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THE EFFICACY OF OZONIZED OLIVE OIL IN THE TREATMENT OF ORAL LESIONS: A CLINICAL STUDY

ЕФИКАСНОСТА НА ОЗОНИРАНОТО МАСЛИНОВО МАСЛО ВО ТРЕТМАНОТ НА ОРАЛНИТЕ ЛЕЗИИ: КЛИНИЧКА СТУДИЈА

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Abstract

The oral cavity functions as a dynamic ecosystem, maintaining a delicate balance between the entry of microorganisms, colonization modalities, nutritional equilibrium, and the host's defenses against their removal. Common entities frequently encountered in clinical practice include aphthous ulcerations, herpes and traumatic lesions, oral candidiasis, oral lichen planus and angular cheilitis. Numerous treatment modalities are available for these lesions. Topical ozone therapy, being an effective non-drug method, offers a minimally invasive technique that can be used for these conditions without any causing any side effects. **The aim of** the study is to evaluate the efficacy of ozonized olive oil in the treatment of recurrent aphthous stomatitis (RAS), herpetic and traumatic lesions. **Materials and methods:** A clinical study was conducted involving 35 patients, comprising 20 cases of aphthous ulcerations, 13 cases of herpetic lesions and 2 cases of traumatic lesions. Ozonized olive oil was topically applied twice daily until the lesion regresses. The size of the lesions and the intensity of the illness, evaluated using VAS scale, were recorded during the first visit and every other day until complete epithelization occurred. The lesions were photographed and documented. **Results:** All types of lesions, including aphthous ulcerations, herpetic lesions and traumatic lesions exhibited rapid regression and reduction of pain within a few days. None of the patients experienced any toxicity or side effects. **Conclusion:** Ozonized olive oil proves to be an effective topical agent for accelerating the healing process and alleviating pain associated with oral lesions, such as recurrent aphthous stomatitis, herpes, and traumatic lesions. **Key words:** Oral lesion, epithelization, ozone olive oil.

Апстракт

Оралната празнина претставува динамична еко-средина, со одржлив баланс помеѓу влезот на микроорганизмите, колонизациските модалитети, нутритивниот внес и одбраната на домаќинот. Некои од најчестите клинички ентитети во усната празнина ги вклучуваат афтозните улцерации, херпетичните и трауматските лезии, оралната кандидијаза, оралниот лихен планус и ангуларниот хеилитис. За овие лезии и состојби се достапни повеќе третмански модалитети. Топичната озон-терапија, како ефективен немедикаментозен метод претставува минимално инвазивна техника, која може да се применува кај овие состојби без никакви несакани ефекти. **Целта на студијата** е да ја проследиме ефикасноста на озонираното маслиново масло во третманот на рекурентниот афтозен стоматит (РАС), херпетичните и трауматските лезии. **Материјал и метод:** Клиничката студија беше спроведена кај 35 пациенти (20 афтозни, 13 херпетични и 2 трауматски лезии). Озонираното маслиново масло беше аплицирано 2 пати дневно, се до комплетна регресија на промените. Големината на лезиите и степенот на болка изразен по ВАС скалата, беа нотирани на првата посета и секој втор ден, до денот на комплетната епителизација. Лезиите беа фотографирани и документирани. **Резултати:** Сите лезии (афтозни улцерации, херпетични и травматски лезии) покажаа брза регресија и намалување на болката за неколку дена. Кај ниту еден пациент не беа регистрирани токсичност и несакани ефекти од препаратот. **Заклучок:** Озонираното маслиново масло претставува ефективен топичен агенс во процесот на заздравување и периодот на исчезнување на болката кај оралните лезии (рекурентниот афтозен стоматит, херпетичните и трауматските лезии). **Клучни зборови:** орални лезии, епителизација, озонирано маслиново масло

Introduction

Ozone, a triatomic gaseous molecule composed of three oxygen atoms, has demonstrated its efficacy in managing various pathologies in the field of medicine and dentistry[1]. Medical-grade-ozone used for medical purposes is a gas mixture consisting of 95–99.95% oxygen and 0.05–5% pure ozone[2].

Ozone therapy has gained a significant attention in the fields of medicine and dentistry. It possesses powerful oxidizing properties and exhibits strong antimicrobial activity against bacteria, viruses, yeasts and protozoa.

Additionally, it can stimulate blood circulation and immune responses, and has analgesic effects[3,4].

