Factors related to pressure ulcer development with diabetic neuropathy

Suhair Shahwan*

Supervising Clinician, RMIT University, Health Science Department, Victoria, Australia

Introduction

Diabetes has been the silent killer disease for many years and on the rise [1]. One of the most reported complications with diabetes is lower limb ulceration with the possibility of leading to amputation [2]. It has been reported that forty thousand cases of lower limb amputation occur yearly in some countries such as the USA [3].

Although, Diabetes has been highly correlated to the development of ulceration, the pathophysiology leading to ulceration is not fully understood [4]. Several studies have shown neuropathy one of the major leading cause to foot ulceration through an increase in the plantar pressure of the foot [4]. Ulceration has also been associated with several risk factors related to diabetic neuropathy such as limited joint mobility, connective tissue deformity [3] history of ulceration and duration of diabetes [4].

In this literature review, there will be a focus on understanding how diabetic patients with neuropathy are at higher risk of developing foot ulcers in comparison to diabetic patients with no neuropathy. Risk factors such as limited joint mobility [5], connective tissue thickness of the sole of the foot [6,7] and level of HbA1C [4] will be further analysed in regards to its relationship with plantar pressure and how it is related to foot ulcers development in the Diabetic patient with insensate feet. The research questions of my literature review is what is most contributing risk factor in increasing plantar pressure and causing the development of neuropathic ulcer? and what is the best off-loading methods for neuropathic pressure ulcer?

Discussion

The typical Diabetic Polyneuropathy (DPN) is defined as “a chronic, symmetrical, length-dependent sensorimotor polyneuropathy (DSPN) and is thought to be the most common type of neuropathy and occurs on with a history of longstanding hyperglycaemia” [8]. Bennet’s 1996 study selection of diabetic patients with neuropathy was determined by using the biothesiometer, which is an electrical device delivering a spectrum of vibration stimuli and a patient who cannot detect vibrations delivered at greater than 30 volts to the plantar skin of the foot was classified as having clinically sever neuropathy. Biothesiometer was found to be the gold standard in evaluating patients with diabetic neuropathy of VPT value of greater than 25 [9]. A second test using the 5.07 Semmes-Weinstein monofilaments was also applied to examine the level of sensitivity to pressure and subjects who were not able to detect pressure in this test were categorised as having peripheral sensory neuropathy [4]. Otherx studies such as Aboueisha studies were also able to select patients with neuropathy based on neurothesiometer test which is a vibration testing using 128HZ tunning fork in addition to the 5.07 Semmes-Weinstein monofilament test [6]. All results from previous studies showed an agreement of these tests as useful tools for peripheral diabetic neuropathy. However based on Jayaprakash study (2011), Biothesiometer was found more sensitive than the other tests but less specific than the Neurothesiometer and Semmes-Weinstein test.

Long term Hyperglycaemia and neuropathic pressure ulcers

Delbridge’s study showed neuropathic ulcers are more common with neuropathic feet than with diabetic patients with no neuropathy [10]. This usually occurs as a result in an increase in the interaction between mechanical factors such as peak plantar pressure and unusual connective-tissue properties associated with loss of joint mobility [2].

Tissue hardness and deformity was commonly linked to accumulation of glycastion products which accelerate age-related changes to the skin and connective tissue and joints. Advanced glycastion products (AGEs), in skin collagen are associated with severity of hyperglycaemia as well as the presence of long term complications [11].

Alteration of foot pressure distribution due to increase in hardness of the tissues in the sole of the foot, was indicated with Periyasamy case control study of 2011. This was significantly clear with long term diabetic patients and with a history of neuropathy [5].

Another study that explained the abnormal loading of the diabetic forefoot in the gait cycle due to an increase of Achilles tendon and plantar fascia thickness was Giacomozzi study of 2005 and again was more evident with neuropathic patients of long duration with diabetes [12].

Finally Bennet et al. [4] case control study, which was conducted to determine the correlation between non-enzymatic glycosylation of collagen and plantar foot pressure with diabetic patients and history of neuropathy, revealed a higher increase in Peak plantar pressure as a risk factor with diabetic neuropathic patients and a history of ulceration in the past year compared to the diabetic control group with no history of ulceration [4]. The control group of the study was matched to the case group by age and sex and were selected on the the basis that they had

Correspondence to: Suhair Shahwan, Supervising Clinician, RMIT University, Health Science Department building 300, University Hill Shopping Precinct 30 Janefield Drive, Bundoora VIC 3083, Australia, Tel: 61497229864, E-mail: sshahwan123@yahoo.com

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attended the hospital diabetic unit at least one time during the previous 12 months and had no history of ulceration [4].

