Prevalence of neuropathic pain and associated factors in diabetes mellitus type 2 patients seen in outpatient setting*

Prevalência de dor neuropática e fatores associados em portadores de diabetes mellitus tipo 2 atendidos em ambulatório médico

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ABSTRACT

BACKGROUND AND OBJECTIVES: Epidemiological data on chronic pain in different populations are scarce in Brazil. This study aimed at investigating the prevalence of neuropathic pain and possible associated factors in diabetes type 2 patients, of a teaching center.

METHODS: This was a transversal study with individuals seen between March 2010 and March 2011, in the Medical Outpatient Setting of Specialties, University of Southern Santa Catarina, Tubarão, SC, with interviews to identify socio-demographic variables of age, gender and time elapsed after diagnosis of diabetes mellitus and application of tools to measure neuropathic pain, depression, glycemia and adhesion to treatment.

RESULTS: Participated in the study 72 subjects, being 69.4% females, 15.3% with controlled glycemia levels at the moment of the interview, 90.3% were adherent to treatment and 33.3% had depressive symptoms. The prevalence of neuropathic pain was 16.7% and this was associated to time of diabetes mellitus 2 (p=0.031).

CONCLUSION: The prevalence of neuropathic pain was similar to that observed in other places of the country and we suggest better follow up of the studied population with regard to depression and adhesion to medication to treat diabetes.

Keywords: Chronic pain, Complications of diabetes, Diabetes mellitus, Diabetic neuropathies.

RESUMO

JUSTIFICATIVA E OBJETIVOS: Dados epidemiológicos sobre dor crônica, em diferentes populações, são escassos no Brasil. O objetivo deste estudo foi investigar a prevalência de dor neuropática e possíveis fatores associados em pacientes portadores de diabetes tipo 2, de um serviço universitário.

MÉTODOS: Realizou-se estudo transversal com indivíduos atendidos entre março de 2010 e março de 2011, no Ambulatório Médico de Especialidades da Universidade do Sul de Santa Catarina, Tubarão, SC, com entrevistas para identificação das variáveis sócio-demográficas de idade, gênero e tempo de diagnóstico do diabetes *mellitus* e aplicação de instrumentos para mensuração de dor neuropática, depressão, glicemia e adesão aos fármacos.

RESULTADOS: Foram entrevistados 72 sujeitos, sendo 69,4% do gênero feminino, 15,3% apresentavam níveis glicêmicos controlados no momento da entrevista, 90,3% eram aderentes ao tratamento e 33,3% apresentavam sintomas de depressão. A prevalência de dor neuropática foi de 16,7% e esta se associou com o tempo de diagnóstico do diabetes *mellitus* 2 (p=0,031).

CONCLUSÃO: A prevalência de dor neuropática foi semelhante à observada em outras localidades do país, e sugere-se melhor acompanhamento da população estudada quanto à depressão e a adesão aos fármacos para tratamento do diabetes.

Descritores: Complicações do diabetes, Diabetes *mellitus*, Dor crônica, Neuropatias diabéticas.

INTRODUCTION

Diabetes mellitus (DM) is considered a disease of worldwide endemic proportions, with increasing number of cases diagnosed every year. In Brazil, DM prevalence is approximately 5% of the population[1], being most of them DM type 2 (DM2).

DM metabolic disorders, which have in common increase blood glucose concentration, may lead individuals to different clinical conditions affecting central and/or peripheral nervous system[2]. Diabetic neuropathy is a chronic complication of this disease, with changes in nervous functions due to their prolonged exposure to increased glucose levels, they symptoms of which may include neuropathic pain[3]. This pain pathogenesis seems to involve progressive sensory fiber axons

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degeneration, as well as oxidative stress caused by increased free radicals formation as a function of high glucose levels, among others[4,5].

Neuropathic pain is a health problem due to its chronic characteristic and may affect any human body nerve, generating major functional incapacity and comorbidities such as depression, anxiety and sleep disorders, among others[6]. Notwithstanding, epidemiological data on the frequency and consequences of this condition are scarce in Brazil and the government, via Ministry of Health, is now encouraging such studies, aiming at the diagnosis and better management of these patients[7].

In light of the above, this study has investigated the prevalence of chronic pain and other possible associated factors in DM2 patients attending a teaching medical outpatient setting.

