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Ozone Therapy in the Management of Recurrent Aphthous Ulcer – A Pilot Study and Review

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ABSTRACT

Ozone,an allotropic form of oxygen is gaining interest in dentistry.It hassuccessfully beenused in dentistry for more than 100 years. Ozone therapy is a form of alternative medicine treatment because of its unique properties like antimicrobial, immunomodulation, immunostimulation, biosynthetic, bioenergetics, antihypoxic,analgesic and hemostatic action and non-invasive nature.This review of literature is an attempt to summarize itsunique properties,different modes of application,its different uses in dentistry,contraindications and toxicity in addition to a pilot study to exhibit the beneficial use of topical ozonatedoil in one of the most common mucosal disorder - Recurrent Aphthous Ulcer.

KEY WORDS

Ozone therapy, Ozone, Immunomodulator, Aphthous Ulcer

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INTRODUCTION

C.F.Shonbein, in 1840, was the first person to name the substance thatgave an odor when Oxygen was subjected to electrical matter (Greek word Ozein-to smell) as Ozone.[1] Ozone is a naturally occurring compound comprising of three oxygen molecules; present in the upper atmosphere which screens the earth from harmful ultraviolet radiations.Thermodynamically, it is a highly unstable compound that decomposes to pure oxygen with a short half-life of 40 minutes at 20° C depending on system conditions like temperature and pressure. It has an oxidation potential that is 1.5 times greater than Chloride when used as an antimicrobial agent.

For more than 100 years, the usage of Ozone therapy in the medical field has been documented in various capacities. Initially,its usewas limited toindustrial purpose likedisinfection of water. Itsentry into the clinical field is seen after the effectiveness of Ozone therapywas proven in treating post traumatic gangreneinfected wounds and fistulas in soldiers of the FirstWorld War.In 1933, E.A Fischbecamethe first person to use Ozone in the dental field during surgeries to aid in disinfection and wound healing.[2]The Ozone used for medical purposes is amixture of pure oxygen (95 to 99.95%) and pure Ozone (.05 to 5%). Due to its unstable nature it has to be preparedright before the procedure and cannot be stored for a long period.In orderto slow downthe decompositionof Ozone to oxygen it is also coupled with a medium which has high viscous properties.[3]

Ozone therapy is a form of alternative medicine treatment that purports to increase the amount of Oxygen into the body through the introduction of Ozone in order to gain from its therapeutic benefits(versatile bio-oxidative therapy).Different modes of administration of Ozone are - Ozone gas,Ozone aqueous solution and Ozone oil. These forms of application are used singly or in combination to treat dental diseases.Ozone gas isgenerated by Ozone generating equipment (Ozone generators) which convertsOxygen to Ozone.Unlike antibiotics,there is no resistance to topical Ozone therapy because the microorganisms cannot escape from itsoxidative nature.Moreover,it disarms the toxins which areresponsible for tissue destruction.[3]However, Ozone gas should not be administered intravenously due to the risk of air embolism.[4]

Table1: Unique properties of ozone [5,6,7]

Unique properties of Ozone	Anti-inflammatory
	Analgesics
	Antioxidant (increases the production of free radical scavengers)
	Antimicrobial Antibacterial-disrupts the membrane by oxidation f lipid,protein and lipo proteins Antiviral –disrupts the envelope,capsid viral DNA Antifungal –inhibits the cell growth
	Hemostasis –helps in platelet aggregation
	Antihypoxic –Reduces clumping of RBC and increases the Oxygen carrying capacity
	Bioenergetics
	Biosynthesis –Activation of metabolism of carbohydrates, lipids and proteins
	Immunomodulator and immune stimulator-cytokine stimulator TGF,IL-2,6,8

Table 2:Uses of ozone in dentistry[8,9,10,11,12]

Indications	Oral Medicine	Aphthous and Herpetic ulcer,Mucositis,Temporomandibular disorders
	Periodontics	Preventing Periimplantitis, promoting osseointegration and for gingival and periodontal problems
	Prosthodontics	Denture cleansers
	Conservative and endodontics	Caries, hypersensitive dentin, bleaching, root canal irrigant
	Oral Surgery	Wound healing after surgery and extraction, refractory Osteomyelitis, preventing the development of Osteoradionecrosis
	Pediatrics	Root caries, pit and fissure caries, root canal therapy of deciduous teeth

Table 3:Toxic nature of ozone [13]

Prolonged exposure damages	Respiratory system
	Extra pulmonary organs
	Skin
Side effects	Epiphora
	Upper respiratory irritation
	Rhinitis
	Cough
	Occasional nausea,vomiting
	Shortness of breath
	Blood vessel swelling
	Poor circulation
	Heart problems, stroke

In case of toxicity, patient should be placed in supine position and treated with vitamin E and n-acetyl cysteine.[14]

Table 4:Contraindicationof ozone [15]

