A comparative study between Dexmedetomidine ,Ozone and Dexamethasone local injection in carpal tunnel syndrome for long-term pain relief

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Introduction

Carpal tunnel syndrome (CTS) is a collection of symptoms and signs associated with median neuropathy at the carpal tunnel. Most CTS is related to idiopathic compression of the median nerve as it travels through the wrist at the carpal tunnel.[1]

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy in the upper limb which is caused by compression of the median nerve as it travels through the carpal tunnel within the flexor retinaculum of the wrist.[2,3]

The incidence of CTS has been reported to be 1–3 per 100 people per year. Surgical release of the retinaculum in advanced cases has been proposed as the method of choice.[4]

The most commonly suggested explaining mechanism is that increased mechanical pressure in the carpal tunnel can lead to compression, inflammation and decreased blood supply to the nerve which all-together can lead to nerve lesion; thereby producing typical symptoms such as pain, numbness, weakness in grip and tingling usually in the thumb, index and middle fingers.[3,4]

Surgery resolves CTS in 70% of cases with clinical remission lasting up to 30 months. Sometimes severe complications may occur such as nerve injury and infection. Considering the burden and possible complications of surgery, many patients with mild to moderate grades might prefer to select one of the conservative treatments including: oral non-steroidal anti-inflammatory drugs (NSAIDs), diuretics, pyridoxine, wrist splinting, physical agent modalities like LASER, ultrasound (US),[5,6] and the most recent method, i.e., local injections of

corticosteroid, ozone ,progesterone and platelet-rich plasma (PRP) etc.[7,8]

Corticosteroid injection is an extensively used and accepted treatment in mild to moderate CTS according to the guidelines of the American Academy of Orthopedic Surgeons [9] as corticosteroids reduce the inflammation and edema associated with CTS. However, there is no guideline as to which corticosteroid has to be used as the standard treatment in CTS.

Triamcinolone acetonide, a commonly used steroid for this indication, is a particulate steroid, which can cause permanent nerve injury if accidentally injected into the nerve [10]. Dexamethasone sodium phosphate is another steroid with a better safety profile that has also been shown to be effective in CTS. It is a non particulate steroid that would not cause permanent nerve damage even if it is accidentally injected into the nerve. [10]

Local ozone injection as a therapeutic option in some musculoskeletal conditions; ozone (O3) gas is a molecule consisting of three oxygen atoms in a dynamically unstable structure. Ozone therapy has been utilized and studied for more than a century. Ozone is a re-emerging substance that has many biological effects such as bactericidal, immune-modulatory, analgesic, anti-inflammatory, anti-oxidative, as well as enhancing the blood circulation. [11]

The most established therapeutic mechanisms are:

A) Indirect mechanical decompression in the site of nerve entrapment by increasing tissue oxygenation with reduced venous or lymphatic stasis.

B) Suppression of the cell-mediated immune response by inhibiting macrophages from the release of proteinase, and also by induction of inhibitory mediators such as interleukin-10 and tissue growth factor beta (TGF-β).

C)Suppression of the humoral immune system, by decreasing the prostaglandins release and pro-inflammatory bradykinins.[12]

Dexmedetomidine is a super-selective α2-adrenergic agonist with considerable sedative and analgesic actions. The mechanism of its intra-articular analgesic action is not yet fully elucidated, but it is similar to clonidine. Clonidine acts on presynaptic receptors, inhibiting the release of nor epinephrine in peripheral afferent receptors, and exhibits local anesthetic action via inhibition of stimuli conduction through C and A-delta fibers. [13]

Aim of the work

The aim of the present study is to compare the analgesic efficacy of Dexmedetomidine, Ozone and Dexamethasone regional injection in carpal tunnel syndrome.

- **primary outcome:** is to evaluate the analgesic efficacy and functional status improvement of Dexmedetomidine, Ozone and Dexamethasone regional injection in carpal tunnel syndrome via assessment of Visual Analogue Scale (VAS) before and after injection.
- **Secondary outcome**: is to evaluate :

1) Median motor and sensory nerve conduction study(NCS) evaluation before and after injection.
2) Analgesic requirement (dose and frequency of oral acetaminophen intake in first 48 hours) for post injection .

Patients and Methods

This prospective randomized study will be carried out in Tanta University Hospitals for a period of nearly one year from February 2023 to February 2024, after approval from institutional ethical committee.

Informed written consent will be obtained from every patient after receiving an explanation of the purpose of the study and every patient will have a secret code number. All data of the patients will be confidential with secret codes and private file for every patient. All given data will be used for the current medical research only.

Any unexpected risks appeared during the course of the research will be cleared to the participants and ethical committee on time.

Inclusion Criteria:

One hundred and thirty five patients aged 20-60 years who are presented to Tanta university outpatient pain clinic at a period from February 2023 to February 2024 with clinical, electro physiologic, and ultrasonographic evidence of mild-to-moderate CTS will be included in this study.

