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Balance And Gait Training In Diabetic Peripheral Neuropathy: A Narrative Review

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INTRODUCTION

Diabetes is a common metabolic disease having serious health implications and its incidence is increasing day by day. The global burden of diabetes is alarmingly high, with over 382 million diabetics in 2013 which is expected to rise up to 592 million by 2035 [1]. 60% of the world diabetic population resides in Asia [1], with Southeast Asia having around 72 million adults with diabetes in 2013 and this figure is expected to rise to 123 million by 2035 [2]. Long-term diabetes presents with various complications including retinopathy, nephropathy, neuropathy, arteriosclerosis etc. One of the many complications of diabetes mellitus is diabetic peripheral neuropathy (DPN), which is defined as "the presence of symptoms or signs of peripheral nerve dysfunction in people with diabetes after exclusion of other causes [3]. It is estimated that 60% to 70% of diabetics have mild to severe forms of nervous system damage [4]. DPN is one of the serious known micro vascular complications of both type 1 and type 2 diabetes mellitus having been diagnosed in 20-50% of the diabetic population [8].
The incidence of developing DPN increases with the chronicity of the disease and poor glycemic control [13,14]. Moreover, balance affliction is found in 16% diabetics [15] which may increase up to 30 to 50% with increase in the severity of the disease [16]. Peripheral neuropathies associated with diabetes are of several types. This review however, focuses on chronic sensorimotor DPN, which is most the common presentation of DPN. Peripheral neuropathies occur deceptively and start with reduced sensitivity followed by motor nerve impairment following distal to proximal pattern [17,18]. About 50% of patients may experience symptoms like burning pain, electrical or stabbing sensations, paraesthesia, hyperaesthesia, and deep aching pain [5]. Sensory disruption in diabetes leads to loss of vibration, pressure, temperature and pain (mediated by small and large afferent fibres). It also contributes to decrease in proprioception and increased reflex reaction time [19-21]. In addition, as many as 30% of people with DPN experience muscle weakness, loss of ankle reflexes, and decreased balance, coordination and gait control [4,22]. All these risk factors limit walking and other activities and increase the incidence of fall- related injuries [20,21,23].
Previous studies have reviewed the gait characteristics in DPN [24] and the effect of various modalities to improve balance in DPN patients [25]. However, they did not take into account balance exercises as an intervention. In addition, the reviews by Liu and Frank [26] and Streckman et al. [27], present the efficacy of exercises to improve balance characteristics in older patients and patients with peripheral neuropathy respectively. This necessitates compiling the findings of studies which examine the effectiveness of balance exercises specifically in patients with DPN. Therefore, the present review aims to discuss the pathogenesis and factors associated with DPN, concept of balance and postural control, balance and gait impairment in DPN and balance exercise interventions used to improve balance and gait parameters in DPN population.

METHODS

A literature search was performed using Google Scholar, PubMed and Cochrane databases. A total of 66 items showed up on PubMed and 20 on Cochrane with the term "balance training in DPN". The search terms used were 'Diabetes mellitus', 'type 2 Diabetes Mellitus', 'Diabetic neuropathy', 'Diabetic peripheral neuropathy', 'Glycemic control', 'balance', 'gait', 'falls risk', 'proprioception', 'postural control', 'postural stability', 'balance exercise' and 'balance training'. A broad research approach was chosen to minimize the chances of missing relevant articles. Articles that assessed variables reflecting balance & gait characteristics and the effect of balance training provided to DPN patients independently or in combination with other exercise, were included. Exercise interventions other than balance training were excluded. The studies were double checked and only full text articles were used for the review. Total 9 studies were selected to emphasize the balance and gait abnormalities in DPN patients and 11 studies were selected to demonstrate the effect of balance exercise in improving balance and gait in DPN patients (summarized in Table 1 and Table 2 respectively). These studies were reviewed in a narrative way.

