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# Efficacy of OLEOZON® compared to Alvogil in the treatment of alveolitis

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## ABSTRACT

Alveolitis is a reversible infection of alveolar process after tooth extraction. Its etiology is unknown, but there are factors increasing its incidence such as traumatisms, infections, decrease of vascular supply of surrounding bone and general systemic status. Aimed at comparing the efficacy of OLEOZON® (ozonated sunflower oil) with Alvogil, treating alveolitis clinically and microbiologically and determining the degree of patients´ satisfaction and side effects. A controlled, randomized, single.blind, phase III clinical trial was conducted at "Reynold García" Polyclinic, Matanzas municipality (Cuba), between January 2007 and May 2010. The sample included 100 adult patients, aging from 20 to 59 years, with diagnostic criterion of alveolitis; 50 patients in the experimental group, to which were applied OLEOZON® and in the other 50 patients, Alvogil, a conventionally used medication of well-known efficacy. Cures were made every 72 hours as well as many visits as necessary to the dentist's office. Healing criterion was formation of granulation tissue and pain relief. Patients were recovered with OLEOZON® by 92% and with Alvogil, by 78%, in the third visit, with significant differences between both groups. The majority of patients needed from 2 to 3 visits to the dentist's office in both groups, though it was observed that there was a greater number of patients recovered in the group treated with OLEOZON® in the second visit, with significant differences regarding the control group. OLEOZON® proved better efficacy than Alvogil. No side effects against the medication under study were observed.

**Keywords**: alveolitis, treatment, Alvogil, OLEOZON®, ozonated vegetable oils, efficacy.

## INTRODUCTION

Primary care is integral part of the National Health System in Cuba, being its basic function and main core and also of the social and economic development of the entire community. It represents the first level of contact of individuals, family and the community with the National Health System, brings health attention closer to the people's place of residence and work and is primary component of a sanitary care ongoing process[1].

Comprehensive General Dentist provides dental care to a population sector of 1200-1300 inhabitants, together with the family doctor and nurse and with community engagement. Those services in which the dentist-inhabitant relationship is not achieved yet, some actions are carried out. However, due to the high demand for treatment assistance, actions are limited to promote health and prevention, thus influencing the oral health indicators of the assisted population[1].

Within those actions, dental emergency treatment is a priority as well as application of alternative methods of treatment, such as Natural and Traditional Medicine[1].

One of the conditions considered as an emergency is alveolitis, since the patient suffers so much pain that this symptom makes him to resort to our services immediately.

Alveolitis or septic osteitis of alveolar socket is a reversible infection, located on the surface after a

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tooth extraction, and is the most frequent and painful complication of exodontia[2].

Cause for alveolitis is unknown, but there are factors which increase incidence of this painful sequel of extractions like traumatisms, infections, decrease in vascular supply of surrounding bone and general systemic status, sclerotic bones, excessive trauma of the alveolus ridges in gums, osseous crushing, tooth extraction with periapical or acute periodontal processes, bad oral hygiene, foreign body in alveolus, radicular remains of cysts or granulomas, systemic diseases, among others[6-8]. The origin can be related to factors preventing adequate nutrition form reaching the recently formed clot inside the alveolus[3-7] .

Conventional treatment used has been based on removal of painful symptomatology and promote healing of alveolar wound. Therefore, application of two medications have been mainly employed: Alvogil or iodoform gauze[4] .

Healing has been demonstrated to have the deoxyribonucleic acid as one of its stimulating elements. Physiologically, healing consists of two phases: initial phase or infiltration and fibroplasia[5-8].

In Natural and Traditional Medicine there are therapeutic modalities that had been used in treating several oral diseases. Ozone therapy is one of them of great efficacy due to its demonstrated scientific properties.

Introduction of ozone in the field of Medicine conditioned the search for new strategies, taking into consideration the properties of this gas. Its use in the form of ozonated water and ozonated oil has also been accepted. Vegetable oils have become adequate medium for ozone therapeutics, basically in dentistry [9,10].

