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Research Article

Is Intradiscal Ozone Injection Effective in Ameliorating Symptoms of Lumbosacral Discopathy?

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Abstract

Background: Oxygen-ozone (O2-O3) gas mixture as a newly prescribed substance became popular among clinicians to relieve low back pain (LBP) in discogenic patients as an alternative method rather than surgery. We developed this study to uncover whether this combination could be helpful in the Middle Eastern population or not.
Methods: In the present randomized clinical trial, we included 40 patients with L1 to S1 disc herniation assigned to schedule for intervention [a single course of ozone (O3) therapy without corticosteroids] or to consider as the control (physiotherapy including exercises based on extension). All patients were followed with a mean time of 12 weeks after injection, and pain severity and level of quality of life (QOL) were assessed. The severity of disc herniations was evaluated by a spine surgeon within the Michigan State University (MSU) classification frame.
Results: The current study represented two identical groups regarding lumbosacral segment involvement during 12 weeks of our survey ($P > 0.05$). The QOL level was equivalent in two groups. The mean pain score was decreased in the intervention group against the control group after two weeks, but it failed to thrive in the further weeks and was raised afterward. On the other hand, the mean pain score for the control group [6.1; 95% confidence interval (CI): 5.4-6.8] proceeded with a steady slope notably lower than the intervention group (7.5; 95% CI: 6.9-8.2) ($P < 0.001$).
Conclusion: Patients with LBP do not get more benefit from O2-O3 mixture injection.

Keywords: Ozone; Intervertebral Disc Displacement; Pain; Quality of Life

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Background

Oxygen-ozone (O2-O3) gas injection into the nucleus pulposus is a viable percutaneous intervention for herniated discs, but using this method is challenging and there is not a same voice about using it (1). It has long been practiced in Europe and there are several studies that investigated its safety and effectiveness in relieving pain and improving function (2-9).

The rational approach of O2-O3 therapy, as well as technique and selection criteria for treating lumbar disk herniations, have recently been refined (10). The action mode in bringing down discogenic pain has been attributed to disk proteoglycans depletion, leading to reduction of disc volume and dehydration, and also modulation of inflammatory cytokines and prostaglandins has been proposed as other effects of this treatment (11-14). Some investigators have built a case on this hypothesis and suggested that ozone (O3) might not irreversibly harm nucleus pulposus cells of the disc (12). Some investigators have suggested the administration of the O2-O3 mixture as a first-choice treatment before resorting to surgery (13-16). However, misconceptions around treatment with O3 and technical errors, along with the lack of clinical trial studies, might have limited the widespread practice on O3 therapy. "The empiric O3 usage by ignorant physicians, lack of proper and standard technique and criteria for patient selection, generators of O3 without a suitable photometer, and lack of data" have all been suggested by Bocci et al. as causes for orthodox medicine to disagree with it (13, 17).

Therefore, in the current study, we aim to examine the effect of O2-O3 mixture injection on pain and quality of life (QOL) of patients with lumbar disc herniation among the Middle Eastern population.

Methods

Study Population: This study was accomplished within the framework of a randomized clinical trial in 2018 and 2019. 40 patients with lower back pain (LBP) and confirmed herniated disks from L1 to S1 were consecutively assigned to either conservative treatment or one course of O3 therapy. Patients were included in the study if they had radicular pain and a compatible contained disc herniation found on magnetic resonance imaging (MRI), which had not responded to six weeks of conservative management, including physical therapy. The patients were excluded if they presented with progressive neurologic deficit, cauda equina symptoms, thoracolumbar fracture, tumor, infection, lumbar canal stenosis, and past medical history of spine surgery, immune deficiency, diabetes, and hyperparathyroidism, or if they were pregnant. The patients were also excluded if they had sequestered or extruded disc herniation or they were found to have active denervation on their electromyographic (EMG) and nerve

conduction velocity (NCV) studies. All patients had been offered a six week course of physiotherapy and had reported no improvement; then they were assigned to two treatment strategies. The control group was offered another course of physiotherapy, and the intervention group was provided with O3 therapy.

Study Interventions: The participants were randomly (using a random number table) assigned to two groups. The intervention included a single course of O3 therapy without corticosteroids that was a combination of O2-O3 with a concentration of O3 being 40 $mg.ml^{-1}$. All the injections were performed with the 18-20 gauge needle in the operation room in the prone position after standard prepping and draping. Moreover, all injections were performed under the guidance of fluoroscopy to target the mid-portion of the nucleus pulposus. Patients were discharged the day after the procedure. Physiotherapy for the control group included exercises based on extension. A sports medicine specialist visited all patients, and the intensity and quality of physiotherapy were modified every two weeks based on the improvement in symptoms. The modification included adding core stabilizing exercises based on self-reported improvements.

