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EFFECTIVENESS OF ULTRASOUND GUIDED LOCAL OZONE INJECTION IN THE TREATMENT OF CARPAL TUNNEL SYNDROME: A RANDOMIZED CONTROLLED TRIAL

Physical Medicine & Rehabilitation

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ABSTRACT

Introduction: Carpal Tunnel Syndrome (CTS) is the most common entrapment neuropathy which is causing work related disability in upper limb. This study aim to assess the therapeutic efficacy of local ozone injection in the management of CTS and to compare it with a control.

Material & Method: This randomized controlled trial (RCT) was conducted in Department of PMR, RIMS Imphal. Thirty two patients with CTS were included in two groups. Both the groups used a resting volar splint for 12 weeks. The intervention group received a single dose (4ml) of local ozone injection and control group received normal saline (4 ml) injection under ultrasound guidance. The outcome measures visual analog scale (VAS) for pain, symptom severity (SSS) and functional status (FSS) based on Boston carpal tunnel questionnaire were reassessed on 2weeks, 4weeks and 12 weeks after injection.

Results: All the outcome measures including VAS, symptom severity and functional status improved significantly in both groups (P=0.00). But when compared between the groups; there was no statistically significant improvement in VAS (P=0.667), SSS (P=0.600), FSS (P=0.596) in the Ozone group.

Conclusion: There is no added benefits with single dose of local ozone injection in the treatment of CTS, however further studies with multiple injection, higher dose and larger sample size is needed to confirm the results. Splinting can be considered as a mainstay in conservative management of CTS.

KEYWORDS

Carpal Tunnel Syndrome, Ozone, Wrist Splint

INTRODUCTION

Carpal tunnel syndrome (CTS) is caused by the compression of median nerve under flexor retinaculum.[1] It is the most common entrapment neuropathy in the upper limb which results in work related disability.[2] There is increased mechanical pressure in the carpal tunnel due to cumulative trauma which can lead to compression, inflammation and decreased blood supply to the nerve results in nerve lesion and producing symptoms such as pain, numbness, weakness in grip and tingling in the thumb, index and middle fingers. It is also called as occupational neuritis or median neuritis.[3]

The AAOS guidelines recommendation for early CTS include both non-surgical and surgical treatments. They also recommend an initial course of conservative treatment.[4] Considering the possible complications of surgery, many patients with mild to moderate grades prefer to select one of the conservative treatments including: wrist splinting, physical agent modalities like ultrasound and local injections of corticosteroid.[5-7] Ozone has been tried in various musculoskeletal conditions in recent times with promising results. But it is rarely studied in CTS and the results are inconclusive.[8]

MATERIALS AND METHODS

This randomized controlled study was a non-blinded trial conducted at Department of Physical Medicine and Rehabilitation (PMR), RIMS Imphal. The protocol was approved by the Research Ethics Board of RIMS and also was registered in the Clinical Trials Registry of India (CTRI/2019/11/022136). Informed written consent was obtained for all participants. A total of 32 patients presented to PMR OPD, with clinically diagnosed CTS with in age group 30-60 years were enrolled from June 2019 to May 2021. Patients with underlying diseases such as thyroid abnormalities, diabetes mellitus and rheumatoid arthritis, those with a history of local corticosteroid injection within last 3 months, thenar atrophy, polyneuropathy or radiculopathy, were excluded from the study. We also excluded pregnant women and participants with a history of G6PD deficiency, thrombocytopenia (<1 lakh), cardio-vascular instability in view of potential risk of ozone gas. Demographic characteristics of the patients such as age, gender, body mass index (BMI), side of affection were recorded. The outcome-measuring tools used were 1) pain intensity using a 10-score visual analog scale (VAS) in which 0 indicated no pain while 10 indicated the maximal imaginable pain. 2) Boston CTS Questionnaire (BCTQ) which had two sections; symptoms severity scale (SSS) in 11 items and functional status scale (FSS) in 8 items. Each of these questions are graded in a scale of 5 in which higher scores indicated the more severity of the condition.[9-10]

