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2025

8th
International
Symposium
Intra
Articular
Treatment

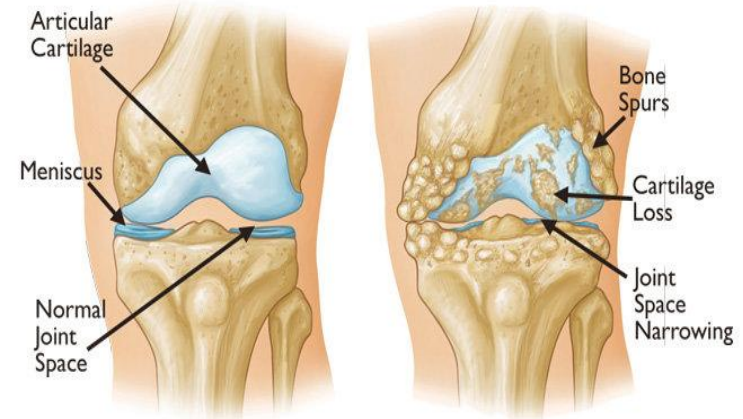


Intra-articular oxygen-ozone therapy: evidence and future perspectives

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- **Osteoarthritis** is a degenerative joint disease characterized by cartilage breakdown, synovial inflammation, subchondral bone changes, and pain with loss of function.
- **Intra-articular injections** are performed to relieve symptoms and improve mobility and functioning:
 - corticosteroids (CS)
 - hyaluronic acid (HA)
 - platelet-rich plasma (PRP)
 - oxygen-ozonotherapy
 - other biologic agents
- Clinical trials and meta-analyses showed that corticosteroid injections provide **short-term relief of pain and stiffness** (e.g. up to 4-6 weeks), but their effects tend to diminish over time and their benefit over placebo is not maintained long term.

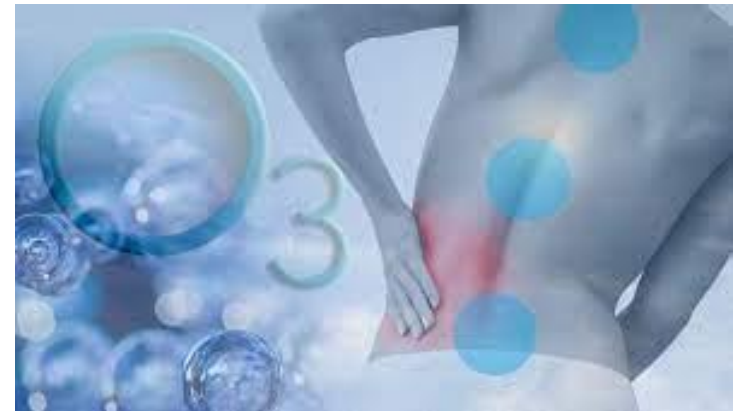


*Bensa et al. J Exp Orthop. 2025
de Sire A et al. J Back Musculoskeletal Rehabil. 2025*



Oxygen-ozone (O_2O_3) therapy:

- method that is old more than a century
- initially relegated to a few operators
- today a remedy used by many doctors and requested by many patients
- recognized as a therapeutic activity





International Journal of
Molecular Sciences

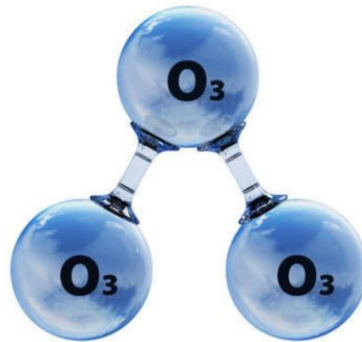


Review

Oxygen-Ozone Therapy for Reducing Pro-Inflammatory Cytokines Serum Levels in Musculoskeletal and Temporomandibular Disorders: A Comprehensive Review

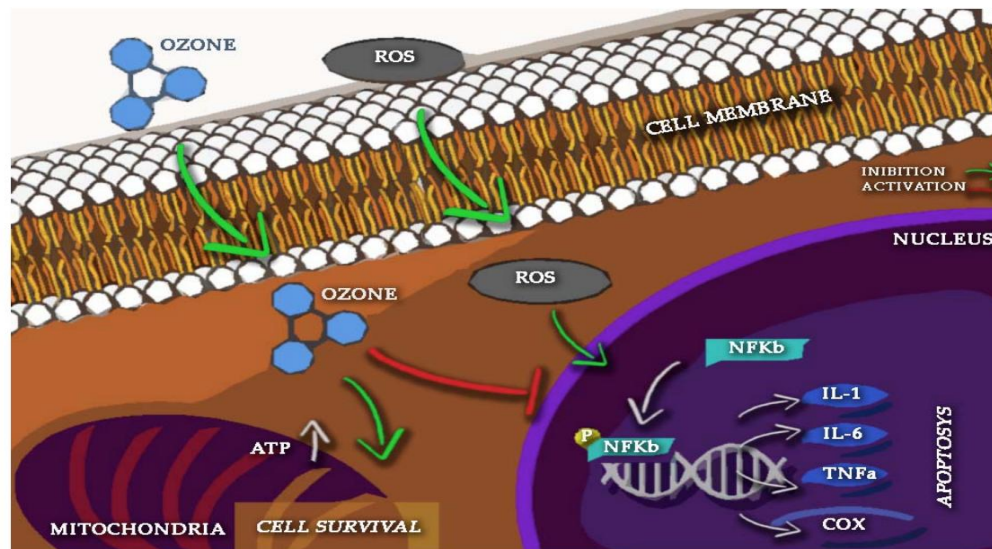
Alessandro de Sire ^{1,*}, Nicola Marotta ¹, Martina Ferrillo ², Francesco Agostini ³, Cristiano Sconza ^{4,5}, Lorenzo Lippi ⁶, Stefano Respizzi ⁴, Amerigo Giudice ², Marco Invernizzi ^{6,7} and Antonio Ammendolia ¹

- O₃ is composed of three oxygen atoms with a cyclic structure.
- It is generated for medical use from pure oxygen passing through a high voltage gradient (5–13 mV) following the reaction: $3\text{O}_2 + 68,400 \text{ cal} \rightarrow 2\text{O}_3$
- The result is a gas mixture composed of no less than 95% oxygen and no more than 5% O₃.
- O₃ is 1.6 times denser and 10 times more soluble in water than oxygen.
- It is an unstable gas that cannot be stored and must be used immediately as it has a half-life of 40 minutes at 20°.
- Like any other gas, O₃ physically dissolves in pure water according to Henry's law with respect to temperature, pressure and ozone concentration.