METHODS

This was a cross-sectional study with all DM2 patients attending the Medical Outpatient Setting of Specialties, University of Southern Santa Catarina, Tubarão, SC from March 2010 to March 2011. Inclusion criteria were diagnosis of DM2 and agreement to participate in the study.

DM2 patients identified in the registry system of patients attending the outpatient setting during the study period were contacted via phone and a home visit was scheduled for data collection. During interview, subjects were explained about study objectives and procedures and have signed the Free and Informed Consent Term.

Study variables were socio-demographic information (age, gender and DM2 diagnosis time), glucose level at interview moment, presence of neuropathic pain, patients' adhesion to drugs prescribed to treat diabetes and the presence of depressive symptoms.

Glycemia level was measured by equipment for glucose measurement by glucose photometric determination (Sistema Accu-Chek Active®), in the minimum interval of 1h and maximum of 2h after last meal, according to manufacturer's recommendations, being patients classified as "controlled glycemia" for glucose values up to 100 mg/dL or "uncontrolled glycemia", for glucose values above 100 mg/dL[8]. Neuropathic pain was evaluated by a single interviewer trained in the sequence of interview stages and in the way questions and sensory tests should be applied. As from scores obtained by the DN4 scale, which is being applied to discriminate sensory pain quality to identify chronic pain associated to central nervous system injury[9], the presence of this condition was classified as "yes" when scores equal to or above 4, or "no", for scores below 4.

For the analysis of adhesion to prescribed drugs, subjects were classified as "adherent" when presenting "high or moderate adhesion", or as "non adherent" when presenting "low adhesion", applying Morisky's Scale as previously used by other authors[10]. Beck Inventory[11] was used to evaluate the presence of depressive symptoms, being this outcome classified as "yes" when scores were above 10 and "no" for scores from zero to 9.

Statistical analysis

Prevalence of neuropathic pain and socio-demographic characteristics of DM2 patients were descriptively analyzed. In addition, possible association between neuropathic pain and related factors such as depression, adhesion to treatment, glucose control and time from diagnosis were also analyzed. Data were recorded in a database created as from the Excel® program and were imported to SPSS 16.0®. Chi-square test or Fisher Exact test was used to compare nominal categorical data, considering significant $p \leq 0.05$.

The study was approved by the Ethics Committee for Studies in Humans (CEP), University of Southern Santa Catarina under protocol 12.395.4.01.III.

RESULTS

From 101 patients assisted during the study period, 4 refused to participate, 4 had death records and 21 have not answered to the phone call for at least three attempts, thus resulting in a total of 72 interviewed subjects. Mean age was 60.6±11.2 years ($CI_{95\%}$ 58.0;63.2) and mean time after DM2 diagnosis was 11.6±8.2 years ($CI_{95\%}$ 9.7;13.5).

Remaining characteristics describing the profile of DM2 patients attending AME in the period were: 69.4% were females, 15.3% had controlled glucose levels at interview moment, 33.3% reported depressive symptoms according to the tool used, 61.1% were classified as adherent to treatment and 16.7% had neuropathic pain.

In the multivariate analysis, neuropathic pain was only associated to time from DM2 diagnosis (Table 1). For this anal-

Table 1. Association of neuropathic pain and related variables in patients with diabetes mellitus type 2. Tubarão, SC, May to July 2009 (n=72)

Variables	Neuropathic pain No (%)	Yes (%)	Total n (%)	p value*
Gender				
Female	10 (13.9)	40 (55.6)	50 (69.4)	0.322
Male	2 (2.8)	20 (27.8)	22 (30.6)	
Controlled glycemia				
Yes	1 (1.4)	10 (13.9)	11 (15.3)	0.677
No	11 (15.3)	50 (69.4)	61 (84.7)	
Depressive symptoms				
Yes (score above 10)	5 (6.9)	19 (26.4)	24 (33.3)	0.616
No (score 0 to 9)	7 (9.7)	41 (56.9)	48 (66.7)	
Adhesion to treatment				
Yes (high & moderate)	5 (6.9)	39 (54.2)	44 (61.1)	0.130
No	7 (9.7)	21 (29.2)	28 (38.9)	
Diagnosis time (median)				
< 10 years	2 (2.8)	31 (43.1)	33 (45.8)	0.031*
≥ 10 years	10 (13.9)	29 (40.3)	39 (54.2)	
Total	12 (27.8)	60 (72.2)	72 (100.0)	

* Fisher Exact test.

ysis, diagnosis time was categorized by the median, which was 10 years of diagnosis.

