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Case Report

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

of NO but those authors had skipped the fact that the superoxide dismutase (SOD) and nNOS remains active at synaptic cleft for just 5 to 7 days [3]. Up to now 2 studies have been done in humans where Tadalafil has been used but without ITSNP [4,5].

We have utilised this intrathecal sodium nitroprusside (ITSNP) to induce 10000-fold effect after 5th day of DMD diagnosis (diagnosed by muscle biopsy) and after skipping the effect of SOD and nNOS and oral Tadalafil also for maintenance.

To quantify the effect, we have utilised AL-TENS (acupuncture like trans epidermal neural stimulation) in pre ITSNP and post ITSNP phase [6].

Case Report

A 22-year-old male presented in normal sensorium in OPD room walking with lurching gate condition with chief complaints of walking with difficulty and difficulty to stand up from sitting for 2 years with upper limbs normal. No history of tuberculosis or diabetes. On examination he has full GCS E54V5M6 (GLASGOW COMA SCALE), cranial nerves examination revealed normal 3, 4, 5, 6, 7, 8, 9 and 10th nerve. Motor examination done with ASIA grading done in motor, sensory and bladder bowel involvement. Motor, normal nutrition of upper limbs but lower limbs both sides having moderate wasting of muscles, tone normal on both sides below C5 myotomes, power 5/5 bilateral below C5 myotomes, grip 100% on both sides. All Deep Tendon Reflexes were normal below C5. Superficial reflexes normal below C5 and lower limb showing normal reflexes but hypotonic gluteal muscles. The patient was asked to stand up from sitting posture then he was climbing on himself. Without any respiratory distress with single breadth count up to 49. Sensory examination is showing 224/224 (all over body normal) without bladder bowel involvement.

MRI of cervical, thoracic and lumbosacral spine done which shows normal spinal cord with thecal sac and cauda equina.

Muscle biopsy done which reported as Duchenne Muscular Dystrophy.

AL-TENS has been done which showed NORMAL on both lower limbs (figure 1, pre ITSNP, figure 2 = 15 days POST ITSNP).

Figure 1: Pre ITSNP ALTENS.

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 DPC[2] 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 anterograde 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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