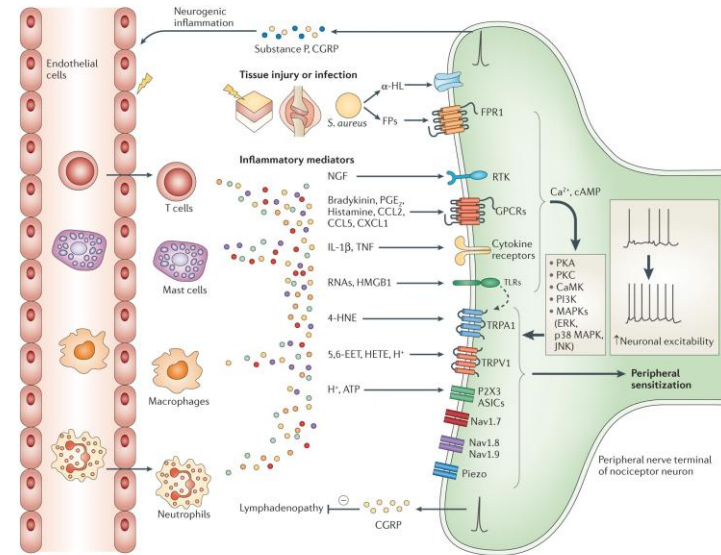
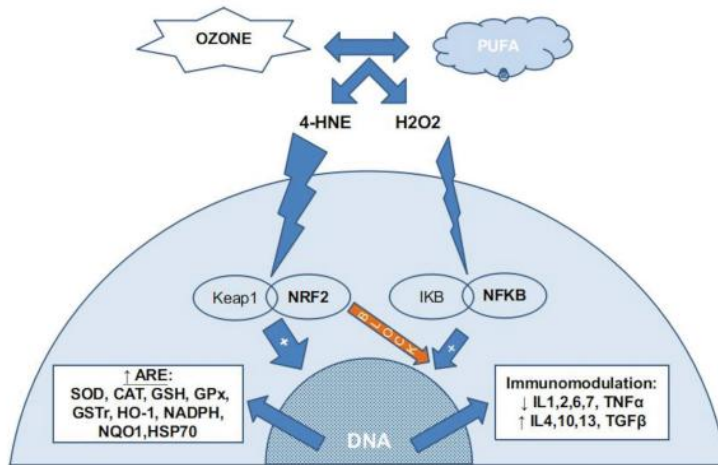


de Sire A. et al. Int. J. Mol. Sci. 2022

- Inhibition of the synthesis of proinflammatory prostaglandins or the release of bradykinin or algogenic compounds
- Neutralization of endogenous ROS by stimulating the local production of antioxidant enzymes
- Inhibition of release of proteinases from macrophages and polymorphonuclear neutrophils
- Increased release of antagonists or soluble receptors capable of neutralizing proinflammatory cytokine arrays
- Reduction of degenerative phenomena through an improvement in micro vascularization and local oxygenation by reduction/resolution of venous stasis - edema - ischemia + pH



de Sire A. et al. *Int. J. Mol. Sci.* 2022



Nature Reviews | Drug Discovery

- Evidence shows that moderate oxidative stress induced by **low doses of ozone** can activate nuclear factor erythroid 2-related factor 2 (**Nrf2**), suppressing transcriptional factor-kappa B (NF-κB) and **reducing inflammatory responses**.

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DOI 10.3233/BMR-245005
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1423

Guest Editorial

Oxygen-ozone therapy for musculoskeletal pain in rehabilitation: Evidence and future perspectives

Marco Invernizzi^{a,b,*} and Alessandro de Sire^{c,d}

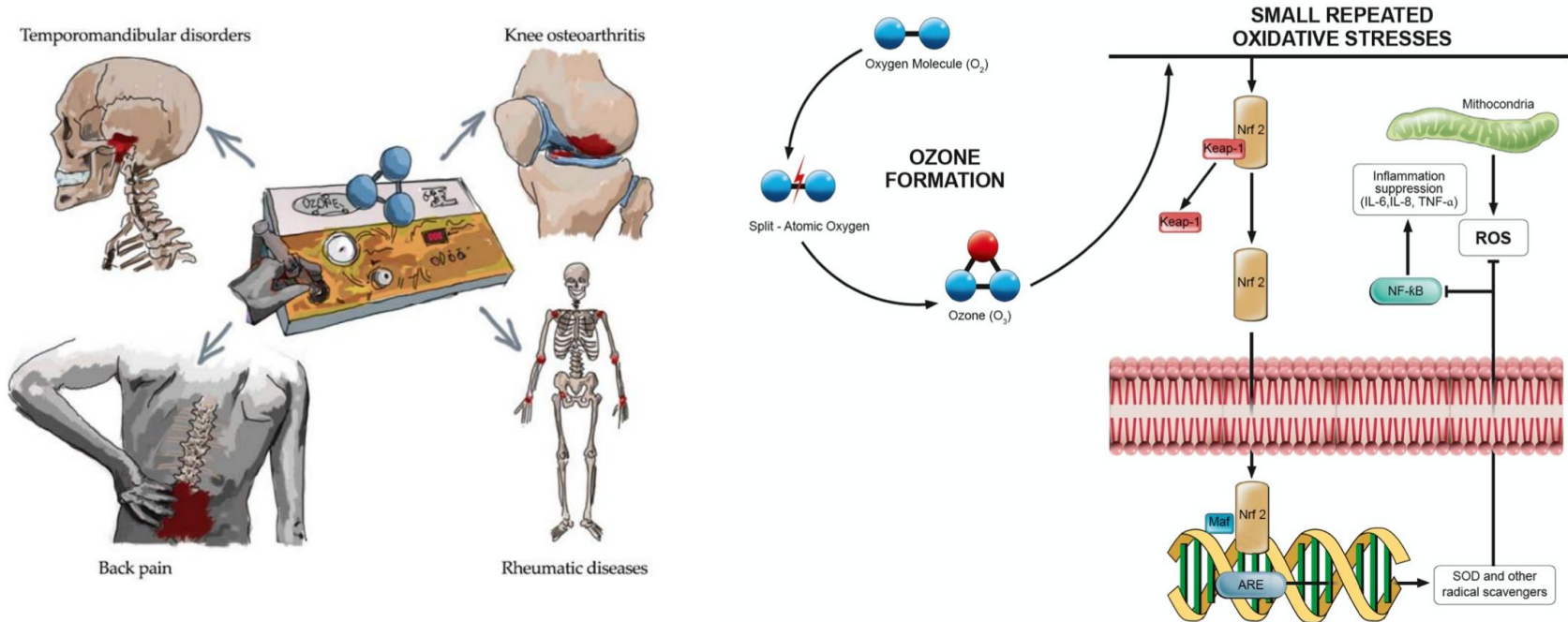
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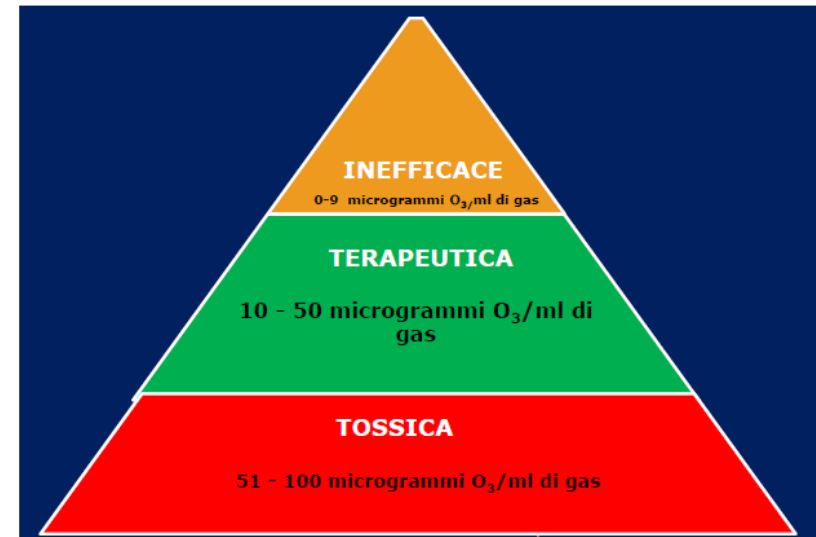
- It is widely recognized that **pain** is a common symptom related to the **inflammatory process** and O₂O₃ therapy could play a key role not only in inflammation management but also in nociceptive perception and modulation
- As far as the analgesic use of O₂O₃ is concerned, after the administration of O₂O₃ an increase in antioxidant molecules (serotonin and endogenous opioids) has been demonstrated, which would induce pain relief by stimulating the antinociceptive pathways



