



Original Article

# COMBINED TREATMENT OF RHIZARTHROSIS WITH LOCAL INFILTRATIONS OF OXYGEN-OZONE AND TOPICAL APPLICATIONS OF ALFA-LIPOIC ACID, CAPSAICIN, CANNABIDIOL, BETA-CARYOPHYLLENE, AND MYRRH

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## ABSTRACT

We describe our experience in the combined treatment of rhizarthrosis with local oxygen-ozone infiltrations and topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh. From March 2022 to December 2023, we selected 58 patients with a diagnosis of rhizarthrosis confirmed by both clinical examination and radiographic findings with standard radiograms of the metacarpal trapezium joint. We treated 43 females and 15 males aged between 49 and 79 years (mean 61.9). Of the patients included, 13 treatments of rhizarthrosis were carried out in both hands (22.41%). The patients included in the study were treated with oxygen-ozone (O<sub>2</sub>-O<sub>3</sub>) infiltrations of the trapezium metacarpal joint – six to ten treatments every two weeks – followed by topical treatment by self-applying the cream on the affected parts three times a day, massaging delicately until completely absorbed. Clinical outcomes were measured using the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire and the Visual Analogue Scale (VAS) scale. The analysis of the results of the DASH questionnaire showed improvement in the perceived disability associated with the symptoms (M = 81.00; SD = 1.77 pre-treatment; M = 17.94; SD = 1.60 after treatment). The VAS questionnaire also showed satisfactory clinical results after treatment (M = 8.31; SD = 0.73 pre-treatment; M = 2.90; SD = 0.73 after treatment). Of 58 patients, 6 (10.34%) reported no benefit and were candidates for possible surgery. These findings suggest that oxygen-ozone therapy with topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh can be considered an ideal treatment for rhizarthrosis.

**KEYWORDS:** oxygen ozone, ozone therapy, rhizarthrosis; thumb osteoarthritis; trapeziometacarpal joint

## INTRODUCTION

Rhizarthrosis is a very common and painful pathology: it consists of degenerative arthritis of the base of the thumb with inflammation, joint swelling, and pain caused by joint instability.

This very common pathology, first described by Forestier in 1937 (1), affects approximately 20% of the adult population, especially women (female:male ratio 4:1, between the fifth and seventh decade of life). In women, it appears more frequently after menopause, while in men, it is more linked to overuse (2-6).

Rhizarthrosis commonly affects one side. The trapezoid-metacarpal joint plays a fundamental role: all gripping actions lead to overloading the trapezoid-metacarpal joint since the thumb axis exerts force and fulcrum at this point. This force transmits stress in a radial direction to the base of the first metacarpal, which over time causes a reduction in the tension of the capsulo-ligamentous apparatus, joint hyperlaxity, and subluxation of the first metacarpal on the trapezium.

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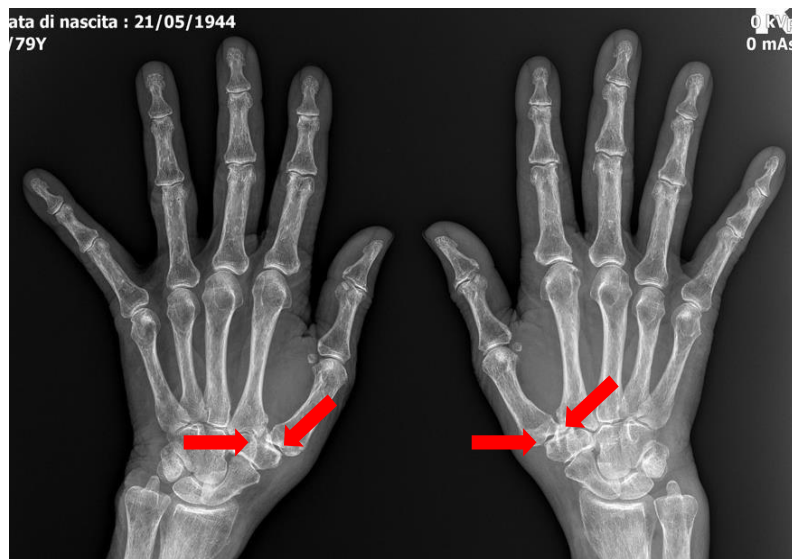
The preternatural movement of the bone heads alters the articular surface, and there is a progressive reduction in cartilaginous thickness, the appearance of pain, and arthrosis.

