Observational Study

SUCCESSFUL USE OF OXYGEN-OZONE THERAPY UNDER CT GUIDE ASSOCIATED WITH ALPHA LIPOIC ACID + PALMITOYLETHANOLAMIDE AND MYRRH IN A 3-YEAR COHORT OF PATIENTS WITH FIRST-DEGREE SPONDYLOLISTHESIS SECONDARY TO SPONDYLOLYSIS

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ABSTRACT

In recent years, there has been an increase in reports on the use of oxygen-ozone therapy for the treatment of non-discogenic low back pain. The aim of our observational study was to compare the therapeutic efficacy of combined oxygen-ozone treatment with the oral administration of 800 mg/day of alpha-lipoic acid (ALA), 600 mg/day of palmitoylethanolamide (PEA), and 200 mg of myrrh in patients with first-degree spondylolisthesis secondary to spondylolysis, against the results obtained with oxygen-ozone treatment alone. From March 2021 to March 2024, we recruited 286 patients diagnosed with first-degree spondylolisthesis secondary to spondylolysis, confirmed through CT and/or MRI studies. All patients were experiencing low back pain and sciatica. Specifically, we treated 161 men and 125 women, aged between 36 and 74 years (mean age: 47.6). All participants in the study received Oxygen-Ozone Therapy, monitored by CT, along with an oral regimen of alpha-lipoic acid (ALA), palmitoylethanolamide (PEA), and myrrh, taking two capsules per day for 30 days. The 286 treated patients were evaluated at the time of recruitment using the Visual Analog Scale (VAS). Clinical outcomes were assessed in the long term at six months, utilizing both the VAS and the modified MacNab method. The results obtained were then compared with those reported in the literature for patients receiving only oxygen-ozone treatment under CT guidance. The VAS questionnaire showed satisfactory clinical results after treatment (M = 8.47, SD = 0.76 pre-treatment; M = 2.48, SD = 1.32 after treatment). These data were also confirmed using the modified Mac Nab method, with which we obtained an excellent result in 185 (64.70%), while in 40 it was satisfactory (13.95%). Out of 286 patients, 38 patients (13.3%) did not report any benefit as reported by the VAS test. These results were then compared with those reported in the literature with oxygen-ozone treatment alone. In light of the results obtained from our observational study involving 286 patients, we compared our findings, combining Oxygen-Ozone Therapy under CT guidance with oral administration of ALA, PEA, and myrrh, to data reported in the literature regarding oxygen-ozone therapy alone. We conclude that this combination therapy results in further improvement over the already excellent outcomes achieved with oxygen-ozone treatment alone. Therefore, we consider this therapeutic combination of ALA, PEA, and myrrh to be a valid alternative to standalone oxygen-ozone therapy.

KEYWORDS: *oxygen, ozone, ozone therapy, spondylolysis, spondylolisthesis*

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INTRODUCTION

Oxygen-Ozone (O_2-O_3) therapy for herniated and protruding discs has become a consolidated clinical practice and is utilized in many countries as a first-line therapeutic approach for patients suffering from this condition. Introduced for the first time in 1985, numerous case studies have been published over the years, reporting positive results ranging from 75% to nearly 90% in the treatment of low back pain, with or without sciatica, due to herniated discs (1-11). In the last fifteen years, many reports have also highlighted excellent therapeutic outcomes achieved with O_2-O_3 therapy in treating pathologies of the posterior spinal compartment (12-21).

In fact, there can be numerous etiologies linked to the vertebral pathology of the posterior compartment: pathology of the articular facets, spondylolysis-olisthesis, stenosis of the spinal canal, radicular cysts, intra and interapophyseal synovitis, Baastrup syndrome, etc. (1-3, 6, 8, 9, 11, 16, 17, 20, 21). It is, therefore, essential to reach a precise diagnosis formulated after a careful objective examination and supported by appropriate instrumental tests, such as (in addition to standard spinal radiographs) Computerized Axial Tomography (CT) and/or Nuclear Magnetic Resonance (MRI) (18) (Fig. 1 A-E, Fig. 2 A-C).

