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Review Article

Is Electrical Stimulation Useful for Patients with Duchenne Muscular Dystrophy? A Mini-review

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ABSTRACT

Duchenne muscular dystrophy (DMD) is a hereditary progressive neuromuscular disease of childhood. The survival rate of DMD patients is extremely low. In physiotherapy, electrical stimulation is frequently applied to rehabilitate these patients. The present study aimed to evaluate the effects of electrical stimulation on the muscles of patients with DMD. In this regard limited relevant studies were found, some of which reported the positive effects of low-frequency electrical stimulation on improving muscle strength. Conversely, there were reports of the detrimental effects of electrical stimulation on muscle fibers. Overall, there is no standard guideline for electrical stimulation in patients with DMD, and further research is required with adequate sample size and follow-up.

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1. Introduction

Duchenne muscular dystrophy (DMD) is a congenital, progressive, X-linked recessive neuromuscular disease caused by the mutated dystrophin gene [1]. The disease presents at birth almost exclusively in males [2] at a rate of 19.8 per 100000 live births [3]. Patients with DMD benefit from various pharmaceutical and other therapies and rehabilitation techniques during their lives [4], helping them survive up to around 30 years [5]. In physiotherapy, exercise therapy and electrical stimulation are traditionally used to stimulate and strengthen muscles [6]. Studies around the 1990s highlighted the beneficial effects of low-frequency electrical stimulation on muscle strength [7-10]; however, some studies have also reported conflicting results [11]. A 1997 study described the destructive effects of electrical stimulation on muscular fibers in dystrophic mice [12]. Despite the contradictory evidence regarding the usefulness of electrical stimulation in patients with DMD, this technique is currently used for patients referring to physiotherapy clinics daily. This study aimed to review and scrutinize the applicability and benefits of electrical stimulation in patients with DMD. This work was approved by the research ethics committee, Hamadan University of Medical Sciences (Registration Code: IR.UMSHA.REC.1401.123). This project has been approved by the Vice-chancellor for Research and Technology of Hamadan University of Medical Sciences (Code No: 14010206834).

2. History of electrical stimulation on the patients with DMD

Scott et al. in 1986 and 1990 conducted studies to assess the effects of electrical stimulation on the tibialis anterior and quadriceps muscles of patients with DMD, regarding the opposite limbs as the control [7, 8]. Evaluation of total muscle strength and percentage of maximum voluntary contraction was performed by an electromyometer device. In their earlier study (number of subjects=16), electrical stimulation (asymmetric biphasic current, 50-microsecond pulse width, 5-8 Hz frequency) was continuously applied on the tibialis anterior muscle for one hour, three times a day for 7-10 weeks, using carbon electrodes (4 cm^2). In their later study (number of subjects=6), electrical stimulation with a pulse width of 290 microseconds (asymmetric biphasic, 8 Hz frequency) was applied on the quadriceps muscle for three hours a day, six days a week, for 7-11 weeks, using 9.5 × 4 cm carbon electrodes. In contrast to the previous study, electrical stimulation in the recent experiment was delivered intermittently with rest and stimulation times of 1.5 seconds each.

These studies showed that in absolute values, electrical stimulation-induced contractions of the tibialis anterior muscle in Duchenne children (mean age 8.7±2.56 years) were about one-third of the healthy children (mean age 7.4±2.58 years), indicating weakness in DMD children compared to healthy children. However, the percent of maximum voluntary contraction following electrical stimulation was comparable between healthy and DMD children (29% vs 22%, respectively), and the coefficient of variation was obtained at 9% and 16% for the normal children and control muscles of DMD children, respectively. Upon 10 Hz electrical stimulation and 2-3 minutes after the quadriceps fatigue test, muscular strength significantly increased in healthy and DMD children.

Also, Zupan et al. in 1992 (number of subjects=9) and 1993 (number of subjects=12) assessed the effects of electrical stimulation on the right tibialis anterior in patients with Duchenne and Baker muscular dystrophy [9, 10]. Their studies applied electrical stimulation (six seconds) and rest episodes (six seconds) using surface electrodes. The electrical stimulation consisted of 0.2-millisecond pulse intervals, 8 Hz frequency, and 100 v amplitude and was applied for one hour twice daily for nine months.

The torque recorded after electrical stimulation was significantly higher for the right side than for the left side. Moreover, the relaxation time ($RT_{1/2}$) was significantly higher in affected versus healthy children. Overall, electrical stimulation did not change the fatigue index in healthy or affected children. After these studies, no studies on the effect of electrical stimulation on patients with DMD have been performed to date.