DPN: Pathogenesis

DPN is said to be caused by both vascular as well as non- vascular abnormalities [28-30]. The theory although controversial, suggests that both mechanisms are a consequence of metabolic aspect (i.e. chronic hyperglycemia). Chronic hyperglycemia impairs micro vascular circulation by disrupting normal cellular communication and initiating signaling cascades [30-32]. The production of end products of advanced glycation signaling cascade of protein kinase C [30-32] leads to the demyelination associated with DPN [33], resulting into axonal thickening with progression to axonal loss[34], basement membrane thickening, pericyte loss [35,36], loss of microfilaments (i.e. cyto skeletal filaments comprising act in and myosin) and decrease in capillary blood flow to C fibers [37] leading to decreased nerve perfusion and endoneurial hypoxia [35,36]. Furthermore, evaluation of C-nociceptive-fiber function using the nerve–axon reflex revealed that small-fibre impairment is an early event during natural history of DPN [38] These cellular-level impairments are manifested as loss of ankle reflexes, decreased position and vibratory sense, and sensory ataxia. In addition, patients with DPN often demonstrate a delay in reflex responses when subjected to postural perturbations due to decrease in nerve conduction velocity, manifested as impairments in balance and thus an increased risk for falls [19].

Sensory nerve impairment

Sensory loss can be restricted to the toes; it can extend over to the feet; or spread over the lower legs or cross the knee level, totally depending on how intense the peripheral nerve lesions are. Later, it may progress to upper extremities and trunk. In most severe cases the summit of the scalp can be affected as a consequence of the involvement of the longest fibres of the trigeminal nerve [39]. In the proximal parts, superficial sensations such as pain and temperature are predominantly affected. Thermal sensibility too gets reduced either individually or along with loss of vibration sense [40]. Loss of large myelinated fibres and other proprioceptive afferent fibres causes disturbed light touch sensation, pressure sensibility, joint position sense and vibration. Disturbed joint position sense leads to increased instability of posture [41].

Motor nerve impairment

Weakness in the distal parts of the body happens late in the natural history of DPN. With increased severity of DPN, a positive Romberg's sign and ataxia may be found due to the weakness in the ankle plantar flexors and dorsiflexors [41]. This instability in the muscles leads to difficulty in maintaining the balance (static as well as dynamic) and it ultimately affect the gait.

BALANCE AND POSTURAL CONTROL

Balance is defined as the ability to maintain or return the body's centre of gravity within the limits of stability that are determined by the base of support [42]. Postural control is the control of the body's position in space for the purpose of balance and orientation [43]. Balance is concerned primarily with preserving, attaining, or restoring the centre of mass in relation to the limits of stability within a given base of support [44,45], and plays an important role in mobility as well as stability. Balance or postural control depends on the interactions between sensory inputs (somato sensory inputs, visual inputs and vestibular inputs) and motor response via central integrative processing systems (Figure 1). If there is any change in the sensory input it would lead to alteration in the motor response, so that appropriate responses to any external or internal perturbation can be chosen during static and dynamic positions of the body [46].

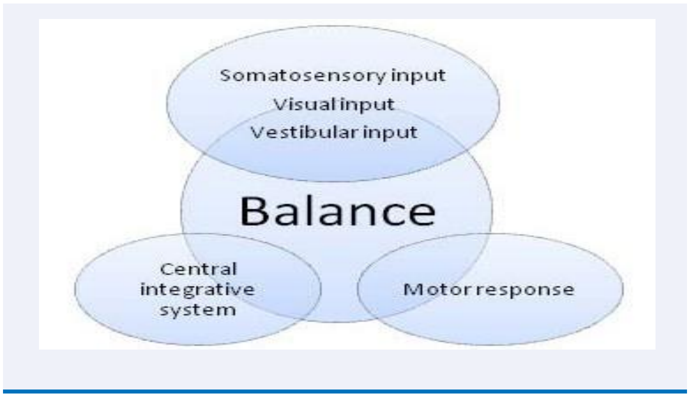

Figure 1 Components of Balance Control.

Somatosensory inputs

In the healthy, somatosensory system is comprised mainly of the proprioception and tactile sensations, where, proprioceptive sense is about joint angles, changes in the joint angles, joint position and muscle length and tension while tactile sensation is associated with sensations of touch, pressure and vibration. Each sensory stimulus makes a unique contribution to control posture.