Contraindications	Pregnancy
	Glucose-6-phosphate dehydrogenase deficiency
	Hyperthyroidism
	Severe anemia
	Severe myasthenia
	Active hemorrhage
	Acute alcohol intoxication
	Recent myocardial infarction
	Ozone allergy

Recurrent Aphthous Stomatitis is a multifactorial inflammatory disorder characterized by recurring ulcers confined to the oral mucosa in patients with no other signs of systemic diseases. Based on the clinical characteristics, it is divided into minor ulcer(< 0.1 cm, most common type, lastsfor 7 -10 days and heals without scars),major ulcer(> 1.0 cm,lastsfor weeksand heals with scarring) and Herpetiformulcers(< 0.1 cm,>10 ulcers dispersed widely over mucosa).There are numerous factors reported to be associated with Recurrent Aphthous Stomatitis like genetics, hematological deficiency, immunological abnormalities, psychological stress ,trauma, smoking, menstruation and food allergy. It shows variability in presentation from mild discomfort to severe pain and debilitating stage which can interfere with speech and eating.The main goal of current therapeutic approaches are management of pain, improving the quality of living and decreasing the duration and recurrence. Digging deep into literature and past researches, we discovered that Ozone therapy has goodtherapeutic benefits in various fields of dentistry when administrated via gas or dissolved in water or oil. It is also observed that most of the literature was in-vitro studies and very few were clinical studies. This motivated us to conduct this study to exhibit the beneficial use of topical Ozonated oil in one of the most common mucosal disorder - Recurrent A phthous Ulcers.

Ozonated oil is produced by fusing ozone through the finest organic cold-pressed Virgin Olive Oil continuously for a long but finite period of time (weeks, sometimes even months of bubbling the oil 24 hours a day). During this procedure, the olive oil changes into an off-white thick paste. The paste formed by this method remains stable and can be stored for up to 17 years.

MATERIALS AND METHODS

A randomized single blind study was conducted in the Department of Oral Medicine and Radiology, Tamilnadu Government Dental College and Hospital. The study sample includes fourteen patients of either sex with age greater than 15 years. The patients who reported for treatment of ulceration on the first day of ulcer with severe pain, inability to speak and inability to swallow food with a history of minimum frequency of 4 outbreaks per year presenting with single ulcers of size

less than 5mm in diameter (Aphthous Minor) were selected. Individuals who had heart,liver, kidney dysfunctions, pregnant and lactating women, ulcerative colitis, Crohn disease, Behcet syndrome, those taking medications within a month before the study and those who are allergic to ozone were excluded .Diagnosis of recurrent Aphthous Ulcer Minor were made based on history and clinical features of round, shallow ulcer with regular border with a surrounding erythematous halo in the non-keratinized mucosa.

Fourteen patients were divided into two groups of seven each - Group A and Group B. Patients were alternatively allotted to the groups. Group A received treatment by ozonated oil along with common supplements like B-Complex and multi vitamins where as Group B received treatment by a gel (anti-inflammatory, anesthetic and antiseptic gel containing Choline Salicylate, Benzalkonium Chlorideand Lignocaine) along with supplements like B-Complex and multi vitamins. Patients were instructed to apply the given medication four to five times daily and were asked to report every day until the lesion completely healed. Pain intensity score at pre-treatment and follow up period were recorded and the duration of each ulcer was recorded. Pain score was measured using Visual Analog Scale (VAS) of 0-10 (0 is no pain and 10 is the worst pain).

STATISTICAL ANALYSIS

Statistical analysis of the data was performed using SPSS for Windows version 17 software. The values were represented and mean ± standard deviation was calculated. Paired t- test was used to analyze the data. Statistical significance was considered to be 5% or $p < 0.05$ level.

