Original Research Article

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AL-TENS as Quantitative Measure for the Feasibility of IASNP in AIS for Physiological Recovery - A Pilot Study of 27 Cases

Vinod Kumar Tewari[1], Neeraj Seth[2], Devesh Johari[3], Lori Tiwari[4]

Abstract

Background: After good recovery noted from Intracarotid Sodium Nitroprusside (ICSNP) previous studies in rats and then humans, there was always a hitch in preinjection period that whether this ICSNP will benefit the recipient or not. Sodium Nitroprusside (SNP) via its 10000 fold effect, is used in out timed InjrTPA (Recombinant Tissue Plasminogen Activator) cases (5 days to 21 days) of ischemic stroke while skipping local induced Nitric Oxide Synthase Enzyme (i NOS) and superoxide (causes destructive effect) formation.

Acupunture Like-Transepidermal Neural Stimulation (AL-TENS) used here for quantitative measure of the stroke recovery bedside other than NIHSS grading to evaluate the ICSNP effect.

AL-TENS causes pain relief by gate theory at spinal cord with negative inputs from brain on Renshaw cells.

Objective: To prognosticate the POST-ICSNP effect by AL-TENS in humans of delayed ischemic stroke from 5th to 21st day by AL-TENS, a Prospective-study.

Material and Methods: 27 ischemic stroke patients (18 male, 9 females) taken. Mean time was 7 days. Dose 0.01 mg/kg/bo/wt at ipsilateral to MRI/CT SCAN indicated infarct, carotid artery direct puncture via 20G Medikit given. Study was monitored by AL-TENS and NIHSS grading.

Results: POST-ICSNP AL-TENS showed 16.66% benefit and 30.12% in NIHSS grading overall. Thus AL-TENS showed a favorable modality to predict the ICSNP feasibility in partial hemiplegia cases that is LACS, PACS and POCS. Complete hemiplegia with major artery block cases, PRE-ICSNP AL-TENS showed 8mAmp or more - no response to ITSNP.

Conclusions: AL-TENS helps us to prognosticate outcome in partial hemiplegia with ICSNP.

Keywords: Acute ischemic stroke; Intracarotid sodium nitroprusside; Acupuncture-like tens (al-tens); The 10,000 fold effect.

Key Message: This study is very crucial one for the acute ischemic stroke cases who comes after the lapse period of rTPA injection that is after 6 hours of acute ischemic infarct.

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Author's Affiliation: [1]Director, Neuro Center, Lucknow Uttar Pradesh 226010, India. [2]Physiotherapist, [4]Statistician, Advance Neuro and General Hospital, Arjunganj, Lucknow, Uttar Pradesh 226002, India. [3]Opthalmologist, Permanent Medical Services, Jodhpur, Rajasthan, India.

Corresponding Author: Vinod Kumar Tewari, Director, Neuro Center, Lucknow Uttar Pradesh, 226010 India.

E-mail: drvinodtewari@gmail.com

Background and Introduction

It has been proved previously via rat[1] and human[2] studies that ICSNP (Intra Carotid Sodium Nitroprusside Injection) gives good recovery (53.42% in rats and 44.58% in humans on 7th day) in delayed cases of ischemic stroke due to serum SOD level (comes to normal after 5th day) and iNOS activity comes to end after 5th day[3,4], whose part of

action was missed in previous studies.

Also it has been well proved in human beings, the efficacy and feasibility of AL-TENS (Acupunture Like-Transepidermal Neural Stimulation) to evaluate ITSNP (Intra Thecal Sodium Nitroprusside Superfusion of Sodium Nitroprusside)[5] in paraplegia patients with inference of 7mAmp or less will show prognostic value from AL-TENS.

Similarly, in cases of acute ischemic stroke while having human studies[2] there was always a hitch from clinician point of view (in pre injection period) that whether this ICSNP will benefit the recipient or not.

Sjölund and colleagues in the 1970s described AL-TENS as a hyperstimulation by current via myotomes placed electrodes having characteristics as "Low-frequency (2–4Hz), higher intensity (to tolerance threshold), longer pulse width (100–400μs)".[4,5]

The different TENS techniques are as follows[6,7] (Fig. 1):

- Conventional TENS (low-intensity, high-frequency) → not helpful.
- Acupuncture-like TENS (high-intensity, low-frequency) → mainly used for ICSNP predictibility done here. Nonpainful.
- Intense TENS (high-intensity, high-frequency) → not helpful. but painful.