Evidence suggests that the body's static and dynamic positions are based on muscle proprioceptive inputs that come from foot and around the ankle joint to give continuous information to the central nervous system about the position of the body for postural regulation [47-49]. Other than this cutaneous sensation from sole of the foot has sufficient spatial relevance to induce adapted regulative posture [50]. Wang & Lin found association between increased severities of loss of plantar cutaneous sensitivity and postural sway. In addition, application of sub sensory mechanical noise reduces the postural sway. During upright stance position, somatosensory information from legs and feet guides both sensory feedback as well as use of experience in scaling the magnitude of the responses. Reduction in the somatosensory information alters the rate as well as the magnitude of postural response.

Visual inputs

Vision has very evident role in postural control resulting from complex synergy that receives multimodal inputs. Visual inputs distinguish between translation and rotation of the head. Static visual cues may slowly control re-orientation or displacement, whereas dynamic visual cues may contribute to fast stabilization of the body [56]. Impairment of vision is strongly associated with falls in the elderly as reported in epidemiological studies.

Vestibular inputs

Vestibular information contributes to stabilization of head during various tasks for gaze control. Head stabilization can optimize postural control when visual information is lacking and during complex equilibrium tasks, it provides a stable reference frame from which to generate postural responses. Vestibular loss will lead to decreased trunk control but less effect would be imposed on the legs, due to legs leading inter segmental relation dynamics.

Motor response

Basic motor response for postural control is tone of the muscle and coordination between movement and posture. Voluntary movements show three main characteristics for postural adjustments: anticipatory movement, adaptation to condition and righting reactions to a certain task that is to be performed. During movement of one segment, if the other segments are disturbed, it will produce instability; therefore, stabilization of proximal segment is essential to produce precise movement of distal segments. Along with this muscle weakness and muscle fatigue are also considered for postural control.

Central integrative system

Another aspect of postural control mechanism is the central integrative processing system, where an individual has to process the information coming from different sensory inputs for the appropriate and accurate response. If the central integrative processing is affected there is an increase in reaction time in case of presentation of conflicting sensory inputs.

DPN: BALANCE AND GAIT DISTURBANCES

Balance and gait characteristics change as one’s age progresses and presence of DPN in elderly populations plays a significant role in the incidence of falls. Static as well as dynamic balance both are affected in DPN. Various factors that affect the balance in this population are a result of significantly impaired sensation, proprioception impairment, movement strategy impairment, biomechanical structural disorders, and disorientation. Examination of static balance includes measurement of one leg stance, tandem stance and centre of pressure (COP) postural sway while for dynamic balance, forward reach, stance on the trampoline or bosu ball measures have been in use. Time up and go (TUG) test has also been used as dynamic balance measure but is more relevant as a mobility and functional task. Patients with diabetic peripheral neuropathy show alterations in the parameters of balance and gait. 39 % of diabetic peripheral neuropathy subjects take more than 10 sec during unilateral leg stance as reported by Goldberg, Russell, & Alexander while Cimbiz and Cakir found maximal reduction in the dominant leg stance time during one leg stance with eyes open and head rotation during static and dynamic balance testing. Cimbiz and Cakir also found reductions in the functional reach in DPN patients on comparison with healthy controls, while Camargo et al., found similar results with no differences between the dominant and non-dominant sides. DPN patients take more time in TUG test, also, DPN women are slower when compared with DPN men and control. The time required to perform the TUG is strongly related to the risk of falls. Healthy adults who are able to perform this test in maximum 10 secs have lesser risk of falls. The presence of neuropathy is associated with an increased body sway, faster sway speed and greater sway dispersion during bilateral stance with eyes open while the values exceed with eyes closed when compared to controls. Maximal step length which has correlation with balance and mobility is found to be reduced in patients with DPN. Proprioception is one of the main causes for alteration in balance in this population and Goldberg, Russell, & Alexander found significantly greater trunk repositioning errors (TREs) in these people. Lower extremity balance performance is found to be lower in diabetic participants when assessed using various scales such as Berg Balance scale (BBS) Short Physical Performance Battery (SPPB) scores (physical performance test) (Table 1).