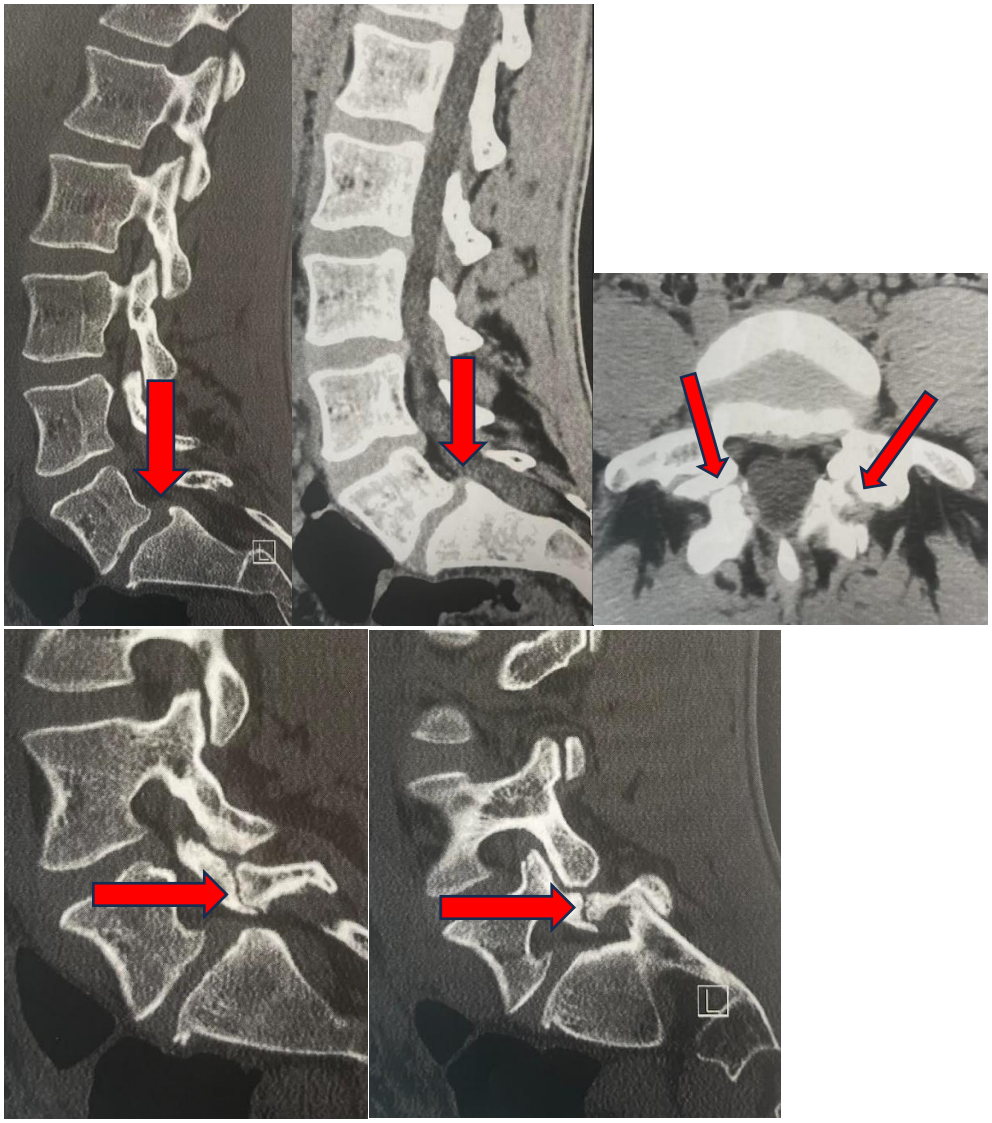

Fig 1. *Meyerding grade I anterolisthesis of L5 on S1 with bilateral isthmic lysis. **A-B**): sagittal reconstructions with algorithms for both bone and parenchyma documenting the listhesis of L5 on S1 (**arrows**); **C**): axial projection documenting bilateral isthmic lysis (**arrows**); **D-E**): sagittal reconstructions with algorithms for bone right (**D**) left (**E**) isthmic lysis (**arrows**).*