On the other hand, there are data indicating increased neuropathic pain as a function of age. We have compared the presence of neuropathic pain considering a possible influence of age and have found no difference for this outcome when individuals were categorized by median of age (60 years, Fisher, p=0.346).

DISCUSSION

Data have shown neuropathic pain in 16.7% of DM2 patients attending a teaching medical outpatient setting, as well as its association with disease evolution time.

Neuropathic pain frequency observed in this study is very similar to that obtained by studies developed with similar populations in other countries. In Turkey, this outcome was recorded for 16.0% of diabetic patients attending a teaching center[12] and in Belgium this value was 14.0% of patients attending clinics for DM1 and DM2 patients[13]. These values are higher for diabetic patients as compared to Brazilian adult population in general, where recent neuropathic pain prevalence has been 1.7%[6].

In Brazil, a cross-sectional study carried out with more than 300 DM2 patients attending a hospital service has identified prevalence of 22.2% of individuals with peripheral diabetic neuropathy[14]. In the same study, although values being close to those found in this study, the slight difference may be explained by the fact that these authors have characterized the condition by other symptoms besides mechanical stimulation sensation changes. However, epidemiological data based on population studies regarding chronic pain frequency, including neuropathic pain, are scarce in the country, which has justified the recent publication of government document approving diagnostic protocols[7] and encouraging this type of study.

Differences in neuropathic pain frequency may also significantly differ among diabetic individuals with different glucose tolerance levels and the general population; factors such as weight, peripheral arterial disease and age are more associated to this outcome[15] With regard to the latter, notwithstanding other authors also reinforcing the idea that the number of individuals with neuropathic pain is higher among older people[16], this outcome was not associated to neuropathic pain in this study, suggesting that the association with time after diagnosis is real not being just a function of longer patients' life.

Our results show that only time after DM2 diagnosis was associated to neuropathic pain; this finding is in line with those recently observed by other authors, that diabetes duration affects other disease comorbidities. In a study carried out in Iran, DM2 time, in addition to age and education level, among other factors, was associated to complications, especially cardiovascular complications[17]. In Canada, a cohort study carried out for more than 20 years with diabetic patients in a young population has also recorded that renal system complications increase with longer DM2 duration[18].

Since neuropathic pain outcome among individuals may also vary according to the evaluation tool, one should highlight that the scale used in this study is being widely adopted in Brazil[19] as well as abroad[9]. Nevertheless, Brazilian Ministry of Health[7] has suggested for this objective the application of a tool validated for the Portuguese language and more recently published[20].

As to remaining characteristics, there have been no associations with other variables for individuals with neuropathic pain. Among patients attending AME, mean time of DM2 diagnosis was 11.6 years, which is in line with other authors[16]. In addition, most patients were females (69.4%), mean age of 60 years, also in line with different studies carried out with similar population.

As to adhesion to pharmacological treatment to control diabetes, 61.1% of patients were considered adherent. This result was below that recently observed (84%) by other authors among DM2 patients attending the public service[22] as well as among diabetes patients attending a university extension center (78.3%) of the state of São Paulo[23]. It is known that values found by different studies for this variable may differ a lot depending on studied population and conditions, as well as on the tool used for its measurement. However, our study calls the attention to the fact that, in addition to this adhesion value being below desirable values (80%), 84.7% of respondents had "uncontrolled glycemia" at interview moment, as described by the method. This suggests the need for further follow-up of this population for better controlling comorbidities associated to diabetic hyperglycemia[21].

With regard to depression risk factor, several studies have shown that depressive symptoms are strongly related to more severity of DM complications[24], showing the importance of its evaluation among diabetic patients; however, our study has observed no association between this variable and the presence of neuropathic pain. On the other hand, as from Beck Inventory, our findings have shown that 33.3% of respondents had depressive symptoms. Although considering that this is not a tool for clinical diagnosis of depression, being more widely used to follow-up therapeutic effect and disease improvement, this high proportion of depressive symptoms suggests the need for further monitoring of this comorbidity in this studied population because, among other reasons, the association of depression and non adhesion to drugs has also been shown[24].

Our results suggest the need for further follow-up of these aspects in the studied population.

CONCLUSION

Our study has shown prevalence of neuropathic pain in DM2 patients and the association of this variable with time after disease diagnosis, as well as a significant number of individuals not adhering to diabetes mellitus therapy.

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