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Original Research Article

Study on Ozonized Water in the Management of Erosive Oral Lichen Planus

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Abstract

Introduction: "Oral Lichen Planus" (OLP) is a chronic inflammatory dermatosis affecting oral mucosa with an unfamiliar cause that affects about 2% of people. It is commonly seen in middle-age (30-60 years), with a woman to man ratio of 2:1. The most common and usually painless forms are reticular, papular, and plaque-like; they resemble white abnormal lesions of oral mucosa like leukoplakia, making an appearance as silvery hyperkeratotic striae or plaques. Treatment mainly focuses on alleviating symptoms and extending relapse free durations, but the whole elimination of the disease is not possible.

Aims and Objectives: The study intends to evaluate the performance indices and efficacy ratings of ozonized water and conventional chemotherapeutic steroids in the management of erosive oral LP.

Methods: A randomized control study was conducted on patients who presented with Oral Lichen Planus (OLP) diagnosed according to WHO criteria. They were divided into 2 groups. Group A received ozonized water treatment, which consisted of 1-minute oral rinses with a double-distilled water-to-ozone ratio of 2:3, repeated four times, twice weekly for four consecutive weeks, for a total of eight applications. Patients in Group B received a placebo treatment, which consisted of oral rinses with double-distilled water that were the same duration and timing as Group A's treatments. Patients were assessed prior to treatment (T0), two weeks later (T1), at the conclusion of treatment (T2), and then again three months later as a follow-up (T3). OLP clinical course was evaluated by gauging pain intensity, lesions' size, clinical indicators, and therapy effectiveness.

Results: 70 individuals with atrophic-erosive OLP completed the study. Four individuals were omitted from the trial because they missed their T2 sessions and follow-up .Among 70 cases 47were women and 23were men. The patient's average age was 65.89. (range 45-84). Both at T1 and T2, group A experienced considerably less pain ($p = 0.05$). At T0, the majority of the patients reported a VAS score of 2, which decreased to a score of 1 or 0 at T2. At both T1 and T2, the difference in VAS scores between the groups was statistically significant ($p = 0.05$). The rate of Thongprasomsign score improvement was higher in group A, but only at T1 ($p=0.001$) there was a statistically significant difference. At every time point, group A's EI of the therapy was considerably higher (p 0.05).

Conclusion: The study concluded that ozone has marked anti-microbial activity. The study has shown that the group which received ozone therapy had reduced candidiasis infection. It has been shown that ozonized water treatment is efficient in managing erosive lichen planus.

Keywords: oral lichen planus, ozone therapy, ozonized water treatment, candidiasis.

Introduction

Lichen planus denotes a commonly diagnosed infection of the skin disease with unknown etiology. It affects 0.5% to 2.2% of the people globally [1]. “Oral Lichen Planus” (OLP) is achronic inflammatory disease of the oral mucosa with an unfamiliar cause that affects about 2% of people [1]. It affects middle-agedpeople (30-60 years old), with a woman to man ratio of 2:1 [2]. Though exact etiology not known, Lichen Planus postulated to be a T cell mediated autoimmune disorder. Dental amalgam, tobacco, betel nut can trigger oral LP. Apoptosis of basal keratinocytes brought by CD8+ T cells in response to unknown antigen is the pathogenic mechanism. Typically, cutaneous LP manifests as multiple violaceous, itchy flat topped papules most of which are bilaterally and symmetric in nature.

Andresen’s classification of OLP differentiates six clinical manifestations: reticular, papular, plaque-like, and atrophic (erythematous), erosive-ulcerous, and bullous erosive [3]. The most common and usually painless forms are reticular, papular, and plaque-like; they resemble white abnormalitiesincluding leukoplakia, makin g an appearance as silver hyperkeratotic str iae or plaques [4]. On the other hand, erosive and atrophic types are frequently related to distress, pain, as well as hostility to spicy as well as hot food consumptions. Furthermore, erosive long-lasting OLP is linked to risk of malignant change [2].As a result, long-standing monitoring, is essential. Management of “erosive OLP” (eOLP) is difficult because there is no definitive cure. Treatment focuses on alleviating symptoms and extending relapse free durations, but the whole elimination of the disease is not possible[5]. There have been wide range of treatment options available, but none of these completely effective. Among these treatments include topical or systemic corticosteroid, topical retinoids, immunosuppressive agents, and anti-inflammatory protective gels [5]. Systemic and topical corticosteroids are widely employed as first-line treatment, however, they have been connected to negative impacts on long term use, limited treatment outcomes[6].Furthermore, research has shown that using corticosteroids for an extended period of time might lead to adverse symptoms such as gastrointestinal, tachyphylaxis, oral mucosa thinning, systemic absorption, and secondary infections [7, 8].