Participants were then randomly divided into two groups using random-sequence generation, with 16 participants in each group. Patients in the both group used a prefabricated wrist-based resting splint with a metal bar on the volar side for 12 weeks (used during night and most possible hours of day) to keep their wrists in the neutral position (0–5-degree angle extension). In addition to splinting, the participants of intervention group received a single local injection of 4 ml ozone (10 micrograms/dl) plus to 1 ml Xylocaine (2%) using a 21 G needle. Whereas control group received 4ml of saline with 1 ml of Xylocaine. Both the injections were given under ultrasound guidance using out of plane technique. The ulnar artery was identified along ulnar aspect at the level of wrist crease. Next the flexor retinaculum was visualized and followed from its proximal to its distal margin. The median nerve was identified at the superficial radial aspect of the carpal tunnel. It was distinguished from the tendon by its isotropic fascicular echo texture and lack of motion as the fingers are flexed and extended. After sterile preparation, local injection with 1 ml of 2% xylocaine was given. A 21 G needle was inserted at the level of distal wrist crease, medial to palmaris longus tendon with a 45 degree angle between needle and skin. Using a 5ml disposable syringe ozone or saline was injected. Participants who were using acetaminophen for post injection pain were recorded. Patients in both groups were reassessed after 2weeks, 4weeks and 12 weeks using VAS score for pain and two parts of BCTQ. Data gathered were analyzed using SPSS V.21. For

descriptive statistics, mean and standard deviation were used. For continuous variables Independent t-test and Chi- square test for categorical variables were used. Within the group comparison was assesses using repeated measures ANOVA. Throughout all analyses, P value < 0.05 was considered as significant.

RESULTS

A total of 32 patients were recruited for the study with a mean age of 45 years were randomized in two equal groups: A single ozone injection along with splinting versus saline injection with splinting. The majority of participants had right sided affection (71%). The mean duration of symptoms was 4.7 months. The baseline characteristics of each groups were comparable (Table 1).

Table 1: Baseline characteristics in both groups

Variables		Ozone Group n = 16 (n %)	Saline Group n = 16 (n %)	P-value
Age in completed years (Mean ± SD)		42.81 ± 8.5	47.19 ± 9.01	0.169
Gender	Male	2 (12.5%)	3 (18.75%)	1.00
	Female	14 (87.5%)	13(81.25%)	
Duration in months (Mean ± SD)		4.44 ± 1.75	4.94 ± 1.56	0.402
Side of Affection	Right	12 (75%)	11 (68.75%)	1.00
	Left	4 (25%)	5(31.25%)	
BMI (Mean ± SD)		24.55±3.70	25±3.8	0.661
VAS Pain		6.81±1.27	6.75±1.23	0.889
Symptom Severity Score		3.05±0.58	3.167±0.64	0.624
Functional Status Score		2.84±0.69	2.97±0.75	0.613

Changes within group

Pain severity (VAS), symptom severity (BQ-SSS) and functional status (BQ-FSS) all showed a statistical significant improvement (P<0.05) at the end of 2 weeks, 4 weeks and 12 weeks in both groups in comparison to pre-treatment scores (Table 2). The pre-treatment mean VAS score of ozone group and saline group were 6.81±1.27 and 6.75±1.23 respectively, 1.69±0.79 and 1.81±0.83 at 12weeks respectively. The pre-treatment mean SSS of ozone group and saline group were 3.05±0.58 and 3.16±0.64 respectively, 1.29±0.29 and 1.28±0.30 at 12weeks respectively. The pre-treatment mean FSS of ozone group and saline group were 2.84±0.69 and 2.97±0.75 respectively, 1.11±0.25 and 1.10±0.25 at 12weeks respectively.

Table 2: Within the group comparison of mean of outcome measures at baseline and 12 weeks.

Variable	Group	Baseline (Mean ±SD)	2 weeks (Mean ± SD)	4 weeks (Mean ±SD)	12 weeks (Mean ±SD)	P value
VAS	Ozone	6.81±1.27	5.0±1.41	4.0±1.21	1.69±0.79	0.00
	Saline	6.75±1.23	5.0±141	3.81±1.04	1.81±0.83	0.00
SSS	Ozone	3.05±0.58	2.27±0.48	1.93±0.41	1.29±0.29	0.00
	Saline	3.16±0.64	2.38±0.54	1.99±0.43	1.28±0.30	0.00
FSS	Ozone	2.84±0.69	2.14±0.73	1.55±0.38	1.11±0.25	0.00
	Saline	2.97±0.75	2.29±0.77	1.62±0.40	1.10±0.25	0.00

Changes between groups

Two groups were compared for the mean change in outcome measures at the end of treatment using independent t-test. The VAS reduction, symptom severity and functional status improvement was comparable between the groups at the end of treatment (Table 3). The mean change of VAS score from pre-treatment to 12 weeks in ozone group and saline group were 5.125±1.258 and 4.938±1.181 respectively (P=0.667). The mean change of SSS from pretreatment to 12 weeks in ozone group and saline group were 1.760±0.618 and 1.883±0.694 respectively (P=0.600). The mean change of FSS from pre-treatment to12 weeks in ozone group and saline group were 1.725±0.730 and 1.869±0.796 respectively (P=0.596).