The first medical application of ozone dates back to 1870 when Dr. C. Lender employed it for purifying blood in test tubes[5].

Clinical literature reveals several studies highlighting the use of medical-grade ozone for the treatment of oral lesions and conditions[6]. Most of these studies focus on the use of the gaseous ozone, generated by specialized "Ozone Generators" which can be very expensive and require direct application to the lesion[7]. Due to the rigidity of this treatment, an alternative method of ozone application has been developed using an ozone solution. Olive oil, a revolutionary component in the solution, ensures better shelf life of the medication due to its chemical properties[8].

The treatment of erosive and ulcerative lesions in the oral cavity poses a significant challenge for dentists across all various specialties due to the chronic nature of the condition. Effective treatment approaches should consider the underlying etiopathogenesis of these lesions.

The oral cavity, due to its anatomical features, is constantly exposed to more than 300 types of microbes, making any erosion in this area susceptible to microbial contact. Many types of treatments have been used to manage oral ulcers, including mouthwashes (such as chlorhexidine), topical corticosteroids, topical tetracycline, immunoregulators, TNF inhibitors, systemic zinc sulphate, monoamine-oxidase inhibitors, low-energy laser, herbs, and others.

However, many of these therapies come with potential consequences such as dysbiosis, fungal infection, the development of microbial resistance and sensitization of the body[9,10]. In contrast, medical ozone has gained popularity as an antibacterial agent in multiple medical areas. Ozone exhibits broad-spectrum antimicrobial properties, effectively killing all kinds of bacteria, viruses, fungi and protozoa. Notably, the antiseptic effect of pure ozone is three hundred times stronger than that of chlorine, while being non-destructive and non-irritating to tissues. Therapeutic doses of ozone also poses antihypoxic and immunoreactive effects, potentiate the action of antibiotics, improve the rheological properties of blood and enhance microcirculation[11-15].

Ozone has been used in the treatment of ulcers affecting other parts of the gastrointestinal tract[16-18] blood vessels[19] and skin[20,21]. However, there is limited research available on the role of ozone in treating recurrent aphthous ulcers in the oral cavity.

This prompted the undertaking of the present study, which aimed to assess the effects of ozone olive oil in the treatment of oral lesions, including aphthous, herpetic and traumatic ulcers.

Material and method

A total of 35 patients participated in this clinical study, with 20 having aphthous lesions, 13 having herpetic lesions and 2 having traumatic erosions. The average age of the patients with aphthous lesions was 26 years, with 11 males and 9 females. The patients with herpetic lesions had an average age of 48 years, with 8 females and 5 males. The patients with traumatic erosions were both male, with one being 45 years old, and the other 8 years old, averaging 26 years (table 1). The study was conducted during the period from 1st of January 2021 until January 2023.

This study was conducted in accordance with ethical principles, specifically those outlined in the World Medical Association Declaration of Helsinki. The study was ethically approved by the Ethics Committee at the Faculty of Dentistry - Skopje, Ss. Cyril and Methodius University in Skopje, Macedonia.

All participants were fully informed about the study, and their informed consent was obtained prior to their participation in the study. All clinical examinations were performed on a dental chair. The diagnosis of all the lesions was based on the clinical presentation and symptoms.

Table 1. Oral lesions included in the study

	NUMBER OF PATIENTS	AVERAGE AGE	MALE	FEMALE
APHTHOUS LESIONS	20	26 years	11	9
HEPRETIC LESIONS	13	48 years	5	8
TRAUMATIC LESIONS	2	26 years	2	/

The main outcome measures of the study were pain levels, lesion size and duration. At the beginning of the study, ulcer size was measured using a periodontal probe which has an accuracy of up to 1 mm. Also, pain assessment was conducted using a VAS score (Visual Analogue Score), ranging from 0 to 10; with 0 indicating no pain and 10 indicating the most severe pain. The participants were instructed not to use any systemic or local drugs for the treatment of the ulcers or symptom relief throughout the period of the study. After establishing the diagnosis for each participant in the study, the size of the lesion was recorded in millimeters and photographed. Pain levels were also recorded using the VAS score. All of the patients were instructed to apply ozone olive oil, as explained in detail, massaging the oil into the affected area of the oral mucosa, twice a day without rinsing or moisturizing the area for 30 minutes after application. Control appointments were scheduled on the 3rd, 5th, 7th day, and so on for the purpose of monitoring the epithelization process of the lesions (as indicated by size reduction) and the reduction of pain levels until complete recovery. The entire process and changes were documented through photographs.

