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Case Report

10,000-Fold Effect by a Nitric Oxide Donor (Sodium Nitroprusside) in Motor Neuron Disease Via Intrathecal Superfusion

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Abstract

Motor Neuron Disease (MND) or Amyotrophic lateral sclerosis (ALS) is a slow fatal neurodegenerative disease characterized by selective and gradual motor neuronal death with unknown aetiology. The insufficient clearance of glutamate through the glutamate transporter and the specific distribution of Ca^{2+}-permeable AMPA receptors in spinal motor neurons, indicates that glutamate-induced neurotoxicity is involved in its pathogenesis. NO is generated by nitric oxide synthase (NOS) which acts via 10000-fold effect to reverse the neuronal death. NO is destructive within 5 to 7 days as noted in earlier study by various authors. We have used intrathecal sodium nitroprusside to activate the 10000-fold effect to modulate the retrograde neuroregulation in MND.

Keywords: Motor Neuron Disease; Amyotrophic Disease; 10000-Fold Effect; Intrathecal Sodium Nitroprusside

Introduction

Nitric oxide donors, like Sodium nitroprusside, modulates the antegrade neurotransmission via retrograde neuroregulation by 10000-fold effect, is well established by the previous authors [1]. In motor neuron disease (MND) or Amyotrophic lateral sclerosis (ALS) the insufficient glutamate transport induced motor neuronal gradual death [2] hypothesized by us that the 10000-fold effect would be one of the remedy in these dreadful conditions. The SNP causes release of NOS and then NO which causes 10000-fold effect which modulates the ANT via RNT. Previous authors also postulated the negative effect of NO but those authors had skipped the fact that the SOD and nNOS remains active at synaptic cleft for just 5 to 7 days [3].

We have utilised this ITSNP to induce 10000-fold effect after 5th day of MND diagnosis and after skipping the effect of SOD and nNOS. To quantify the effect we have utilised AL-TENS (acupuncture like transepidermal neural stimulation) in pre ITSNP and post ITSNP phase [4].

Case Report

A 42-year-old female presented in normal sensorium in OPD room on wheel chair bound condition with chief complaints of headache and fever off since NOV 2019, severe headache since march 2020 with upper limbs and lower limbs on both side (right more weak as compared to left side) with nasal voice and difficulty of deglutination and sore throat. No history of corona contact, tuberculosis or diabetes. On examination she has full GCS E54V5M6

(GLASGOW COMA SCALE), cranial nerves examination revealed normal 3, 4, 5, 6, 7, 8 nerve. 9th, 10th involved with nasal voice and loss of deglutination reflex. Motor examination showed right weaker as compared to left side. ASIA grading done in motor, sensory and bladder bowel involvement. Motor, normal nutrition of upper limbs and lower limbs both sides, tone increases on both sides below C5 myotomes, power 3/5 bilateral below C5 myotomes, grip 25% on right and 50% on left side. All Deep Tendon Reflexes were exaggerated below C5. Superficial reflexes absent below C5 and lower limb showing Clonus too. Sensory examination is showing 224/224 (all over body normal) without bladder bowel involvement. To secure airway we did tracheostomy as the lower cranial were involved and thus micro aspiration was one of the possibilities for chest infection.

MRI of brain stem done which showed some myelopathic changes in brain stem without any significant findings in rest of the cranial spinal axis (Figure 1).

AL-TENS has been done which showed 3 and 4 CN+ at left lower limbs (Figure 2-5 pre ITSNP, 2 hrs post ITSNP 2 hrs, 3 post ITSNP 24 hrs, 4 post ITSNP 7 days, 5 post ITSNP 14 days).

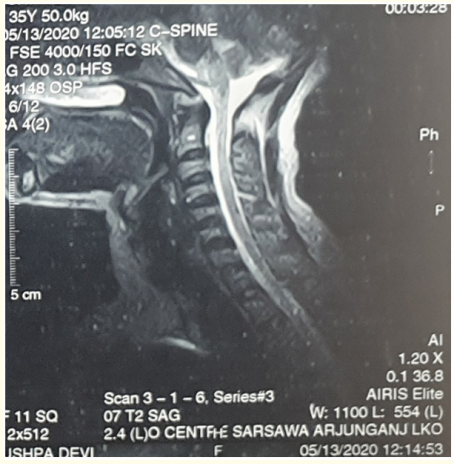

Figure 1: MRI of brain stem.

