Acupuncture-like TENS (AL-TENS) as a Quantitative Measure for the Feasibility of Intrathecal Sodium Nitroprusside Superfusion in Paraplegics for Physiological Recovery—A Pilot Study (13 Cases)

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ABSTRACT

Background and introduction: Intrathecal sodium nitroprusside (ITSNP) has shown marked recovery in various causes of paraplegias after proper surgical decompression of the spinal cord and stabilization of vertebra. Until now, we were unable to predict paraplegias' recovery post-ITSNP bedside effectively, either by clinical or by any investigatory modality (somato sensory-evoked potential (SSEP) and motor-evoked potential (MEP)).¹ We present our work on the grading system and predictability for paraplegics using acupuncture-like TENS (AL-TENS) with ITSNP in various thoracolumbosacral cases. AL-TENS causes pain relief by well-known gate theory at the spinal cord by activating A-alpha nerve fibers which activates A-delta fibers for muscle spindle, and then pain fibers are inhibited by Renshaw cells at the spinal cord. The present work uses this cascade of various transmissions of nerves via a normal or damaged (complete or partial) spinal cord and utilizing this pathway to predict the feasibility of ITSNP in paraplegics. Our hypothesis works on this fact that the various nerves passing through the spinal cord and toward the brain can be utilized to use the quantitative measure for spinal cord injured patients and their recovery.

Aims/study design: The aim of the study is to prognosticate the post-ITSNP effect by AL-TENS in thoracolumbosacral paraplegia cases in the pre-ITSNP phase, a prospective study.

Materials and methods: Thirteen paraplegia patients (11 male patients and 3 females, and 3 complete paraplegias and 10 partial paraplegias) with zone of partial preservation (ZPP) cases were considered in whom pre-ITSNP-AL-TENS and post-ITSNP-AL-TENS have been done. The mean time for superfusion was 9.69 months. ITSNP was administered at a dosage of 0.2 mg/kg body weight at the L3/4 level using a 20G LP needle. Pre- and post-ITSNP was monitored by AL-TENS.

Results: Post-ITSNP-AL-TENS showed 23.84% benefit overall and 23.32% in American Spinal Injury Association (ASIA) grading in thoracolumbosacral paraplegia cases. Complete paraplegia cases did not show any change while partial paraplegias (with ZPP) showed 31% recovery in post-ITSNP-AL-TENS and 33.34% in ASIA grading. Thus, AL-TENS showed a favorable modality to predict the ITSNP feasibility in thoracolumbosacral paraplegia cases. If pre-ITSNP-AL-TENS showed 8 mAmp or more, there will be no response to ITSNP. This effect of post-ITSNP-TENS has increased to 34.96% after 24 hours. After 1 week, it became 39.19% and after 21 days, it had reached 44.16%.

Conclusion: ITSNP with the help of TENS done in paraplegic cases helped us to prognosticate the future outcome.

Keywords: Acupuncture-like TENS, Intrathecal sodium nitroprusside, Paraplegias, The 10,000 fold effect.

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Background and Introduction

Intrathecal sodium nitroprusside (ITSNP) has shown marked recovery in various causes of paraplegias after proper surgical decompression of the spinal cord and stabilization of vertebra.¹ Until now, we were unable to predict the recovery of paraplegias' recovery bedside effectively, either by clinical or by any investigatory modality (somato sensory-evoked potential (SSEP) or somato sensory-evoked potential (MEP)) and motor evoked potential (MEP). We have used acupuncture-like TENS (AL-TENS) to predict ITSNP feasibility in paraplegics. AL-TENS is a form of hyperstimulation described by Sjölund and colleagues in the 1970s. The characteristics of AL-TENS as “low-frequency (2–4 Hz), higher intensity (to tolerance threshold), longer pulse width (100–400 μs).” The intention of AL-TENS is to stimulate small diameter, high threshold peripheral afferents (A-delta) in order to activate extrasegmental descending pain inhibitory pathways. Non-painful muscle twitches occur during stimulation causing activity in small diameter muscle afferents. Electrodes are positioned over myotomes, trigger points, and acupuncture points.²

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Activity in peripheral nociceptive afferents releases excitatory neurotransmitters causing activity in second-order nociceptive transmission cells in the central nervous system, which leads to pain. Activation of large diameter non-nociceptive afferents by TENS causes the release of inhibitory neurotransmitters, which reduce activity in second-order nociceptive transmission cells. The reduction in nociceptive input to the brain results in pain relief. TENS-induced activity in non-nociceptive transmitting pathways in the central nervous system results in a sensation of electrical paresthesia.