Inclusion criteria will include numbness and pain in the median nerve (MN) distribution persisting for minimum of 3 months , nerve conduction studies (NCS) consistent with carpal tunnel syndrome (CTS) as per the American Association of Neuromuscular and Electro diagnostic Medicine (AANEM) guidelines, and an median nerve (MN) cross-sectional area (CSA)at the wrist >12 mm2 suggesting mild-to-moderate CTS forms. [14]

CTS grade	NCS finding
-Minimal	-Abnormal segmental or comparative tests only
-Mild	-Abnormal SNCV only with normal DML
-Moderate	-Abnormal SNCV and abnormal DML
-Severe	-Absent sensory response and abnormal DML
-Extreme	-Absence of motor and sensory responses

AANEM grading of CTS based on NCS findings
AANEM: American Association of Neuromuscular and Electro diagnostic Medicine
CTS: carpal tunnel syndrome
NCS: nerve conduction study
SNCV: sensory nerve conduction velocity
DML: distal motor latency

In the case of bilateral involvement, only the side with more severity was included.

Exclusion Criteria:

- Patient refusal.
- Patients with severe symptoms and signs of CTS as identified per the American Association of Neuromuscular and Electro diagnostic Medicine (AANEM) guidelines,[14] as this is an indication for surgery,
- Patients who show improvement on medical treatment,
- previous surgical or injectional CTS treatment,
- Pregnancy ,co existence of brachial plexopathy, or thoracic outlet syndrome, polyneuropathy, radiculopathy and peripheral nerve lesion in upper limb.
- Severe cardiovascular disease
- Morbid obese patients (body mass index (BMI) of >35 kg/m^2)
- Infection at site of injection.
- Bleeding diathesis

- History of thyroid deficiency, uncontrolled diabetes mellitus , rheumatoid arthritis and history of glucose-6-phosphate dehydrogenase (G6PD) deficiency
- History of Ozone or Dexmedetomidine allergy.
- End stage renal and hepatic disease.
- History of inflammatory joint , connective tissue disorders, , burns, any local tissue contractures and history of wrist trauma.
- Patients who will not consent to completing The visual analogue scale (VAS) for pain or nerve conduction study before and after injection.

Methods:

The patients will be randomly classified into three equal groups (45 patients each). Group allocation will be done by computer generated random numbers and closed opaque envelopes:

Group A (n=45): the participants will receive a single local injection of 4 ml ozone (10 micrograms/dl) plus to 1 ml lidocaine (1%) using a 25 G needle.

Needle insertion using ultrasonography will be on the volar side (conventional midline approach), one finger-breadth proximal to distal wrist crease (between the tendons of flexor Carpi radialis and Palmaris longus) with a 45-degree angle between needle and skin. US-guided intracarpal injection using ultrasonography (SonoScape E1Exp; Shenzhen, China) with a 10–18 MHz linear array transducer will be performed by the same physician who will not be aware of study groups, 3 mL of solution will be injected through the in-plane ulnar approach, to detach the MN from the transverse carpal ligament, and an additional 2 mL will be injected to separate the MN from the underlying flexor tendons.

Group B (n=45): patients will receive a single local injection of 5 mL (3 mL lidocaine (1%) and 2 mL [8 mg] dexamethasone) via the same technique.

Group C (n=45): patients will receive injection of 1 microgram/kg dexmedetomidine average (70-100-microgram) (0.7-1ml) plus 4ml lidocaine injection nearby median nerve via the same technique.

During the preoperative assessment, all enrolled patients will be informed about the study objectives and protocol.

Full history, clinical examination, complete blood count, coagulation profile, blood sugar, renal and hepatic profile, ECG, and echocardiography will be performed in all patients .

After establishing an intravenous access (20 G), Patients will be monitored for noninvasive blood pressure, ECG, and peripheral oxygen saturation.

All blocks will be performed by one pain physician who will neither be aware of study groups nor participate in data collection or analysis.

All patients will be observed for 30-min post injection for possible side effects before discharge.

All patients will be allowed to use acetaminophen in the case of possible post injection pain during the first 48 hrs.

- Sample size Justification :

The sample size and power analysis was calculated using Epi-Info software statistical package created by World Health organization and center for Disease Control and Prevention, Atlanta, Georgia, USA version 2002.

The criteria used for sample size calculation were as follows:

- 95% confidence limit
- 80% power of the study
- Expected long term pain relief among 90% in best treatment groups as compared to 65% in least favorable treatment groups.

The sample size based on the previously mentioned criteria was found at N=44 in each group. The researcher will increase the sample size to 45 cases to compensate for incomplete results.

Measurements:

All measurement will be recorded by an investigator who will not be aware about the study design or intervention.

1) Age, gender, and BMI of the patients will be recorded.

2) Visual Analogue Scale (VAS) used as an effective tool to detect intensity of pain will be recorded;
- "0" represents no pain ,"10" worst pain, "1-3" mild pain,"4-6 " moderate pain and" 7-10 " severe pain. [15]
Each patient will be assessed at the baseline (before injection) , at 1week, 1month, 3month, and 6month intervals after injection.

3) Median motor and sensory nerve conduction study(NCS): the grade of CTS, determined via electrophysiological study, will be classified as mentioned before at the American Association of Neuromuscular and Electro diagnostic Medicine (AANEM) guidelines. [14]
Only participants with mild to moderate CTS will be included in the study. Each patient will be assessed regarding electrophysiological

changes sensory nerve conduction velocity in millimeter/seconds and distal motor latency in milliseconds at the baseline (before injection)
, at 1week, 1month, 3month, and 6month intervals after injection.

4) Analgesic requirement (Dose and frequency of oral acetaminophen intake in first 48 hours) for post injection .

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