Patients complain of pain at the base of the thumb when performing daily activities such as turning a key, opening a car door, picking up a book, or threading a needle. People who suffer from this pathology tend to drop objects and feel a loss of strength between their thumb and forefinger. Joint deformity is very painful and can even prevent sleep. Therefore, normal functions of the thumb, such as gripping and fine joint movements like drawing and embroidery, are compromised, significantly impacting the patient's quality of life.

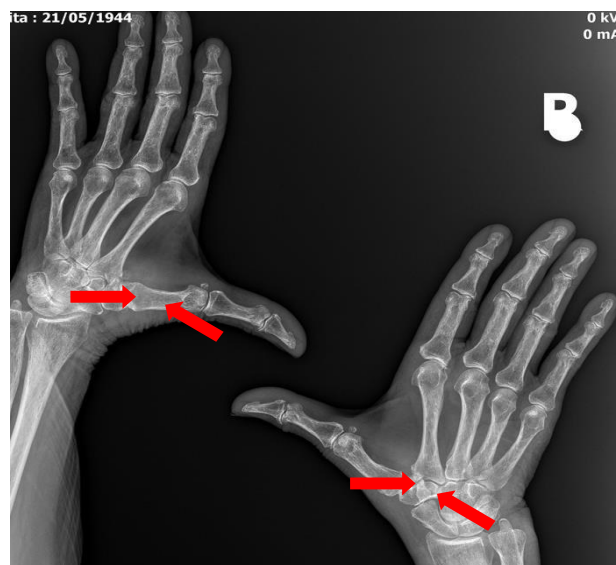
Conservative management includes the administration of anti-inflammatory drugs, splints to immobilize the joint, or intra-articular cortisone injections temporarily. A specific palmar splint may be of therapeutic use to block the joint, at least at night. Analgesics like paracetamol and non-steroidal anti-inflammatory drugs may also be helpful in the most painful stages. Local treatment with hyaluronic acid injections has also proved effective (7-16). In case of failure, surgery is performed. The most satisfying surgery is the so-called biological arthroplasty (17-25).

Rhizarthrosis can be so painful that, in the most severe cases, it is necessary to resort to surgery. Pain can regress after many years, at the cost of stiffness in adduction of the first metacarpal and hyperextension of the phalangeal metacarpal of the thumb.

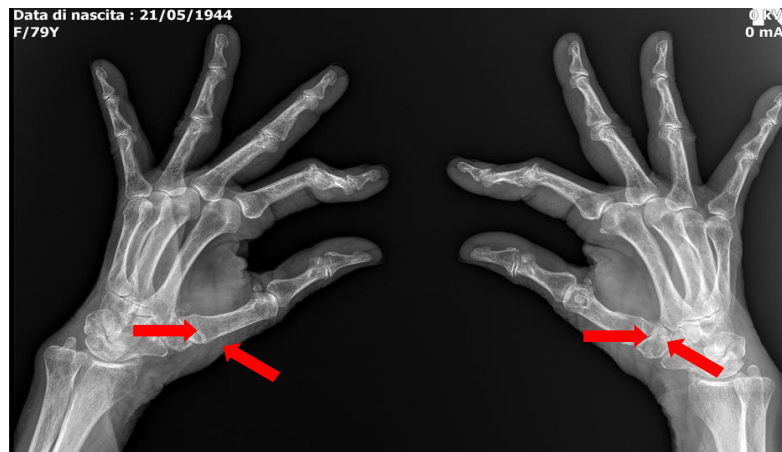
The diagnosis of rhizarthrosis is clinical and radiographic, with the use of anteroposterior and oblique radiographs and the Kapandji projection to evaluate the thumb base joint (Fig.1-3), according to the Eaton-Littler setup modified by Brunelli (Table I).



**Fig. 1.** Antero-posterior radiograph projection of both hands documenting grade 2 bilateral rhizarthrosis with slight reduction of joint space (arrows).



**Fig. 2.** Kapandji radiographic projections of both hands documenting grade 2 bilateral rhizarthrosis with slight reduction of joint space (arrows).



**Fig. 3.** Latero-lateral radiographic projection of both hands documenting grade 2 bilateral rhizarthrosis with slight joint space reduction.