This cascade of pain relief is a well-known entity to the medical world, which needs normal transmitting nerves via the normal spinal cord and brain. Thus, the present work uses this cascade of various transmissions via this neural pathway of non-nociceptive (A-alpha) and nociceptive (A-delta) afferents via a normal or damaged (complete or partial) spinal cord. Our hypothesis works on this fact that the various nerves (A-alpha and A-delta) passing through the spinal cord and toward the brain can be utilized to use the quantitative measure for spinal cord-injured patients and their recovery. The TENS activates the A-alpha nerve fiber which in turn activates the A-delta nerve. Then, this A-delta nerve activates the muscle spindle pathway from muscle to respective areas of the spinal cord, thereby the neuronal pathway from the spinal cord to Renshaw cells and the brain is activated, thus, completing the whole pain modulating pathway. The injured (complete or partial) spinal cord will have a partial or complete derangement of TENS reflex in pre-ITSNP and post-ITSNP phases, which can be utilized to prognosticate the pre-ITSNP and post-ITSNP response. With this ITSNP and TENS, we should be able to generate and access the whole pathway within intact or partial/complete spinal cord damage, respectively.

Different TENS techniques are used to selectively activate populations of nerve fibers to elicit mechanisms leading to pain relief (Fig. 1):

- Conventional TENS (low-intensity and high-frequency)—not helpful.
- Acupuncture-like TENS (high-intensity and low-frequency)—mainly used for ITSNP predictability here.
- Intense TENS (high-intensity and high-frequency)—not helpful.

We have selected to perform ITSNP on fifth day of decompression of the spinal cord and well stabilized vertebra due to the serum superoxide dismutase (SOD) level (comes to normal after 5 days) and iNOS (nitric oxide synthase) activity comes to end after the fifth day.

**Aims/Study Design**

The aim of this study is to prognosticate the post-ITSNP effect by AL-TENS in thoracolumbosacral paraplegia cases, a prospective study.

**Materials and Methods**

This prospective study has been done from May 2018 to December 2018 at Advance Neuro and General Hospital (ANGH), Lucknow, U.P., India, on thirteen paraplegia patients of various etiologies. The effect of ITSNP on the fifth day in a decompressed spinal cord and stabilized vertebra was evaluated. Neurological clinical scoring was analyzed on the basis of ASIA grading after 2 hours, 24 hours, 1 week, and 3 weeks of superfusion in all operative cases. All the selected cases were thoracic, lumbar, or lumbosacral cases. The mean time for superfusion was 9.69 months. Written consent was taken from every patient telling all untoward reactions to the patients and their relatives too.

Pre-ITSNP-TENS was recorded in all cases in ward with a “Medilap Two Channel TENS” machine, and ITSNP was done in operation theater and then post-ITSNP-TENS was again checked after 2 hours in ward.

The SNP injection (made with 200 mL of dextrose 5% with 50 mg of the SNP, 0.2 mg/kg body/wt) was superfused via the lumbar puncture route at the L3/4 level, i.e., around 8 mL of cerebrospinal fluid (CSF) was taken out and 8 mL of the SNP solution was put in slowly, about in 30 seconds. After waiting for 10 minutes, again superfusion was done slowly and the recovery is noted. Meticulous photoprotection and the sterile technique were done for all aspects of delivery of the medication as well as its formulation.

