DE GRUYTER OPEN

http://www.jrdiabet.ro
Rom J Diabetes Nutr Metab Dis. **23**(1):067-072
doi: 10.1515/rjdnmd-2016-0008

COMPARATIVE EVALUATION OF SEVERAL SIMPLE SCREENING TESTS FOR RISK OF NEUROPATHIC ULCERATIONS OF FEET IN PATIENTS WITH DIABETES MELLITUS

Monica Lasca [1], ***Andreea Larisa Tăut*** [1,✉], ***Ioan Andrei Vereşiu*** [1,2]

[1] Diabetes, Nutrition and Metabolic Diseases Department, Emergency Clinical County Hospital, Cluj-Napoca, Romania
[2] University of Medicine and Pharmacy "Iuliu Haţieganu" Cluj-Napoca, Romania

received: February 01, 2016 *accepted*: February 26, 2016
available online: March 15, 2016

Abstract

Background and Aims: *The aim of this study is to compare and evaluate three semi-quantitative screening methods used to predict ulceration risk in diabetic patients: 10 g Semmes-Weinstein monofilament (SW), 128-Hz tuning fork and VibraTip® device.* ***Material and Method:*** *This case-control study was carried out at the Diabetes, Nutrition and Metabolic Diseases Department Cluj-Napoca and included 90 persons distributed into three groups: group A: 30 patients with diabetes mellitus and one or more active neuropathic ulcerations at one foot, group B: 30 patients with diabetes mellitus without ulceration and group C: 30 apparently healthy subjects. The subjects were examined by two independent examiners, using the three screening methods.* ***Results:*** *The agreement kappa coefficient between the two examiners was high and statistically significant. The SW monofilament presented a sensitivity of 71.67% and a specificity of 91.67%. The 128 Hz tuning fork presented a sensitivity of 60% and a specificity of 89.17%. VibraTip® device recorded a sensitivity of 76.66% and a specificity of 77.5%.* ***Conclusions:*** *The highest sensitivity is encountered at the use of VibraTip® device, and the highest specificity is presented by SW monofilament.*

key words: *neuropathy, ulceration, VibraTip®, monofilament, tuning fork*

Background and aims

Symmetrical Peripheral Sensorimotor Polyneuropathy (SPSP) represents the most common form of manifestation of diabetic neuropathy (DN). It is defined by the presence of symptoms and/or signs of dysfunction of peripheral nerves in patients with diabetes mellitus, after the exclusion of other causes [1]. The distribution of manifestations is distal and symmetric, with initial involvement of lower limbs followed by the upper limbs [2]. The early symptoms are represented by paraesthesia, numbness, followed by the installation of pain. Peripheral diabetic polyneuropathy is one of the decisive factors associated with the occurrence and development of ulcerations in feet, amputations, Charcot osteoarthropathy and other complications of diabetic feet [3]. Diabetic foot represents a major cause of morbidity and one of the main reasons for the hospitalization of diabetic patients [4]. The adequate management

✉ 72 Madach Imre Street, Cluj-Napoca, Cluj, Romania; Postal code 400464; Phone number: +40752016106; *corresponding author e-mail*: andreeataut@yahoo.com

of risk factors and early recognition of manifestations specific to polyneuropathy are essential. The strict glycaemic control is an effective strategy in the prevention or delay in progression of SPSP both in patients with type 1 diabetes mellitus and in patients type 2 diabetes mellitus [5].

