Screening of Distal Symmetric Polyneuropathy in Hospitalized Diabetic Patients

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Abstract:

Introduction: Distal symmetric polyneuropathy (DSPN) is a frequent, catastrophic and underdiagnosed complication of diabetes mellitus. The authors have hypothesized that hospitalization could be an opportunity to screen DSPN and also pretend to compare two different diagnostic methods.

Material and Methods: This was a prospective and multicentre study that enrolled diabetic patients admitted consecutively to internal medicine wards, between May and October 2015. Patients were evaluated using the MNSI (Michigan Neuropathy Screening Instrument) and the SWME (10 g- Semmes-Weinstein monofilament examination). A score > 2 in the clinical examination of MNSI or ≤ 7 positive answers in a total of 10 in SWME were considered diagnostic of DSPN.

Results: Eighty-eight patients were included; average age was 77 (13) years and 45% were males; most were type 2 diabetic patients, 7% had a previous diagnosis of DSPN. DSPN prevalence was 75% using MNSI, SWME was abnormal in 38% of these patients. The agreement rate between MNSI and SWME was 44.3%. A percentage of 92.4% of the patients with a diagnosis of DSPN in the study did not have a previous diagnose.

Discussion: The number of underdiagnosed cases in this study is alarming but had been previously detected in studies regarding outpatient; it might represent a problem of registry or an omission in the screening of neuropathy.

Conclusion: We have concluded that DSPN is a high prevalent disease in hospitalized patients in Portugal, which remains underdiagnosed. MNSI can be a good instrument to screen neuropathy and SWME should not be used exclusively for this purpose.
Introduction

Distal symmetric polyneuropathy (DSPN) is one of the most frequent complications of diabetes; it can affect up to 50% of patients with type 2 diabetes mellitus (T2DM), and 60% of patients with type 1 diabetes mellitus (T1DM). The pathogenesis of this condition is still unclear, however, both metabolic and ischemic alterations are thought to contribute to the pathogenesis of this condition.2,3 The duration and severity of hyperglycaemia seems to be the major risk factor, but glycaemia variability, age, dyslipidemia, hypertension and smoking have also been pointed as risk factors.4

In clinical practice, DSPN is defined as the presence of symptoms and/or signs of peripheral nerve dysfunction in patients with diabetes after exclusion of other causes. The diagnosis of DSPN is predominantly clinical. A combination of typical symptomatology and symmetrical distal sensory loss or typical signs in the absence of symptoms in a patient with diabetes is highly suggestive of DSPN and may not require additional evaluation. As up to half of the patients may be asymptomatic, a diagnosis may only be made on examination or, in some cases, when the patient presents with a painless foot ulcer.5 The American Diabetes Association (ADA) recommends the use of more than one test, with 10 g·Semmes-Weinstein monofilament examination (SWME) being added to at least one of three: pinprick, temperature or vibration sensation using 128 Hz tuning fork.6 In DSPN, small and large fibers are affected, producing different signs and symptoms. SWME is worldwide used and in Portugal is recommended to identify feet in risk to ulceration.6 It tests large fibers lesions, which explains some lack of accuracy to diagnose earlier stages of neuropathy.5,7 Scales like Michigan Neuropathy Screening Instrument (MNSI), United Kingdom Screening Test (UKST), Neuropathy Symptoms Score (NSS) or Diabetic Neuropathy Score (DNS), which combine some of the tests, have been developed to facilitate the diagnosis of DSPN.8,11

MNSI has been recently validated to the Portuguese population; it is an easy scale with a sensitivity/specificity of 86%/61% and a positive predictive value of 73% / 79%.12

The early diagnosis of this condition allows the proper education of patients to prevent its catastrophic complication, like diabetic foot lesions and subsequent amputation.5,13 Diabetes is a prevalent condition in Portugal, especially in hospitalized patients, where it affects 10% to 43% of the inpatients.14

Hospitalization could be an opportunity to screen diabetic neuropathy and a window to education of these patients in an attempt to reduce the burden of foot lesions and amputations. The authors have hypothesized that hospitalization of diabetic patients could be an opportunity to screen DSPN and to educate patients. Authors also intended to compare SMWE and MNSI performance.