AL-TENS delivers non-painful muscle twitchings which causes stimulation of small diameter muscle afferents, high threshold peripheral afferents (A-delta) in order to activate extrasegmental descending pain inhibitory pathways thus causes pain relief by the well known gate theory at Renshaw Cells at spinal cord. These Renshaw Cells are influenced by the inhibitory circuits from brain (cerebellum and cerebral cortex)[6,7] C fibers produces[6,7] excitatory neurotransmitters causing pain via activity in transmission cells in the central nervous system.[6,7] Activation of A- Delta fibers by AL-TENS[8] causes the release of inhibitory neurotransmitters which reduce activity in transmission cells.[8,9,10,11] This cascade of pain relieve is well known entity to medical world, which needs a normal transmitting nerves via normal spinal cord and normal brain (as brain influences the pain pathways via inhibitory pathways).

The ischemic brain (complete or partial) will have a partial or complete derangement of AL-TENS reflex in PRE-ICSNP and POST-ICSNP phase which can be utilized to prognosticate the PRE-ICSNP and POST-ICSNP response in ischemic stroke cases too.

Thus the present work uses this cascade of various transmissions via this neural pathway of A-ALPHA and A-DELTA via a normal spinal cord but the ischemic brain and to use the quantitative measure for ischemic brain and their recovery when added with ICSNP.

Objective

To prognosticate the PRE-ICSNP and POST-ICSNP effect by AL-TENS in ischemic stroke cases, Prospective-study.

Materials and Methods

This is a prospective study and has been done from May 2018 to Dec 2019 at Advance Neuro And General Hospital (ANGH) Lucknow, UP, India on 27 Acute Ischemic Stroke patients of various etiologies after taking ethical committee clearance from local hospital ethical committee. The effect of ICSNP on mean 7th day in acute ischemic infarct cases of various etiologies was studied. Neurological clinical scoring was analyzed on the basis of NIHSS grading after 2 h, 24 h, 1 week and 3 weeks of ICSNP in all cases.

All the selected cases were according to the Oxfordshire Community Stroke Project (OCSP) classification clinically subdivides cerebral infarction into total anterior circulation (TACS), partial anterior circulation (PACS), posterior circulation (POCS) and lacunar (LACS) syndromes.[12]

1. Lacunar Strokes (LACS) - 9 cases.
2. Partial Anterior Circulation Strokes (PACS) – 6 cases.
3. Total Anterior Circulation Strokes (TACS) – 5 cases.
4. Posterior Circulation Strokes (POCS) – 7 cases.

Written consent was taken from every patient informing all untoward reactions to the patients and their relatives too. Total 56 acute ischemic stroke cases arrived after the prescribed timings of Inj rTPA in ANGH; 29 were disqualified, and 27 qualified for the studydue to intracerebral-hemorrhage (n=22), a non-stroke diagnosis (n=5)

and minor or rapidly resolving symptoms (n=2). With mean age of our patients was 62.25 years (range 55-70) and Co-morbid-illnesses in form of hypertension/diabetes/hypercholesterolemia were present in 27/18/12 patients, respectively. Additionally, atrial fibrillation/congestive-heart-failure/coronary-artery-disease were present in 10/5/5 patients, respectively.

These cases were having prior stroke in 4 patients. Blood pressure at admission was 168/98 and mean-maximum-pretreatment was 182/100 mmHg. 12 were smokers.

Extensive neurological examination including BASELINE NIHSS was performed in all patients. Other parameters noted were demographic profile, stroke risk factors, ECG examination, baseline CT scan findings/MRI study, platelet aggregation activity monitoring (bleeding-time), PT/PC/APTT and INR level.

Patients received pretreatment for nausea in form of ondansetron HCl (32.0mg/IVpush) 15-minutes before treatment. Powdered-SNP was sterilely (photoprotection) reconstituted with 200ml 5% dextrose with 50mg of the SNP. Patients were hydrated and ICSNP given with simultaneous IV injection of 1 ml mephentermine to combat the ensuing SNP-related hypotension (if any).