Connective tissue thickness was measured through peripheral joint flexibility and it was assessed and compared to the measurement of HbA1c which determines the amount of connective tissue that has been affected by non-enzymatic glycosylation over 36 months prior to the study. A minimum of three test results were documented at more than six monthly intervals and results showed the peak plantar pressure was increased with prolonged hyperglycaemia (10.4% ± 1.9) of patients with diabetic neuropathy and history of ulceration compared to diabetic patients with no neuropathy (8.9% ± 1.3) [4].

Bennet case control study revealed more reliable results compare to other methods used in other studies such as Periyasamy or Giacomozzi that used either durometer or ultrasound instead of HbA1c to evaluate any increase in tissue thickness in long term diabetes. HbA1c is the best biomarker for tissue dysfunction compared to other indirect measure such as pulse wave analysis or direct markers such as skin autofluorescence [13].

**Limited Joint mobility as a risk factor in Diabetic neuropathy ulceration studies**

Limited joint mobility in the ankle was also studied as a risk factor in the development of ulcer with diabetic patients and history of neuropathy. It was suggested that limited joint mobility at the ankle contribute to the development of tissue damage by resulting in abnormal pressure at the susceptible site [5,10,14]. According to Periyasamy case control studies, Limited ankle and subtalar joint mobility was more significant with diabetic patients with neuropathy and with a history of long term diabetes [5].

The results of these measurements were highly accurate due to the instruments that have been been utilised. Ankle joint and hallux joint mobility were measured using a Goniometer with 2-degrees increments [5,4,15]. The ankle joint was measured by having the patient sit comfortably and both legs were suspended in a relaxed manner without applying any stress to the ankle joint and ankle joint dorsiflexion and plantar flexion were both measured [5].

The P value for the association between limited joint mobility and neuropathic patients concluded a strong correlation between the reduction of joint mobility and neuropathy [5]. Bennet study showed similar results in regards to a decrease ankle joint and hallux mobility with long duration diabetic patients and history of neuropathy [4]. However Bennet’s technique used in range of motion measurement had a different technique than other studies such as Periyasamy study. Bennet’s method measuring the range of motion with the goniometer was similar to Mueller study of 1989 and was done by measuring ankle and the subtalar joint range of motion while patient in a prone position and it was done by the same tester to avoid any standard error [13].

Bennet study was more thorough because he also measured flexibility of the metacarpophalangeal joint of the hand, following Delbridge study of 1988 [10].

**Peak pressure effect on limited joint mobility and tissue thickness in diabetic neuropathy**

Results with Bennet study showed a significant elevation in plantar pressure in patients with history of neuropathy and ulceration in comparison to the control group. Bennet study recorded plantar pressure through the Musgave footprint which is dependent on a computer for automatic analysis using Musgave software. Dynamic pressure was calculated through six foot prints and the highest and lowest pressure prints were not included [4]. The remaining four foot prints were used to determine pressure analysis at the most frequent sites for plantar foot ulceration, which are the metatarsal heads, hallux and heel and the maximum peak pressure (kg/cm2) was recorded for statistical analysis [4].

Other studies such as Abouaesha study in 2001, showed opposite studies of Bennet. According to Abouaesha study (2001) the results showed a strong inverse relationship between plantar tissue thickness and dynamic foot pressure measurement [6]. However the reason for other studies conflict with Bennet study could be due to variable techniques used of measuring tissue thickness and patient selection of VPT of greater than 25 was the inclusion criterion in a longitudinal study thus only a relative small range of VPT was measured in this study [6].

**Data Analysis with several studies**

Several studies such as Zimmy in 2004, Mueller in 1989 and Periyasamy in 2011 showed similarities in their results with Bennet study. Bennet study used more tests to confirm the results of his tests. The Wilcoxon signed rank test was used to determine the normal distribution of the mean and standard deviation for each test utilised [4]. The t test was also utilised in all to determine the significance of differences between cases and control subjects and all results showed a normal distribution. Other methods such as Conditional logistic regression, (CLR) was a good test to apply to confirm the association between the factors tested and the risk of diabetic foot ulceration through the exclusion of the odd ratio [4].

This CLR test is conducted to compare the strength of association between the factors examined and the risk of diabetes ulceration. Studies such as Periyasamy, Zimmy and Abouaesha did not provide these further studies to confirm the association of strength between factors tested for the association of ulceration with diabetic patients with neuropathy [5,6,14].

Bennet study also showed a value of the plantar pressure threshold of 8.0 Kg/cm² that other studies was not able to confirm. However he had excluded the influence of other potential risk factors for foot ulceration such as age, sex, body mass index, type and duration of diabetes and this was ignored by matching case and control subjects for their variables [4]. Although, Bennet’s study did focus on the area of the sole of the foot with the highest amount of peak plantar pressure (PPP) which are metatarsal heads, hallux and heel, other variables was ignored which is measuring the in shoe pressure upon weight bearing. Several studies has shown that the inability to assess the forces acting on the shoe during gait analysis will be a potential source of errors in the examination of the genetic effect of foot orthosis [16].