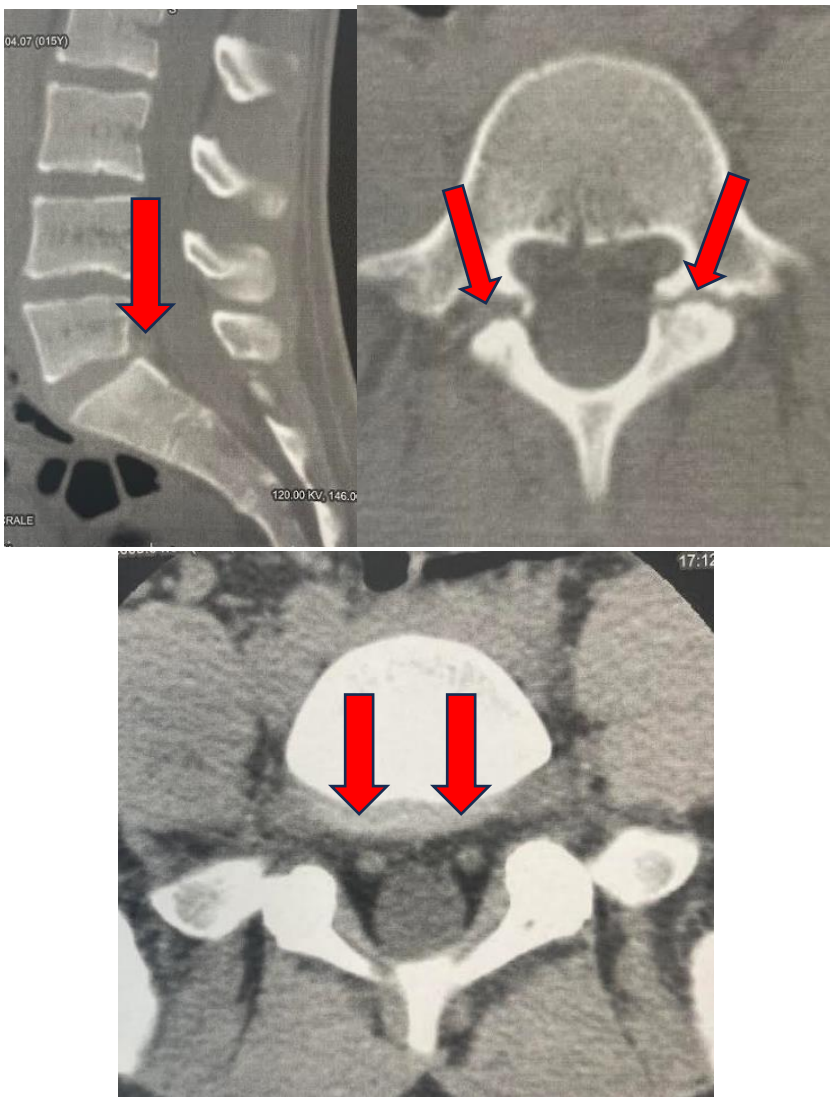

Fig 2. ***A****): millimetric anterolisthesis of L5 on S1 (****arrows****); **B**): bilateral isthmic lysis (****arrows****); **C**): accompanying bilateral paramedian median protrusion (****arrows****).*

As indicated in scientific literature, the therapeutic action of the O_2-O_3 mixture (1-21) is well-established. Furthermore, several studies have also considered the therapeutic potential of ALA, PEA, and myrrh when administered orally in the management of pain (22-37).

ALA has been shown to reduce oxidative stress, thereby preventing damage from oxygen free radicals and providing thioctic acid with a broad spectrum of antioxidant activity (22-35). In contrast, PEA functions as a biological modulator that promotes the physiological response of tissues (36-39). MyrLiq® myrrh is a dry extract derived from the gummy resins of *Commiphora myrrha*, characterized by a high content of bioactive furanodienes, which are preserved through a patented extraction process that maintains the properties of the original raw material (40-42).

In the observational study, the authors present results from treating patients with low back pain and/or sciatica secondary to first-degree spondylolisthesis with associated spondylolysis, which may be responsible for the observed symptoms. The outcomes of CT-guided O_2-O_3 therapy were compared with those from a combined treatment regimen that involved O_2-O_3 therapy, along with oral administration of ALA, PEA, and myrrh over a 30-day period within a three-year cohort. Patients were evaluated long-term, six months post-treatment.

The research design aims to explore the integration of two therapeutic approaches. This association has begun to be studied (21), driven by the intention to optimize patient recovery through a combined approach that addresses immediate symptoms and underlying pathogenic factors.