Each of our patients received 0.01mg/kg of ICSNP, up to a maximum of 2ml (0.5mg), based on titration of hypotension (stoped at the start of hypotension) via 20 G viggo/Medikit directly into the ipsilateral carotid artery (ipsilateral to MRI/CT scan demostrated infarct).

Aftre 2 hours POST-ICSNP AL-TENS done. NIHS-scores were recorded at baseline 2-h, 24-hrs, 7-days and 2-months. The Barthel index for stroke recovery was recorded at 2-months.

This study corroborates earlier impressions regarding the safe limits of doses of SNP in intrathecal, intraventricular, intra-arterial and intracarotid[1-5] administration.

Heparin/aspirin/clopidogrel/&/Antihyper-tensives were given as usual.

The Mean-Baseline-Nihss-Score Was 21.11 (range 10-33). Pre ICSNP and post ICSNP clinical examination with AL-TENS was recorded in all cases in ward with "Medilap Two Channel TENS" machine.

Neurological Assessment

The neurological assessment was performed PRE and POST ICSNP (2 hours), to get the exact improvement by ICSNP using NIHSS grading system. Upon settling of nausea and apprehension by giving Ondansteron and mild sedative like Inj diazepam, patients returned to wards. The scores of neurological assessment obtained after testing on each grade were summed up and denoted as neurological deficit score.

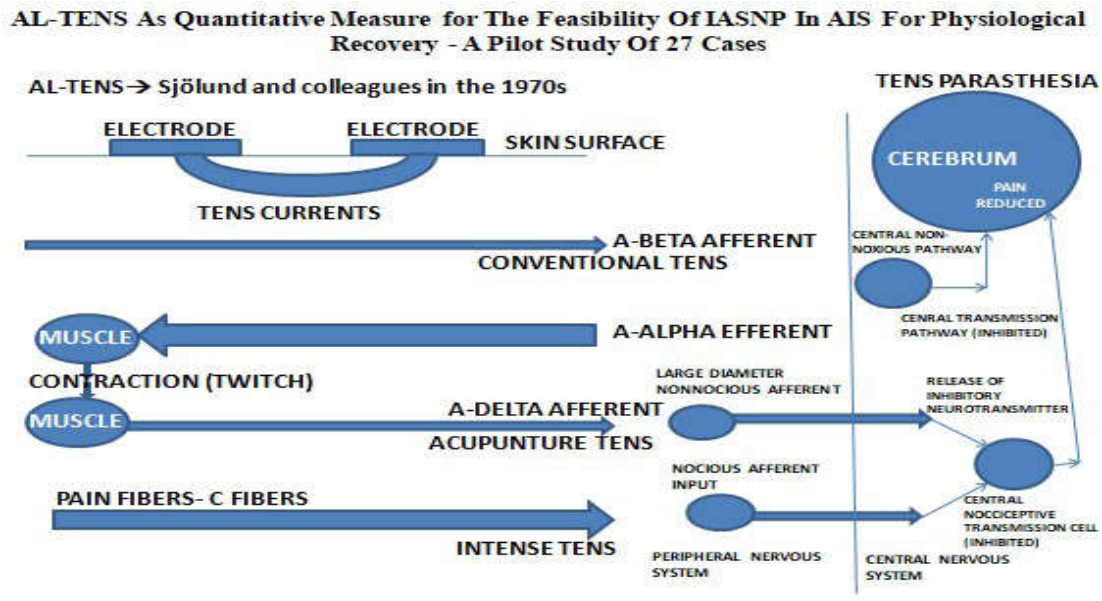

Fig. 1: AL-TENS as Quantitative Measure for the Feasibility of IASNP in AIS for Physiological Recovery - A Pilot Study of 27 Cases.

Table 1: Acute Ischemic Stroke Cases According To The Oxfordshire Community Stroke Project (Ocsp) Classification Clinically Subdivides Cerebral Infarction Into Total Anterior Circulation (Tacs), Partial Anterior Circulation (Pacs), Posterior Circulation (Pocs) And Lacunar (Lacs) Syndromes And Icsnp Feasibility Via Al-Tens.