Material and Methods

STUDY DESIGN AND PATIENT POPULATION

This was a prospective and multicentre study that enrolled diabetic patients admitted consecutively to internal medicine wards, between May and October 2015. Patients were enrolled in two central hospitals: Hospital de Santo Antonio (HSA) and Hospital de Vila Real (HVR). HSA is also a teaching hospital. Patients were enrolled in the study if they had a diagnosis of diabetes previous to admission. Other causes of peripheral polyneuropathy were excluded through patients interview and electronic medical records query (hospital and national electronic health records: SClinico® and RSE®, respectively), including alcohol, HIV infection, hypothyroidism, vitamin B12 deficiency, renal chronic failure, paraproteinemias, malignant disease, personal or familial neurological disease and use of neuropathy-inducing drugs (Appendices 1). Demographic variables (sex, age) and data regarding the medical history of diabetes mellitus (type, years of evolution and HbA1c value) were also obtained by patients interview and consulting electronic medical records. Vascular complications (neuropathy, retinopathy, cerebrovascular disease, coronary heart disease and/or peripheral arterial disease) were considered if reliably described in electronic medical records (yes or no answers). In concern to diabetic nephropathy, it was taken into account if described in electronic medical records or microalbuminuria results in the past year.17 Laboratory results (HbA1c and microalbuminuria) were also analysed if undone in the previous three months prior to hospitalization.

DSPN SCALES

The SWME and the MNSI were applied to each patient by one of two neurology residents in each centre in order to reduce interobserver variability. A 10 g-monofilament was used to press 10 different points in each foot as proposed by the practical guideline from Michigan Diabetes Research and Training Center.18 A normal response corresponded to 8 or more correct answers, 7 or less correct answers was considered an abnormal response predictive of DSPN. MNSI includes two separate assessments: a 15-item questionnaire (Section A) and a lower extremity examination (Section B). Section A is self-administered by the patient and assesses the clinical symptoms through 15 “yes” or “no” questions, regarding foot sensations, numbness, temperature alterations, general asthenia, and peripheral vascular disease. In the original version, “yes” responses to items 1 to 3, 5 to 6, 8 and 9, 11 and 12, 14 to 15 count as 1 point each. For items 7 and 13 a “no” response counts as 1 point. Items 4 (a circulation assessment) and 10 (a general status measurement) are excluded in the original scale. Section B includes (1) the inspection of both feet (for dry skin, callouses, fissions or deformities); (2) the assessment of ulcerations; (3) the examination and grading of the muscle stretch reflexes as either normal, reduced, or absent (if necessary, the ankle reflex [AR] may be elicited using the
Jendrassik maneuver, which is defined as “presence with reinforcement”); and (4) the determination of vibration sensation (VS) at the interphalangeal joint of the hallux, using a 128-Hz tuning fork. A score > 2 in this section defined neuropathy.10 The prevalence of DSPN was calculated through results of Section B. The validation of MNSI for Portuguese population occurred after this study was performed, so we applied the cut offs suggested by Feldman et al. in the original article.19

STATISTICAL ANALYSIS

The data study was analysed using SPSS version 24.0.0. Shapiro-Wilk test was used to test normality. Duration of diabetes (years), HbA1c (%) and age were not normally distributed and so described as median ± interquartile amplitude. Mann-Whitney test was used to compare median of continuous variables. Chi-square test and Fisher test were performed to determine the significance of categorical variables. The global agreement rate between MNSI and SWME was based on positivity or negativity for both tests in the same patient. A p-value < 0.05 was considered significant.

ETHICAL STATEMENT

This study was reviewed and approved by both institutional and ethics committee. All patients signed informed consent. Information about diabetic neuropathy and how to prevent amputation was given to all patients with a probable diagnosis of DSPN.

Results

During the study period, 343 diabetic patients were evaluated (225 in HVR and 117 in HSA); of these, 88 patients (65 in HVR and 23 in HSA) were included in this study. The median (interquartile amplitude) age of patients was 7713 years and 45% were males. Most were type 2 diabetic patients (93.2%) and the median duration of diabetes was 1011 years; populations from both hospitals had similar demographic and clinical characteristics (Table 1). Macrovascular complications were present in 40% of the patients and 26% had at least one microvascular complication; of these, 7% had a previous diagnosis of diabetic neuropathy (Table 2).