Ozone is a form of oxygen, which is colorless and is made up of three oxygen atoms. Ozone(O3) treatment is becoming increasingly common in both the healthcare and dental industries due to its potent antimicrobial properties and its anti-inflammatory properties. Furthermore, it possesses analgesic effects, in addition to its ability to boost blood flow and also the immune response [9]. Oral diseases treatment and control, dental protein denaturation, disinfection of dental plaque, teeth bleaching, pain control, TMJ problems, root canal system therapeutic interventions, tissue formation, were some of the dental indications for which ozone treatment was performed. In the past, ozone treatment has developed as a non-pharmaceutical option that may be utilized in the treatment of OLP [10].

Ozone treatment is also not widely employed due to significant worries about the potentially harmful effects[11]. Recent studies have shown that lower O3 levels promote cell defense functions and nuclear expression without inducing cellular injury or changing cell growth [11, 12]. Considering these pharmacological factors

ozone postulated to lessen the symptoms associated with OLP and speed up the recovery of lesions. The process of treatment of water with ozone gas leads to the formation ozonated water which accelerates the wound healing by increasing oxygen supply and increasing the metabolic process by increasing the local temperature.

Advantage and benefits of ozonated water is that, it overcomes the challenges associated with gas oxygen, including gas diffusion, which might result in lung damage. The focus of this study is to evaluate the performance indices and efficacy ratings of ozonized water and conventional chemotherapeutic steroids in the management of eOLP.

Materials and Methods

Study design

A randomized control study was conducted on patients who came to the outpatient department of our hospital from December 2021 to November 2022. The study randomly assigned patients into two groups. Patients in Group A received ozonized water treatment, which consisted of 1-minute oral rinses with a double-distilled water-to-ozone ratio of 2:3, repeated four times, twice weekly for four consecutive weeks, for a total of eight applications. Patients in Group B received a placebo treatment, which consisted of oral rinses with double-distilled water that were the same duration and timing as Group A's treatments. Five minutes before application, water was ozonated at each visit. Every patient got standard topical corticosteroid therapy (betamethasone sodium phosphate 500 mg soluble Tablets, 2 rinses per day for 4 weeks). Patients were assessed prior to treatment (T0), two weeks later (T1), at the conclusion of treatment (T2), and then again three months later as a follow-up (T3). OLP clinical course was evaluated by gauging pain intensity, lesions' size,and therapy effectiveness.

Inclusion and exclusion criteria

Patients who visited the hospital's outpatient department and provided informed consent were included. Inclusion criteria included: (a) OLP histological diagnosis in accordance with traditional WHO criteria (b) A clinical erosive type that meets van der Meij and van der Waal's clinical criteria (c) Symptomatic lesions

Patients who did not provide consent were not included in the study. Oral lichenoid lesions, dysplastic lesions, lesions indicating candidiasis, and individuals who had corticosteroids or another immunosuppressive therapy were excluded from the study.

Statistical analysis

The statistical analysis was carried out using IBM SPSS Statistics, and all data were entered into Microsoft Excel datasheets. Data were given as frequency, percentage, mean, standard deviation, median, and interquartile range after descriptive analysis. The distribution of the data was evaluated using the Kolmogorov-Smirnov test. Non-parametric tests were employed since the data did not have a normal distribution. The Wilcoxon matched paired test was used to assess any differences between groups in terms of pain and clinical scores, and the U-Mann-Whitney test was employed to assess any differences over time. Using the Chi-square or Fisher's exact test, percentages of EI values, improvements, relapses, and candidiasis rates were compared. Assuming alpha 0.05 and beta 0.20 (study power = 80%) and estimating a modest improvement (E.I. 2) at the conclusion of therapy in 90% of cases for the ozone-treated group and in 55% for the control group, the minimal number of patients for the study was calculated to be 50. (at least 25 per group).