3. Discussion

Initially, Duchenne stated that electrical stimulation could be beneficial for patients with muscular dystrophy [13]. Limited studies have investigated this issue, particularly in patients with DMD. Four studies by Scott et al. and Zupan et al., conducted around 30 years ago, confirmed the positive effects of continuous low-frequency electrical stimulation on patients with DMD. Nevertheless, there is a paucity of well-designed studies with large sample sizes on this issue.

Preliminary studies have shown that the properties of muscle fibers vary depending on functional patterns dictated by the central nervous system. Likewise, electrical stimulation promotes a specific functional pattern in muscles [14, 15]. Studies have reported slow contraction and relaxation times and decreased ability of the sarcoplasmic network for calcium uptake in patients with DMD [16]. The typical firing

pattern of immature muscles in animal models has been a pattern of low-frequency activity [16]. However, detrimental effects have also been noted for high-frequency (30 Hz) stimulation, while at low-frequency (8 Hz) pulses, therapeutic effects may not persist [17]. Efforts have been directed toward using low-frequency stimulation (5-8 Hz).

The subjects in the four studies that examined electrical stimulation in Duchenne patients were boys ranging in age from 2 to 13 years. In Scott's first study, out of 16 people, 12 were able to walk independently, 2 needed help to walk, and 2 were wheelchair users. In the second Scott study and the two Zupan studies, all patients were able to walk, and the functional status of the Vignus-scale Zupan patients was about 3.

According to Scott et al. (1986 and 1990), if persistent low-frequency stimuli are applied when there is still no significant disability and loss of muscular mass, they can deliver positive outcomes by a) slowing the loss of available muscle fi $RT_{1/2}$ bers, b) promoting and accelerating the growth of regenerated fibers, and c) inducing the hypertrophy of available healthy fibers [7, 8].

Studies have reported no changes in muscle strength during fatigue tests and also declared no changes in fatigue index in children with DMD and their healthy counterparts following low-frequency electrical stimulation, possibly because muscle fibers are thin and effectively deliver oxygen in healthy children and due to prolonged contraction and relaxation times in affected children [9, 18]. It has also been reported that dystrophic muscles are more resistant to fatigue than healthy muscles [15]. Despite this, the use of high-duty cycle stimulation (50-100%) in these studies to increase strength is not justified and no cause has been reported. According to Scott et al., preserving the features of the "slow" muscle is the primary outcome of treatment, and low-frequency electrical stimulation does not alter muscle fibers' contractile properties [7].

Disease progression and its impacts should always be considered during any therapeutic intervention. The coefficients of variation have been reported at 16% and 27% in the studies of Scott et al. (1986) and Edwards et al. (1988), respectively, probably reflecting the lower age spectrum of children in Scott et al.'s study [8, 19]. Long-term low-frequency electrical stimulation was reported to improve the strength of the tibialis anterior and quadriceps muscles in patients with Duchenne and progressive muscular dystrophy [7, 8, 20], which are critical muscles for walking. Therefore, strengthening these muscles can delay disease progression and forthcoming disability. Furthermore, electrical stimulation has been described to promote sensory feedback and heat sensation in the target leg, improve blood circulation and metabolic function, and prevent connective tissue proliferation [7, 10].

However, Brown et al. declared that electrical stimulation did not affect the strength of the tibialis anterior muscle [11], contradicting the findings of Scott et al. (1986 and 1990) and Zupan et al. (1990 and 1993). As an explanation, it should be noted that Brown et al. enrolled adult patients with neuromuscular diseases and applied high-frequency stimulation (30 Hz). It is also noteworthy that studies reporting positive electrical stimulation effects on patients with DMD suffer from limitations such as small sample sizes and lack of adequate follow-up [4]. Moreover, Yoshida et al. (1997) declared that electrical stimulation could exaggerate muscular fiber degeneration in dystrophic mice, partly due to the intracellular accumulation of calcium and activation of proteases [12]. Unfortunately, no comprehensive studies have been conducted in recent years to divulge the beneficial or adverse effects of electrical stimulation on patients with DMD.

4. Conclusion

According to what was previously mentioned, the possible positive effects of continuous low-frequency electrical stimulation on Duchenne dystrophic muscles are not clearly understood. Thus, physiotherapists are recommended to be vigilant when using electrical stimulation in patients with DMD and employ alternative exercise therapy programs [21]. It is also recommended to conduct a comprehensive study with a sufficient sample size and an appropriate follow-up period to shed light on this issue.

Ethical Considerations

Compliance with ethical guidelines

This work was approved by the Research Ethics Committee, Hamadan University of Medical Sciences (Code: IR.UMSHA.REC.1401.123). This project has been approved by the Vice-Chancellor for Research and Technology of Hamadan University of Medical Sciences (Code: 14010206834).

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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