The clinical examination of MNSI (section B) was positive in 66 patients (52 patients in HVR and 14 patients in HSA) reflecting a global prevalence of DSPN of 75% without significant differences between centres (Table 3); of these, 49 patients (55.7%) had a score ≥ 4 in the questionnaire (section A) and 82 patients (93.2%) had at least one symptom of neuropathy.

Most patients (92.4%) with a diagnosis of DSPN done during hospitalization did not have their condition diagnosed previously. Six patients had a previous diagnosis of DSPN; of these, 4 (66.7%) had a positive MNSI and 2 (33.3%) had a negative one. One of these patients had 11 points in Section A and the other had 3 points.

SWME was abnormal in 25 of the DSPN patients (38%); more patients in HSA presented a positive SWME (71% vs 29%, p = 0.005) (Table 4). One of these 25 patients had a previous diagnosis of DSPN.

The global agreement rate between MNSI and SWME was weak (44.3%). We identified that 25 (28.4%) out of 88 patients had both tests positive (MNSI and SWME), and 14 (15.9%) had both tests negative (Table 5). This agreement rate was significantly higher in HSA than in HVR (61% vs 39%). MNSI score was significantly higher in SWME positive patients, in global group and in HSA (Table 6).

Discussion

This study found that 75% of the hospitalized diabetic patients had DSPN and 92% of these patients were not previously diagnosed.

In Portugal this is the first study to estimate the prevalence of diabetic neuropathy in hospitalized patients. This is a higher percentage than has been described in the outpatient’s studies.20,21 For instance, Barbosa AP et al reported a prevalence of 32.3% of DSPN, based on signs and symptoms, among outpatients in the north side of the country.20,21 Our result reflects a bias towards older patients, with longer duration of diabetes and with more associated comorbidities in inpatients. However, the inclusion of two different centres in the north of Portugal, with similar inpatient population and with the same prevalence of DSPN in both centres when using MNSI criteria, is a positive aspect of this study.

The number of underdiagnosed cases of neuropathy in this study is alarming. Silva AM et al have already noticed that most inpatients electronic clinic registries lack documentation of vascular complications, particularly microvascular ones.20 Our percentage of underdiagnosed neuropathy, 92% of the cases, can represent either a problem of registry or an omission in the screening of neuropathy in diabetic patients. This study reinforces that hospitalization can be a window of opportunity to screen the neuropathy in the diabetic population and also to educate these patients in order to reduce the number of amputations.

Another aspect that can contribute to our results is the diagnostic tests used to detect DSPN. Abraham et al postulated that ankle reflex in addition to vibration or pinprick sensation is a sensitive combination for diagnosing polyneuropathy.22 In our study, we verify that reflexes and vibration sensation were the tests that contributed mostly to the positivity of MNSI. We also verify that there was a higher proportion of patients with reduced or abolished reflexes in one centre; however, the number of cases of DSPN using MNSI was not significantly different between the two centres, suggesting that this can be a good tool to screen neuropathy in hospitalized patients. One of the limitations of this work is absence of electrophysiological tests to confirm the MNSI results.

We found a high variability in DSPN detection when we used SMWE, with a significantly higher percentage of detected cases in one centre. This result suggests that there is an important interobserver variability in monofilament examination, which can limit the use of this test in the diagnosis of neuropathy and reinforces that this test should not be used isolated in the diagnosis of DSPN. This difference in monofilament test results also contributes to agreement rate of MNSI and SMWE in HSA.
The cut-off point of MNSI has been an issue of debate. In this study, the cut-off point of 2 was considered but our results suggest that higher cut-off points could contribute to higher agreement between tests. However, the ROC results (unpublished data) don’t confirm an alternative cut-off point.

Conclusion
In this study we conclude that DSPN is a high prevalent disease in hospitalized diabetic patients in Portugal but remains mostly underdiagnosed. This reinforces that hospitalization is an opportunity to screen neuropathy in diabetic patients and to educate these patients. Our result suggests that MNSI can be a good instrument to screen neuropathy and that SWME should not be used exclusively for this purpose. The validation of the MNSI for Portuguese population, after our work, reinforces the possibility of using this scale as a screening test.

REFERENCES