Ethical approval

The patients were given a thorough explanation of the study by the authors. The

concerned hospital's ethical committee has accepted the study's methodology.

Results

According to the inclusion criteria, 70 individuals with atrophic-erosive OLP were chosen for the study. Four individuals were omitted from the trial because they missed their T2 sessions. 70cases in total (47women and 23 men) were therefore included. The patient's average age was 65.89. (range 45-84). The buccal mucosa, gums, and dorsum of the tongue were the oral locations affected. Both groups' initial demographic and clinical characteristics were comparable (p>0.05) (table 1).

Table 1: Baseline characteristics of the patient's

	Group A (n=35)	Group B (n=35)	*p-value*	Total (n=70)
Male- Female	11:24	12:23	0.57	23:47
Age (mean/range)	66.09 (48-84)	65.12 (45-82)	0.65	65.89 (45-84)

Table 2 lists the VAS clinical characteristics for evaluating pain. Both at T1 and T2, group A experienced considerably less pain (p = 0.05). At T0, the majority of the patients reported a VAS score of 2, which decreased to a score of 1 or 0 at T2. At both T1 and T2, the difference in VAS scores between the groups was statistically significant (p = 0.05).

Table 2: VAS pain distribution at T0, T1, T2.

	Group A	Group B	*p value*	Total
VAS median (IQR)				
T0	5.9 (2)	5 (5)	0.198	5 (4)
T1	3 (3)	4 (5)	0.019*	4 (3)
T2	0.7 (2)	2 (2)	0.041*	2 (1)
VAS SCORE median (IQR)				
T0	3 (2)	3 (2)	267	3 (2)
T1	1.5 (0)	1.5 (1)	0.012*	1.5 (0)
T2	0.7 (1)	1.5 (1)	0.015*	1.5 (1)
VAS SCORE DISTRIBUTION number of cases (n%)				
T0				
0	0 (0%)	0 (0%)		0 (0%)
1	11 (31.4%)	16 (45.7%)		13 (37.1%)
2	23 (65.7%)	20 (57.1%)		21 (60%)
3	1 (2.8%)	3 (8.6%)		1 (2.8%)
T1				
0	5 (14.2%)	3 (8.6%)		4 (11.4%)
1	31 (88.6%)	21 (60%)		26 (74.3%)
2	0 (0%)	12 (34.3%)		6 (17.1%)
3	0 (0%)	0 (0%)		0 (0%)
T2				
0	18 (51.4%)	9 (25.7%)		13 (37.1%)
1	18 (51.4%)	20 (57.1%)		19 (54.3%)
2	0 (0%)	7 (20%)		3 (8.6%)
3	0 (0%)	0 (0%)		0 (0%)
VAS IMPROVE a number				

of cases (%)				
T1				
Yes	27 (77.1%)	11 (31.4%)		19 (54.3%)
No	8 (22.8%)	24 (68.6%)		16 (45.7%)
T2				
Yes	14 (40%)	10 (28.6%)		12 (34.3%)
No	22 (62.8%)	25 (71.4%)		23 (65.7%)

IQR (interquartile range)

The lesions ranged in size from 2 to 20 mm. Table 3 shows measurements and Thongprasom sign scores. At T1 (p=0.05) and T2, the difference in the size of the lesions between the groups was statistically significant. (Fig. (Fig.2) (Fig.2) 2) At baseline, the majority of patients had Thongprasom scores of 2 and 4, which often improved to grade 1 after treatment (T2). The rate of Thongprasom sign score improvement was higher in group A, but only at T1 (p0.001) there was a statistically significant difference.

Table 3: Lesion size and signs score (Thongprasom score) at T0, T1, T2.