**Neurological Assessment**

The neurological assessment was performed pre- and post-ITSNP (2 hours), to get the exact improvement by ITSNP using the ASIA...
ITSNP’s Feasibility Assessed by Acupuncture-like TENS

grading system and according to the method developed in ITSNP cases. Upon setting of nausea and apprehension by giving ondansetron and mild sedative like injection diazepam, patients returned to wards. Briefly, the neurological assessment was done using the ASIA grading system. The scores of neurological assessments obtained after testing on each grade were summed up and denoted as the neurological deficit score.¹

Measurement of the TENS Score
Pre-ITSNP and post-ITSNP-TENS (2 hours, 24 hours, 1 week, and 3 weeks) were done to get the various neurological assessments. TENS employed here was AL-TENS.

RESULTS
The effect of ITSNP on the fifth day in a decompressed spinal cord and stabilized vertebra was evaluated. Neurological deficit (ND) scoring was analyzed on the basis of ASIA grading after 2 hours, 24 hours, 1 week, and 3 weeks of superfusion in all operative cases. All the selected cases were thoracic, lumbar, or lumbosacral cases.

Upon search of literature, we could not find any grading system of paraplegics based on TENS to quantify the paraplegia patients or the ITSNP effect.

Our following work has been based on the following parameters based on TENS (Table 1).

There were 11 males and 2 females and all cases taken were thoracic,⁵ lumbar,⁵ or lumbosacral ones.⁷ Males showed 25% and females showed 23.33% of recovery. Thoracic showed 23.33% of recovery post-ITSNP-TENS. Lumbar showed 22% of recovery post-ITSNP-TENS. Lumbosacral showed 30% of recovery post-ITSNP-TENS. Complete paraplegia cases did not show any change while partial paraplegias (with ZPP) showed 31% recovery in post-ITSNP-TENS and 33.34% in ASIA grading. While, overall, there was a change of 23.84% in post-ITSNP-TENS and 23.32% in ASIA grading. Cases having less than or equal to 6 months presentation showed post-ITSNP-TENS 24.28% and more than 6 months showed 23.33% benefit. The pre-ITSNP-TENS of those cases who showed 8 mAmp or more than 8 mAmp muscle twitching did not get any benefit post-ITSNP-TENS. This effect of post-ITSNP-TENS has increased to 34.96% after 24 hours. After 1 week, it was 39.19%, and after 21 days, it had reached 44.16%.

DISCUSSION
SNP being a nitric oxide donor (NOD) acts at postsynapse’s nNOS and releases NO which acts presynaptically and generates the impulse via a 10,000-fold effect.¹ ITSNP in cases of paraplegias with clinical ZPP and investigatory SSEP and MEP deflection has been shown to be highly effective previously by the authors.¹ The main hindrance of the use of ITSNP in paraplegics was unpredictability which was mainly based on the clinical finding of ZPP, and investigatory findings of SSEP and MEP. We were using SSEP and MEP for paraplegics, but the interpretations of SSEP and MEP were very subjective and we always need a neurologist (so exhaustive and an impractical tool). So, clinically ZPP gets the sole responsibility of judging the feasibility of ITSNP.

TENS is being used here to get some pre-ITSNP predictability, so that one can predict whether ITSNP is going to get some benefit in these cases or not. TENS is very much objective and a mere twitching of the myotomes, or if there is a slightest muscle flickering, suffices the need for ITSNP.

SNP and TENS both are universally available and affordable with a minimum adverse effect.

It was earlier demonstrated by the authors that intracarotid administration of SNP reduces infarct size after the fifth day of infarct due to synaptic cleft’s superoxide formation¹¹ and its neutralization by serum superoxide dismutase (takes 5 days) and iNOS (neurotoxic) degradation in 5 days.¹² Also, in paraplegics, the use of ITSNP has been successfully done previously in the literature.¹ This is well known as the rule of five after a well-decompressed spinal cord and stabilized vertebra.

So, the authors again strictly followed the rule of five for ITSNP along with TENS.