de Sire A. et al. *Int. J. Mol. Sci.* 2022

The **concentration of ozone** and the consequent production ROS/LOP are the main factors of oxygen-ozone therapy:

- Too low ROS/LOP levels are ineffective
- **Moderate ROS/LOP levels induce enzyme activation and are found to be effective and therapeutic**
- Too high ROS/LOP levels are toxic with irreversible cellular damage



Oxygen-ozone therapy through a transient production of oxidants determines a correction of the redox imbalance in chronic oxidative stress pathologies



biomolecules



Review

Oxygen–Ozone Therapy in the Rehabilitation Field: State of the Art on Mechanisms of Action, Safety and Effectiveness in Patients with Musculoskeletal Disorders

Alessandro de Sire ^{1,*}, Francesco Agostini ², Lorenzo Lippi ³, Massimiliano Mangone ², Simone Marchese ², Carlo Cisari ³, Andrea Bernetti ² and Marco Invernizzi ^{3,4}

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- Injections of HA vs O₂O₃: Intra-articular infiltrations of HA appear to be associated with similar pain relief.

*Li Q. et al. Int. J. Surg. 2018.
Hedayatabad, J.J. et al. Arch. Bone Jt. Surg. 2020.*

- The efficacy of O₂O₃ in pain relief is significantly superior to placebo and not statistically different from other treatments (HA, dextrose and air injection). O₂O₃ may have a role in the short-term non-surgical (3-6 months) mild to moderate pain.

*Raeissadat, S.A. et al. J. Pain Res. 2018.
Noori-Zadeh A. Complement. Ther. Med. 2019.*

- Safe and effective technique in reducing pain in the short to medium term.

Sconza C. et al. Arthroscopy 2020.

Randomized Controlled Trial

> Knee Surg Sports Traumatol Arthrosc. 2017 Feb;25(2):485-492.

doi: 10.1007/s00167-016-4110-5. Epub 2016 Apr 7.

Choice of intra-articular injection in treatment of knee osteoarthritis: platelet-rich plasma, hyaluronic acid or ozone options

Tahir Mutlu Duymus¹, Serhat Mutlu², Bahar Dernek³, Baran Komur², Suavi Aydogmus⁴,
Fatma Nur Kesiktas⁵

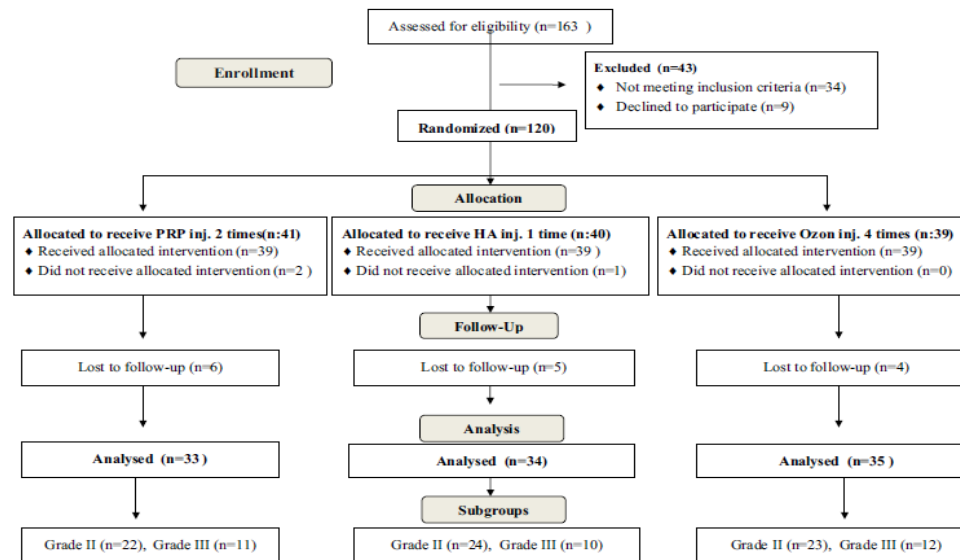
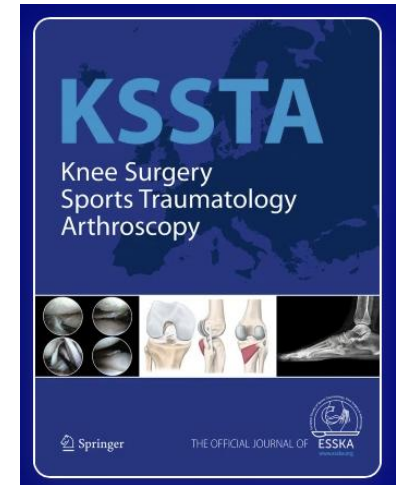




Fig. 2 VAS scores of the groups pre- and post-treatment

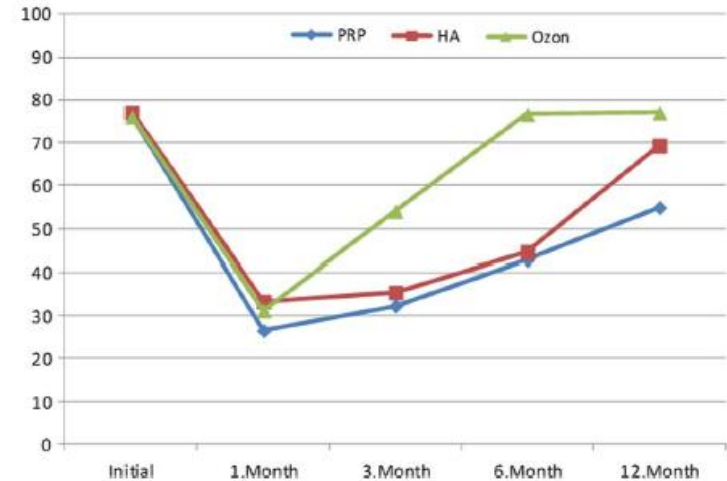


Fig. 3 Total WOMAC scores of the groups before and after treatment

Conclusion In the treatment of mild–moderate knee OA, PRP was more successful than HA and ozone injections, as the application alone was sufficient to provide at least 12 months of pain-free daily living activities.