In general Bennet study results show more strength than other studies in regards to the correlation between neuropathy and its associated factors in increasing plantar pressure with diabetic foot ulceration. His case control study design was ideal for the investigation in the relationship between Hyperglycaemia and increase in plantar pressure with diabetic neuropathy. Methods used in Bennet study in 1996 were also more reliable and sensitive towards the results of his study. Bennet study in 1996 also included patients with history of ulcers which other studies did not [6]. Bennet study also had better data analysis than other studies [4].
Best modalities to reduce pressure pressure at the neuropathic ulcer site

Reducing plantar pressure is important in preventing ulceration and limb amputations [17]. These treatments usually work by transferring weight bearing forces away from the ulcer site [17,18]. A number of off-loading devices have been considered for ulcer prevention and according to Fleischli et al. [18], a number of off-loading modalities have been reviewed for its effectiveness in reducing peak plantar pressure at the site of neuropathic ulceration. Fleischli study in1997 was conducted on 26 patients (16 males and 10 females). Patients were recruited from the clinics at the university health system in San Antonio, Texas [18].

Patients were divided in two groups and consent form was obtained prior to clinical trials. The first group, 19 patient had a current ulceration at the metatarsal head area of the foot and the second group consisted of seven patients who had a current ulceration at the great toe [18]. The neuropathy measurement was utilised using biosiometer. Pressure on the sole of the foot was evaluated using the Pedar in shoe pressure measurement system [18].

Offloading modalities that were evaluated for effectiveness were five treatment devices which are total contact cast, DH Pressure relief Walker, Darco ortho Wedge Shoe, Darco rigid- soled post-operative shoe and finally accommodative felt and foam dressing [18]. Rubber-soled canvas oxford was used to establish baseline pressure values [18]. These modalities were applied with certain techniques. For example, the total contact cast with rocker bottom cast boot was applied using the Colman techniques, with the exceptions of applying plywood [18]. The outer layers of fibreglass cast material was applied over the total contact layer and splints and this was performed to help the patient to walk immediately after application [18].

The accommodative felt and foam dressing was applied based on procedures used by the Josline Diabetic centre, Boston [18]. This techniques was done to promote weight bearing by the healthy surface of the forefoot.

Treatments were evaluated in random order. For each treatment, subjects were instructed to walk with their offloading devices until they feel adequate in walking with their new offloading device [18]. This would help with their gait pattern and data will be more consistent across all the trials. Subjects were advised to walk at their own pace with their modality after break-in period [18]. Four gait trials were performed for each device, with eight mid gait steps from each trial used for final analysis. Only mid gait steps were analysed for each treatment due to variability of initial and ending treatment means [18]. Results was analysed based on the mean peak pressure and percent change from baseline. All results from these off-loading modalities showed an effectiveness in reducing foot pressure at ulcer sites [18]. The DH pressure relief walker was just as effective as the total contact cast in reducing peak pressure. However the DH pressure relief walker was a better off loading modality for hallux ulcers than the total contact cast. Ulcers located under the ball of the foot was managed better with total contact cast than with the DH modality [18]. Half-shoes were consistently the third most effective method in reducing pressure ulcers and the felt and foam dressing slightly more effective than rigid-soled postoperative shoe [18]. The healing time was also much shorter with total contact cast followed by half shoes then accommodative orthotics and wheelchairs and crutches [18].

In general according to this study, the total contact cast is the gold standard for off-loading a pressure ulcer and this agrees with Snyder, R. study in 2014. Although total contact cast is not the ideal off-loading modalities for elderly people, it was still found there was less recurrence of complication in comparison with crutches and wheelchairs [18]. The other down side about total contact cast is the inability to view the ulcer progression on daily basis and any signs of infection while patient is being treated and in addition to the fact that there is a certain technique when applying the total contact cast [18]. Many practitioners do not utilise this offloading modality in their office due to the fact of the inability of the patient to inspect their wound on daily basis for infection and the possible of developing an iatrogenic ulcer [18].

In general, removable walking cast was shown to be as effective as total contact cast in Fleischli study in 1996 and more effective than other removable casts such as air cast pneumatic Walker and CAM walker [18]. The later information is based on easy application, reusability and control over monitoring the ulcer. Half shoe was also found to be convenient in reducing plantar pressure but not as good as total contact cast and the DH pressure relief walker [18]. The pressure reduction by the half shoe was just as good as some of the commercially available removable cast [18].

Conclusion

Diabetic neuropathy ulcers are multifactorial in origin and are on the rise .Although not all diabetic foot ulcers can be prevented, it is feasible to decrease the incidence of morbidity through suitable foot screening and management. Fleischli et al. has indicated there has been no previous clinical studies to compare off-loading modalities for its effectiveness [18]. As a result, the practitioner needs to consider all other variables when treating a neuropathic pressure ulcer such as patient’s agreement, cost and compliance for optimum results.

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