Olive oil is most commonly used in Europe. The germicidal properties of ozonated olive oil was demonstrated in its use against *Staphylococcus aureus* as experimental model resulting in 99% of death of the microorganism after 13 hours[10].

At the National Center for Scientific Research (CNIC), a study was conducted in sunflower oil in place of olive oil. Both ozonated oils were assessed for their microbicidal power, using growth of yeast species of *Candida tropicalis* as experimental model. Results showed feasibility to use sunflower oil with advantages over olive oil, due to its germicidal power[11].

When vegetable oils are ozonated, chemical compounds are obtained (ozonides and peroxides) with strong germicidal characteristic against viruses, bacteria and fungi, making it useful in treating infected wounds, fistulae and other local septic processes, due to its direct attack to the microorganisms. Also, peroxides and ozonides develop several functions in the body which include stimulation of enzyme redox systems, positive influence on oxygen transportation to tissues and in the respiratory mitochondrial chain; blockade of viral receptors and death of infected cells by virus as well as a synergy on reinforcement of the phagocytic capacity[12,13].

It has also been proven in the mouse tail model, an increase in superoxide dismutase in animals treated with OLEOZON® with respect to control group, showing its protective action[14].

Furthermore, OLEOZON® provides a less costly therapeutic alternative for it is produced domestically; besides its economic advantage, it has passed satisfactorily dermal irritability and ophthalmic preclinical assays, acute and sub chronic toxicity studies, mutagenesis and teratogenesis assays, guaranteeing innocuity of the product, made known in published clinical assays[15-21].

**Objective**

To compare OLEOZON efficacy with that of Alvogil, in treating alveolitis, regarding clinical and microbiologic aspects, as well as to determine the degree of satisfaction of patients and side effects.

## PATIENTS AND METHODS

A controlled randomized single-blind phase III clinical assay was carried out. It was registered with code number 015 as an institutional project of the Directorate of Science and Technique of the University of Medical Sciences of Matanzas (Cuba) and in the Directorate of Postgraduate, since it became an issue for research in a thesis of Comprehensive General Dentistry specialty following a Branch Project.

Study universe was made up of all patients with alveolitis who resorted to the Dentistry Department of "Reynold García" Polyclinic of Matanzas between January 2010 and May 2013. Number of patients was 247. Sample chosen, accordin. exit criteria was of 100 patients, aged between 20 and 59 years of either sex, who attended our dental consultation with diagnosis of alveolitis. They were distributed into two groups: 50 patients in the experimental group treated with OLEOZON® and

50 patients in the control group treated with Alvogil, according to the random table (Annex I).

Inclusion criteria:

- ➢ Patient with diagnostic criteria of alveolitis.
- ➢ Ages between 20 and 59 years.
- ➢ Patient of either sex or race.
- ➢ Patient who voluntarily gave his/her informed consent to participate in the research. (Annex II)

Exclusion criteria:

- ➢ Patient in pregnancy status.
- ➢ Patient with antecedents or presence of neoplastic processes.
- ➢ Patients with antecedents of irradiated bone and immunodeficiency diseases.
- ➢ Patient with physical or mental disability.

Exit criteria:

- ➢ Patient, who for reasons such as: change of domicile address, death, prolonged hospitalization and other similar cannot continue the proper course of the research.
- ➢ Patient who in the course of the study was first diagnosed with systemic diseases (acute or chronic) such as Diabetes Mellitus, infectious, metabolic or immunodeficiency diseases or those requiring irradiation treatment.
- ➢ Patient who died during the course of research due to reasons beyond the treatment.
- ➢ Once it was verified that the patient was not following indications of the study.
- ➢ Once the patient decided to abandon treatment voluntarily.

Primary Care Clinical Record was obtained from all the patients included in the study; asepsis and antisepsis was performed, anesthesia was placed with lidocaine 2% at a distance and the alveolus was treated and irrigated with physiologic serum to eliminate all fragments of necrotic clot and inadequate content of alveolus. Once the alveolus has been carefully dried with sterile cotton swabs, it was softly covered with Alvogil (control group). The experimental group was treated in the same way. Patients were applied OLEOZON® in the alveolus without prescription of any other medication in none of the groups.