Table 3: Comparison of mean change in outcome measures between the groups

Variable		Study N=16 (Mean ± SD)	Control N=16 (Mean ± SD)	P- value
VAS	0-2 weeks	1.813± 0.84	1.750 ± 0.775	0.827
	0-4 weeks	2.813 ± 0.981	2.938 ± 0.854	0.703
	0-12 weeks	5.125 ± 1.258	4.938 ±1.181	0.667
SSS	0-2 weeks	0.779 ± 0.315	0.785 ± 0.290	0.955
	0-4 weeks	1.136 ± 0.422	1.170 ± 0.475	0.832
	0-12 weeks	1.760 ± 0.618	1.883 ± 0.694	0.600
FSS	0-2 weeks	0.700 ± 0.354	0.676 ± 0.307	0.839
	0-4 weeks	1.289 ± 0.475	1.350 ± 0.480	0.720
	0-12 weeks	1.725 ± 0.730	1.869 ± 0.796	0.596

DISCUSSION

The present study findings based on assessing pain, symptom severity and functional status showed that ozone injection added to wrist splinting, does not have any added benefits in improving signs and symptoms of CTS. Previously some trials have studied the effectiveness of ozone injection in CTS treatment, with some variation in their injection protocols, medications, and follow-up periods. A similar study conducted by Bahrami MH et al[11] with similar injection protocol and splinting as present study and without placebo control showed effectiveness in clinical improvement with ozone injection at the end of 10 weeks without statistically significant improvement in electro diagnostic evaluation. Present study also showed improvement in ozone group but the failed to show improvement when compared with the placebo control. In a similar study conducted by Zambello et al[12] had evaluated the efficacy of ozone injection in 112 CTS patients; injection schedule used was 2–3 mL with 10 mg/ml concentration injection twice a week for five weeks (10 sessions), and then two more injections with a 14 day interval. The study had multiple injection protocol and showed statistically significant improvement in clinical symptoms.

Elwamy A et al[13] conducted study on CTS of patients with systemic sclerosis. 50 patients were studied and compared ozone therapy with steroid injection. They used oxygen ozone concentration of 25 microgram/ml in 20ml. There was improvement in pain and hand function at the end of 3 months and 6 months. Forogh B et al[14] conducted a study in 40 patients with mild to moderate CTS and compared ozone with steroid injection. The study showed statistically significant improvement in clinical symptom at the end of 6 weeks and 12weeks. But they also failed to show improvement in elctrodiagnostic and ultrasound criteria.

From the previous researches there is no conclusive evidence that ozone is effective in the treatment of CTS. Present study also could not confirm the definite effect of ozone in CTS. But some of the previous study with higher concentration, higher volume of ozone and repeated injection protocol showed clinical improvement. But still, they all lack improvement in electro diagnostic or ultrasound criteria. The mechanism of action ozone is hypothesized to be anti-inflammatory action through mild oxidative stress. Ozone is a toxic gas which use should be restricted if the benefits is not outweighing the risk. In the present study, both the groups were given wrist splinting treatment for a period of 12 weeks, which showed significant improvement in clinical symptoms. This also confirms that splinting can be considered as a conservative method of CTS treatment.[15]

During the present study there was no adverse effects reported with ozone injection. Few patients had a poor compliance with the wearing schedule of wrist splint which was reinforced at 2 week follow up. One of the drawback of the study was that it doesn't incorporated electro diagnostic criteria either in diagnosis or follow up which would have made the study better.

Limitation of study

There was no blinding done in the study. The follow up period was short and sample size was small. Ozone may have better outcome in longer follow up.

CONCLUSION

Present study showed that there is no added benefits in treatment with single dose injection of ozone (10microgram/ml in 4ml) in CTS. Splinting can be considered as an option for conservative management of CTS. However, further randomized controlled studies with larger sample size and higher dosing with repeated injection protocol are warranted to confirm these results.

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