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Case Report

10,000-fold Effect by a Nitric Oxide Donor (Sodium Nitroprusside) in Parkinsonism Via Intrathecal Superfusion

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Abstract

Parkinsonism is a slow but nonfatal neurodegenerative disease characterized by hypokinesia, rigidity, postural instability and tremors, due to low quantity or deficient in dopamine neurotransmitter at Substantia Nigra, parkinsonism develops in, may be because of toxins, head injury or infections or drugs. Dopamine release is also regulated by NO (Nitric Oxide) which is generated by nitric oxide synthase (NOS) and NO acts via 10000-fold effect to reverse the neuronal parkinsonism clinical features. We have used intracarotid and intrathecal sodium nitroprusside to activate the 10000-fold effect to modulate the retrograde neuroregulation in Parkinsonism as a pilot study. The postural instability vanishes completely in 24 hours, loss of tremors was in just 48 hours, loss of rigidity around 5 days and hypokinesia improvement (to 75%) more than 30 days.

Keywords: Parkinsonism; 10000-fold Effect; Intrathecal Sodium Nitroprusside

Introduction

Parkinsonism is a slow, nonfatal but causes life difficult. Parkinsonism is a neurodegenerative disease characterized by hypokinesia, rigidity, postural instability and tremors due to drugs, toxins trauma and infections.

In Parkinsonism extensive and progressive loss of dopaminergic neurons in the substantia nigra pars compacta is noted. Molsidomine, a nitric oxide donor, modulates rotational behaviour and monoamine metabolism in 6-OHDA lesioned rats treated chronically with L-DOPA in rats in an experimental study [1].

In humans the role of nitric oxide synthases in Parkinson's disease as a virtue of the antioxidant and anti-inflammatory activity of polyphenols has been established [2]. Nitric oxide donors, like Sodium nitroprusside, modulates the antegrade neurotransmission via retrograde neuroregulation by 10000-fold effect, is well established by the authors [3,4]. The SNP causes release of nNOS (neuronal nitric oxide synthase) and then NO which causes 10000-fold effect which modulates the ANT via RNT. Previous authors also postulated the negative effect of NO (as double-edged sword if used within 5 days) but those authors had skipped the fact that SOD (superoxide dismutase) and iNOS (inducible nitric oxide synthase) remains active at synaptic cleft for just 5 to 7 days [4].

The pathological neural circuits for tremors are also well known and it is GABAergic neuron at cerebellar dentate nucleus, brain stem (locus ceruleans and inferior olives) and thalamus is involved causes

tremulous activity within the cerebellothalamocortical circuits [6]. The GABAergic neurons are also in turn controlled by the very sensitive 10,000-fold effect circuits via Nitric Oxide [7,8] (checked by PNAS-Pico Nanosecond Absorption Spectroscopy [9]).

We have utilised this IASNP {Intraarterial (Common Carotid Artery) Sodium Nitroprusside} and ITSNP (Intrathecal Sodium Nitroprusside) to induce 10000-fold effect after 5th day of Parkinsonism diagnosis and after skipping the effect of SOD and nNOS to induce the dopamine formation at substantia nigra pars compacta. To quantify the ITSNP effect we have utilised video recordings of pre ITSNP and POST ITSNNP clinical examination.

Case Report

A 52-year-old male presented in normal sensorium in OPD room on wheel chair bound condition with chief complaints of hypokinesia, rigidity, postural instability and tremors since NOV 2015. He has been treated with nearly all anti parkinsonism drugs of nearly each group since 2015. Then he was planned for DBS (deep brain stimulation). No history of chronic infection like tuberculosis, no drug induced history, no head injury or diabetes. On examination he has full GCS E54V5M6 (Glasgow Coma Scale), cranial nerves examination revealed normal 3,4,5,6,7,8, 9, 10, 11 and 12th nerve. Motor examination showed normal with ASIA grading done in motor, sensory and autonomic examination and found to be normal. Clinical features showed hypokinesia (especially fascial region), rigidity (clasp knife rigidity), postural instability (can't walk fast) and tremors (around 6 hertz per seconds) of whole body. Motor examination showed normal nutrition of upper limbs and lower limbs both sides, tone increases on both sides, power 5/5 bilateral all myotomes, grip 100% on both sides. All Deep Tendon Reflexes and Superficial reflexes were normal. Sensory examination is showing 224/224 (all over body normal) without bladder bowel involvement.

MRI of brain stem done which showed normal features in T1 and T2 and flair images.

After well informed consent and telling all untoward action (like sweating and apprehension) of ITSNP we did IASNP {Intraarterial (Common Carotid Artery) Sodium Nitroprusside} and superfused ITSNP (Intrathecal Sodium Nitroprusside) 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 clinical examination done with video recordings after 2 hours, 24 hours, 7th day and 14th day.

Discussion

Parkinsonism slow progressive disease. Most cases are due to progressive loss of dopaminergic neurons in the substantia nigra pars compacta [1]. 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 to release dopamine [2,3].

In our pilot study case, we have noticed the postural instability vanishes completely in 24 hours, which may be due to the fact of SNP causing better neuronal activity as a whole of all neurotransmitters in the brain due to its very potent and apt 10000-fold effect. we have noticed the loss of tremors was in just 48 hours, that may be due to the local activation of GABAergic neuron. Loss of rigidity took around 5 days and thus proving the activation of Dopaminergic neurons causing rigidity. The hypokinesia improvement took more than 30 days but still we find around 25% left. As this was the pilot study and we are not well equipped with PNAS (Pico Nanosecond Absorption Spectroscopy) facility in our institution, so the actual 10000-fold effect study remains in dark to prove herewith.

Positron emission tomography (PET) and single photon emission tomography (SPECT) provide sensitive means for quantifying the loss of nigrostriatal dopaminergic fibres in Parkinson's disease and for detecting the presence of dopaminergic dysfunction in asymptomatic at-risk relatives and patients with isolated tremor [10,11], this modality is still not available within institution.

YouTube URL of PRE ITSNP and POST ITSNP phase is:

Pre ITSNP phase

- https://youtu.be/uZz0MBE0Iag
- https://youtu.be/9dTYPlwt8M0

- POST ITSNP 5 DAYS LATER
- https://youtu.be/kpRu3QP8Hco
- https://youtu.be/A1jJZ6c5cFo
- POST ITSNP 38 DAYS LATER
- https://youtu.be/1upa2Qr4df4
- https://youtu.be/PZJ8oBP9Lv4

Limitations

- As only one case is studied as a pilot study, we are unable to prove many of the mechanisms but as the results were highly promising so this study needs a future case studies in the form of randomised control trial,
- We are not having PNAS (Pico Nanosecond Absorption Spectroscopy) with us so study should have been added with the investigations part too which is deficient here,
- The clinical improvement is being seen by only a panel of 4 doctors, which should have been seen by 2 groups or more doctors so that bias can be nullified,
- Patient himself and his wife are highly satisfied along with the patient relatives but more of the social gathering should be involved in the study.

Conclusion

This case was well diagnosed as Parkinsonism clinically and after giving ITSNP and IASNP to induce the 10000-fold effect got 85% (as per patient's clinical response and in his own words) improvement on 38th day of post ITSNP and IASNP phase.

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