**Table I.** Radiographic staging according to Eaton-Littler.

Grade 1	Normal joint surfaces, with increased joint space due to synovitis
Grade 2	Reduction of joint space due to deficit or laxity of the ligaments
Grade 3	Marked narrowing of the joint rim, subchondral cystic formations, bone sclerosis, and subluxation of the first metacarpal with respect to the trapezium greater than 2 mm. Trapezoid scaphoid joint intact.
Grade 4	Complete joint deterioration, associated with involvement of the trapezoid-scaphoid.

Over the years, natural products have contributed enormously to developing important therapeutic drugs currently used in modern medicine.

Alpha-lipoic acid (ALA), which, as is known, is a natural sulfur compound produced in small concentrations by all cells. ALA is a key compound in some mitochondrial enzyme complexes (pyruvate dehydrogenase and ketoglutarate dehydrogenase), which play a central role in oxidative metabolism. ALA can reduce oxidative stress, preventing damage caused by oxygen free radicals. Unlike other antioxidants that fully function in aqueous or fatty tissues, ALA exerts its antioxidant function in water and fats. This property gives lipoic acid a broad spectrum of antioxidant action (26-31).

Capsaicin is an organic compound in chili peppers, which is responsible for their spicy flavor. There are various beneficial properties attributed to capsaicin; it can bind to some pain receptors, desensitizing them, so much so that it has now consolidated pain-relieving properties.

Cannabidiol (CBD) is a non-psychoactive component of Cannabis with proven anti-inflammatory action (32-34).  $\beta$ -caryophyllene (BCP) is a plant compound, a member of bicyclic sesquiterpene. In nature, it mainly occurs as trans-caryophyllene (E)-BCP mixed with small amounts of its isomers, (Z)- $\beta$ -caryophyllene (iso-caryophyllene) and  $\alpha$ -humulene ( $\alpha$ -caryophyllene), as well as its oxidation derivative,  $\beta$ -caryophyllene oxide (BCPO). BCP-induced effect of analgesia is obtained with endocannabinoid system (ECS) involvement. BCP binds to peripheral cannabinoid receptor type 2 (CB2), leading to  $\beta$ -endorphin release from keratinocytes and activation of opioid receptors (35-36).

Myrrh is a natural compound secreted by shrubs of the *Commiphora* genus of the Burseraceae, whose analgesic effect has long been known. Myrrh is a dry extract with a high content of bioactive furanodienes obtained through a patented extraction process, which allows the preservation of all the properties of the original raw material (37).

Excellent results were recently obtained with treatment with oxygen-ozone therapy in rhizarthrosis. The rationale for anti-inflammatory treatment by intraarticular oxygen-ozone infiltration is based on an attempt to relieve the inflammation with analgesic action. The oxygen-ozone gas mixture injected is thought to normalize the level of cytokines and prostaglandins, increase superoxide dismutase (SOD), minimize reactive oxidant species (ROS), and improve local circulation with a eutrophic effect (38-45).

In this observational study, we wanted to evaluate the clinical results obtained in the treatment of 58 selected patients diagnosed with rhizarthrosis treated with oxygen-ozone therapy and topical applications of alfa-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh.

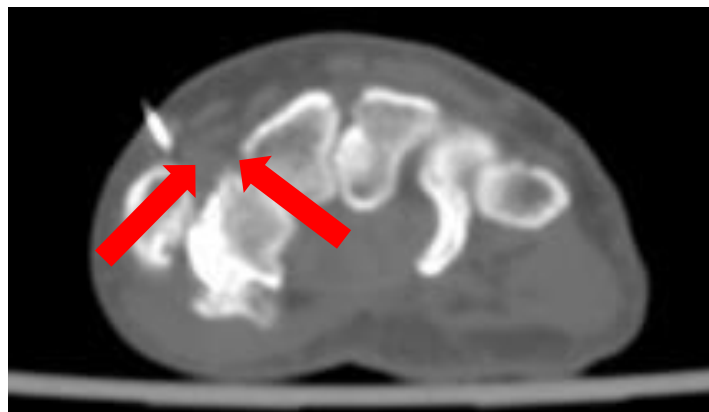
## MATERIALS AND METHODS

We describe our experience treating rhizarthrosis by administering oxygen-ozone (O<sub>2</sub>-O<sub>3</sub>) and topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh.