Long-term observation of patients, six months post-treatment, allows for the assessment of not only the immediate efficacy of the combined therapy but also its sustainability over time. This research design intends to provide more detailed clinical evidence and better understand the mechanisms through which these substances can work synergistically, thus offering a more comprehensive framework for treating chronic pain related to spondylolisthesis and spondylolysis.

MATERIALS AND METHODS

In this observational study, we evaluated the therapeutic efficacy of treatment in patients with first-degree spondylolisthesis (antelisthesis less than 33%), bilateral isthmic lysis (Fig. 2 A-B-C), and associated disc pathology (herniated disc or protrusion). The treatment comprised oxygen-ozone therapy administered under CT guidance, combined with alpha lipoic acid (ALA), palmitoylethanolamide (PEA), and oral myrrh for 30 days in a cohort of patients.

Clinical evaluations were conducted using the Visual Analog Scale (VAS) questionnaire and the modified MacNab method both prior to treatment and six months post-therapy. We then compared the results of our treatment approach with those reported in the literature for cases that involved only CT-guided infiltrative treatment with oxygen-ozone therapy.

Infiltration technique

Following the acquisition of written informed consent from the participants, the appropriate injection level was determined based on comprehensive neuroradiological findings and the presenting clinical symptoms. This selected level was further confirmed through preliminary computed tomography (CT) scans conducted with the patient positioned in the prone stance, enabling accurate identification of the needle entry point.

Subsequently, the skin over the targeted site was meticulously disinfected with a polyvinylpyrrolidone iodine solution, after which local anesthesia was administered via ethyl chloride spray to ensure patient comfort during the procedure. A CT-guided puncture was then executed utilizing 22-gauge needles, with real-time CT guidance employed to verify the precise positioning of the needle within the anatomical structures (Fig. 3, 4).

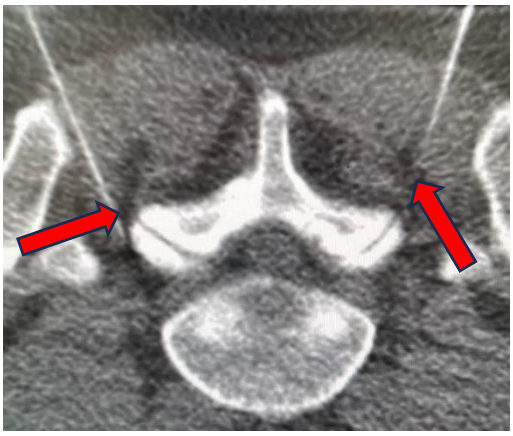

Fig 3. *CT scan check of correct needle placement (**arrows**).*

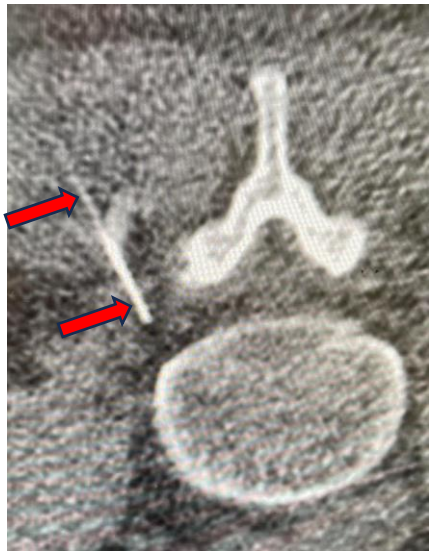

Fig 4. *CT scan check of correct needle placement (**arrows**).*

To uphold stringent aseptic standards, a 10 ml polyethylene syringe was prepared, containing a 3 ml oxygen-ozone gas mixture at 25 µg/ml concentration. This mixture was injected through a microporous filter to minimize any potential contamination risk during the procedure.

Following the infiltration, additional CT scans were performed to confirm the correct distribution of the gas mixture at the designated treatment site, ensuring that the therapeutic agent was adequately administered (Fig. 5, 6). Post-procedure, the patient was observed for approximately 30 minutes to monitor for any immediate adverse effects or complications, after which they were safely discharged.