After well informed consent and telling all untoward action (like sweating and apprehension) of ITSNP we superfused ITSNP about 15 ml of the SNP given of 50 mg of SNP dissolved in 200 ml of Dextrose 5% solution with full photoprotection and freshly prepared. Post ITSNP AL-TENS done again after 2 hours, 24 hours, 7th day and 14th day and video recordings done also.

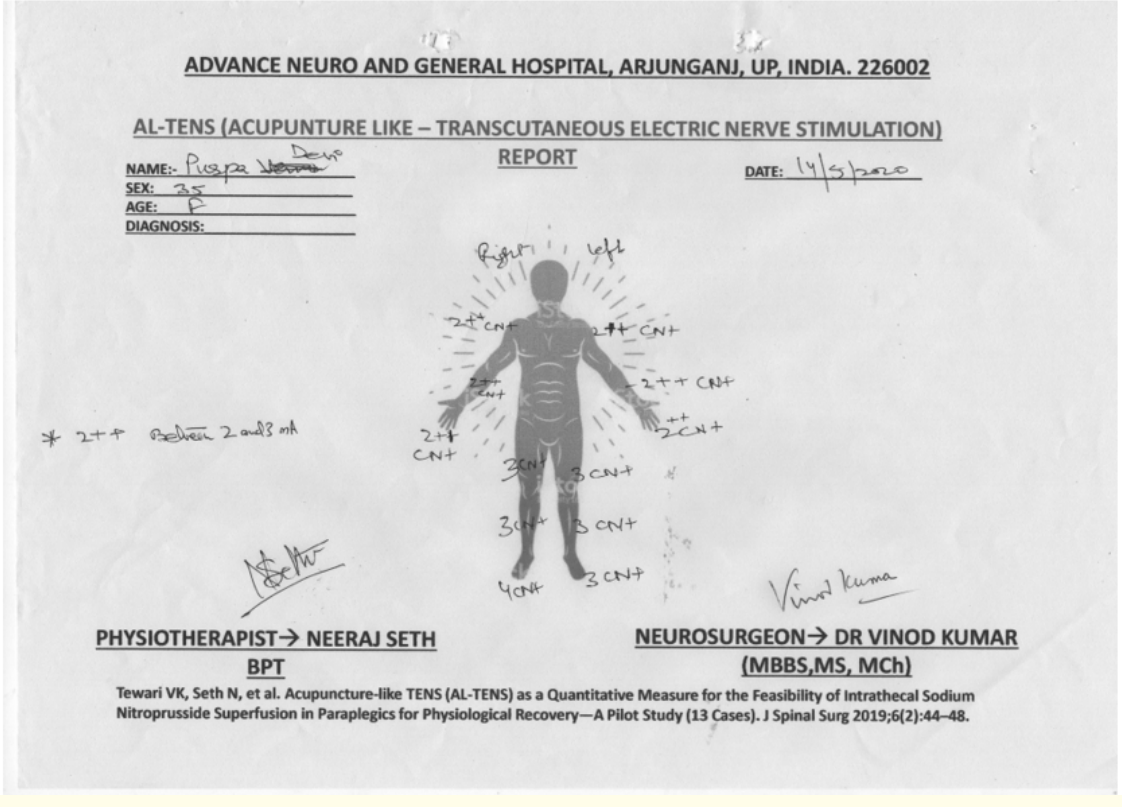

Figure 2: Altens-1[4] = Pre ITSNP Altens examination = Shows the right upper and lower limbs are more affected. Altens in right upper limb is at 2/10 all joints, right lower limbs 3/10 at left hip joint and knee joint and 4/10 left ankle joint, left upper limbs 2/10 all joints and left lower limbs 3/10 all joints.