Study Measurement and Following-up: A predetermined questionnaire was used and information on age, sex, body mass index (BMI), visual analog scale (VAS), and 36-Item Short Form Survey (SF-36) was collected. At baseline examination and during each follow-up visit, patients were asked to report their pain intensity based on VAS score, with 0 meaning no pain and 10 meaning intolerable pain. Collection of SF-36 data and investigating the MRI findings were performed at the baseline and the 12-week follow-up. The severity of discopathy was measured by a spine surgeon who was blind to the intervention status of the participants. The severity of the discopathy was classified using Michigan State University (MSU) classification (18). Patients were followed-up for the study endpoints at the day after injection and also, 2, 4, and 12 weeks after the intervention.

This study was accomplished after confirmation of the Ethical Committee of Tehran University of Medical Sciences, Tehran, Iran, and for all the patients, informed written consent was obtained. The investigations reported herein have been carried out in accordance with the principles of the Declaration of Helsinki as revised in 2008.

Statistical Analysis: Data were reported as either mean and standard deviation (SD) or frequency and percent for continuously and categorically-distributed variables. Generalized estimating equations (GEE) were used to compare repeated measurements at different examination time points. We set the statistical significance level at a two-tailed type I error of 0.05 and used Stata software (version 16.0, Stata Corporation, College Station, TX, USA) for all statistical analyses.

Results

We included 40 patients in the study but nine were lost to follow-up and finally, we reported the data on 31 participants who attended the baseline and all follow-up examinations. The baseline characteristics of the control and intervention groups have been compared and the age, sex, and smoking distributions were not statistically different.

As shown in table 1, the two groups were alike regarding the lumbosacral segments involved.

Table 1. Baseline characteristics of the participants by intervention status

Item	Intervention	Control	P-value
Age (year)	33.7 ± 5.4	34.6 ± 7.9	0.660
Height (cm)	171.5 ± 9.9	175.1 ± 8.7	0.224
Weight (kg)	82.3 ± 26.4	77.4 ± 12.1	0.455
BMI (kg/m2)	27.9 ± 8.0	25.1 ± 2.0	0.140
Smokers	3 (15.0)	1 (5.0)	0.605
Male gender	12 (40.0)	12 (40.0)	> 0.999
Segment(s) involved			
L4-L5	4 (20.0)	1 (5.0)	0.990
L5-S1	13 (65.0)	5 (25.0)	
L4-L5-S1	3 (15.0)	12 (60.0)	
Herniation extension			
1A	12 (41.3)	13 (44.8)	0.779
1B	1 (3.4)	1 (3.4)	
2AB	7 (23.8)	6 (20.7)	
2A	4 (13.7)	3 (10.3)	
2B	3 (10.3)	3 (10.3)	
2C	2 (6.9)	2 (6.9)	
3A	0 (0)	1 (3.4)	

Data are presented as mean ± standard deviation (SD) or number and percent
BMI: Body mass index

Results indicated that the means of SF-36 scores were not statistically different at the baseline and remained the same at the end of the study (Table 2). The steepness of the slope of the trivial changes in the mean SF-36 score was similar among the intervention and control groups.

As shown in figure 1, the mean VAS score of the intervention group decreased significantly two weeks after the injection, but it started to increase at the end of the study as shown in table 3. The mean VAS score of the control group [6.1; 95% confidence interval (CI): 5.4-6.8] was significantly lower than that of the intervention group (7.5; 95% CI: 6.9-8.2) (P for interaction < 0.001).

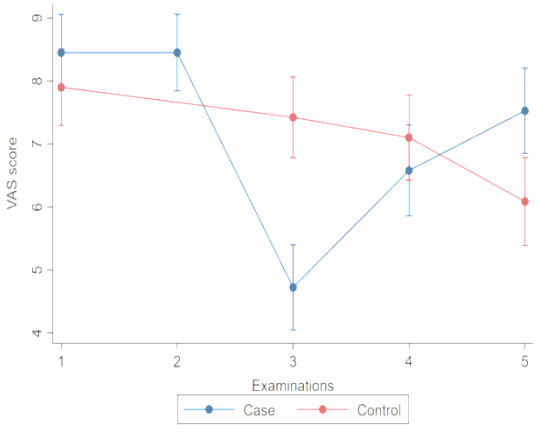

Figure 1. Mean visual analog scale (VAS) score of intervention and control groups