S. No	Groups-4	27 Cases	Duration	Pre-Icsnp-Al-Tens	Post-Icsnp-Al-Tens	% Change	Pre Icsnp Nihss Grading	Post (2 Hrs) Icsnp Nihss Grading	Post (24 Hrs) Icsnp Nihss Grading	Post (7 Days) Icsnp Nihss Grading	Ost (7 Days) Icsnp Nihss GradingPost (21 Days) Icsnp Nihss Grading	Post (3 Months) Icsnp Nihss Grading
1	Lacs (Lacunar Strokes)	9	7 Days	5 to 6 mAmp	3 to 5 mAmp	20%	28	12	10	8	6	4
2	Pacs(Partial Anterior Circulation Strokes)	6	9 Days	3 to 5 mAmp	2 to 3 mAmp	15%	24	10	8	6	6	6
3	Tacs (Total Anterior Circulation Stroke)	5	6 Days	more than 8 mAmp	more than 8 mAmp	0%	32	32	32	32	30	30
4	Pocs (Posterior Circulation Strokes)	7	7 Days	5 to 7 mAmp	4 to 5 mAmp	15%	30	18	16	12	12	10

Measurement of the TENS Score

PREITSNP and POSTITSNP TENS (2 hours, 24 hours, 1 week and 3 weeks) done to get the various neurological assessment. TENS employed here was AL-TENS.

Results

The effect of ICSNP on 5th day onwards in an acute ischemic stroke cases was evaluated using NIHSS and AL-TENS current delivery readings. Neurological deficit (ND) scoring was analyzed clinically on the basis of NIHSS grading after 2 h, 24 h, 1 week and 3 weeks of ipsilateral intracarotid injection. All the selected cases were of LACS, PACS, TACS and POCS,

Our following work has been based on the following parameters based on TENS.

There were 18 males and 9 females and according to the Oxfordshire Community Stroke Project (OCSP) classification clinically subdivides cerebral infarction into total anterior circulation (TACS), partial anterior circulation (PACS), posterior circulation (POCS) and lacunar (LACS) syndromes. (Table 1).

Lacunar strokes (LACS) - 9 cases. 20% recovery seen in POST-ICSNP TENS and NIHSS recovery was 38%

Partial Anterior Circulation Strokes (PACS) – 6 cases. 15% recovery seen in POST-ICSNP TENS and NIHSS recovery was 23.8%

Total Anterior Circulation Strokes (TACS) – 5 cases. No recovery seen in POST-ICSNP TENS and NIHSS recovery was 0%

Posterior Circulation Strokes (POCS) – 7 cases. 15% recovery seen in POST-ICSNP TENS and NIHSS recovery was 28.57%.

Complete hemiplegia due to TOCS didn't show any change. While overall there was a change of 16.66% in POSTICSNP TENS and 30.12% in NIHSS grading. The PREICSNP-TENS of those cases who showed 8 mAmp or more than 8 mAmp muscle twitching did not get any benefit POSTICSNP-TENS. This effect of POST-ICSNP-TENS has increased from overall 16.66% to 24.96% after 24 hours. After 1 week overall 39.19% and after 21 days it has reached to 42.16%.

Discussion

Activated nerve impulses originated from AL-TENS after activating the A-DELTA nerve fibers via various cascades of neural connections from skin (dermatome) to muscle spindle enters spinal cord and thereafter brain, thereby inhibition by cerebrum and cerebellum on Renshaw cells, relieves the pain. Thus the various pathologies of spinal cord and then brain can have the predictability value of physiological damage and their recovery by AL-TENS and ICSNP at bedside itself in PRE-ICSNP phase and post ICSNP phase.

SNP (Sodium Nitroprusside) being a NOD (Nitric Oxide Donor) acts at postsynapse's nNOS (Neuronal Nitric Oxide Synthase) and releases NO (NITRIC OXIDE) which acts presynaptically and generates the impulse via 10000 fold effect[1,2,5], The Retrograde Neuroregulation.