Level of evidence Therapeutic study, Level I.

Randomized Controlled Trial > J Back Musculoskelet Rehabil. 2020;33(3):347-354.

doi: 10.3233/BMR-181294.

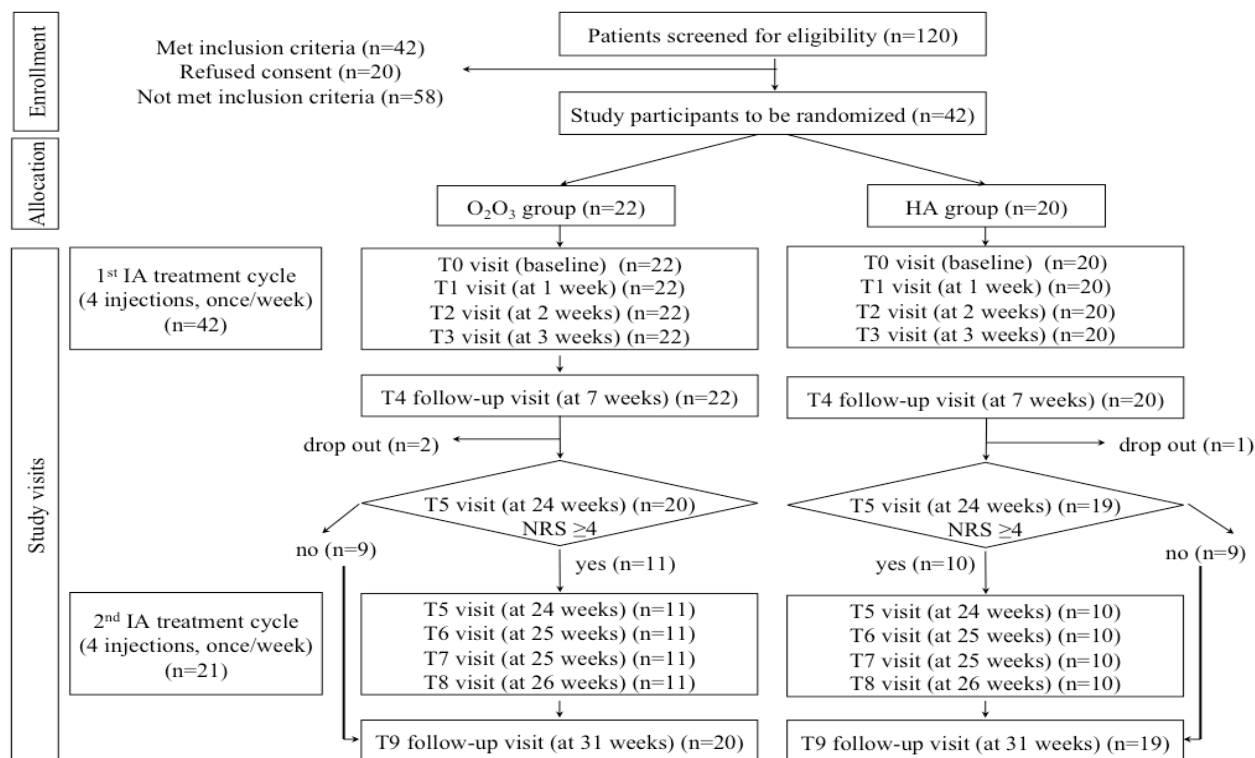
Long-term effects of intra-articular oxygen-ozone therapy versus hyaluronic acid in older people affected by knee osteoarthritis: A randomized single-blind extension study

Alessandro de Sire ^{1 2}, Davide Stagno ¹, Marco Alessandro Minetto ³, Carlo Cisari ^{1 4},
Alessio Baricich ^{1 4}, Marco Invernizzi ¹



de Sire A. et al. J Back Musculoskelet Rehabil. 2020

Figure 1. Study flow chart.



de Sire A et al. J Back and Musc Rehab 2020

A. de Sire et al. / Long-term effects of intra-articular oxygen-ozone therapy versus HA in older people affected by KOA

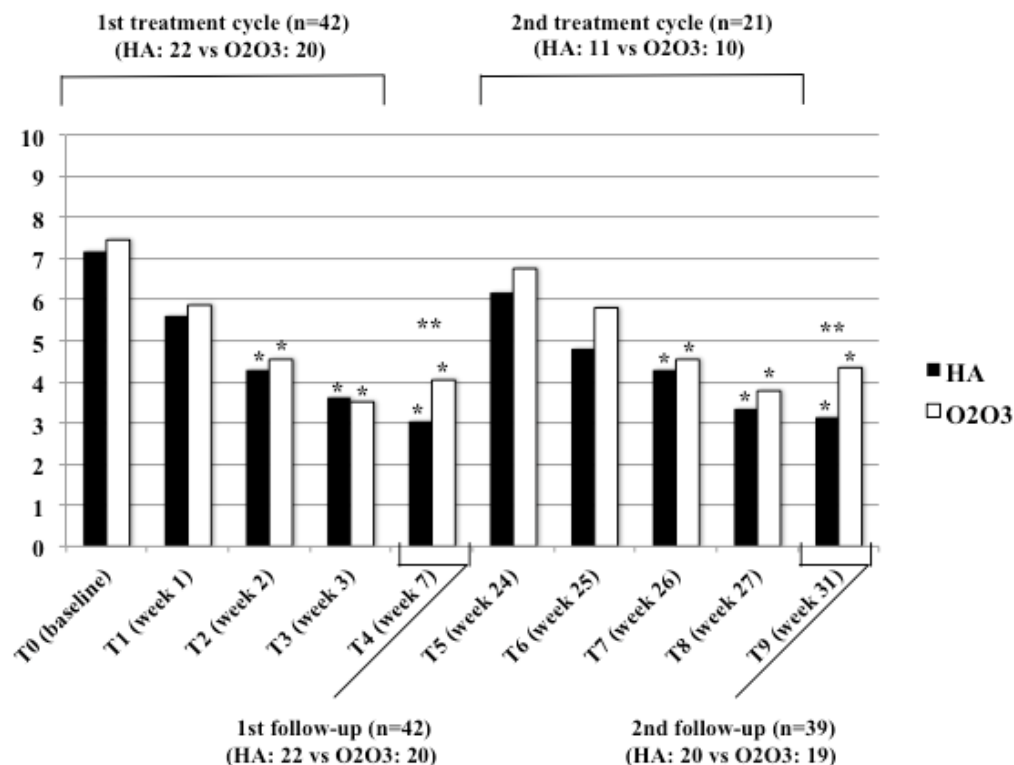
Table 1
Anamnestic and demographical characteristics of study population at baseline ($n = 42$)