Patients with DPN walk slower with shorter stride length and lower cadence when compared with healthy controls during self-paced as well as maximal speed conditions due to prolonged double limb support and widened base so as to increase stability during walking. Petro sky and colleagues found reaction time to be two times higher in diabetic patients versus age-matched controls as one of the factors for widened base and slower gait. Although researchers found increased gait variability (stride time variability as well as stride length variability) in DPN subjects which suggested that they have lesser stable walking pattern. Ko et al., found proportionally longer gait cycle duration in DPN patients on comparison with non-neuropathy diabetic people (Table 1).

Table 1: Outcomes measures examined for balance and gait impairment in DPN.

Authors and year	**Sample size / group**	**Mean age ± SD**	**Outcome measures**
Cimbiz and Cakir, 2005	60 30 DPN 30 CG	DPN: 57.6 ± 3.9 CG: 55.6 ± 6.1	⁎ Static one leg stance with eyes open and eyes closed (dominant as well as non-dominant leg) ⁎ Dynamic one leg stance with eyes open and eyes closed (dominant as well as non-dominant leg) ⁎ Physical fitness tests ⁎ FRT
Goldberg, Russell, & Alexander, 2008	16 8 DPN 8 CG (age matched)	DPN: 60.1 ± 2.4 CG: 60.0 ± 2.6	⁎ One leg stance — TUG — Maximal step length ⁎ Trunk reposition errors (degrees)
Camargo et al., 2015	60 30 DPN 30 CG	DPN: 59 ± 8 CG: 65 ± 5	⁎ TUG ⁎ FRT ⁎ Muscle strength (planter flexors and dorsi flexors) ⁎ Step length ⁎ Cadence ⁎ Gait speed
Vaz et al., 2013	62 13 DPN 19 DM 30 NC	DPN: 54.6 ± 5.5 DM: 53.8 ± 7.7 NC: 54.1 ± 5.7	* BBS * TUG — Maximum AP displacement of trunk during FTSST * Time spent to perform the FTSST * Maximum AP displacements of the trunk during the upright balance (unstable platform eyes closed) — Maximum ML of the trunk during the upright balance
Boucher et al., 1995	29 17 DPN 12 CG	DPN: 62.5 ± 7.4 CG: 60.6 ± 5.6	⁎ AP range of sway (mm) ⁎ ML range of sway (mm) ⁎ Scalar range of sway (mm) ⁎ Sway speed (mm/s) ⁎ Dispersion of sway (%) (presence as well as absence of vision)
Chiles et al., 2014	983 126 Diabetes 107 IFG 750 No diabetes	Diabetes: 75.4 ± 7.5 IFG: 74.8 ± 6.8 No diabetes: 74.6 ± 7.4	* Nerve conduction velocity — CMAP * 4.31 Monofilament — 4.56 Monofilament — Vibration sensitivity * Neuropathy score Physical performance test * SPPB score * Walk score * Balance score * Chair score * Usual walking speed
Mueller et al., 1994	20 10 DPN 10 CG (age matched)	DPN: 57.7 ± 14.5 CG: 56.8 ± 11.3	* Ankle ROM (gait) * Ankle ROM (goniometer) * Ankle moment — Hip and Knee moment * GRF (AP and ML) * Walking velocity * Stride length * Planter-flexor peak torque — Cadence

			— Gait cycle time
Katoulis et al., 1997	80 20 NC 20 DM 20 DPN 20 DNU	NC: 50.6 ± 8.6 DC: 47.6 ± 10.7 DN: 52.9 ± 8.8 DNU: 54.1 ± 7.1	DPN Vs NC and DM ∗ Moment arm (meters) at hip joint in frontal plane ∗ Moment (Newton-meter) at ankle joint and hip joint DNU Vs NC and DM ∗ Ankle angle in sagittal plane ∗ Knee angle in sagittal plane ∗ GRF total ∗ GRF vertical ∗ GRF antero-posterior
Ko et al., 2011	186 26 DM 160 NC	DM: 70.00 ± 1.43 NC: 70.45 ± 0.58	— Speed — Stride length — Cadence ∗% gait cycle — Stride width