	Group A	**Group B**	***p-value***	**Total**
Lesion diameters mm - median (IQR)				
T0	6 (4)	6 (5)	0.841	6 (5)
T1	5 (5)	5 (4)	0.023*	6 (5)
T2	1.7 (1)	4 (8)	0.002*	3 (2)
Thongprasom score median (IQR)				
T0	4 (2)	3 (2)	0.694	4 (3)
T1	3 (2)	3 (3)	<0.002*	3 (3)
T2	2 (1)	3 (3)	<0.002*	2 (2)
Thongprasom score distribution number of cases (%)				
T0	0 (0%)	0 (0%)		0 (0%)
T1	0 (0%)	0 (0%)		0 (0%)
T2	14 (40%)	12 (34.3%)		13(37.1%)
T3	6 (17.1%)	4 (11.4%)		5 (14.3%)
T4	10 (28.6%)	12 (34.3%)		11 (31.4%)
T5	5 (14.3%)	6 (17.1%)		7 (20%)
T1				
0	0 (0%)	0 (0%)		0 (0%)
1	15 (42.9%)	0 (0%)		8 (22.9%)
2	15 (42.9%)	18 (51.4%)		16 (45.7%)
3	0 (0%)	4 (11.4%)		2 (5.7%)
4	5 (14.3%)	10 (28.6%)		8 (22.8%)
5	0 (0%)	3 (8.6%)		1 (2.8%)
T2				
0	11 (31.4%)	3 (8.6%)		7 (20%)
1	20 (57.1%)	9 (25.7%)		15 (42.8%)
2	4 (11.4%)	16 (45.7%)		10 (28.5%)
3	0 (0%)	4 (11.4%)		2 (5.7%)
4	0 (0%)	4 (11.4%)		2 (5.7%)
5	0 (0%)	0 (0%)		0 (0%)
Thongprasom improve the number of cases (%)				

T1				
Yes	32 (91.4%)	10 (28.6%)		22 (62.8%)
No	1 (2.8%)	25 (71.4%)		13 (37.1%)
T2				
Yes	26 (74.3%)	23 (65.7%)		24 (68.6%)
No	9 (25.7%)	13 (37.1%)		11 (31.4%)

IQR (interquartile range)

Table 4 displays data on the effectiveness index (EI), relapse rates, and candidiasis rates. At the conclusion of the treatment, the majority of patients in both groups displayed a moderate improvement (EI=2). At every time point, group A's EI of the therapy was considerably higher (p 0.05).

Table 4: Efficacy Index (EI), relapse rate, and candidiasis rate distribution

	Group A	**Group B**	***p value***	**Total**
Efficacy index (EI) mean %				
T0-T1	45.26	13.12	< 0.002*	28.56
T1-T2	50.35	29.89	0.023*	39.24
T0-T2	73.12	37.87	<0.002*	55.98
EI score distribution number of cases (%)				
T0-T1				
0	1 (2.8%)	20 (57.1%)		10 (28.6%)
1	0 (0%)	9 (25.7%)		4 (11.4%)
2	34 (97.1%)	7 (20%)		20 (57.1%)
3	0 (0%)	0 (0%)		0 (0%)
4	0 (0%)	0 (0%)		0 (0%)
T1-T2				
0	7 (20%)	11 (31.4%)		9 (25.7%)
1	0 (0%)	7 (20%)		3 (8.6%)
2	20 (57.1%)	16 (45.7%)		18 (51.4%)
3	1 (2.8%)	2 (5.7%)		1 (3.8%)
4	7 (20%)	0 (0%)		3 (8.6%)
T0-T2				
0	0 (0%)	6 (17.1%)		3 (8.6%)
1	0 (0%)	7 (20%)		4 (11.4%)
2	19 (54.3%)	17 (48.6%)		18 (51.4%)
3	9 (25.7%)	6 (17.1%)		7 (20%)
4	7 (20%)	0 (0%)		3 (8.6%)
Relapse (T3) number of cases (%)	12 (34.3%)	14 (40%)	0.456	13 (34.3%)
Candidiasis number of cases (%)	4 (11.4%)	11 (31.4%)	0.076	8 (22.8%)

Efficacy Index (EI) 0: no improvement, 1: mild improvement, 2: moderate improvement, 3: marked improvement, 4: healed.

