10,000-fold Effect by a Nitric Oxide Donor (Sodium Nitroprusside) in Duchenne Muscular Dystrophy (DMD) Via Intrathecal Superfusion and Oral Tadalafil - A Case Report

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Abstract

Duchenne Muscular Dystrophy (DMD) is a slow, progressive and fatal X-linked neuromuscular disorder due to loss of dystrophin that links the contractile apparatus to the sarcolemma via the dystrophin-associated protein complex (DPC).

The NOD (Nitric Oxide Donor) causes release of Nitric Oxide (NO) by nitric oxide synthase (NOS) and then via 10,000-fold effect NOR (Nitric Oxide Receptor) it acts to release cGMP thus modulates DPC and improves the skeleton muscle functionality.

We have used intrathecal sodium nitroprusside to activate the 10000-fold effect to modulate the retrograde neuroregulation in DMD (diagnosed by muscle biopsy) and oral Tadalafil as NODs and well checked by AL-TENS (acupuncture like transepidermal neural stimulation) in pre ITSNP and post ITSNP phase.

Keywords: Duchenne Muscular Dystrophy (DMD); 10000-fold Effect; Intrathecal Sodium Nitroprusside; Oral Tadalafil

Introduction

Duchenne Muscular Dystrophy (DMD) is a slow, progressive and fatal X-linked neuromuscular disorder due to loss of dystrophin that links the contractile apparatus to the sarcolemma via the dystrophin-associated protein complex (DPC). If the DPC is defective then the contractile apparatus of muscle is damaged via excessive inward flow of calcium from extracellular compartment which leads to loss of regeneration and thus fibrosis of muscle fibres [1].

With the various modalities one can modulate the DPC and get better results. Like Restore NO bioavailability in dystrophic muscle including nNOS overexpression, L-arginine administration, Phosphodiesterase (PDE) inhibition and nitrate supplementation, with a focus on the effects on the architecture, function and metabolism of dystrophin-deficient skeletal muscle [1].

The nNOS (neuronal NITRIC OXIDE SYNTHETASE) is being released at the postsynaptic membrane at neuromuscular junction after activated by NMDA receptor and this in turn releases NO (NITRIC OXIDE) in the synaptic cleft which is being taken up by NOR (NITRIC OXIDE RECEPTOR). This NO donors (NODs), like Sodium nitroprusside (SNP), modulates the antegrade neurotransmission via retrograde neuroregulation by 10000-fold effect, is well established by the previous authors [2].

In Duchenne Muscular Dystrophy (DMD) the skeleton muscle is fibrosed due to defective DPC [1]. With the more bioavailability of NO by NODs like SNP via inducing nNOS at presynaptic membrane at neuromuscular junction, the DPC acts fast. The SNP causes release of NOS and then NO causes 10000-fold effect which modulates the anterograde neurotransmission (ANT) via retrograde neurotransmission (RNT). Previous authors also postulated the negative effect

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AL-TENS (ACUPUNCTURE LIKE – TRANSCUTANEOUS ELECTRIC NERVE STIMULATION)

NAME:- <u>RAKESH</u>	REPORT	DATE: <u>11-06-2020</u>
SEX: <u>Male</u>	<u>Post ITSNP</u>	
AGE: <u>22y</u>		
DIAGNOSIS: <u>DMD</u>		

PHYSIOTHERAPIST → NEERAJ SETH BPT	NEUROSURGEON → DR VINOD KUMAR (MBBS, MS, MCh)
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Tewari VK, Seth N, et al. 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). J Spinal Surg 2019;6(2):44–48.

Figure 2: Post ITSNP 15th day ALTENS.

After taking written confirmation that the patient in the study has given consent for the video recording and its clinical study to be published and well informed consent about 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 7 days and 14th day and video recordings done also. Then after ITSNP patient was given ORAL TADALAFIL 20 mg 1 TDS for next 7 days.

YouTube URL of PRE ITSNP and POST ITSNP phase is:

Video 1- Pre ITSNP phase.

Typical of DMD

Video 2- Post ITSNP 7 days

<https://youtu.be/0HRab6XLDuc>

<https://youtu.be/bg2vpQWNK7s>

Video 2- Post ITSNP 2 months

<https://youtu.be/uN9mOjWtoSc>

<https://youtu.be/XbaXBfDi8P0>

Discussion

The DMD is a dreadful slow progressive disease. Mostly affects due to defective DPC² mechanism. The NOD releases NO which causes modulation of ANT via RNT by 10000-fold effect, thus increases the ANT impulses in those defective DPC by bypassing the routine ANT impulses [1-3].

After cGMP activation via NOR, cGMP activates DPC and then the contractile apparatus causes appropriate contraction of muscle as such. With the deficient DPC, excessive intake of calcium is seen inside the sarcolemma and thus muscle's regeneration is hampered with excessive damage and fibrosis. With the increased nNOS activation via NOD the DPC gets optimal activation instead of low frequency, so the muscle contraction is benefitted with each antero-grade neurotransmission.

As far as human's use of TAB TADALIS is concerned it has been used in humans in two studies and both reported good recovery, we have used oral Tab TADALIS along with ITSNP so that the 10000-fold effect will cause swift modulation and then oral TAB TADALIS will maintain the effect later on. And got an excellent result.

The previous studies has been based on the muscle ischemia studies but we have utilised AL-TENS to quantify the neuromuscular junction functionality.

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 well tested via AL-TENS [5,6].

Conclusion

This case was well diagnosed as DMD and after giving ITSNP to induce the 10000-fold effect got 35% improvement on 15th day of post ITSNP phase.

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