Results

As a result of the insufficient number of participants needed for statistical representation of data, we were able to report average values for certain parameters, including the initial size of the lesions (measured in mm), average pain levels, average epithelialization time and time of pain disappearance. These average values are presented in table 2.

For aphthous lesions, the average size was 3.35 mm, the average initial pain level was 4.16, the average epithelialization time was 4.3 days and the average time of pain disappearance was 3 days (figure 1-6).

Aphtae minor

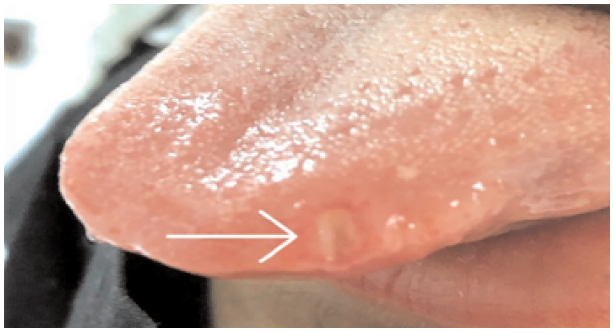

Figure 1. *First day (6 mm; VAS = 7)*

Figure 2. *Third day (2 mm VAS = 0)*

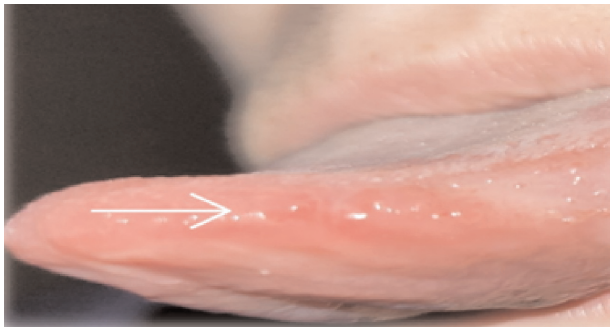

Figure 2. *Fifth day (0 mm VAS =0)*

Table 2. Average size of lesions, average pain levels, epithelization time and disappearance of pain numbered in days

	NUMBER OF PATIENTS	INITIAL AVERAGE SIZE OF LESIONS (мм)	INITIAL AVERAGE PAIN LEVELS VAS (1 -10)	AVERAGE EPITELIZATION TIME (days)	AVERAGE TIME OF DISAPPEARANCE OF PAIN (days)
APHTHOUS LESIONS	20	3,35	4,16	4,3	3
HEPRETIC LESIONS	13	8,87	4,37	4,25	3,75
TRAUMATIC LESIONS	2	5,5	4	2	3

Aphtae major

Figure 4. *First day (25 mm VAS =8)*

Figure 5. *Third day (15 mm VAS = 1)*

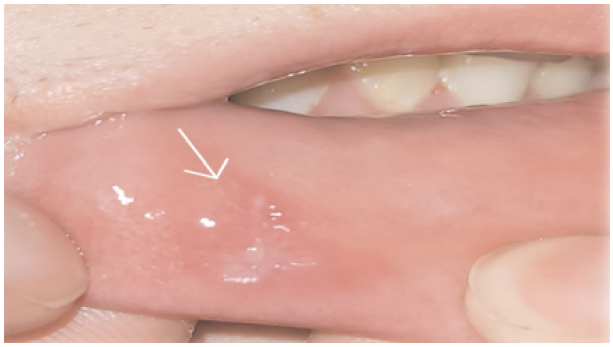

Figure 6. *Fifth day (0 mm VAS = 0)*

Herpes simplex recidivans

Figure 7. *First day (8mm VAS=5)*

Figure 8. *Third day (4mm VAS =0)*

Figure 9. *Fifth day (0mm, VAS =0))*

Herpes simplex recidivans

Figure 10. *First day (10 mm, VAS=3)*

Figure 11. *Third day (4mm, VAS=0)*

Figure 12. *Fifth day (0 mm, VAS=0)*

Erosio traumatica

Figure 13. *First day (5mm, VAS=5)*

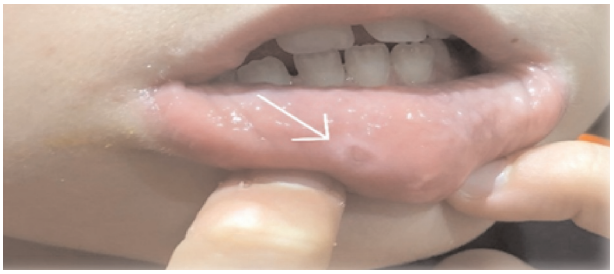

Figure 14. *Third day (2mm, VAS=0)*

Figure 15. *Fifth day (0mm, VAS=0)*

In the case of herpetic lesions, the average size was 8.87 mm, the average pain levels were 4.37, the epithelialization time was 4.25 days and the average time of pain disappearance was 3.75 days (figure 7-12).