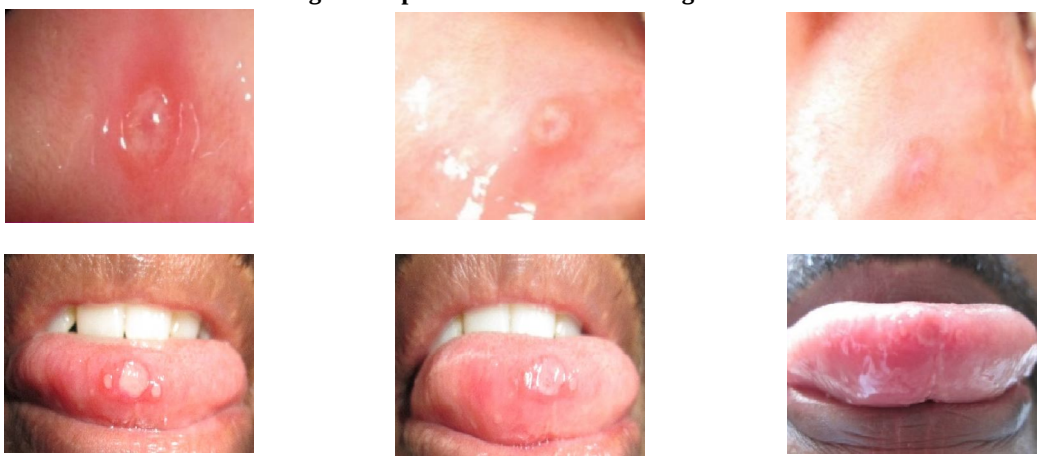
RESULTS

No one from the study was unhappy with the treatment or discontinued the treatment. Every patient reported regularly for the follow-up and reported no side effects. Patients under Group A showed significant reduction in pain on the very first day of the treatment. They were happy because the mainstay palliative care were achieved i.e. the symptoms were resolving after applying Ozonated oil. Along with the reduction in pain, the erythema around the lesion reduced indicating an accelerated healing. On the third day of the treatment lesions further reduced in size with re-epithelialization and pain reduced by 85% compared to pre-treatment. The lesion completely healed in the range of 5-6 days of the treatment with 98% resolution of symptoms.

Ozone therapy Group A demonstrated faster healing duration than Group B(mean of 5.43 days for Ozone therapy versus mean of 6.29 days for conventional treatment) on Recurrent Apthous Ulcers ($p<0.05$) as shown in Table 6, Figure 1 and Graph 1.It was noticed that there was significant reduction in pain on the first and second day of the treatment with Ozonated oil Group A(46% and

73% respectively) when compared with the conventional approach Group B(35% and 58% respectively) as shown in Table 5.

Figure 1:Aphthous ulcer treated using ozonated oil



Day 1 Day 2 Day 3

Table 5: Mean ± standard deviation of pain score between two groups

Time interval	Group	Numbers	Mean ±SD	% reduction from the pretreatment	P value
Pretreatment	Group A	7	5.86±.69		
	Group B	7	5.71 ±.95		
Day1	Group A	7	3.14 ±.38	46	.03*
	Group B	7	3.71±.49	35	
Day2	Group A	7	1.57±.53	73	.01*
	Group B	7	2.43± .53	58	
Day 3	Group A	7	0.86± .90	85	.29
	Group B	7	1.29 ±.49	78	
Day 4	Group A	7	0.29 ±.49	95	.32
	Group B	7	0.57±.53	90	
Day 5	Group A	7	0.14±.38	98	.27
	Group B	7	0.43±.53	93	
Day 6	Group A	7	0.0±0.0	100	.
	Group B	7	0.14±0.38	98	
Day 7	Group A	7	0.0±0.0	100	-
	Group B	7	0.0±0.0	100	
Day 8	Group A	7	0.0±0.0	100	-
	Group B	7	0.0±0.0	100	
Day 9	Group A	7	0.0±0.0	100	-
	Group B	7	0.0±0.0	100	
Day10	Group A	7	0.0±0.0	100	-
	Group B	7	0.0±0.0	100	

***p value < .05 – statistically significant**

Table 6: Mean ± standard deviation of days required for healing between two groups

	Days required for healing Mean ±SD	P Value
Group A	5.43 ± .53	.03*
Group B	6.29 ±.76	

***p value < .05 – statistically significant**

Graph 1: Comparison of average number of days for healing between the two groups

DISCUSSION

From this pilot study it was found that Ozone therapy reduced the healing duration compared to conventional approaches in Aphthous Ulcers. Further detailed studies are required in the future with larger samples to make use of this beneficial effect of Ozone therapy.

Although Aphthous Ulcers are episodic and self-limited, ulceration is painful and debilitating for the patient by interfering with eating, speaking and swallowing. Ozone therapy accelerates the healing time. A previous study conducted by Logan has demonstrated the beneficial use of topical application of Ozone in long standing Aphthous Ulcer. There was complete resolution of the symptoms due to accelerated healing of the ulceration.[9] Its usage also extended to Herpetic Ulcers, in which it neutralizes the virions, stimulates healing and inhibits supra added bacterial infections.

Immunomodulating, analgesic, antimicrobial and the capacity to promote blood circulation arethe reasons behind faster healing of ulcers due to Ozone therapy.Immunomodulating effects of Ozone therapy are related to an increase in the production of cytokines such as interleukin-2,interleukin -6, tumor necrosis factor –α and transforming growth factor –β and stimulation of blood circulation is mainly due to eliminating the clumping and by restoring the flexibility of the red blood cells.

CONCLUSION

Even though Ozone therapy existed in the medical field for more than 100 years, the sudden increase of different scientific and clinical papers in the recent years has madeOzone therapy gain a lot of interest lately. In spite of promising beneficial effects, it is still considered limited because of the toxicity and side effects.Further studies with establishment of safe and well defined parameters like dosage and application time areneeded to establish Ozone as a good alternative treatment modality in different fields of dentistry.

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