Table 2. 36-Item Short Form Survey (SF-36) component indices by intervention

Item	Control		Intervention		P-value		
Variable	Baseline	Follow-up	Baseline	Follow-up	Within subjects	Between subjects	Interaction
General health	13.3 ± 1.8	13.7 ± 1.9	13.5 ± 2.1	13.6 ± 2.0	0.965	0.299	0.455
Physical functioning	18.1 ± 3.9	18.3 ± 5.2	17.3 ± 3.6	17.4 ± 4.0	0.579	0.621	0.959
Role limitations due to physical health	5.8 ± 1.2	6.0 ± 1.4	5.7 ± 1.3	5.6 ± 1.4	0.617	0.715	0.525
Role limitations due to emotional problems	22.6 ± 1.1	23.0 ± 1.3	21.6 ± 2.6	22.9 ± 1.7	0.292	0.065	0.329
Pain	6.8 ± 1.6	7.0 ± 1.4	7.2 ± 1.4	7.1 ± 1.4	0.629	0.806	0.410
Social functioning	7.5 ± 1.0	7.8 ± 1.3	7.9 ± 1.1	7.3 ± 1.4	0.872	0.538	0.141
Energy/fatigue	16.6 ± 2.5	16.6 ± 2.6	17.2 ± 2.5	16.8 ± 3.0	0.717	0.424	0.424
Emotional well-being	4.9 ± 1.2	4.8 ± 1.1	5.1 ± 1.4	5.2 ± 1.3	0.526	0.934	0.423

Data are presented as mean ± standard deviation (SD)

Table 3. Changes in the pain score in the intervention group

Item	Group	Pain score	95% CI	P-value
Baseline examination	Control	7.9	7.3-8.5	< 0.001
	Intervention	8.5	7.9-9.0	
After injection	Control	7.9	7.3-8.5	
	Intervention	8.5	7.9-9.0	
At 2-week follow-up visit	Control	7.4	6.8-8.0	
	Intervention	4.7	4.1-5.4	
At 4-week follow-up visit	Control	7.1	6.5-7.8	
	Intervention	6.6	5.9-7.3	
At 12-week follow-up visit	Control	6.1	5.4-6.8	
	Intervention	7.5	6.9-8.2	

CI: Confidence interval

Discussion

We have investigated the impact of O3 therapy on pain reduction and QOL improvement against conservative treatment, like therapeutic exercise. No favorable effect was observed unless for the amelioration of pain two weeks post injection that was annihilated by increasing pain at the end of the study. Several studies have previously reported on the effectiveness of O3 therapy among patients with disc herniation. However, a vast majority of the previous studies have used O3 in combination with corticosteroids (19). Haseeb et al. have recently examined the effectiveness of O3 therapy for lumbar disc herniation, alone and in combination with steroids and they observed that these two approaches might have similar outcomes (4).

However, many other studies have reported steroids and O3 being more effective than each alone (19).

We used only the intradiscal injection in the current study and did not perform an intraformational injection. Most of the favorable outcomes have been obtained from the studies investigating intradiscal O3 injection combined with intraformational O3 injection (20). It might explain why we observed the favorable results obtained from the previous studies. Although a considerable number of studies have shown percutaneous intradiscal O3 injection to be an effective and safe treatment for lumbar disc herniation (21), recently, it has been shown that this treatment might impose serious complications.

Beside reporting various advantages, there are also reported complications. A case of paradoxical embolism has been reported following intradiscal O2-O3 therapy. The embolism caused anterior spinal cord syndrome and acute myocardial infarction (MI) (22). Chirchiglia et al. have described a suspected pulmonary embolism case that has caused sudden death in an elderly woman after O2-O3 injection for lumbar disc herniation (23).

A case of pneumocephalus has been reported by Andreini et al. as a complication of O3 therapy (24). Other complications reported are insomnia, itching, dermatologic inflammations, gastrointestinal (GI) disturbances, lightheadedness, tachycardia, and hot flushes. Vanni et al. have gathered a list of other relatively rare complications (25) and have called for refinement of the guidelines and protocols related to O3 therapy application (26).

The strength of the current study lies on its ability to investigate the effect of just intradiscal injection of the O3 therapy independently of the effects of the intraformational injection and those resulting from steroids. It might have clinical relevance in that it might help refine the guidelines for applying the O3 therapy for lumbar disc herniating.

Our findings, however, need to be interpreted in the backdrop of these limitations. The efficacy of O3 therapy has been reported to vary with types of disc herniation (27-29). Our limited sample size did not enable us to perform a subgroup analysis.

Conclusion

Having controlled for confounding bias from intraformational injection and steroids, we observed that intradiscal injection of O3 alone improved neither radiologic nor clinical outcome of the lumbar disc herniation.

Conflict of Interest

The authors declare no conflict of interest in this study.

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