Discussion

Veneri et al. (2020) conducted and reported on a randomized controlled trial. 51 members are usually divided into one of two treatment groups: the research project (n=26) obtained ozonized treatment, whereas the positive control (n=25) got placebo therapy (i.e. double-distilled water). Four 1-minute oral rinses were given weekly for 4 weeks as part of the therapy strategy. Both groups received

regular external cortisone treatment. The size of the lesions, and discomfort ratings were evaluated previous to treatments, after two weeks of treatments (T1), and at conclusion of the 4-week treatment period (T2). This study evaluated Medication "Efficacy Index"(EI), and recurrence rate. T1 scores acquired: Thongprasom 92.2% against 28.0%; VAS pain 76.9% versus 32.0%; p0.05. The control subjects had a greater incidence of infection (32% versus 11.5%) and poor prognosis (40% versus 34.6%), but these changes were not statically important. Within the limits of this research, ozonized water appears to be an effective additive treatment whenever paired with systemic corticosteroids for the management of eOLP [13].

Furthermore, the use of oxygen (O3) in the therapy of OLP has come to prominence. O3 is a highly powerful antioxidative substance utilized as a disinfectant and germicide in healthcare. Furthermore, it enhances blood flow and possesses anti-inflammatory effects [13-15]. Whenever oxygen and external steroids have been used, a case-controlled study suggested that lesions size, Thongprasom score, and pain were reduced considerably when compared to the control group [13]. Several additional investigations by Mustafa et al. and Bayer et al. [14, 15] confirmed this result. When used in combination with systemic corticosteroids, ozone treated water appears to be a beneficial additional treatment in the treatment of eOLP(10). Several organic medicines, including lycopene, curcumin, and aloe vera, have also been examined in the treatment of OLP, with variable outcomes [16, 17].

Significant medicinal effects of oxygen include immunity regulation, analgesic, and activation of metabolic action, antioxidant, antibacterial, and tissue repair qualities. Furthermore, it increases muscle blood flow to the brain. Although both oxygen and laser treatments increased bone growth in rat hard tissue abnormalities, Kazancioglu et al. observed that oxygen treatment was more beneficial than PBMT [18]. Erdemici et al. [19] shown in an induced study that oxygen has positive benefits on the recovery process of both soft and hard tissues in in addition to improving physiological pathways and reactive processes. In the present study, experts discovered a decrease in the symptoms of atrophic-erosive OLP. Lesion size, Thongprasom score, and discomfort were reduced considerably in the combination treatment with oxygen and external steroids compared to those who were treatment with corticosteroids only.

Furthermore ozone demonstrated significant antibacterial activity. In the present study, infection rate was lower in the group A. It was indeed consistent with the results of Arita et al., who determined that ozonated water might be useful in reducing the counts of oral Candida Albicans on resin denture plates [20] due to its potent antifungal capabilities.

El Meligy et al. (2020) examined and confirmed the success of oleozon gel in the therapy of atrophic/erosive lichen planus. 20 people with severe atrophic/erosive OLP were assigned randomly to either 0.1% triamcinolone acetonide solution or oleozon gel. The discomfort level and cancer necrosis response were measured at the base, 30 days to 3 months. The decrease in pain intensity scale rating and cancer response factor did not differ significantly between both two treatments. Based on the results, the oleozon solution was just as successful as triamcinolone acetonide in ora-base (0.1% gel) for the therapy of macular OLP in people with poor health. [21,22]

Conclusion

The study concluded that ozone has marked anti-microbial activity. The study has also shown that the group which received ozone therapy had reduced candidiasis infection. It has been shown that efficacy of ozonized water treatment has been efficient in managing erosive lichen planus as

quantified or determined by several scoring systems. Relapse has been much lowered in ozonized treatment group as compared to the controls. The study is limited by smaller size of sample. There is a need to conduct more similar studies to find out more effective results which can be generalized more easily for the whole population.

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