All patients chosen here were operative cases on whom the decompression of the spinal cord and stabilization of vertebra was done. Pre-ITSNP TENS status of paraplegics showed muscle twitching/flickering with high intensity and minimum frequency (AL-TENS type). Post-ITSNP TENS (noted after 2 hours of ITSNP) status showed muscle twitching/flickering with low intensity and minimum frequency and the change noted was 23.84% benefit from pre-ITSNP status. This showed that the TENS has activated the A-alpha nerve fiber which in turn activated the A-delta nerve. Then, this A-delta nerve activated the muscle spindle pathway from muscle to respective areas of the spinal cord, thereby the neuronal pathway from the spinal cord to Renshaw cells and the brain is activated, thus, completing the whole pain modulating pathway. With this ITSNP and TENS, we were able to generate and access the whole pathway within intact or partial/complete spinal cord damage, respectively. The injured (complete or partial) spinal cord had a deranged TENS reflex in pre-ITSNP and post-ITSNP phases.

This effect of post-ITSNP-TENS has increased to 34.96% after 24 hours. After 1 week, it was 39.19% and after 21 days, it had reached 44.16%, thereby showing an incremental increase too.

The intact A-delta nerve pathway denotes that the spinal cord is intact with its various synapses, where the SNP has worked via a 10,000 fold effect via nNOS.¹ Thereby, the various pathologies of the spinal cord after proper decompression and stabilization of vertebra can have the predictability of physiological recovery by TENS and ITSNP at bedside itself in the pre-ITSNP phase.

We did not get any benefit in those cases in which pre-ITSNP TENS was having 8 mAmp or more than 8 mAmp readings for muscle twitchings. This shows that the TENS has activated the intense TENS instead of AL-TENS, and the patient is having complete paraplegia at that myotome.

In one patient (number 4 traumatic paraplegia L2 fracture with ZPP below L3 and complete below L5 level bilaterally), we got two kinds of responses in pre-ITSNP-TENS and post-ITSNP-TENS. Below L5, we got 8 mAmp and at L3 or L4 TENS was 4 mAmp pre-ITSNP-TENS and post-ITSNP-TENS showed 8 mAmp below L5 and 3 mAmp below L3 and L4. This shows that the L5 nerve is damaged completely, but L3 and L4 were partially damaged.