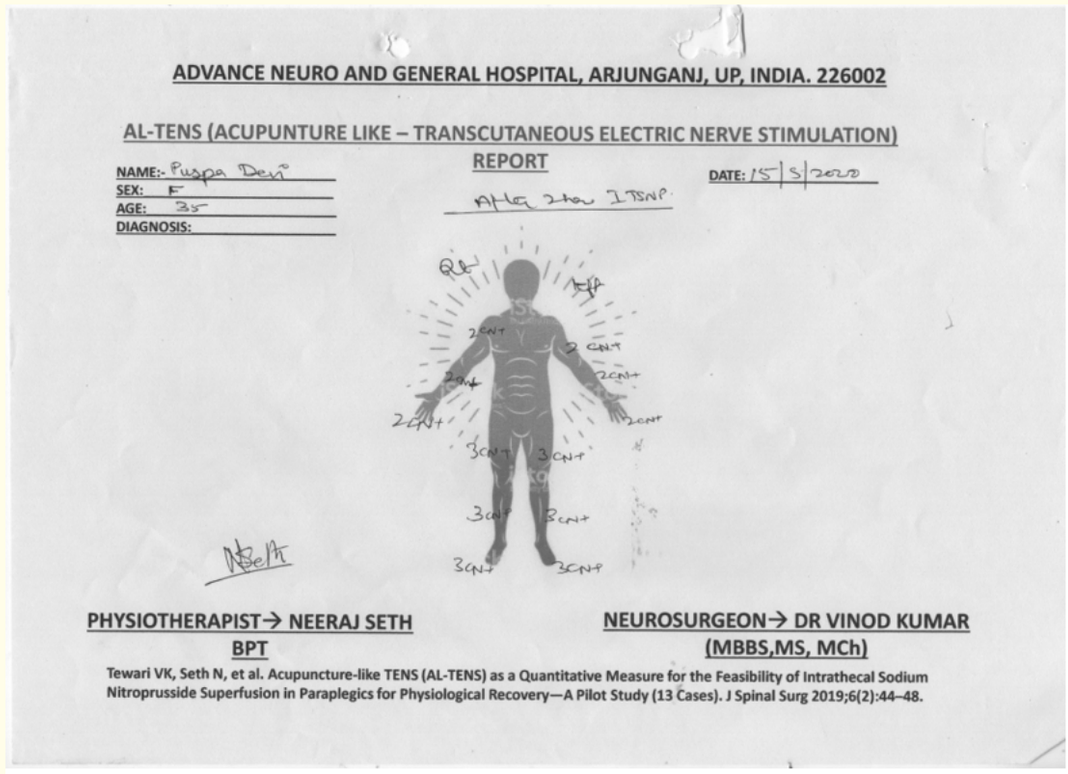

Figure 3: Altens-2[4] = Post ITSNP 2 hours Altens examination = Shows the right upper and lower limbs are more affected. Altens in right upper limb is at 2/10 all joints, right lower limbs 3/10 at all joints, left upper limbs 2/10 all joints and left lower limbs 3/10 all joints.