We treated 58 patients between March 2022 and December 2023. with a diagnosis of rhizarthrosis confirmed both by clinical examination and by radiographic findings with standard hand radiographs; in particular, we treated 43 females and 15 males between 49 years and 79 years (average age: 61.9).

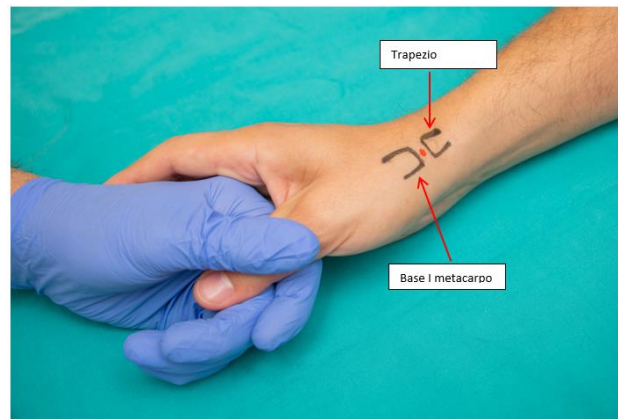
Subject to informed consent to the treatment, we proposed a therapeutic path with local injection with oxygen-ozone at a concentration of 20 µg /ml and topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh.

For the treatment with O<sub>2</sub>-O<sub>3</sub>, we used 25 G 5/8 orange Terumo code needles, injecting the gaseous mixture at a concentration of 20 µg/ml directly into the trapezoid metacarpal joint. The first treatment was always performed under CT guidance to ensure perfect joint access and control the distribution of the gas mixture (Fig. 4).



**Fig. 4.** *The first treatment is performed with CT guidance to identify the trapezium and base of the first metacarpal correctly. The infiltration point is marked with a dermographic pencil. Using CT, it is possible to verify the correct positioning of the needle (arrows).*

Once the correct entry point was identified, it was marked on the skin with a dermographic pencil, and this point remained constant for subsequent treatments (Fig. 5, 6). On average, six to ten oxygen-ozone injections were given twice a week, depending on the severity: 26 (44.8 %) patients received six treatment sessions, 11 (19%) received eight, and the remaining 21 (36.2 %) had ten injections. Since the area to be treated is susceptible, local anesthesia was administered via ethyl chloride spray before infiltration.



**Fig. 5.** With a dermographic pencil, identify the trapezium and the base of the first metacarpal,



**Fig. 6.** Infiltration with an oxygen-ozone mixture.

All patients tolerated the injections well and then underwent clinical follow-up one month after the end of treatment. Following the treatment with oxygen-ozone, topical application of a cream containing alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh was carried out on the affected parts, massaging delicately until completely absorbed. The applications were carried out 3 times a day, approximately every 8 hours. They were always well-tolerated, with an immediate sensation of relief on the skin thanks to the calming effect linked to the antioxidant properties of alpha-lipoic acid and the hydrating properties.

To fully evaluate the experience of pain, it is important to assess patients' perceived disability associated with the symptoms and involve them actively in rating their algic experience. To this regard, we decided to adopt two self-report surveys, both of which have demonstrated adequate metric properties in literature, both in terms of validity and reliability.

During the treatment period, we consensually decided with the patient to suspend any anti-inflammatory therapies in progress. Every participant was asked to fill out the DASH (46-48) questionnaire before starting treatment with  $O_2-O_3$  – on the occasion of the first medical consultation – and one month after the end of the treatment (Table II). The experience of pain was assessed before and after treatment using the VAS scale (49-51), with the same timing applied to the DASH.