DPN: Diabetic peripheral neuropathy; CG: Control Group; NC: Normal control; DM: Diabetes mellitus; DNU: Diabetic neuropathy with ulceration; IFG: Impaired fasting glucose; FRT: Forward reach test; TUG: Time up and go test; AP: Antero-posterior; ML: Medio-lateral; FTSST: Five times sit to stand tests; BBS: Berg balance Scale; GRF: Ground reaction force; CMAP: Compound muscle action potential; SPPB: Short Physical Performance Battery; * : shows significant difference; ↔: shows no difference

Table 2: Balance training interventions in DPN.

Authors and year	**Study design (Sample size)**	**Type of exercise**	**Duration / frequency**	**Outcome measures**
Akbari et al., 2010	CCT (age matched) 10 IG 10 CG	Progressive Biodex stability and rocker and wobble-board training	10 session / 2 times per session	Eyes open ↑ Over all stability index ↑ Antero-posterior stability index ↑ Left-right stability index Eye closed ↑ Over all stability index ↑ Antero-posterior stability index
Allet et al., 2010	RCT 35 IG 36 CG	Gait and balance exercises with function orientated strengthening	12 weeks / twice Weekly	↑ Walking speed ↑ Walk over beam ↑ Biodex sway index ↑ Performance oriented mobility ↑ Ankle plantar flexor strength ↑ Hip flexor strength ↑ Degree of concern about falling
Song et al., 2011	RCT 19 IG 19 CG	Balance exercise program for 60 min.	8 weeks / 2 times per Week	↑ Postural sway (eyes open and eyes closed) ↑ One leg stance (eyes open, eyes closed and head rotation) ↑ FRT ↑ TUG ↑ 10 m walk ↑ BBS score
Salsabili et al., 2013	QE-TS design 19 IG	Standing balance trainings on Biodex Stability System for 30 min.	10 sessions / 3 times	Eyes open ↑ Medio-lateral sway — Antero-posterior sway Eyes closed

			per week	— Medio-lateral sway – Antero-posterior sway
Richardson et al., 2001	CCT 10 IG 10 CG	Balance exercises	3 weeks / 5 or more per week	↑ Unipedal stance ↑ Tandem stance ↑ FRT — ABC Scale
Lee, Lee & Song, 2013	RCT 19 IG-1 18 IG-2 18 CG	IG-1: Whole body vibration (WBV) for 3 min. + balance exercise (BE) for 60 min. IG-2: Balance exercise for 60 min.	6 weeks / balance exercise - twice weekly WBV - three times per week	WBV+BE with BE and CG ↑ Postural sway (all conditions) ↑ One leg stance ↑ FRT ↑ TUG ↑ Five times sit to stand ↑ BBS BE with CG — Postural sway ↑ One leg stance ↑ FRT
Kruse et al., 2010	RCT 41 IG 38 CG	Leg strengthening and balance exercises and a graduated, self-monitored walking program for 20 min.	3 months / twice per Week	– one leg stance – TUG – Rt. Ankle Strength – BBS – FFIDSS – FESS
Raghav et al., 2013	CCT (two intervention) 15 IG-1 15 IG-2	IG-1: Focussed balance exercise for 30 min. IG-2: Strengthening exercise 3 set of 10 repetitions	3 weeks / 5 times per week	IG-1 ↑ Stride length ↑ Cadence ↑ Dynamic gait index
Mueller et al., 2013	RCT (two intervention) 15 IG-1 14 IG-2	IG-1: Progressive balance, flexibility, strengthening, and aerobic exercise conducted standing and walking (WB) IG-2: Progressive balance, flexibility, strengthening, and aerobic exercise conducted sitting or lying (NWB)	12 weeks / 3 times per week	IG-1 ↑ 6MWD ↑ Daily step counts ↑ HBA1C
Morrison et al., 2010	CCT (age matched) 16 type 2 diabetic patients 21 CG	Both group: Balance exercise and resistance strength training	6 weeks / three times per week	↑ Proprioception ↑ Quadriceps and Hamstring strength ↑ Hand and foot reaction time ↑ Risk of fall
Londhe and Ferzandi, 2012	RCT (two intervention) 12 IG-1 12 IG-2	IG-1: balance + resistive exercise for 45 to 60 min. IG-2: balance exercise for 45 to 60 min.	8 weeks / 6 days per Week	IG-1 ↑ BBS ↑ ABC

