Comparison of local methylcobalamin injection versus subcutaneous lidocaine injection in patients with subacute herpetic neuralgia

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STUDY SITE:-DEPARTMENT OF DERMATOLOGY,COMBINED MILITARY HOSPITAL,MULTAN,PAKISTAN

STUDY DESIGN:-RANDOMIZED CONTROLLED TRIAL

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Introduction

Trigeminal, autonomic, and dorsal root ganglia are latent sites for neurotropic varicella zoster virus (VZV).[1] While varicella vesicles can form in any dermatome, axonal injury and myelin disruption are the hallmarks of shingles (zoster) and mononeuritis, which cause discomfort associated with zoster.[2] Even while there may be cutaneous spread beyond initially afflicted dermatome, the discomfort is frequently limited to a single dermatome.[3]

Pain that lasts longer than the acute phase and lasts between 30 and 120 days after vesicles first appear is known as subacute herpetic neuralgia (SHN).[4] All cases of post-herpetic neuralgia (PHN) cannot be fully managed by current treatments, such as systemic medications or localized therapy.[5] A neurotrophic substance with a unique affinity for brain tissues is cobalamin (Cbl). Peripheral nerve regeneration, axonal cytoskeleton trafficking and myelination, and nervous system maintenance are all facilitated by it.[6] In a number of illnesses, high-dose Cbl treatment may have significant pharmacological effects on brain function. Clinical experience has demonstrated that Cbl treatment relieves autonomic dysfunction and peripheral neuropathy symptoms.[7] Parenteral Cbl therapy should be considered because delayed therapy can result in irreparable neurological damage.[8]

Ninety-eight individuals (aged ≥50) with unilateral dermatomal pain that persisted for 30 days following rash development were included by Xu G et al. For four weeks, the patients were randomly assigned to receive subcutaneous 1% lidocaine injection (LD, n = 32), oral methylcobalamin (OT, n = 33), or local methylcobalamin injection (MB, n = 33). According to the authors, 72.7% of MB group, 6% of OT group, and 12.5% of LD group had pain NRS (numeric rating scale) <3 at the end point ($p<0.001$). Compared to the OT

(25%) and LD (26%) groups, the MB group had fewer patients using analgesics at the end point (3%).[9]

This research has been planned to compare local methylcobalamin injection with subcutaneous lidocaine injection in individuals who present with SHN in our local setting. It is crucial to compare these two approaches in order to ascertain which offers better and lasting pain relief, lesser side effects, and improved patient satisfaction. The results will direct medical professionals toward a more effective localized SHN treatment plan. Sleep, movement, mood, and day-to-day functioning will all improve with relief from chronic pain. Effective early intervention will reduce long-term handicap in the community by preventing the development of post-herpetic neuralgia.

Objective: To compare efficacy of local methylcobalamin injection versus subcutaneous lidocaine injection in patients with subacute herpetic neuralgia.

Operational definitions

Subacute herpetic neuralgia: Patients with dermatomal neuropathic pain > 30 and ≤ 120 days after rash onset (clinical history of vesicular rash in dermatomal distribution) will be labelled as having subacute herpetic neuralgia.

Pain score: Pain will be assessed through Visual analogue scale ranging from 0 (no pain) to 10 (maximum bearable pain). Pain will be assessed at baseline and at 28 days after randomization.

Efficacy: Pain score < 3 after 28-days of treatment will be taken as efficacious.

Diabetes mellitus: DM will be deemed positive if known case of diabetes mellitus on hypoglycemic therapy for ≥ 1-year – assessed on history and medical record.