The screening of SPSP should be done every year for all the patients with diabetes mellitus [5] using easy to apply screening methods such as: 10 g Semmes-Weinstein monofilament (SW), 128-Hz tuning fork, or the VibraTip® device. SW monofilament (method patented in 1950s by Josephine Semmes and Sidney Weinstein) is one of the most frequently used devices in current practice [1,6-8], which can identify the loss of protective sensitivity. The 128-Hz Rydel-Seiffer tuning fork is used to evaluate the vibration perception threshold. The absence of vibration at hallux is significantly associated with a high risk for ulceration occurrence [1,6,9-11]. The VibraTip® device [7] is an instrument used for testing the perception of vibratory sensitivity threshold; it issues a vibration of 128-Hz at each activation. The aim of our study was the comparative evaluation of these three simple screening tests, for detecting the risk of neuropathic ulcerations in the feet of patients with diabetes mellitus, having as reference the presence of neuropathic ulceration.

Material and Method

The study is a prospective case control study performed at the Diabetes, Nutrition and Metabolic Diseases Department Cluj-Napoca, Romania. It included 90 subjects distributed into three study groups: group A included 30 patients with type 1 or 2 diabetes mellitus and one or more active neuropathic ulcerations at one foot; group B included 30 patients with type 1 or 2 diabetes mellitus without ulceration and group C included 30 apparently healthy subjects (without known diabetes mellitus). In group A were included all patients with neuropthic ulceration hospitalized in Diabetes, Nutrition and Metabolic Diseases Department Cluj-Napoca between first of March 2015 to first of June 2015. Subjects in groups B and C were simple randomly selected from the general population. The evaluation of the subjects was done using three screening methods for tactile and vibratory sensitivity: 10 g SW monofilament, 128-Hz Rydel-Seiffer tuning fork and VibraTip® device. They were applied to the foot without ulceration in the experimental group (group A) and in both feet in the control groups (B and C), taking into consideration the foot with the lower sensitivity.

Exclusion criteria: subjects who presented peripheral neuropathies of any other cause than diabetes, persons with neurological disorders of any other cause than diabetes, those with neuro-ischemic ulcerations, persons with psychiatric diagnosis, pregnant women, breastfeeding women and the persons who did not give their consent to participation.

We also analyzed other parameters recognized as predictive factors for ulceration risk: the type of diabetes mellitus, duration of diabetes, the value of the last glycated haemoglobin (HbA1c), the presence of peripheral arterial disease diagnosis, the presence of peripheral diabetic polyneuropathy (PDPN) diagnosis, PDPN symptomatology and the treatment followed by the subjects, the age and localization of neuropathic ulceration, the existence in the personal history of other neuropathic ulcerations of diabetic cause.

Statistical analysis and graphic representations were carried out with the SPSS 20 (Statistical Package for the Social Sciences) software. For the evaluation of the agreement coefficient between the two investigators we used the Cohen's kappa coefficient. Descriptive statistics of variables was used. In addition, we used the ANOVA One-Way (Bonferroni post-

hoc test) method for comparing the variables evaluated in the three groups.

Experimental procedures:

A. The procedure with 10 g Semmes-Weinstein monofilament: the patient in dorsal decubitus position was asked to close his/her eyes during the examination. The filament was applied to the plantar face of the hallux, finger III, finger V and on the plantar face of the hallux at the ball of foot. From the four areas established, we randomly touched three areas and a touch was fictitious. The patient was asked to answer ''YES'' when he/she felt the touch of the monofilament. We did not apply the monofilament on ulcerated, hyperkeratosis areas, on scars or necrosed tissue. We considered the tactile sensitivity present if the patient answered correctly to at least two of the three touches. The tactile sensitivity was considered absent if at least two incorrect answers to the three touches.

B. The 128-Hz Rydel-Seiffer tuning fork was used according to the qualitative method (Yes/No). The patient in dorsal decubitus was asked to close his/her eyes during the examination. We induced the vibration of the tuning fork, then we placed it in vertical position at a constant pressure on the hallux tip or at the basis of amputation stump of metatarsus I. We did not apply it on ulcerated areas, hyperkeratosis areas, on scars or necrosed tissue. We considered the vibratory sensitivity present if the patient felt the vibration and absent if the patient did not feel the vibration.