**Table II.** DASH questionnaire.

<b>DISABILITIES OF THE ARM, SHOULDER AND HAND</b>					
Please rate your ability to do the following activities in the last week by circling the number below the appropriate response.					
	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. Open a tight or new jar.	1	2	3	4	5
2. Write.	1	2	3	4	5
3. Turn a key.	1	2	3	4	5
4. Prepare a meal.	1	2	3	4	5
5. Push open a heavy door.	1	2	3	4	5
6. Place an object on a shelf above your head.	1	2	3	4	5
7. Do heavy household chores (e.g., wash walls, wash floors).	1	2	3	4	5
8. Garden or do yard work.	1	2	3	4	5
9. Make a bed.	1	2	3	4	5
10. Carry a shopping bag or briefcase.	1	2	3	4	5
11. Carry a heavy object (over 10 lbs).	1	2	3	4	5
12. Change a lightbulb overhead.	1	2	3	4	5
13. Wash or blow dry your hair.	1	2	3	4	5
14. Wash your back.	1	2	3	4	5
15. Put on a pullover sweater.	1	2	3	4	5
16. Use a knife to cut food.	1	2	3	4	5
17. Recreational activities which require little effort (e.g., cardplaying, knitting, etc.).	1	2	3	4	5
18. Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g., golf, hammering, tennis, etc.).	1	2	3	4	5
19. Recreational activities in which you move your arm freely (e.g., playing frisbee, badminton, etc.).	1	2	3	4	5
20. Manage transportation needs (getting from one place to another).	1	2	3	4	5
21. Sexual activities.	1	2	3	4	5

DISABILITIES OF THE ARM, SHOULDER AND HAND					
	NOT AT ALL	SLIGHTLY	MODERATELY	QUITE A BIT	EXTREMELY
22. During the past week, to what extent has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups? (circle number)	1	2	3	4	5
	NOT LIMITED AT ALL	SLIGHTLY LIMITED	MODERATELY LIMITED	VERY LIMITED	UNABLE
23. During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem? (circle number)	1	2	3	4	5
Please rate the severity of the following symptoms in the last week. (circle number)					
	NONE	MILD	MODERATE	SEVERE	EXTREME
24. Arm, shoulder or hand pain.	1	2	3	4	5
25. Arm, shoulder or hand pain when you performed any specific activity.	1	2	3	4	5
26. Tingling (pins and needles) in your arm, shoulder or hand.	1	2	3	4	5
27. Weakness in your arm, shoulder or hand.	1	2	3	4	5
28. Stiffness in your arm, shoulder or hand.	1	2	3	4	5
	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	SO MUCH DIFFICULTY THAT I CAN'T SLEEP
29. During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? (circle number)	1	2	3	4	5
	STRONGLY DISAGREE	DISAGREE	NEITHER AGREE NOR DISAGREE	AGREE	STRONGLY AGREE
30. I feel less capable, less confident or less useful because of my arm, shoulder or hand problem. (circle number)	1	2	3	4	5

**DASH DISABILITY/SYMPТОM SCORE** =  $\frac{(\text{sum of } n \text{ responses}) - 1}{n} \times 25$ , where n is equal to the number of completed responses.

A DASH score may not be calculated if there are greater than 3 missing items.

## RESULTS

All patients included in the study were clinically evaluated before treatment and one month after the end of the therapy. Analyzing the results of the first access to the clinic, the DASH evaluation reported, in most of the skills tested, considerable difficulties and very significant disability (e.g., unscrewing a tightly closed lid) with an average score of 81.00 (SD = 1.77) out of 100. After the therapy with local infiltrations of oxygen-ozone and topical applications of alfa-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh, the skills in daily activities were generally reported in association with lower complications (Mean DASH score after treatment: 17.94; SD = 1.60). Regarding the experience of pain measured by the VAS scale, the ratings before treatment ranged from 7 to 9, with a mean score of 8.31 (SD = 0.73), while after treatment, the mean score was 2.90 (SD = 1.36). Only 6 patients (10.34%) reported no benefit and were candidates for possible surgery (Tables III-VIII).

**Table III.** DASH and VAS test results before treatment.

<i>Instrument Scale</i>	<i>Mean Score (Standard Deviation)</i>	<i>Range Of Scores</i>
DASH	81.00 (1.77)	76-87
VAS	8.31 (0.73)	7-9

**Table IV.** DASH and VAS test results after treatment.

<i>Instrument Scale</i>	<i>Mean Score (Standard Deviation)</i>	<i>Range Of Scores</i>
DASH	17.94 (1.60)	12-20
VAS	2.90 (1.36)	1-6

**Table V.** DASH pre-treat.

<b>Standard Deviation</b>	<b>s = 1.7671466</b>
Variance	s <sup>2</sup> = 3.122807
Count	n = 58
Mean	$\bar{x}$ = 81
Sum of Squares	SS = 178