Material & methods

Setting: Department of Dermatology, Combined Military Hospital Multan

Study design: Randomized Controlled Trial

Duration: Six months after approval of synopsis

Sample size[9]: Sample size is obtained through OpenEpi online software using formula for randomized controlled trial. Where,

Efficacy of local methylcobalamin injection = 72.7% Power of the study = 80%

Efficacy of subcutaneous lidocaine injection = 12.5% Confidence level = 95%

Sample size = **60** (30 in each group)

Sampling technique: Non-probability consecutive sampling

Inclusion Criteria: Patients 40 – 70 years of age, either male or female gender, unilateral subacute herpetic neuralgia as per operational definition and baseline pain score > 6 VAS

Exclusion Criteria: Diffuse neuropathic pain outside the dermatome distribution, cognitive impairment, topical agent or nerve blocking agents within 10 days prior to enrollment and immune compromised (on steroids >14 days at 2mg/kg/day, chemo-therapy)

Data collection procedure

The research will be performed after taking approval from the ethics review committee and CPSP. A total of 60 patients presenting to dermatology department, meeting the enrollment criteria, will be recruited in the study after written informed consent. Patient characteristics like age, gender, duration of SHN (months), dermatomal location of (Trigeminal, Cervical, Thoracic, Lumbar, sacral), laterality (right / left), prior antiviral treatment (yes/no) and current pain medications (paracetamol, ibuprofen, gabapentin, pregabalin, tramadol) will be recorded. All the patients will be assessed for baseline pain score using VAS and sleep disturbance score – on a numeric rating scale 0 (no disturbance) to 10 (severe disturbance). Patients will be randomly assigned to group A (methylcobalamin injection) or group B (lidocaine injection) through simple lottery methods and allocation will be concealed in sealed opaque envelopes.

The treating dermatologist (expert in both types of treatments) will open the assigned allocation. Due to nature of the injection color the dermatologist and patients will not be

blinded to assigned treatment. Patients in group A will be given subcutaneous methylcobalamin injections (1.0 mg / 2 ml), once every morning at fixed time, six times / week for 4 weeks. Similarly, patients in group B will be given local subcutaneous lidocaine injection (1%) 2ml once every morning at fixed time, six times / week for 4 weeks. Sterile, hypodermic, 25-gauge needles will be used for all patients. Based on patient reports of painful areas 0.5 ml study medication will be injected into up to four painful areas. Patients will be observed for redness, swelling, hematoma formation, dizziness, and urticaria for one hour and then sent home.

At every visit patient will be counselled for treatment adherence. Total number of injections received by each patient will be recorded. At the conclusion of treatment, the pain score and sleep disturbance score will be assessed by dermatologist neither involved in the study, not aware of the assigned treatment. All the participants will be instructed not to inform them of the treatment they have received. All the data will be recorded on proforma (attached)

Data analysis

SPSS version 27 will be utilized for data analysis. Normality of numerical data will be assessed through Shapiro-Wilk test. Age, duration of SHN, number treatment dose taken, baseline and end of treatment pain and sleep disturbance score will be presented as mean and standard deviation (median and IQR if not normally distributed). Gender, dermatomal location, laterality, prior antiviral use, current pain relief medication, any adverse effects and efficacy of treatment (as per operational definition) will be presented as frequency and percentages.

End of treatment pain and sleep disturbance score between the groups will be compared through independent sample t-test. Adverse effects and efficacy between the treatment will be compared through chi-square test. P-value <0.05 will be considered significant. Data will be stratified on age, gender, dermatomal location, laterality and prior antiviral

use to determine the effects on distribution of efficacy between the groups. Post stratification chi-square test will be applied and p-value < 0.05 will be taken as significant.

References

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Proforma

Comparison of local methylcobalamin injection versus subcutaneous lidocaine injection in patients with subacute herpetic neuralgia

Group A (Methylcobalamin injection)

Group B (Lidocaine injection)

Case No. ---------- **Registration No. ----------**

Name: ---------- **Age (years): ----------**

Gender: M / F

Duration of SHN (months): ----------

Number of treatment doses taken: ----------

<u>Baseline:</u> **pain score: ----------** **sleep disturbance score: ----------**

<u>Dermatomal location:</u>

Trigeminal / Cervical / Thoracic / Lumbar / sacral

Laterality: Right / Left

Prior antiviral use: Yes / No

<u>Current pain relief medication:</u>

Paracetamol / Ibuprofen / Gabapentin / Pregabalin / Tramadol

Any adverse effect: Yes / No

Efficacy of treatment: Yes / No

<u>At the end of treatment:</u> **pain score: ----------** **sleep disturbance score: ----------**