	Total ($n = 42$)	O ₂ O ₃ group ($n = 22$)	HA group ($n = 20$)	<i>P</i> values
Age (years)	70.5 $\pm$ 5.8	70.3 $\pm$ 6.5	70.7 $\pm$ 5.4	ns
BMI (kg/m ²)	27.0 $\pm$ 1.8	27.1 $\pm$ 1.9	26.8 $\pm$ 1.7	ns
Sex (female/male)	29/13	16/6	13/7	ns
Smokers	9 (21.4)	5 (22.7)	4 (20.0)	ns
Previous treatment with NSAIDs and/or GC	7 (16.7)	5 (22.7)	2 (10.0)	ns
Kellgren-Lawrence Grade II	29 (69.0)	15 (68.2)	14 (70.0)	ns
Kellgren-Lawrence Grade III	13 (31.0)	7 (31.8)	6 (30.0)	ns

Continuous variables are expressed as means $\pm$ standard deviations, categorical variables are expressed as counts (percentages).
Abbreviation: BMI = Body Mass Index; NSAIDs = nonsteroidal anti-inflammatory drugs; GC = glucocorticoids.

de Sire A et al. J Back and Musc Rehab 2020

Figure 2. Visual analogue scale (VAS) modifications in HA and O₂O₃ groups at different study visits. *Within-group differences compared to T0 (p<0.013); ** Between-group differences (p<0.013).



de Sire A et al. J Back and Musc Rehab 2020



International Journal of
Molecular Sciences



Article

Ozone Therapy versus Hyaluronic Acid Injections for Pain Relief in Patients with Knee Osteoarthritis: Preliminary Findings on Molecular and Clinical Outcomes from a Randomized Controlled Trial

Cristiano Sconza ^{1,2}, Berardo Di Matteo ^{1,2}, Paolo Queirazza ^{1,2}, Arianna Dina ³, Roberta Amenta ⁴, Stefano Respizzi ^{1,2}, Giuseppe Massazza ⁵, Antonio Ammendolia ⁶, Elizaveta Kon ^{1,2}
and Alessandro de Sire ^{6,*}

- KOA for at least 3 months
- Double blind RCT versus hyaluronic acid
- At 1-3 and 6 months, evaluating pain stiffness and function
- 52 participants, 8 drop out
- 22 patients in group A and B

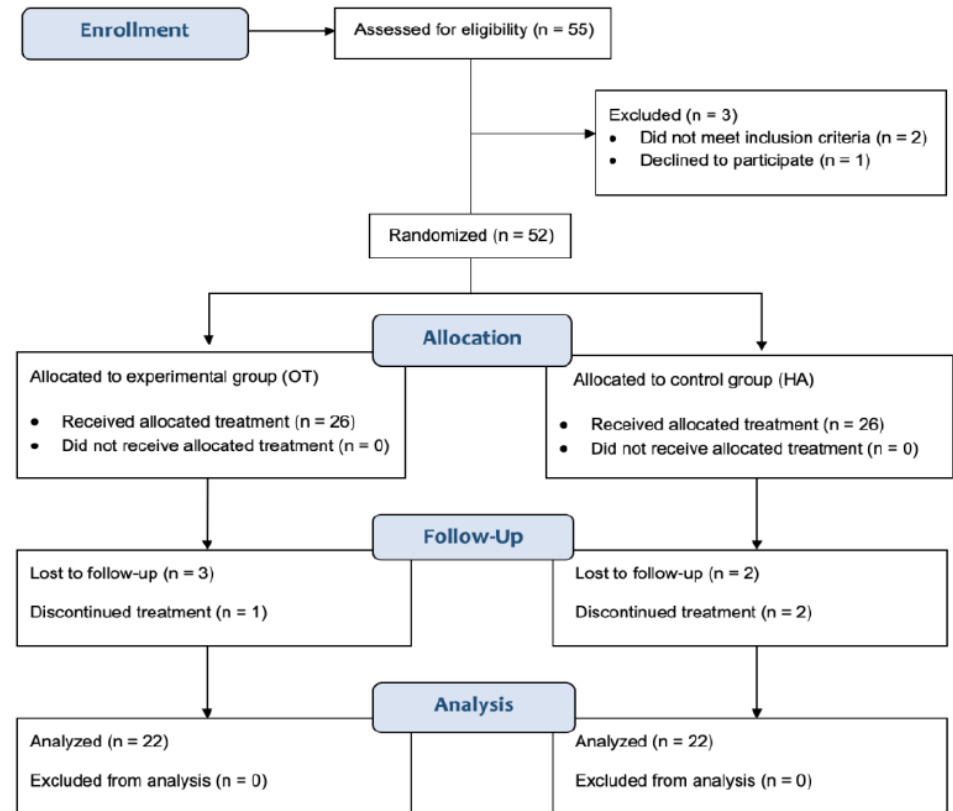


Figure 1. PRISMA Flow Diagram.

Sconza C. et al. *International Journal of Molecular Sciences* 2023.

	Baseline		1 Month		3 Months		6 Months		p Value
	OT	HA	OT	HA	OT	HA	OT	HA	
n	22	22	22	22	22	22	22	22	
WOMAC pain subscore	6.8 ± 2.7	7.3 ± 3.7	3.7 ± 3.1	2.8 ± 3.1	3.7 ± 2.7	2.9 ± 3.1	4.4 ± 3.1	3.9 ± 3.8	0.001
WOMAC total score	45.6 ± 15.1	45.8 ± 20.1	18.7 ± 14.3	14.0 ± 13.1	17.7 ± 14.0	14.8 ± 16.4	20.9 ± 15.8	17.9 ± 16.7	<0.001
KOOS	79.1 ± 24.9	72.2 ± 27.3	40.0 ± 26.2	32.4 ± 26.9	38.9 ± 28.1	30.9 ± 32.8	44.8 ± 30.5	35.8 ± 32.3	<0.001
NRS	5.6 ± 2.2	5.8 ± 1.7	2.3 ± 2.2	2.6 ± 2.2	2.9 ± 2.6	2.5 ± 2.3	3.6 ± 2.6	3.2 ± 2.7	<0.001