In a previous article[5], ITSNP (Intra Thecal Sodium Nitro Prusside), in cases of paraplegias with clinical ZPP (Zone of Partial Preservation) and AL-TENS deflection has been shown highly effective previously by the authors.

AL-TENS is being used here in this present study too in a similar way as that for ITSNP[5] to get some PRE-ICSNP predictability, so that one can predict whether ICSNP is going to get some benefit in these cases (ischemic stroke) or not. AL-TENS is very much objective and a mere twitching of the myotomes or if there is a slightest muscle flickering with minimal current flow, suffices the need for ICSNP.

It was earlier demonstrated by the authors that ICSNP reduces infarct size after 5th day of infarct in rats.[1] The synaptic cleft's superoxide formation and its neutralization by serum superoxide dismutase (takes 5 days) and iNOS (neurotoxic) degradation in 5 days[3] gave an excellent idea in rat experimental study. This is well known as Rule of Five after well decompressed spinal cord and stabilized vertebra.

So authors again strictly followed the "Rule Of Five" for ICSNP along with AL-TENS. All patients chosen here were strictly 5th post ischemic days. PRE-ICSNP AL-TENS status of cases showed a 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 42.84% benefit from PRE-ICSNP status. This showed the AL-TENS has activated A-ALPHA nerve fiber which in turn activated A-DELTA nerve thereafter activated muscle spindle pathway from muscle to respective area of spinal cord, thereby the neuronal pathway from spinal cord to RENSHAW cells and brain is activated, thus, completing the whole pain modulating pathway. With this ICSNP and AL-TENS we were able to generate and access the whole pathway within intact or partial/complete ischemic damage respectively.

Upon search of literature we could not find any grading system of paraplegics based on TENS to quantify the ICSNP effect.

This effect of POST-ICSNP-TENS has increased from overall 16.66% to 24.96% after 24 hours. After 1 week overall 39.19% and after 21 days it has reached to 42.16% thereby showing an incremental increase too.

The intact A-DELTA nerve pathway denotes spinal cord is intact with its various synapses, where the SNP has worked via 10000 fold effect via nNOS.[5]

We didn't get any benefit in those cases in which PRE-ITSNP-TENS was having 8mAmp or more than 8mAmp readings for muscle twichings. This shows that the TENS has activated the Intense-TENS instead of AL-TENS and the patient is having complete paraplegia at that myotomes.

Limitations

The limitations of this study were the number of humans itself and not able to evaluate the 10000 fold effect via Pico Nano Second Absorption Spectroscopy (PNSAS) being no availability of the PNSAS at our setup. Our TENS machine has not got the facility of tracings, in fact we didn't find in literature that any TENS machine is having this tracing facility which can give any objective traceable document of effective muscle twitching. We didn't compare between AL-TENS and the SSEP and MEP while doing this study. Absence of clonus study. Reflexes can be judged by DTR and tens but power can't be judged by TENS or DTR. Power determination is done by clinical study only but we are not having any device/instrument which can grade the power of a particular myotome (on searching of literture).

Conclusions

ICSNP with the help of AL-TENS helps us to prognosticate the future outcome in partial hemiplegia. POST-ITSNP-AL-TENS after 2 hours showed 16.66% benefit overall and 30.12% in NIHSS grading. Complete paraplegia cases didn't show any change. This effect of POST-ICSNP-TENS has increased from 16.66% to 24.96% after 24 hours. After 1 week 39.19% and after 21 days it has reached to 42.16%.

Thus AL-TENS showed a favorable modality to predict the ICSNP feasibility in LACS, PACS, TACS AND POCS stroke cases. If PREICSNP TENS showed 8 mAmp or more there will be no response to ICSNP.

The above findings recommend the use of AL-TENS in PREICSNP stroke assessment after 5th post stroke day. In this study ICSNP with the help of AL-TENS done in Acute Ischemic Stroke cases helped us to prognosticate the future outcome of these cases.

Recommendations

Future study should include AL-TENS with tracing facility along with ICSNP

Number should be increased to around 100s so that exact conclusions can be drawn well.

If possible Pico Nano Second Absorption Spectroscopy (PNSAS) should be done in each excellent responding case to get 10000 fold effect's evaluation which can open up a plethora of research work further.

Disclosures: None.

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