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BENEFICIAL LOW INTENSITY EXERCISE IN DIABETIC PERIPHERAL NEUROPATHY PATIENTS

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ABSTRACT

The American Diabetic Association standards of medical care for diabetic patients recommends Moderate intensity exercise to help manage diabetes; however, this recommendation may be unmanageable for Patients who have become inactive or unable to reach this intensity Exercise training is an established method for increasing the different components of physical fitness, including enhancing body composition and improving Neuromuscular strength.

KEYWORDS: Neuromuscular function, Diabetic peripheral neuropathy, Diabetes mellitus, Hyperglycemia, Physical training.

INTRODUCTION

Diabetic peripheral neuropathy (DPN) is a Complication of both type 1 and type 2 diabetes.[1] DPN has a complex pathogenesis marked by both Metabolic and vascular factors.[2] Even though Diabetes is a precursor to neuropathy,hyperglycemia is only one of the many key metabolic events known to cause axonaland micro vascular injury.[2] It has been suggested that damage to small nerve fibers May precede damage to large nerve fibers which Convey proprioception, innervate skeletal muscles, and mediate tendon reflexes.[1] Metabolic Syndrome and obesity have also been linked to DPN.[3,4] In order to better manage diabetes, metabolic Syndrome, and obesity, the recommendation for Diabetic patients based on the ADA Guidelines is 150 Minutes per week of moderate intensity exercise.[5] For patients who have become inactive or unable to reach that intensity, this recommendation may be Unmanageable. Symptoms that become uncontrolled can lead to a decreased quality of life, increased risk of amputation, and increased medical costs.[6] Therefore, by incorporating low-intensity exercises into initial therapy, small Increases in both the Vascular and metabolic pathways could have Potential to decrease painful

neuropathic symptoms.

A muscle's ability to respond to an exercise stimulus is likely related to thedistal to proximal progression of vascular and nervous system disease associated with DPN. The Vascular and nervous system mediators of neuropathic muscle adaptation that may be Critical are muscle specific micro vascular perfusion, glucose uptake, and neural drive How Ever, the current standard measures of these mediators are not precise or muscle specific. For example, (1) micro vascular dysfunction from type 2 diabetes-associated peripheral Neuropathy is not detected with common microvascular assessments (ankle brachial index); (2) muscle specific metabolic function is not adequately measured with whole body Indices (homeostatic model assessment of insulin resistance score); and (3) muscle strength, A measure of motorneuropathy, is unable to decouple neural transmission from a muscle's Intrinsic contractility.

PATHOPHYSIOLOGY

Diabetic peripheral neuropathy results from various biochemical perturbations and is categorized by widespread damage to the peripheral nerve fibers, which can lead to Pain, foot ulcers, diminished mobility, impaired quality of life, and significant morbidity. The exact mechanisms behind the pathogenesis of DPN are still unknown due to the Multi factorial nature of the disease; however, chronic hyperglycemia with a significant Drop in insulin sensitivity seems to be at the forefront of DPN causes.[18] Muscle specific Glucose uptake, microvascular perfusion, and neural drive seem to be key components in the development of DPN and important mediators of the response to exercise interventions Among those with type 2 diabetes (T2D).

METHOD

Detailed search of PubMed, EMBASE, Scopus and Web of Science databases was conducted from their inception to March 2021 for the following key terms: 'diabetic new- Rotates' OR 'diabetic peripheral neuropathy' OR 'diabetes 'AND 'muscle' OR 'peripheral nerves' OR 'neuromuscular system' AND 'exercise training' OR 'aerobic training' OR 'resistance training' or 'combined training'. The systematic Reviews and original research papers were selected according To their scientific relevance.

We systematically searched PubMed, SCOPUS, and Cochrane Library databases for studies on exercise Therapy from 2013 to December 2017. We narrowed the search of "exercise

therapy" AND "peripheral Neuropathy" to a more focused "low-intensity Exercise" AND "peripheral neuropathy" within the Realm of diabetes. Other searches used to find Clinical trials and literature reviews include: "aerobic Exercise" AND "peripheral neuropathy" and "yoga" AND "peripheral neuropathy." In looking at what to Consider low-intensity, we followed the Centers for Disease Control and the U.S. Department of Health And Human Servicesphysical activity guidelines (Figure 1).