	OT Group (Group A)	HA Group (Group B)	p Value
WOMAC total score (baseline)	45.6 ± 15.1	45.8 ± 20.1	0.888
WOMAC total score (1 month)	18.73 ± 14.3	14.04 ± 13.14	0.223
WOMAC total score (3 months)	17.69 ± 14.0	14.81 ± 16.4	0.500
WOMAC total score (6 months)	20.86 ± 15.8	17.86 ± 16.7	0.544
KOOS (baseline)	80.91 ± 21.0	73.13 ± 29.4	0.319
KOOS (1 month)	39.96 ± 26.2	32.42 ± 26.9	0.311
KOOS (3 months)	38.92 ± 28.1	30.92 ± 32.8	0.349
KOOS (6 months)	44.77 ± 30.5	35.77 ± 32.3	0.347
NRS (baseline)	5.81 ± 2.2	5.86 ± 1.6	0.939
NRS (1 month)	2.35 ± 2.2	2.58 ± 2.2	0.707
NRS (3 months)	2.92 ± 2.6	2.50 ± 2.3	0.538
NRS (6 months)	3.60 ± 2.6	3.23 ± 2.7	0.653

- At different time points, significant improvements with comparable outcomes between groups

Sconza C. et al. International Journal of Molecular Sciences 2023.

Research article

Intra-articular injections of oxygen-ozone versus hyaluronic acid for the treatment of knee osteoarthritis: A randomized controlled trial

Journal of Back and Musculoskeletal
Rehabilitation
1–12

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DOI: 10.1177/10538127251358732

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Cristiano Sconza¹, Andrea Parente², Nicola Marotta^{3,4}, Giacomo Fari⁵, Dalila Scaturro⁶, Michele Vecchio^{7,8}, Giulia Letizia Mauro⁶, Antonio Ammendolia^{2,4}, Alessio Baricich^{1,9} and Alessandro de Sire^{2,4}

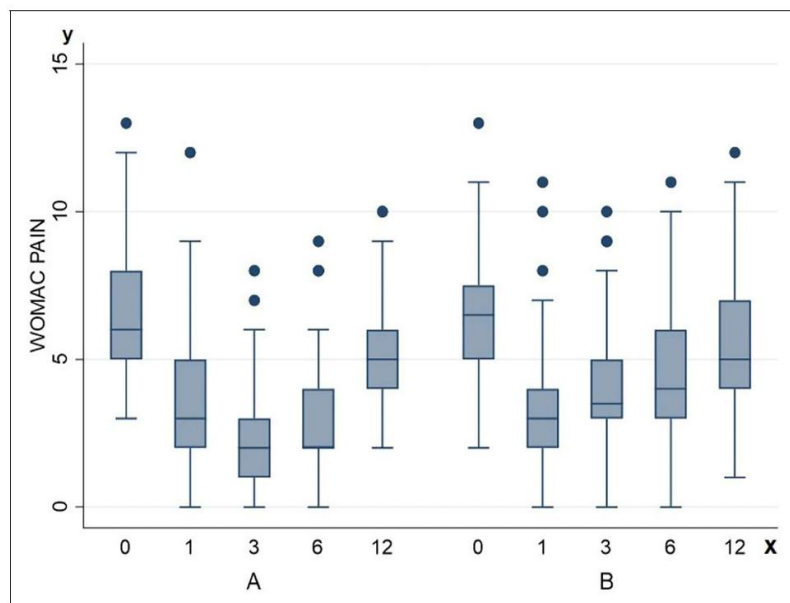


Figure 2. Intra-group analysis of the primary outcome WOMAC LK 3.1 pain subscale score in the groups of HA (A) and O₂O₃ (B).

Table 3. Between-group differences in the primary outcome.

WOMAC LK 3.1 pain score	HA Group (Group A)	O ₂ O ₃ Group (Group B)	P value
Baseline	6.77 ± 2.53	6.50 ± 2.24	0.735
1 month	3.66 ± 2.57	3.45 ± 2.30	0.501
Δ 1 month - baseline	3.10 (2.31; 3.91)	3.05 (2.38; 3.73)	
3 months	2.36 ± 1.67	3.89 ± 2.16	<0.001
Δ 3 month - baseline	4.41 (3.73; 5.09)	2.61 (1.94; 3.27)	
6 months	2.98 ± 1.89	4.50 ± 2.46	< 0.001
Δ 6 month - baseline	3.78 (3.09; 4.47)	2.00 (1.13; 2.77)	
12 months	5.04 ± 1.97	5.63 ± 2.25	0.271
Δ 12 month - baseline	1.73 (1.10; 2.35)	0.88 (0.36; 1.40)	

Continuous variables are expressed as means ± standard deviations; categorical data are expressed as counts (percentages). Abbreviations: O₂O₃: Oxygen-ozone therapy; HA: hyaluronic acid; Δ: delta; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

Conclusion

Major findings of our trial showed that administration of O₂O₃ and HA injections might provide positive results in pain control and motor function recovery in patients affected by KOA. Both treatments were also comparably safe. O₂O₃ seems to have a faster effect than HA, but only in the first month of treatment. HA, on the other hand, is more effective in the medium to long term.

Therefore, O₂O₃ could be considered as a potential treatment for KOA, thanks to its anti-inflammatory and analgesic properties, especially in the short-term.

Sconza C. et al. J Back Musculoskelet Rehabil. 2025.

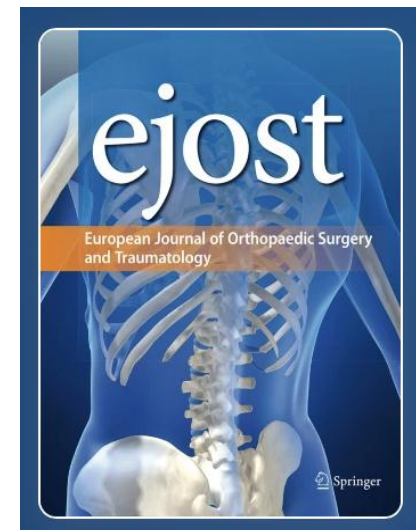
Meta-Analysis

> Eur J Orthop Surg Traumatol. 2024 Nov 23;35(1):20.

doi: 10.1007/s00590-024-04135-x.