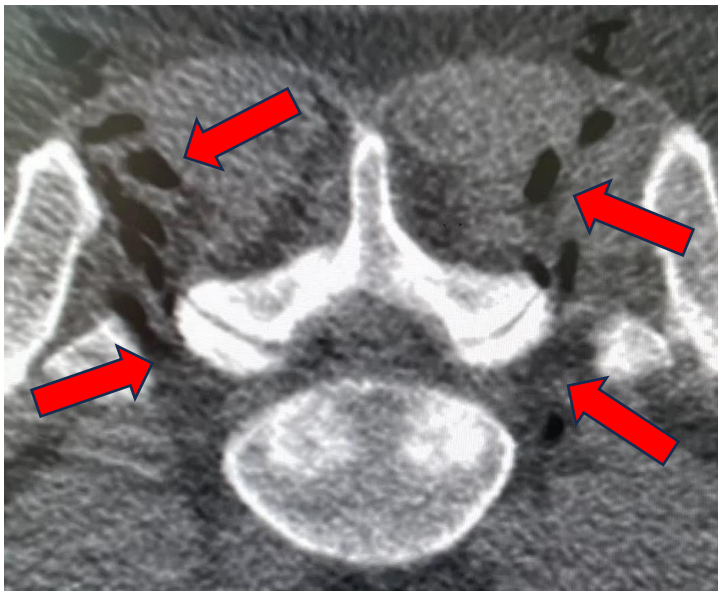

Fig 5. *Control of the gas mixture distribution at the foraminal level and in correspondence with the paravertebral muscles (**arrows**).*

The clinical outcomes in all patients were assessed through long-term follow-up over six months. This evaluation was conducted using a modified version of the McNab method (Table I). The Visual Analog Scale (VAS) questionnaire was utilized to quantify pain levels.

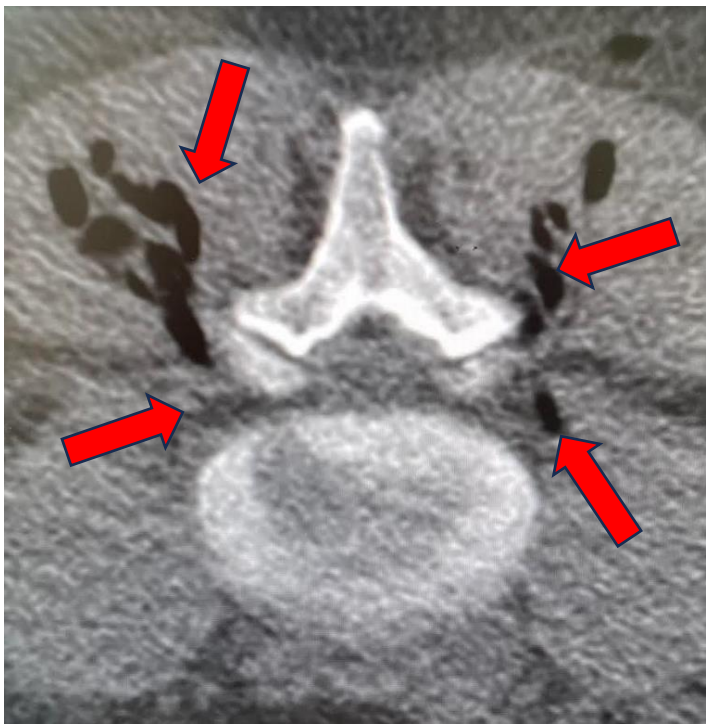

Fig 6. *Control the gas mixture distribution at the foraminal level and in correspondence with the paravertebral muscles (**arrows**).*

Table I. *Modified McNab method.*

Items	Explanation
a) Excellent	Resolution of pain and return to normal activities performed prior to the onset of pain.
b) Good or Satisfactory	Pain reduction greater than 50%.
c) Fair or Poor	Partial pain reduction of less than 50%.

RESULTS

Analysis of results

After therapy with local O_2-O_3 infiltrations and the use of ALA, PEA, and myrrh, as for the experience of pain measured by the VAS scale, the ratings before treatment ranged from 7 to 9, with a mean score of 8.47 (SD = 0.76), while after treatment the mean score was 2.48 (SD = 1.32). Only 38 patients (13.3%) reported no benefit, as indicated by VAS scores that were unchanged (Table II, III).

Table II. *VAS test results before treatment.*

Instrument Scale	*Mean Score (Standard Deviation)*	*Range Of Scores*
VAS	8.47 (0.76)	7-9

Table III. *VAS test results after treatment.*

Instrument Scale	*Mean Score (Standard Deviation)*	*Range Of Scores*
VAS	2.48 (1.32)	1-7

Using the modified Mac Nab method in the long term (clinical follow-up at 6 months), 185 patients (64.70%) continued to report an excellent clinical result obtained with the therapy, while 40 (13.95%) reported a satisfactory result, and 61 (21.35%) were patients who had not experienced substantial benefits (Table IV).