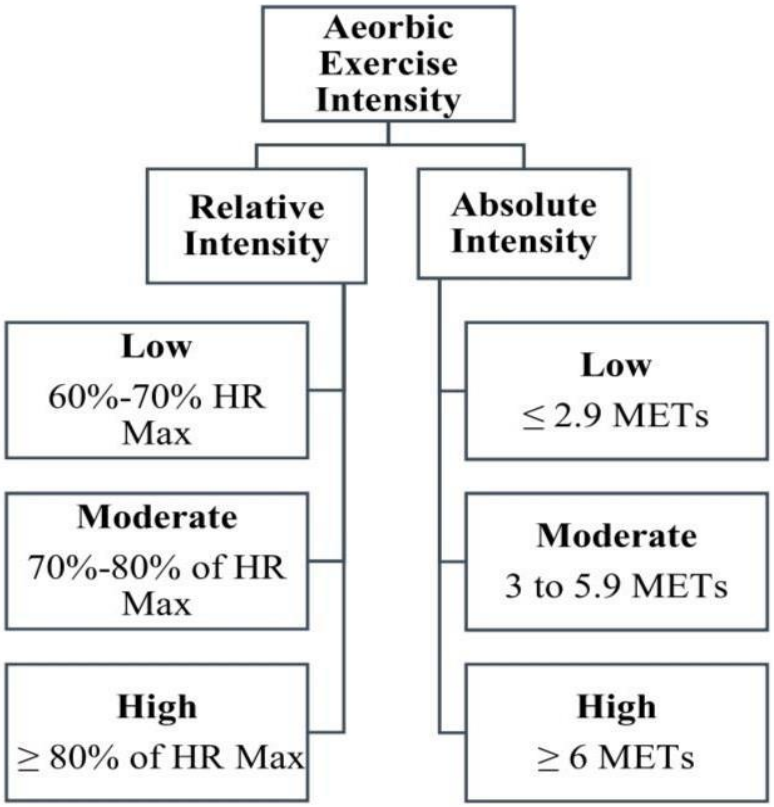

Figure 1: Categorizing Exercise Intensities. HR Max refers to the maximum heart rate of patient. MET refers to metabolic equivalent tasks this information is adapted from the Centers for Disease Control, the Office of Disease Prevention and Health Promotion.[7,8]

Neuromuscular Function and Diabetic Peripheral Neuropathy

Neuromuscular dysfunction is a typical complication of DPN, Characterized by loss of muscle strength (i.e., force-producing Capacity) and power (i.e., force velocity) that is attributable To both a loss of muscle mass (atrophy) and poor muscle quality (i.e., low/reduced force per unitof muscle area).[10-16] In Addition to a progressive loss of contractile tissue (atrophy), There is also an accumulation of intra- and inter-muscular Adipose tissue, capillary rarefaction and loss of oxidative Capacity.[11,13,17] Muscle

abnormalities first occur distally in the toes and feet before gradually spreading to the leg And thigh muscles.[2]

Structural and functional deficits of The muscle progress with the severity of DPN.[18] Major detrain Mental effects have been documented in the ankle (i.e., ankle Plantar flexors) and foot muscles (i.e., intrinsic foot muscles)[12,13,16] although a recent study has reported similar strength reductions (-30%) in ankle and knee extensors in a strength reductions (-30%) in ankle and knee extensors in a Mixed group ofdiabetic patients with and without DPN.[17]

Several cross-sectional studies in large numbers of both T1DM and T2DM patients with DPN[6,10,14,24,25] have Reported that neuromuscular dysfunction is an early, rather Than a late complication of DPN as previously postulated by. Andersen et al.[26] and that muscles that are seemingly Not affected by peripheral neuropathy (e.g., upper body). May also be involved. For instance, 20% 40% lower muscle Strength during dynamic andstatic tasks was detected in Boththe upper (i.e., shoulder and arm muscles) and lower Body (i.e., thigh and hip muscles) of patients with mild to Moderate DPN compared to healthy individuals.[10,14,25] These findings indicate that muscle dysfunction is an early Hallmark of DPN that is only partly explained by peripheral Motor nerve damage. There is also evidence that muscle Function impairment is an independent correlate not only of DPN but also of autonomic neuropathy and diabetic retinae Thy, promoting the concept that the combination of more Complications is related to the greatest muscle decline.[6,24]

NEURAL AND MUSCULAR FACTORS UNDERLYING THE LOSS OF NEUROMUSCULAR PERFORMANCE

Although the mechanisms underlying the impaired neuro-muscular function in diabetes and DPN are complex and Not entirely clear, it is important to note that chronic hyper - glycemia is capable of altering the vascular and sensory Motor systems. Indeed, as showed in Fig. 1, chronic hyperglycemia may cause not only denervation by damage of the peripheral nerves but may also alter muscle fiber function Through several mechanisms among which non-enzymatic gyrationof skeletal muscle proteins.