Both groups underwent cures every 72 hours and they made visits to the consultation as required.

Samples of exudates were taken from 20 patients of each group at the beginning of research and after 96 hours of treatment, for microbiologic analysis carried out at the Provincial Center of Hygiene and Epidemiology by a laboratory technician to detect presence or not of pyogenic microorganisms.

The following variables were taken into account: age, sex, possible causes for alveolitis, clinical and microbiologic assessment and patient's level of satisfaction, which were operationalized in the research protocol.

Patients were assessed clinically by the assessor, a comprehensive general dentist at 72 hours (second visit), 96 hours (third visit) and one week of treatment (fourth visit) to assess remission of signs and symptoms in the affected zone.

For the clinical evaluation of patients were taken into consideration:

- ❖ Recovered: when pain and inflammation clinical signs disappeared and the alveolus was in a healing phase.
- ❖ Improved: when pain and inflammation clinical signs decreased and the alveolus was in the healing phase.
- ❖ Same: pain maintains same intensity and inflammation clinical signs persist.
- ❖ Worse: Increased pain and inflammation clinical signs persist or got worse.

For the microbiological evaluation:

- ❖ Infected alveolus: presence of pyogenic microorganisms.
- ❖ Alveolus free of infection: absence of pyogenic microorganisms.

For efficacy evaluation:

- ❖ Good: Patients with clinical progress following criterion of recovered and microbiologic course with criterion of alveolus free of infection.
- ❖ Acceptable: Patients with clinical course following criterion of improved and microbiologic course with criterion of alveolus free of infection.
- ❖ Bad: Patients with clinical course following criterion of same or worse and microbiologic course with criterion of infected alveolus.

Information was processed in a SPSS statistical package; Fisher's Chi Squire and exact test was applied.

Ethical considerations were taking into account, principles for the studies in human beings like the informed consent, no malice, respect, justice and principles of the Declaration of Helsinki of World Medical Association.

## RESULTS

Distribution of patients according to age and sex can be observed in Table 1. By Chi square test, homogeneity between groups was demonstrated ($p > 0.05$), regarding age of patients since it influences the body's response.

Relation between alveolitis and possible causes for its occurrence for both study groups was shown in Table 2. Among factors influencing the most in alveolitis, were traumatic extractions and Diabetes Mellitus.

Results regarding patient's progress were shown in Table 3. Regarding clinical assessment, it was observed that 41 patients (experimental group), only needed two visits to be in the category of recovered, while in the control group these were 29. While analyzing the number of patients who needed three visits to heal, we observed 5 patients in the experimental group and 10 in the control, but at the end of the assessment only one patient of the experimental group treated with OLEOZON®, needed more than 4 visits against 9 patients from control group, with significant statistical differences.

TABLE 1. Distribution of number of patients according to age and sex in both study groups.

| Study Group | 20-34 years | | | | 35-59 years | | | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | | Female | | Male | | Female | | Male | | Female | |
| | No | % | No | % | No | % | No | % | No | % | No | % |
| Experimental (n=50) | 10 | 20.0 | 12 | 24.0 | 14 | 28.0 | 14 | 28.0 | 24 | 48.0 | 26 | 52.0 |
| Control (n=50) | 9 | 18.0 | 7 | 14.0 | 23 | 46.0 | 11 | 22.0 | 32 | 64.0 | 18 | 36.0 |
| Total (n=100) | 19 | 19.0 | 19 | 19.0 | 37 | 37.0 | 25 | 25.0 | 56 | 56.0 | 44 | 44.0 |

TABLE 2. Relation between alveolitis and its possible causes for occurrence

| Group | Number of patients | | | | | |
|---|---|---|---|---|---|---|
| | Diabetic | | Traumatic Extractions | | Smokers | |
| | No | % | No | % | No | % |
| Experimental (n=50) | 18 | 36.0 | 32 | 64.0 | 17 | 34.0 |
| Control (n=50) | 21 | 42.0 | 30 | 60.0 | 16 | 32.0 |
| Total (n=100) | 39 | 39.0 | 62 | 62.0 | 33 | 33.0 |