Abbreviations: CCT: Clinical Control Trial; RCT: Randomized Control Trial; QE-TS: Quasi Experimental - Time Series; IG: Intervention Group; CG: Control Group; WB: Weight Bearing; NWB: Non-Weight Bearing; FRT: Forward Reach Test; TUG: Time up and Go Test; ABC: Activities Specific Balance Confidence Scale; BBS: Berg Balance Scale; FFIDSS: Foot Function Index Disability Scale Score; FESS: Falls Efficacy Scale Score 6MWD: Six Minute Walk Distance; ↑ shows improvement; ↔ Shows No Improvement

DPN: BALANCE TRAINING

Balance training is considered to be a very important tool for prevention of falls in older population. It has been shown to produce improvements in different aspects of postural control, balance and gait. Previous researches have studied balance exercises as an intervention in DPN patient and have demonstrated its efficacy when used individually or in combination

with other interventions. More specifically, balance training enhanced balance sway index, with significant improvement in antero-posterior sway index, medio-lateral sway index and overall sway index with eyes open as well as eyes closed condition. There was improvement in static balance such as one leg stance, tandem stance as well as in the dynamic balance such as forward reached test, walk over beam and five times sit to stand. A marked progress in the gait parameters such as gait speed, stride length and cadence as well as in 10 min walk time, 6 min walk distance, was also recorded following balance training. Functional and mobility task as a dynamic balance measure like time up and go test or performance-oriented mobility also improved post balance training. Balance exercise also helped in decreasing reaction time, consequently reducing the risk of falls. (Table 2)
Balance training has also shown improvements in balance performance scales like Berg balance Scale (BBS) and activities specific balance confidence (ABC) scale. It has been shown that balance exercises when used along with other exercises show better results. Lee, Lee & Song compared two interventions; whole body vibration with balance exercise in experimental group and balance exercises alone in control group. The combination group was found to exhibit significant improvement in balance measures when compared to only balance exercise group. Kruse et al., and Mueller et al., chose a combination of aerobic exercises and strengthening exercises along with progressive balance exercises. Mueller and colleagues compared weight bearing group with non-weight bearing group while Kruse and colleagues compared leg strengthening, balance exercise and graduated, self-monitored walking program with control group. Mueller et al., found significant improvement in 6 min walk distance and daily steps count in weight bearing group in comparison to the non-weight bearing group whereas Kruse et al., found no significant improvement in the strength and balance measures, which may be accounted to the assessment of measures that were taken 6 month and 12 month following an intervention that was provided for a duration of 3 months (twice/week) (Table 2).
Kruse and colleagues reported no adverse effect of exercises while Mueller and colleagues reported calf pain in one patient [88] and Allet and colleagues reported pain in Achilles tendon in two patients. Other than these, none of the researchers reported adverse events with balance training in DPN population.

FUTURE PERSPECTIVE

Future studies investigating balance exercise training in patients with DPN should present higher levels of evidence. Randomized control trials with an adequate sample size enhance the quality of research. Furthermore, the studies should discuss the precise training protocol with progression of exercise and heterogeneous in nature; also, information regarding duration, intensity and frequency is imperative to assist replication and examine efficacy. Detailed inclusion, exclusion criteria and meaningful outcome measures could also influence the effects. More studies must explore the role of balance training as a preventive measure rather than just a rehabilitative tool.

CONCLUSION

Current data suggests that balance exercises and gait training are feasible and safe, and have the potential to improve balance and gait. Also, reduction in the risk of fall and fall-related injuries in DPN patients can be achieved. These exercises can be use in clinical setup if the patient is affected with DPN. Therefore, balance exercises should be used as a supportive therapy along with medication and diet control in DPN patients.

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