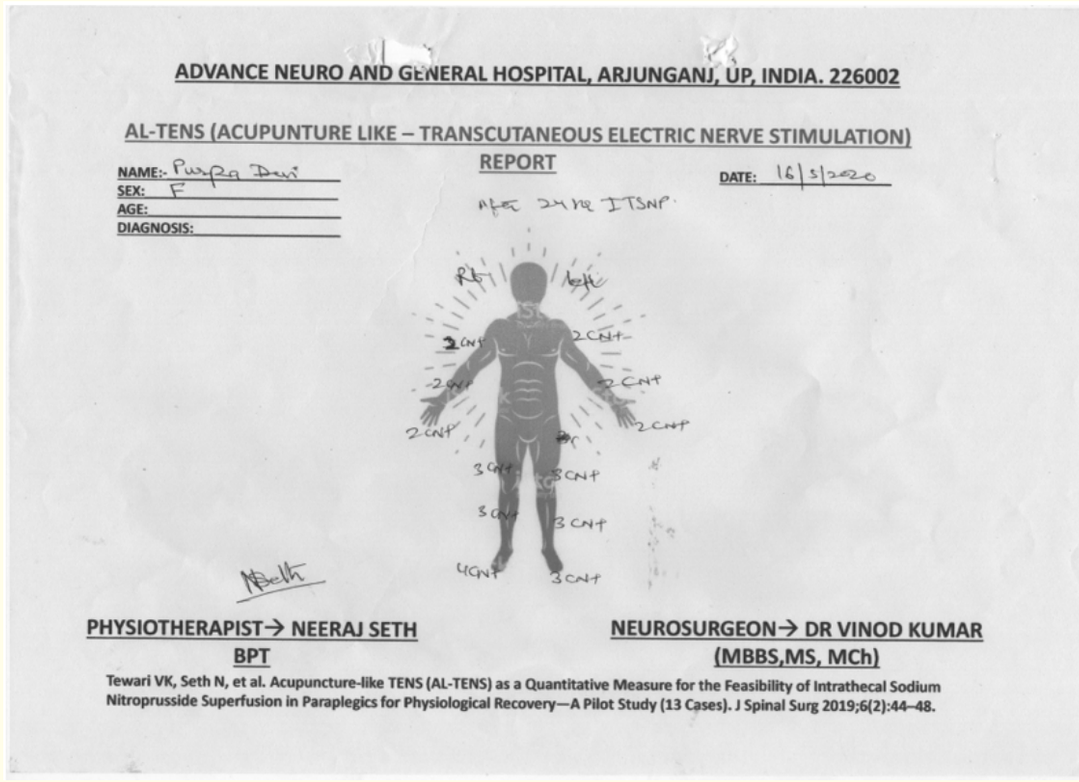

Figure 4: Altens-3[4] = Post ITSNP 24 hours Altens examination = Shows the right upper and lower limbs are more affected. Altens in right upper limb is at 2/10 all joints, right lower limbs 3/10 at left hip joint and knee joint and 4/10 left ankle joint, left upper limbs 2/10 all joints and left lower limbs 2/10 all joints.