**Table VI.** DASH post-treat..

<b>Standard Deviation</b>	<b>s = 1.6050623</b>
Variance	s <sup>2</sup> = 2.576225
Count	n = 58
Mean	$\bar{x}$ = 17.948276
Sum of Squares	SS = 146.84483

**Table VII.** VAS pre-treat.

<b>Standard Deviation</b>	<b>s = 1.3852564</b>
Variance	s <sup>2</sup> = 1.9189353
Count	n = 58
Mean	$\bar{x}$ = 2.8965517
Sum of Squares	SS = 109.37931

**Table VIII.** VAS post-treat.

<b>Standard Deviation</b>	<b>s = 0.7304624</b>
Variance	s <sup>2</sup> = 0.53357532
Count	n = 58
Mean	$\bar{x}$ = 8.3103448
Sum of Squares	SS = 30.413793

## DISCUSSION

Considering our experience in oxygen-ozone therapy and the well-known mechanism of action of the oxygen-ozone gas mixture in the analgesic purposes of treatment of rhizarthrosis, we aimed to evaluate the results of the action of local oxygen-ozone therapy and topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh (52-55).

In rhizarthrosis, the arthrosis process causes the cartilage that lines the two bones in contact between them (trapezius and first metacarpal bone) to always thin, causing friction, further wear, and pain. In the first phase of the disease, conservative treatment did not propose a single protocol. The main symptom is pain, which appears when the patient performs simple gripping and gripping movements with your thumb, for example, removing the lid of a jar, turning the key in a lock, grasping a door handle, and opening the door of the car.



Studies have demonstrated the beneficial properties of alpha-lipoic acid, capsaicin, cannabidiol,  $\beta$ -Caryophyllene, and myrrh regarding the treatment of musculoskeletal pathologies and the perception of pain associated with it, even in joint treatments with oxygen-ozone therapy infiltrations.

In this observational study, we found that treatment with O<sub>2</sub>-O<sub>3</sub> + topical application of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh allowed to obtain excellent results also confirmed with DASH and VAS evaluations.

In recent years, several studies have demonstrated the usefulness of oxygen-ozone therapy in the treatment of rhizarthrosis as well as the known analgesic potential of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh, acting as biological modulators, favoring the physiological response of fabrics. The curative possibility, therefore, of oxygen-ozone, which is in this regard high due to the improvement of local circulation being able to normalize the level of cytokines and prostaglandins with anti-inflammatory and pain-relieving action, associated with the topical use of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh justifies the excellent result.

From the results obtained, it can be deduced that from the first treatment to the clinical control at thirty days, the association of a minimally invasive therapy such as oxygen-ozone therapy and the topical administration of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh can be considered an excellent therapeutic solution capable of further improving the good final clinical result with better control of symptoms, particularly in the first phase of the disease, to offer a valid conservative alternative to a possible surgical solution.

The results of the present study align with what is reported in the literature, confirming the beneficial effects of the joint action of these therapies, both in terms of pain perception and improvement of the functionality of the trapezium-metacarpal joint.

## CONCLUSIONS

Our findings suggest that oxygen-ozone therapy with topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh can be considered an ideal rhizarthrosis treatment. Although ours is a small cohort, oxygen-ozone treatment of trapezius metacarpal rhizarthrosis appears to be a valid alternative to NSAIDs and/or steroids, especially in the early stage of illness. Further studies could investigate these factors in greater detail in broader samples and randomized controlled studies.

In our opinion, the brilliant results obtained in our series are linked to some of the main activities of oxygen-ozone therapy. The improvement of intra- and trans-tissue oxygenation with consequent improvement of both hypoxia and venous stasis and lymphatic in addition to the well-known anti-inflammatory, analgesic, and eutrophicating activities of ozone. Given these results, we can conclude that oxygen-ozone therapy, associated with topical applications of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh – can be considered an excellent therapeutic approach for patients afflicted with rhizarthrosis.

These promising data, therefore, suggest the usefulness of carrying out a randomized and controlled study to definitively ascertain the efficacy of the topical use of alpha-lipoic acid, capsaicin, cannabidiol, beta-caryophyllene, and myrrh in addition to O<sub>2</sub>-O<sub>3</sub> therapy for the treatment of rhizarthrosis.

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