TABLE 3. Clinical assessment of patients according to the treatment used and number of visits they needed.

| | OLEOZON® | | | Alvogil | | |
|---|---|---|---|---|---|---|
| Category | 2 v | 3 v | ≥4v | 2 v | 3 v | ≥4v |
| Recovered | 41** | 5** | 3 | 29** | 10** | 2 |
| Improved | 4 | 4 | 1 | 12 | 7 | 9 |
| Same | 5 | 0 | 0 | 6 | 3 | 0 |
| Worse | 0 | 0 | 0 | 3 | 1 | 0 |

V: number of visits to consultation. * Non-significant (p=0.117). ** Significant (p=0.004).

In Table 4, microbiologic assessment of 20 patients revealed that at 96 hours of treatment, 13 patients of the group treated with OLEOZON® showed criteria of alveolus free of infection against 6 of the control group.

A greater number of patients who only needed 2 to 3 visits to consultation to get cured was observed in the group treated with OLEOZON®, in compare with results in the group treated with Alvogil, with significant differences between the groups (p<0,004).

In Table 5, when analyzing efficacy of both medications, it was seen that OLEOZON® showed good efficacy for 92%, while Alvogil obtained 78%, with important statistical differences.

The 100% of patients showed satisfaction with the treatment no matter what group they belonged to. No second effects were found.

TABLE 4. Microbiologic evaluation of patients according to treatment employed.

| | OLEOZON® | | Alvogil | |
|---|---|---|---|---|
| Category | beginning | 96 hours | beginning | 96 hours |
| Infected alveolus | 20 | 7** | 20 | 14** |
| Alveolus free of infection | 0 | 13** | 0 | 6** |

** Significant (p=0,004).

TABLE 5. Efficacy of OLEOZON and of Alvogil in patients with alveolitis.

| | OLEOZON® | | Alvogil | |
|---|---|---|---|---|
| Category | No | % | No | % |
| GOOD | 46 | 92.0 | 39 | 78.0 |
| ACCEPTABLE | 4 | 8.0 | 10 | 20.0 |
| BAD | 0 | 0 | 1 | 2.0 |
| TOTAL | 50 | 100.0 | 50 | 100.0 |

** Significant (p=0,004).

## DISCUSSION

In the study carried out it was observed that the greatest number of patients treated was between 35 and 59 years; this could be related to the fact that within this range of age is when the greatest amount of teeth are lost. Actually, this figure is not high compared to national and international standards thus proving the effectiveness of promotion and prevention actions in the Cuban health system, as well as the increase in conservative treatments in dental practice that avoid resorting exodontia.

Among factors mostly influencing alveolitis are traumatic extractions and Diabetes Mellitus, for both study groups.

Horta[5] coincides in his study with that Diabetes Mellitus is one of the systemic diseases mostly associated with a loss of dental organ, mainly after 35 years old, and that alveolitis is the most frequent complication arising in these patients after undergoing exodontia.

Martínez de Santelices[6] consider that a stronger association is with Type II Diabetes because despite it is the most frequent in the Cuban population and the world, it is related to lifestyles and genetic conditions that pose risk factors coinciding with other oral pathologies such as periodontitis, also responsible for dental loss at these ages.

This is explained by the altered metabolism of diabetic patients and glucose increase in blood, making them more susceptible to infections, mainly if they are decompensated.

Results regarding patients´ progress showed that the experimental group treated with OLEOZON® needed less visits to achieve the category of cured than in the control group.

Martínez,[18] in his study in chronic gingivitis, refer that the group treated with OLEOZON® needed less visits that the control group to achieve healing, which coincides with results of the current research.

Cruz *et al*.[20] developed one of the first studies published in Cuba about alveolitis treated with ozone. They found 46% of patients healed with OLEOZON® and 41% with Alvogil, without significant differences between both groups. The majority of patients needed 2 to 3 visits to consultation in the two groups. Despite efficacy of OLEOZON® is proven, these results do not coincide with those of the current study.