Intra-articular injections of ozone versus hyaluronic acid for knee osteoarthritis: a level I meta-analysis

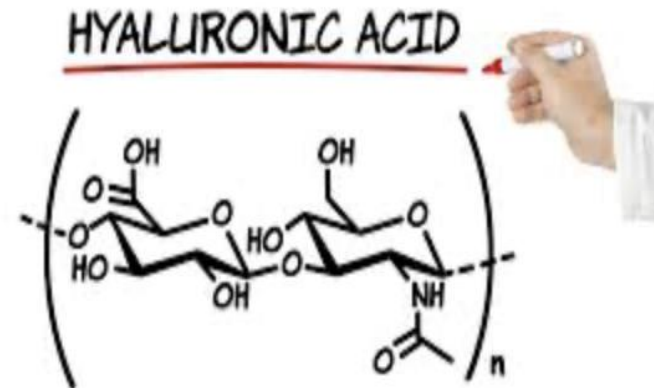
Filippo Migliorini ^{1 2 3}, Riccardo Giorgino ⁴, Manuel Giovanni Mazzoleni ¹, Luise Schäfer ³,
Francesca Alzira Bertini ¹, Nicola Maffulli ^{5 6 7}



Results: Data from 424 patients were collected. 74% (314 of 424 patients) were women. The mean age of the patients was 61.1 ± 4.5 years, and the mean BMI was 27.8 ± 0.8 kg/m². Compatibility was found in the mean age, mean BMI, PROMs, and the percentage of women. No difference was found in VAS at follow-up ($P = 0.4$).

Conclusion: The current level I evidence suggests that ozone and HA intra-articular injections achieve similar pain control between 4 and 6 months of follow-up.

Level of evidence: Level I.



Complementary Therapies in Medicine 93 (2025) 103238



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Complementary Therapies in Medicine

journal homepage: www.elsevier.com/locate/ctim



Comparing the efficacy of combining ozone therapy with hyaluronic acid versus using hyaluronic acid alone for pain relief in patients with knee osteoarthritis: A randomized clinical trial



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G. Akhavanakbari et al.

Complementary Therapies in Medicine 93 (2025) 103238

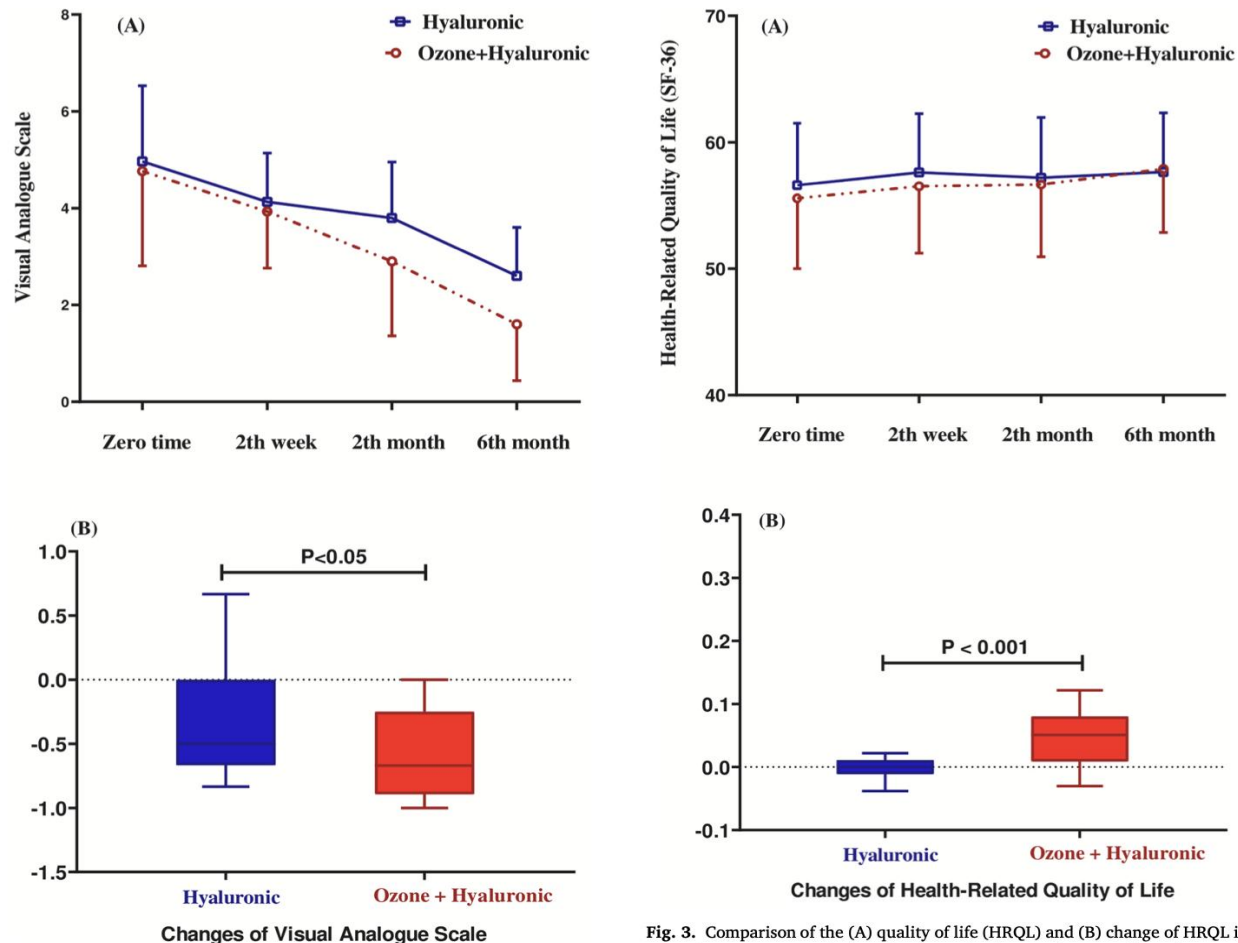


Fig. 2. Comparison of (A) the pain scores (VAS) and (B) change of VAS score in HA and OZ+HA groups in baseline (Zero time), 2 week, 2 month, and 6 month after intervention. Values are represented as mean±SD or median (interquartile range). VAS: Visual Analogue Scale. For each group, n = 30.

Fig. 3. Comparison of the (A) quality of life (HRQL) and (B) change of HRQL in HA and OZ+HA groups in baseline (Zero time), 2 week, 2 month, and 6 month after intervention. Values are represented as mean±SD or median (interquartile range). PSQI: Pittsburgh Sleep Quality Index. For each group, n = 30.

Pain Physician 2025; 28:347-357 • ISSN 1533-3159

Observational Study

Ozone and Hyaluronic Acid, Alone and in Combination: Exploring Temporal Dynamics and Synergies in Intraarticular Therapy for Knee Osteoarthritis

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Table 3. Mean difference within groups at the end of treatment and at one month, 3 months, and 6 months posttreatment.

	T0-T1	T0-T2	T0-T3	T0-T4
NRS-11				
Group O ₃	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Group HA	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Group O ₃ +HA	< 0.001*	< 0.001*	< 0.001*	< 0.001*
WOMAC P				
Group O ₃	< 0.001*	< 0.001*	< 0.001*	0.004*
Group HA	< 0.001*	< 0.001*	< 0.001*	0.004*
Group O ₃ +HA	< 0.001*	0.001	< 0.001*	< 0.001*
WOMAC S				
Group O ₃	0.003*	< 0.001*	< 0.001*	0.003*
Group HA	0.003*	< 0.001*	< 0.001*	0.003
Group O ₃ +HA	< 0.001*	< 0.001*	< 0.001*	0.001*
WOMAC Ph				
Group O ₃	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Group HA	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Group O ₃ +HA	< 0.001*	< 0.001*	< 0.001*	< 0.001*

CONCLUSION

Our study suggests that intraarticular O₃ therapy and HA therapy, alone or combined, provide distinct and complementary benefits for KOA. O₃ therapy offers immediate pain relief, while HA contributes to sustained improvements in pain and function. The combination demonstrates a synergistic effect,

enhancing joint functionality and quality of life. O₃ therapy is well-tolerated with no clinically relevant side effects. Despite study limitations, our findings emphasize the potential of combined therapies in optimizing short- and long-term outcomes for patients with KOA.

