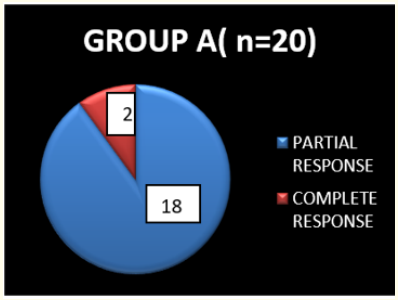


Figure 8: Inter group comparison (follow up 2 of group A and group B).

Table 6 and figure 9 pie chart: Shows the response to treatment for both the groups. In group A 18 patients showed partial response whereas in group B 12 patients showed partial response. Complete response was seen in 8 patients in group B and with 2 patients in group A at the end of the treatment.

Response	Group A (n = 20)	%	Group B (n = 20)	%
Partial response	18	90	12	60
Complete response	2	10	8	40

Table 6



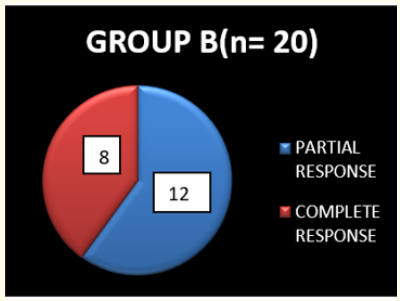


Figure 9

Discussion

Uses of PDT in dentistry are growing rapidly: the treatment of oral cancer, as well as bacterial and fungal infections, and the photodynamic diagnosis (PDD) of the malignant transformation of oral lesions [9]. Photodynamic therapy comprises of 2 components, a non-toxic light- sensitive dye called a photosensitizer (PS) combined with harmless visible light of the appropriate wavelength to match the absorption spectrum of the PS. After photon absorption the PS gets excited and reacts with ambient oxygen, resulting in the formation of reactive oxygen species (ROS). PDT is a highly selective modality as (i) the PS can be targeted to the unwanted cells or tissue (ii) cell death is spatially limited to regions where light of the appropriate wavelength is applied [10,11].

The treatment of DS can be considered difficult and complex due to its multifactorial etiology, common recurrences, lack of antifungal drug efficacy, as well as the development of antifungal resistant by *Candida* species. Therefore, PDT has been suggested as a promising treatment for this infection [8]. This result may be explained by the fact that the interaction of the reactive oxygen species (ROS) generated by PDT with organic molecules is not specific, for this reason, any organelle of the cell can be a potential target of the ROS [12]. Thus, PDT can cause cell damage for both fungal and bacterial cells. Although *Candida* species are considered important pathogens in the occurrence of DS, bacteria may contribute to the colonization and proliferation of *Candida* strains in the oral cavity [13]. On the oral microbiota, fungal and bacterial species are living in harmony with each other and forming a polymicrobial biofilm.

For this reason, the ability of PDT to kill both fungal and bacterial species is another advantage over conventional drugs for the management of DS.

The dilution effect of saliva and cleansing action of the tongue and oral musculature may decrease the concentration of topical drugs, such as clotrimazole mouth paint, to sub therapeutic levels, requiring multiple doses, which can lower patient's compliance. Moreover, high recurrence rates after antifungal treatment have been reported [14]. In the case report by Mirelamaver-Biscanin., *et al*. [15], both patients showed partial response to low level laser therapy whereas in our study 40% patients had shown complete response to photodynamic therapy. In the case series by Mima., *et al*. [2], all patients showed DS type II at baseline, similar observations were seen in our study. And the results are also similar to our study i.e. PDT is effective in the treatment of DS. In the study by Maciel., *et al*. [5], all patients showed type II DS at baseline, similar observations were seen in our study. In their study miconazole showed better results than PDT which is contrary to results of the present study. The difference in the results is maybe because of the use of different wavelength of laser [15].

Conclusion

Methylene blue mediated photodynamic therapy provides better results than clotrimazole mouth paint. Further studies with the larger sample size and multicentric trials are required to prove its efficacy in the treatment of denture stomatitis.

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