Martínez[21] evaluated microbiologically patients with periodontitis, treated with OLEOZON® and demonstrated its germicidal power by finding a notable decrease of bacterial cargo in the evaluations.

Several authors[10-12] evidence ozone's oxidant power and its application as germicide in its ozonated oil modality by means of preclinical studies which supports its use in clinical assays in medicine and dentistry to control infections.

Pérez[19] describes the clinical changes occurring in the damaged tissue by an infectious process after applying ozone therapy, a fact proven in the study.

Guanche,[16,17] in studies carried out, proposed ozone's mechanisms of actions related to oxidative stress and response to antioxidant systems, as well as the stimulating power of tissue healing or restoration.

Though both, the group treated with OLEPOZON® as well the one treated with Alvogil, progressed satisfactorily, a greater number of patients recovered was achieved in the experimental group compared with the control group. Patients in the experimental group recovered faster than those in the control group.

By analyzing efficacy of both medications, OLEOZON® showed a much better efficacy than Alvogil, due to the high germicidal power of OLEOZON® and its capacity to stimulate tissue restoration.

All patients were satisfied with the treatment whether they were in one group or the other. They indicated the strong smell of OLEOZON® and oily flavor in the mouth but referring that it was not bitter and that relief of symptoms was so rapid that they were pleased with the treatment. Those in the control group did not state anything related to Alvogil medication but showed themselves grateful and satisfied as well.

The study demonstrated that OLEOZON® can be considered as an effective medication in the treatment of alveolitis. It is innocuous and economic, and since it is a national manufactured product, its use can be proposed in the emergency dental services to substitute imports. Likewise, no adverse reactions or side effects to OLEOZON® were found.

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**Annex I.** Random Table

| | | | | |
|---|---|---|---|---|
| 1-B | 21-B | 41-B | 61-B | 81-B |
| 2-B | 22-B | 42-A | 62-B | 82-B |
| 3-A | 23-B | 43-A | 63-A | 83-B |
| 4-B | 24-B | 44-A | 64-B | 84-B |
| 5-A | 25-B | 45-A | 65-A | 85-B |
| 6-A | 26-B | 46-A | 66-A | 86-B |
| 7-B | 27-A | 47-B | 67-B | 87-A |
| 8-A | 28-A | 48-B | 68-A | 88-A |
| 9-A | 29-A | 49-A | 69-A | 89-A |
| 10-B | 30-A | 50-B | 70-B | 90-A |
| 11-B | 31-B | 51-A | 71-B | 91-B |
| 12-B | 32-A | 52-A | 72-B | 92-A |
| 13-A | 33-A | 53-B | 73-A | 93-A |
| 14-A | 34-A | 54-B | 74-A | 94-A |
| 15-A | 35-B | 55-A | 75-A | 95-B |
| 16-A | 36-B | 56-B | 76-A | 96-B |
| 17-A | 37-A | 57-B | 77-A | 97-A |
| 18-B | 38-B | 58-B | 78-B | 98-B |
| 19-A | 39-B | 59-A | 79-A | 99-B |
| 20-B | 40-B | 60-A | 80-B | 100- |

**Annex II.** Informed consent.
"Efficacy of OLEOZON and Alvogil in the treatment of Alveolitis"

Informed consent of the patient (ethics)
I _____ agree to engage in clinical this research.
I have been explained that:

- This is a pharmaceutical of national production.
- Patients included in this research shall be treated with the product and conventional treatment (Alvolgil).
- Entering in the study is absolutely voluntary.
- If I do not agree to this, I shall receive proper medical and dental attention not impairing my relationship with the dentist or health area.
- Though in studies conducted to date no side effects have been shown to the experimental product, the patient must go in to the dentist's office in case any side effect occurs or if treatment fails and shall be guaranteed with all the necessary attention.
- By signing this document I authorize my inclusion within this research and for the record, I sign the document herein.

Done on day_____ of the month of _____of_____.
Signature: _____.
Name and signature of responsible dentist_____.