Table 2. Mean difference between groups at treatment end (T1), at one month (T2), 3 months (T3) and 6 months (T4) posttreatment.

NRS-11, mean (SD)	T0 (Baseline)	T1	T2	T3	T4
Group O ₃	6.43 (1.07)	3.14 (1.78)	3.25 (1.17)	2.96 (1.59)	2.82 (2.37)
Group HA	6.08 (1.29)	4.24 (1.94)	3.20 (2.19)	2.56 (1.92)	2.08 (2.49)
Group O ₃ +HA	6.25 (1.17)	3.29 (1.74)	2.64 (1.74)	2.36 (1.49)	1.82 (1.84)
P Value - O ₃ vs HA		0.031*	0.697	0.293	0.111
O ₃ vs O ₃ +HA		0.937	0.026*	0.118	0.128
HA vs O ₃ +HA		0.023*	0.170	0.742	0.848

WOMAC P, mean (SD)	T0 (Baseline)	T1	T2	T3	T4
Group O ₃	7.93 (2.51)	3.61 (2.57)	3.64 (2.07)	2.86 (1.35)	4.14 (5.12)
Group HA	6.72 (3.02)	5.80 (3.63)	3.28 (2.65)	1.80 (2.61)	1.88 (2.59)
Group O ₃ +HA	6.96 (3.23)	4.04 (3.60)	3.46 (3.40)	2.89(2.15)	1.75 (1.83)
P Value - O ₃ vs HA		0.018*	0.354	< 0.001*	0.039*
O ₃ vs O ₃ +HA		0.783	0.168	0.323	0.034*
HA vs O ₃ +HA		0.011*	0.783	0.019*	0.652

WOMAC S, mean (SD)	T0 (Baseline)	T1	T2	T3	T4
Group O ₃	3.14 (1.99)	1.98 (1.63)	1.29 (1.38)	1.07 (1.08)	1.46 (1.55)
Group HA	2.6 (2.1)	0.80 (1.26)	1.00 (1.15)	1.44 (1.29)	1.16 (1.14)
Group O ₃ +HA	2.43 (1.99)	1.21 (1.85)	0.89 (0.95)	0.64 (0.98)	0.82 (1.19)
P Value - O ₃ vs HA		0.014*	0.613	0.370	0.619
O ₃ vs O ₃ +HA		0.047*	0.395	0.137	0.110
HA vs O ₃ +HA		0.519	0.780	0.006*	0.208

WOMAC Ph, mean (SD)	T0 (Baseline)	T1	T2	T3	T4
Group O ₃	27.32 (9.05)	14.89 (9.47)	13.68 (8.72)	10.86 (7.44)	10.79 (4.55)
Group HA	23.0 (11.03)	18.36 (12.9)	10.76 (9.66)	7.12 (8.74)	7.32 (9.41)
Group O ₃ +HA	23.89 (13.99)	12.39 (10.3)	9.50 (9.93)	6.32 (6.58)	4.86 (5.97)
P Value - O ₃ vs HA		0.376	0.170	0.023*	0.029*
O ₃ vs O ₃ +HA		0.105	0.011*	0.010*	0.001*
HA vs O ₃ +HA		0.048*	0.591	0.966	0.706

Randomized Controlled Trial

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The efficacy of ultrasonography-guided oxygen-ozone therapy versus corticosteroids in patients with knee osteoarthritis: A multicenter randomized controlled trial

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Table 2
Summary of implications for principal outcomes

	Score (mean $\pm$ SD)			Within-group change score (mean (95%CI))			Repeated measure ANOVA F (p)	
	Baseline	4 weeks	12 weeks	Baseline vs. 4 weeks	Baseline vs. 12 weeks	4 weeks vs. 12 weeks	Time	Time*group
VAS rest								
Corticosteroid	5.53 $\pm$ 2.15	2.68 $\pm$ 1.81	2.27 $\pm$ 1.80	2.85 (2.31, 3.38)*	3.25 (2.62, 3.88)*	0.40 (0.05, 0.75)*	259.29 (= 0.000)**	1.12 (0.31)
Ozone (O ₂ -O ₃)	5.26 $\pm$ 2.03	2.85 $\pm$ 1.92	2.18 $\pm$ 1.99	2.40 (1.88, 2.93)*	3.08 (2.46, 3.70)*	0.67 (0.32, 1.08)*		
VAS movement								
Corticosteroid	7.87 $\pm$ 1.39	4.48 $\pm$ 2.02	4.17 $\pm$ 2.02	3.38 (2.64, 4.12)*	3.70 (2.9, 4.48)*	0.31 (−0.14, 0.78)	283.17 (= 0.000) **	2.02 (0.135)
Ozone (O ₂ -O ₃)	7.32 $\pm$ 1.40	4.20 $\pm$ 1.74	3.18 $\pm$ 1.81	3.12 (2.39, 3.84)*	4.14 (3.37, 4.91)*	1.02 (0.56, 1.47)*		
WOMAC								
Corticosteroid	72.54 $\pm$ 18.89	45.95 $\pm$ 17.30	37.10 $\pm$ 19.87	26.59 (21.18, 31.99)*	35.44 (28.87, 42.00)	8.85 (6.24, 11.45)*	305.3 (= 0.00)**	0.105 (0.79)
Ozone (O ₂ -O ₃)	68.23 $\pm$ 20.18	42.99 $\pm$ 18.67	33.43 $\pm$ 18.24	25.23 (19.94, 30.53)*	34.80 (19.94, 30.53)*	9.56 (7.01, 12.11)*		

* $p < 0.000$; ** $p < 0.05$; VAS: Visual analog scale; WOMAC: The western ontario and mcmaster universities osteoarthritis index.

- **Oxygen-ozone therapy** is a promising conservative and minimally invasive treatment for **musculoskeletal pain**
- Supporting evidence is mainly for **knee OA** patients **in the short-term** (despite the few studies of comparison with corticosteroids)
- To date, the evidence showed that **hyaluronic acid** **has longer-term effects**
- More high-quality studies are needed to fully understand the therapeutic effects of the **combination of oxygen-ozone therapy and hyaluronic acids injections**



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Intra-articular oxygen-ozone therapy: evidence and future perspectives

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