Regarding traumatic lesions, the average size was 5.5 mm, the average pain level was 4 , the average epithelialization time was 2 days, and the average time of pain disappearance was 3 days (figure 13-15).

Some of the photos were taken by the patients, at home, so they are without protective gloves.

Discussion

Ozone is an inactivate form of oxygen (O_2) that exists as a trivalent molecule (O^3). Ozone naturally breaks down into two atoms of regular oxygen by releasing an atom of singlet oxygen over a period of approximately 20–30 minutes[22,23]. Despite being recognized as one of the most powerful oxidants in nature, the precise mechanisms underlying its therapeutic effects are unclear. Several theories have been proposed based on clinical observations. These theories include the generation of peroxides by ozonolysis of unsaturated fatty acids in cell membranes, activation of reactive oxygen species that act as physiological enhancers of various biological processes (including increased production of adenosine triphosphate), and increased expression of intracellular enzymes with antioxidant activity. It has been reported that exposure to ozone results in changes in the levels of many biological substances, such as cytokines (Interferon C, TNFs, TGFβ and IL-8), acute phase reactants and adhesion molecules from the integrin family such as CD11b.

Other reports have indicated increased motility and adhesion of peripheral blood polymorphonuclear cells to

epithelial cells after exposure to ozone. Similarly, major autohemotherapy-induced leukocytosis and enhanced phagocytic activity of polymorphonuclear cells have been reported.

Ozone therapy has proven to be useful in various ways for treating different diseases, thanks to its unique properties, including antimicrobial, immunostimulant, analgesic, antihypnotic, detoxicating, bioenergetic and biosynthetic actions.

Ozone causes inactivation of bacteria, viruses, fungi, yeast and protozoa. It disrupts the integrity of the bacterial cell membrane through the oxidation of phospholipids and lipoproteins. Even at low concentration of 0.1 ppm, ozone is sufficient to inactivate bacterial cells, including their spores[24]. In fungi, ozone inhibits cell growth at certain stages, with budding cells being the most sensitive[25]. In the case of viruses, ozone damages the viral capsid and disrupts the virus-to-cell contact though peroxidation, thereby disrupting the reproductive cycle[26].

Ozone therapy leads to an increase in the rate of red blood cell glycolysis. This stimulation results in the production of 2,3-diphosphoglycerate, leading to an increased release of oxygen in the tissues. Ozone activates the Krebs cycle by enhancing the oxidative carboxylation of pyruvate, stimulating production of ATP. It also causes a significant reduction in NADH and aids in the oxidation of cytochrome C. Moreover, it stimulates the production of enzymes that act as free radical scavengers and cell-wall protectors, such as glutathione peroxidase, catalase and superoxide dismutase and prostacyclin, which is a vasodilator[27].

When administered at a concentration between 30 and 55 µg /cc, ozone causes the greatest increase in the production of interferon and the greatest output of tumor necrosis factor and interleukin-2, triggering a cascade of subsequent immunological reactions[28].

Conclusions

The results obtained from this study indicate the following:

- A relatively fast epithelialization process of recurrent aphthous lesions, herpetic lesions and traumatic erosions, accompanied by a reduction in pain over a short period of time after treatment was observed.
- None of the patients experienced adverse effects or toxicity resulting from the topical agent, further confirming its safety.
- The application of ozone therapy was atraumatic, painless and noninvasive and the patients generally responded positively to the topical agent.

The current clinical literature lacks sufficient data on the utility of ozone therapy as a treatment option for certain oral condition, despite numerous studies available for conventional treatment modalities.

However, despite the study's limitations due to the small number of participants, the results were clear. The quick and effective healing of the lesions and reduction in pain levels over a short period of time are just two of the many benefits of localized ozone therapy that justify its long-term use in treating different types of periodontal conditions.

The main takeaway from this study is that ozone therapy is poised to revolutionize the field of dentistry in the near future.

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