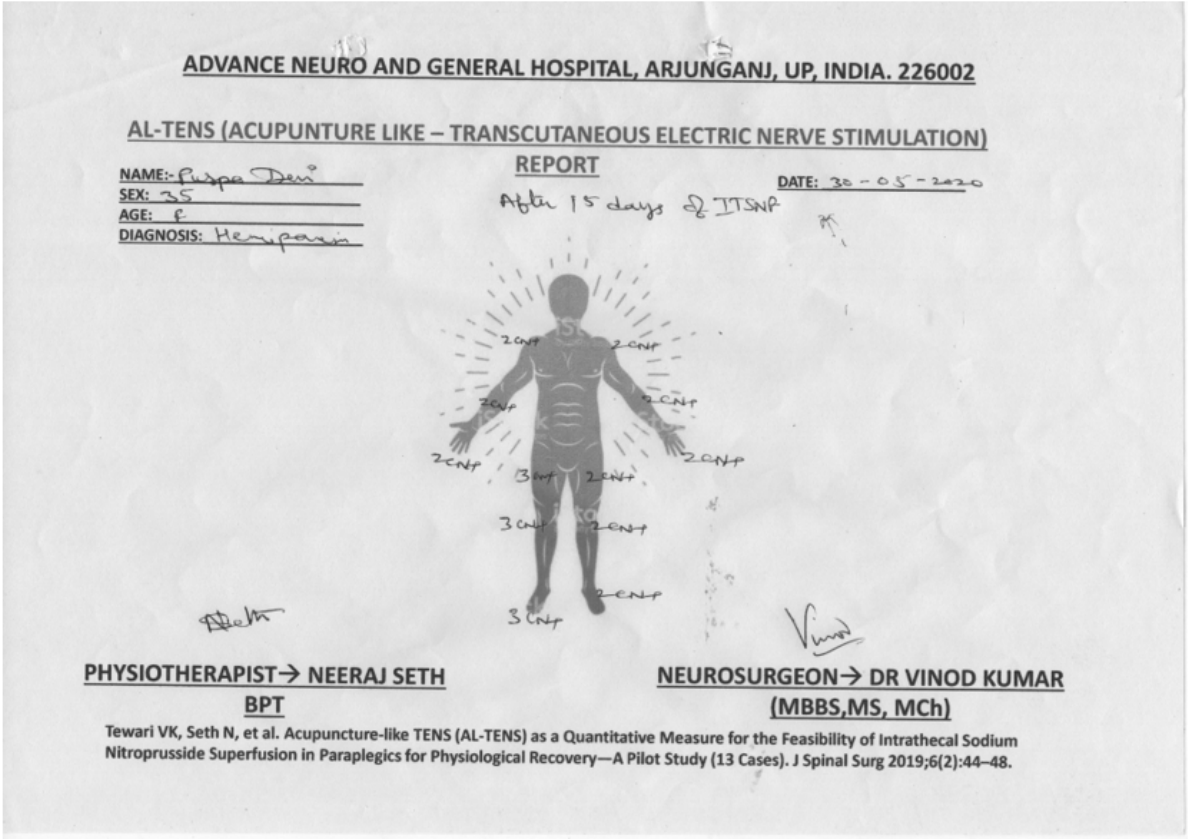

Figure 4: Altens-5[4] = Post ITSNP 14 days Altens examination = Shows the right upper and lower limbs are more affected. Altens in right upper limb is at 2/10 all joints, right lower limbs 3/10 all joints, left upper limbs 2/10 all joints and left lower limbs 2/10 all joints.

Discussion

The MND/ALS is a dreadful slow progressive disease. Mostly affects due to unknown aetiology but a proposed mechanism of MND/ALS pathophysiology is via insufficient glutamate transport induced motor neuronal gradual death [2]. The NOD releases NO which causes modulation of ANT via RNT by 10000-fold effect, thus increases the ANT impulses in those defective synaptic portions by bypassing the routine ANT impulses [1,3].

Reports showed no difference in the concentration of NO derivatives in the cerebrospinal fluid among several neurodegenerative diseases, including ALS [5] and moreover, nNOS-knockout mice with mutant SOD1 transgene showed the same clinical onset and duration as nNOS-expressing mutant SOD1-transgenic mice [6].

To secure airway we did tracheostomy as the lower cranial were involved and thus micro aspiration was one of the possibilities for chest infection.

Previous authors have proposed a negative remark in the use of NOD that the NO will produce a negative effect in MND/ALS [2]. But from our work [3] it was well proved that the SOD level and nNOS level comes to normal after 5 to 7 days and if we skip this time the 10000-fold effect comes to action to generate the ANT via RNT.

YouTube URL of PRE ITSNP and POST ITSNP phase is:

Pre ITSNP Phase

https://youtu.be/haFr8chkuVQ

Post ITSNP 24 hrs upper limbs movements

https://youtu.be/PUk0CF8fR0o

Post ITSNP 24 hrs lower limbs movements

https://youtu.be/P53J4wMwJAs

Post ITSNP phase 14th day

https://youtu.be/_eGFoWfJ0Kc

Post ITSNP 14th day

https://youtu.be/1wVT4k9Cz5Q

https://youtu.be/5RsEsOlJE40

Post ITSNP 15 days upper and lower limbs

https://youtu.be/eeZBZ3Wwc1U

Video 8- Post ITSNP 16 days upper and lower limbs

https://youtu.be/e2gSva-4xdc

Video 8- Post ITSNP 16 days upper and lower limbs

https://youtu.be/gghsypRdvQc

Video 9- Post ITSNP 18 days upper and lower limbs

https://youtu.be/wLrE16tWnVI

Conclusion

This case was well diagnosed as MND and after giving ITSNP to induce the 10000-fold effect got 75% improvement on 15th day of post ITSNP phase.

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