Table IV. *McNab test results after treatment.*

	O_2-O_3 treatment and ALA+PEA+Mirrh in 286 patients		
outcome	*excellent*	*good*	*poor*
at 6 months	185 (64.70%)	40 (13.95%)	61 (21.35%)

In particular, the control CT in patients who, in addition to listhesis, presented a herniated disc (84 patients, 29.33% of the total) documented a complete dehydration of the hernia in 50 patients (17.48 % of the total), obviously without any change in the degree of listhesis. After six months, we requested a neurosurgical evaluation of the situation, and in 17 cases (5.94%), the neurosurgeon-surgeon colleague opted for a spinal stabilization intervention, while in 40 cases (13.99%), the patients continued exclusively a rehabilitation program of physiokinesitherapy.

DISCUSSION

In this observational study, we compared the results obtained with the combined treatment of oxygen-ozone under CT guidance associated with oral treatment with ALA+PEA+myrrh in 286 patients monitored six months after the end of therapy using both the VAS questionnaire and the modified Mac Nab method and then compared the results obtained with those recommended in the literature with oxygen-ozone treatment alone.

In literature, at a six-month clinical follow-up, studies analyzing the association between O_2-O_3, ALA, PEA, and myrrh demonstrated effectiveness from an exclusively analgesic perspective in 58.3% (21) of the treated patients. Our study achieved a therapeutic success rate of 78.65%.

In this regard, we believe that intraforaminal ozone administration in CT-guided mode guarantees perfect control of the needle path. In this regard, the possibility of curative oxygen-ozone is high for the improvement of local circulation with eutrophication in the proximity of the nerve root, compressed and suffering from both muscle spasms. It can normalize the level of cytokines and prostaglandins with anti-inflammatory and analgesic action. It increases the production of superoxide dismutase (SOD) with minimization of oxidizing reagents (ROS). Finally, the proximity to the herniated/protruded material causes accelerated dehydration or destruction of non-vascularized tissue that justifies the good final result.

Therefore, confirming how the rapid resolution of pain without complications, the ease of execution of the method and the complete control of the infiltration by CT allow today to propose the technique of oxygen-ozone therapy guided by CT as a method of choice among conservative therapies in the treatment of first-degree spondylolisthesis with associated spondylolysis.

The association with a minimally invasive therapy such as oxygen-ozone therapy under CT and the oral administration

of 800 mg/day of ALA + 600 mg/day of PEA + 200 mg of myrrh to these patients can be considered an excellent therapeutic solution capable of further improving the good final clinical result with better control of symptoms. Certainly, this result is attributable to the combined action of ALA+PEA+myrrh which consists in further and effectively alleviating neuropathic symptoms.

Based on the results we obtained in this observational study on a sample of 286 patients, we believe this additional therapeutic option can be offered to patients with Meyerding's first-degree listhesis. We also believe that to obtain a satisfactory clinical result, a multidisciplinary therapeutic approach to this problem is highly effective and that the support of the physiotherapist colleague is essential to plan a subsequent postural re-education intervention aimed at maintaining the acquired therapeutic result over time. In cases where the therapeutic result has been poor or unsatisfactory, in addition to the intervention of the physiatrist colleague, a neurosurgical reassessment of the situation is essential to decide whether or not a spinal stabilization intervention is necessary.

CONCLUSIONS

In consideration of the findings from our observational study involving 286 patients who were evaluated six months post-therapy, we analyzed the therapeutic outcomes associated with a treatment regimen that incorporated O_2-O_3 therapy administered under CT guidance, in conjunction with the oral supplementation of ALA, PEA and myrrh.

Subsequently, we performed a comparative analysis of our results with existing data in the literature pertaining to the efficacy of O_2-O_3 therapy as a standalone treatment.

Our investigation indicates that the combination of these oral adjuncts, i.e., ALA, PEA, and myrrh, yields a significant enhancement of the already favorable outcomes observed with O_2-O_3 therapy alone. Thus, we can conclude that this integrated approach not only maintains but also amplifies the therapeutic benefits of O_2-O_3 treatment in patients with the specified conditions.

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