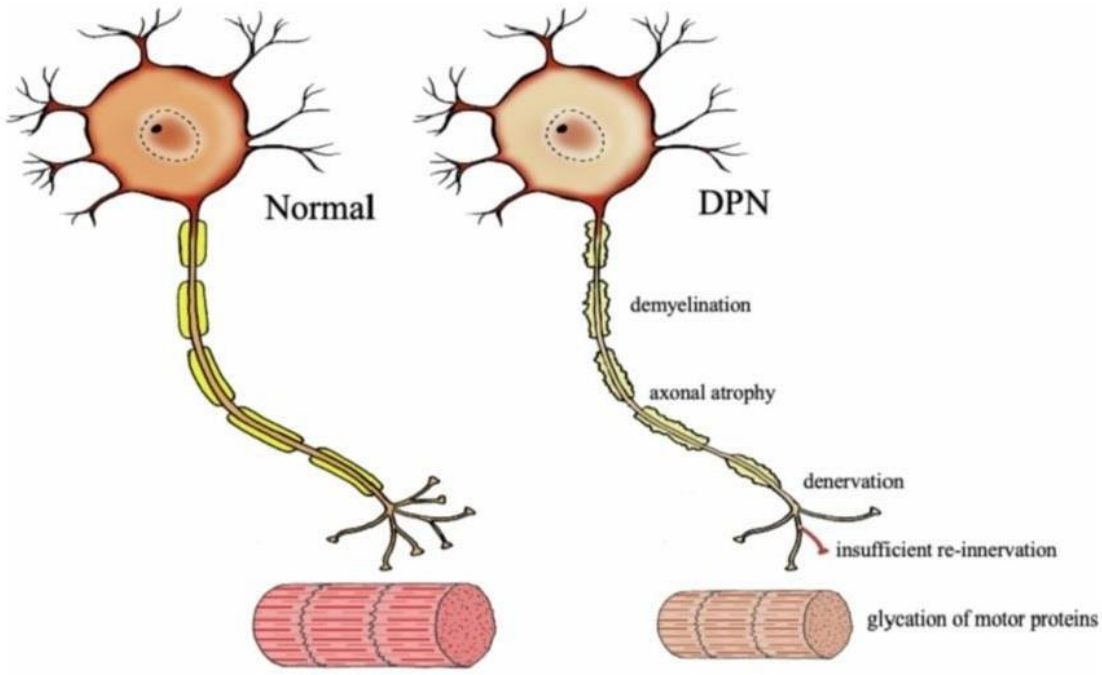

Fig. 1: Effects of diabetic peripheral neuropathy on motor nerve and muscle fiber.

EXERCISE BASED INTERVENTION

Aerobic Exercise Training

Aerobic exercise is one of the most studied exercise modalities. It recruits large muscle groups to perform dynamic, rhythmic movements done over a prolonged period of time (e.g., walking, jogging, cycling, and swimming). Engagement in regular aerobic exercise Sessions is typically done to improve endurance; however, it produces a wide range of additional health benefits. increases in cardiorespiratory fitness is largely associated with A reduction in all- cause mortality, specifically from cardiovascular disease, and those With high levelsof cardiorespiratory fitness have a greater level of habitual physical Activity.[68-72] previous research investigating the effects of aerobic exercise intervention Among individuals with T2D has observed many favorable changes in metabolic health, Body composition, and maximal oxygen consumption.[73,74]

Physical Fitness

Sedentary behavior has been a longstanding global pandemic and is recognized As one of the top five leading contributors to premature mortality.[88,89] Moreover, An individual's level of cardiorespiratory fitness is strongly associated with their premature death from all causes and how much physical activity they engage in.[90] Fatigue during common daily activities is a common symptom reported by individuals with Type 2 diabetes and DPN, further propagating a sedentary lifestyle potentially resulting in Lower cardiorespiratory fitness, decreased

muscular strength, and increased body fat.[91,92] Morrison et al.[36] had 16 individuals with DPN complete 12 weeks of aerobic exercise Sessions occurring three times per week. Subjects were randomly assigned to one of two Is caloric aerobic exercise training groups.

Hyperglycemia

Chronic hyperglycemia plays a key role in the pathogenesis of DPN.[66,67] Through Several disturbances in the metabolic pathways, hyperglycemia leads to abnormalities in Nerve polyol, hexamine and protein kinase C pathways.[68] This triggers the release of PR inflammatory cytokines [poly ADP-ribose polymerase (PARP)], the accumulation of advanced gyration end products (AGEs) and generation of reactive oxygen species[68] [60new Simultaneously, microangiopathic changes of the vasa nervous result in Neurochemical.[69] This is further exacerbated by impaired endothelial nitric-oxide Mediate vasodilator mechanisms (nitrosamine stress).[70] Separately and in concert, these Glucosemia metabolic and ischemic changes lead to DPN by producing nervous system Oxidative stress and apoptosis of both neurons and supportingglia.

CONCLUSION

It appears that muscular dysfunction In DPN is caused by a synergistic effect of the diabetic state and motor nerve damage. Such deficits present in the early stages of DPN and progress withthe severity of peripheral nervous system damage. Loss of functional motor units, neuromuscular Transmission Impairment and gyration of myofibril proteins in muscle Fibers have been proposed as the primary factors contributing to muscular system impairments in diabetes patients. Muscle Function deficits are particularly severe in the lower extremities. Given the significant role of neuromuscular complications in impaired physical function, these deficits should be monitored, and strategies aimed at alleviating them should Be included in the standard care of DPN patients.

AUTHOR'S CONTRIBUTION

The work was designed by corresponding author Mr. Rakesh Jadhav, reviewed the manuscript, and also put a lot of efforts to improve the quality of the manuscript.The data collection and manuscript writing was carried out by Mr. Darshan Ekhande, Miss. Roshani Gharate and Mr. Santosh Borase.

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