C. Procedure with Vibra Tip® device: the patient in dorsal decubitus was asked to close his/her eyes during the examination. We slightly touched the intact skin of patients on the plantar face of hallux, twice every time for about one second, with the round tip of VibraTip®, explaining that 'this is the first touch', and 'this is the second touch'. VibraTip® was randomly activated either at first touch or at the second touch, by pressing the device firmly between the thumb and index finger. The patient was asked which of the two touches was associated with vibration. We did not apply VibraTip® on ulcerated areas, hyperkeratosis areas, on scars or necrosed tissue. We considered the vibratory sensitivity present if the patient identified the touch associated with vibration [7] and absent if the patient did not identify the touch associated with vibration.

The evaluation of the subjects using these three screening methods was done by two independent examiners at a 15 minutes distance between them. To perform the examinations, the same set of instruments was used by both examiners. We assured the thermal, phonic and psychic comfort of patients. All patients signed an informed consent prior to inclusion in the study which was approved by the local ethics committee.

Results

In Table 1 we presented the demographic and clinical features of the three groups that were studied.

The gender, age and presence of peripheral arterial disease were compared for groups A with B and A with C; the type and duration of diabetes and the level of HbA1c were compared for group A with B.

Duration of diabetes in patients from groups A and B is given in Figure 1.

As for the symptoms of peripheral diabetic polyneuropathy (PDPN), only 23.3% of patients were asymptomatic, more than half (63.3%) presented numbness, 56.7% had paraesthesia and 43.3% had pain. A total of 76.6% of patients with ulceration were treated with benfotiamine, 60% with alpha lipoic acid, 13.3% did not follow any treatment, and 3.3% of patients followed treatment with ketoprofen, respectively 3.3%

with gabapentin. A total of 36.7% of the subjects were patients at their first ulceration. More than two thirds of ulcerations had an evolution of less than 6 months. 13.3% of ulcerations had between 6 and 12 months, 6.7% between 12 and 24 months and 6.7% over 24 months.

Table 1. Demographic and clinical features.

Characteristics	Group A	Group B	Group C	p
Men	22 (73.3%)	17 (56.7%)	19 (63.3%)	0.398
Diabetes mellitus type 1	5 (16.7%)	5 (16.7%)	-	0.001
Diabetes mellitus type 2	25 (83.3%)	25 (83.3%)	-	0.001
Duration of diabetes (years)	16.83 (years)	14.80 (years)	-	0.426
HbA1c	8.93	8.85	-	0.364
PAD*	13.3%	3.3%	3.3%	0.200
Average age (years)	60	59	61	0.001