LIMITATIONS
The limitations of this study were

• Number is too small, being a pilot study
• And we were not able to evaluate the 10,000-fold effect via pico nano second absorption spectroscopy (PNSAS) being non availability at our setup.
• Our TENS machine has not got the facility of tracings, in fact, we did not find in the literature that any TENS machine has this
| S. no. | Sex age name | Case briefings | Duration | Operation | Pre-ITSNP-TENS level | Post–ITSNP-TENS level (after 2 hours) | % change | Power pre-ITSNP | Power post-ITSNP (after 2 hours) | ASIA grading |
|-------|--------------|----------------|----------|-----------|---------------------|---------------------------------------|----------|----------------|----------------------------------|--------------|
| 1     | M/44 years   | T11, T12 ligamental hypertrophy | 12 months | T11, 12 decompression | 7 mAmp, L3 | 4 mAmp, L3 | 30 | 2 | +4 | |
| 2     | F/56 years UD | Left L5/S1 PIVD with complete foot drop left | 6 months | L5 laminectomy with discectomy L5/S1 | 7 mAmp, S1 | 5 mAmp, S1 | 20 | 0 | 2 | |
| 3     | M/35 years   | T10 ligamentum hypertrophy with TCS | 12 months | T10 laminectomy with decompression | 6 mAmp bilateral below thigh | 3 mAmp below L1 | 30 | +4 | 5 | |
| 4     | M/55 years HNS | L2 fracture with partial paraplegia below L3 and complete paraplegia below L5 bilateral | 2 months | Decompression and fixation L2 | 8 mAmp below L5, 7 mAmp AT L3, 4 bilateral | 8 mAmp below L5, 3 map and 4 mAmp at L3, 4 bilateral | 0 | Below L5 → 0, AT L3, 4 → 3 | Below L5 → 0 AT L3, 4 → 4+ | |
| 5     | M/55 years   | T12, L1 ligamental hypertrophy with thoracic spinal cord compression | 16 months | Decompression | 7 mAamp below L2 | 4 mAmp below L2 | 30 | Below L2 → 3/5 bilateral | Below L2 → 4+/5 bilateral | |
| 6     | M/14 years AG | T10/T11 thoracic ligamental hypertrophy | 20 months | Decompression | 6 mAmp below L1 | 4 mAmp below L1 | 20 | Below L1 → 2/5 bilateral | Below L1 → 4+/5 bilateral | |
| 7     | M/80 DSS     | L2/3 PIVD (left > right) | 2 months | L2 and L3 laminectomy with L2/3 discectomy | 7 mAmp below L2 | 4 mAmp below L2 | 30 | Below L2 → 3/5 bilateral | Below L2 → 4+/5 bilateral | |
| 8     | M/18 years R | T10, T11, T12 ligamental hypertrophy | 26 months | T10, 11, 12 decompression | 6 mAmp below L1 | 3 mAmp below L1 | 30 | Below L2 → 3/5 bilateral | Below L1 → 4+/5 bilateral | |
| 9     | F/55 years MO | L4/5 PIVD left L5 radiculopathy | 14 months | L4 and L5 laminectomy with L4/5 discectomy | 8 below left L5 | 8 below L5 | 0 | Left foot drop complete | Same | |
| 10    | M/45 years H | L1/2 Pott’s spine with below L3 partial paraplegia bilateral | 4 months | L1 and L2 laminectomy with fixation | 6 below L3 bilateral | 3 below L3 bilateral | 30 | Below L3 → 2/5 bilateral | Below L3 → 4+/5 bilateral | |
| 11    | F/55 years UD | L4/5 PIVD right L5 radiculopathy | 3 months | L4 and L5 laminectomy with L4/5 discectomy | 8 below right L5 | 3 below L5 left | 50 | Below L5 → 1/5 left foot drop | 4+/5 L5 foot drop left improved | |
| 12    | M/27 years K | T9,10,11 Pott’s spine with bilateral complete paraplegia | 6 months | T9, 10, 11 laminectomy and transpedicular fixation | 9 below T11 bilateral | 9 below T11 bilateral | 0 | Below T11 0/5 bilateral | Below T11 0/5 bilateral | |
| 13    | M/55 years NA | L5/S1 Pott’s spine with S1 bilateral radiculopathy | 3 months | L5 laminectomy and transpedicular fixation L4, S S | 7 below L5 bilateral | 3 below L5 bilateral | 40 | Bilateral S1 3/5 power | Bilateral S1 4+/5 power | |
| AV    | 13 cases    | Thoraco, lumbar, and sacral cases | 9.69 months | | 7.07 mAmp | 4.69 mAmp | 23.84 | 23.32% | | | |
tracing facility, which can give any objective traceable document of effective muscle twitching.

- We did not compare between AL-TENS and the SSEP and MEP while performing this study.
- Absence of clonus study.
- Reflexes can be judged by DTR and TENS but power cannot be judged by TENS or DTR.
- Power determination is done by clinical study only, but we do not have any device/instrument which can grade the power of a particular myotome (on searching of literature).

**Conclusion**

Post-ITSNP-AL-TENS showed 23.84% benefit overall and 23.32% in ASIA grading in thoracolumbosacral paraplegia cases. Complete paraplegia cases did not show any change while partial paraplegias (with ZPP) showed 31% recovery in post-ITSNP-TENS and 33.34% in ASIA grading. This effect of post-ITSNP-TENS has increased to 34.96% after 24 hours. After 1 week, it was 39.19% and after 21 days, it had reached 44.16%. Thus, AL-TENS showed a favorable modality to predict the ITSNP feasibility in thoracolumbosacral paraplegia cases. If pre-ITSNP-TENS showed 8 mAmp or more, there will be no response to ITSNP. In view of the above findings, we recommend the use of AL-TENS in pre-ITSNP thoracolumbosacral paraplegia assessment after the fifth post paraplegia day of the decompressed spinal cord or cauda equina nerve roots and stabilized vertebra cases. In this study, ITSNP with the help of TENS done in paraplegic cases helped us to prognosticate the future outcome.

**Recommendations**

- Future study should include TENS with tracing facility along with ITSNP.
- Number should be increased to around 100, so that exact conclusions can be drawn well.
- If possible PNSAS should be done in each excellent responding case to get 10,000-fold effect’s evaluation which can open up a plethora of research work further.

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