*PAD - peripheral arterial disease

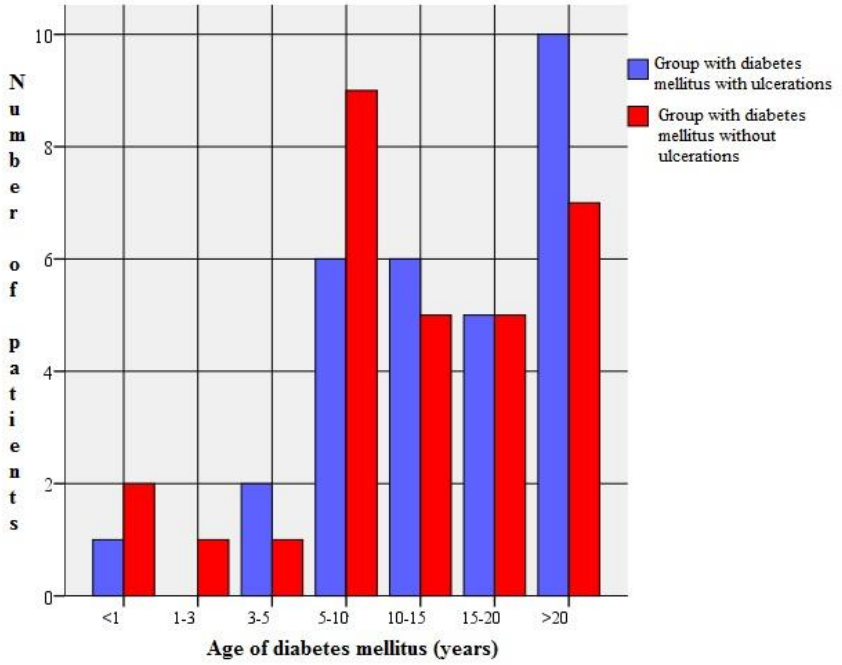

Figure 1. *Duration of diabetes in groups A and B.*

In order to measure the agreement between the two evaluators we used the Cohen's kappa coefficient. For tactile sensitivity (TS) assessment, the agreement between the two evaluators was strong and statistically significant (kappa=0.760; p<0.001). There was a statistically significant agreement (kappa=0,860; p<0,001) between vibratory sensitivity (VS) determined using the 128-Hz tuning fork indicated by the first examiner (A.T.) and that indicated by the second examiner (M.L.). As for the examinations of VS with VibraTip® performed by the two evaluators, the kappa agreement coefficient was 0.701 (p<0.001), indicating a high value of agreement between the observations of the two examiners.

Having in view the statistically significant agreement between the results obtained by the two examiners, we made an average grade of the results in order to assess the power to predict ulceration of the three methods of neuropathy testing. The results are given in Table 2.

Table 2. Predictive power for foot ulceration of the three methods of neuropathy assessment.

	Se	**Sp**	**PPV**	**NPV**
TS (monofilament)	71.67 %	91.67 %	81.07 %	86.66 %
VS (tuning fork)	60 %	89.17 %	73.82 %	81.71 %
VT (VibraTip®)	76.66 %	77.5 %	62.93 %	87.06 %

Se - Specificity; Sp -Specificity; PPV - Positive predictive value; NPV - Negative predictive value.

Discussions

Randomized prospective trials showed that intensive treatment of diabetes mellitus with achievement of glycaemic values as close as possible to normal prevents and/or delays the appearance and progression of PDPN, diabetic retinopathy, and diabetic renal disease [1,5]. As for diabetes duration, the longer time of disease in group A compared to group B suggests that the alteration of nervous fibres evolves over time, contributing to the development of irreversible complications of the feet (complete anaesthesia, necrosis, amputations), as also reported by other authors [2,3,12-15]. The information, awareness and education of patients regarding the routine of daily care for their feet, the risks to which they expose themselves by not following this routine and the long-term disability consequences represent methods just as important for control, prevention and reduction of morbidity [1,3,5,13,14].

The pharmacological management of PDPN uses medication that mainly address the specific symptoms of PDPN [2,12,15]. At present the most common medication used for fighting the symptoms in Romania are benfotiamine, respectively alpha-lipoic acid. Alpha-lipoic acid administered intravenously represents the only pathogenetic treatment with confirmed effectiveness in the treatment of symptoms of painful PDPN following several randomized trials and one meta-analysis (evidence level A) [1].

The screening for prevention and/or early diagnosis of peripheral diabetic polyneuropathy in patients with diabetes still remains a real challenge. In the daily practice one can use several screening methods, easy to apply, for checking the presence or absence of sensitivity in feet of patients with diabetes mellitus. The anamnesis and objective examination remain the generally accepted methods, the most commonly used and safest methods in getting information on the natural history of the disease and the risk factors with role in its progression, but they are not sufficient. According to the recommendations of American Diabetes Association (ADA) [5], the screening of peripheral diabetic polyneuropathy should be carried out every year for all the patients with diabetes mellitus and the standard manoeuvre in the foot examination should be the application of the 10 g SW monofilament, to which should be added another one of the specific instrumental methods. The data from various trials which compared and analysed different screening methods of PDPN proves that these simple instruments are efficient in detection of diabetic foot at risk [1,5-11,16,18].

Conclusions

Our analysis proves that 10 g SW monofilament has the highest specificity and that the highest sensitivity was encountered at the use of VibraTip® device. We think that the accuracy of PDPN diagnosis is increased if we associate the two instruments. Considering the current

conditions in our country, each practitioner (diabetologist, neurologist, general practitioner) should use in current practice at least one of the screening methods described.

REFERENCES

1. Tesfaye S, Boulton AJM, Dyck PJ et al. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. *Diabetes Care* 33: 2285-2293, 2010.

2. Vereşiu IA. *Piciorul diabetic*. Cluj-Napoca (România): Echinox; 2005.

3. Boulton AJM, Vileikyte L. *Neuropatia diabetică în practica clinică.* Târgu Mureş (România): FarmaMedia; 2013.

4. Vereşiu IA, Bondor C, Iancu SS. Sex differences in lower extremities amputations in patients with diabetes-five year nationwide follow-up using DRG data in Romania. *Rom J Diabetes Nutr Metab Dis* 22: 53-59, 2015.

5. ADA. Standards of medical care in diabetes-2015. *Diabetes Care* 38[Suppl. 1]: S62-S64, 2015.

6. Cornblath DR. Diabetic neuropathy: diagnostic methods. *Adv Stud Med* 4: 650-661, 2004.

7. Bowling FL, Abbott CA, Harris WE, Atanasov S, Malik RA, Boulton AJM. A pocket-size disposable device for testing the integrity of sensation in the outpatient setting. *Diabet Med* 29: 1550-1552, 2012.

8. Rayman G, Vas PR, Baker N et al. The Ipswitch Touch Test: a simple and novel method to identify inpatients with diabetes at risk of foot ulceration. *Diabetes Care* 34: 1517-1518, 2011.

9. Perkins BA, Olaleye D, Zinman B, Bril V. Simple screening tests for peripheral neuropathy in diabetes clinic. *Diabetes Care* 24: 250-256, 2001.

10. Gin H, Rigalleau V, Baillet L, Rabemanantsoa C. Comparison between monofilament, tuning fork and vibration perception tests for screening patients at risk of foot complication. *Diabetes Metab* 28: 457-461, 2002.

11. Al-Geffari M. Comparison of different screening tests for diagnosis of diabetic peripheral neuropathy in Primary Health Care setting. *Int J Health Sci* 6: 127-134, 2012.

12. Sima A, Şerban V. *Tratat român de boli metabolice*. Timişoara (România): BrumaR; 2011.

13. Pavel P, Vereşiu IA. Piciorul diabetic. În: Moţa M, coord. *Ghidul educatorului pentru educaţia terapeutică a pacientului cu diabet*. Bucureşti (România): Ilex; 2010. p. 245-254.

14. Popescu R. Neuropatia diabetică periferică şi autonomă. În: Moţa M, coord. *Ghidul educatorului pentru educaţia terapeutică a pacientului cu diabet*.. Bucureşti (România): Ilex; 2010. p. 234-242.

15. Vereşiu IA, Negrean M, Ştirban A. Farmacoterapia neuropatiei diabetice. În: Hâncu N, Roman G, Vereşiu IA. *Farmacoterapia diabetului zaharat*. Cluj-Napoca (România): Echinox; 2008. p. 441-448.

16. Baraz S, Zarea K, Shahbazian HB, Lafiti SM. Comparison of the accuracy of monofilament testing at various points of feet in peripheral diabetic neuropathy screening. *J Diabetes Metab Disord* 13: 19, 2014.

17. International working group on the diabetic foot. *Ghid practic al managementului şi prevenţiei piciorului diabetic*. România; 2002.

18. Konopka KH. *Quantitative sensory testing (QST). Does assessing sense make sense?* Groningen (The Netherlands): Ipskamp Drukkers; 2012.