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Journal Code: EJP	Proofreader: Mony
Article No: EJP350	Delivery date: 07 Jun 2013
Page Extent: 9	

EJP
European Journal of Pain

ORIGINAL ARTICLE

Diagnostic accuracy of two questionnaires for the detection of neuropathic pain in the Spanish population

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Funding sources
This study was supported by grants CTS-109 and FQM-235 from the Junta de Andalucía (Regional Government of Andalusia, Spain).

Conflicts of interest
None declared.

Accepted for publication
16 May 2013

doi:10.1002/j.1532-2149.2013.00350.x

Abstract

Background: Several questionnaires have been developed for the detection of neuropathic pain.
Objectives: This study aimed to compare the diagnostic accuracy of the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale and the Douleur Neuropathique en 4 questions (DN4) questionnaire for the detection of peripheral neuropathic pain in the Spanish population, and to analyse in detail the diagnostic quality of each item in these questionnaires.
Methods: A total of 192 patients were enrolled. We compared the validity of the DN4 and LANSS questionnaires by studying sensitivity and specificity and using receiver operating characteristic (ROC) curve analysis. We also analysed the validity of each item in the questionnaires.
Results: The sensitivity of the DN4 questionnaire with an accepted cut-off value of ≥4 was 95.04% and that of the LANSS questionnaire with an accepted cut-off value of ≥12 was 80.17%. The specificity of the DN4 instrument was 97.18% and that of the LANSS instrument was 100%. The estimated area under the ROC curve (95% confidence interval) was 0.989 (0.977–1) for the DN4 instrument and 0.973 (0.956–0.991) for the LANSS questionnaire. The area under the ROC curve was significantly larger for the DN4 than the LANSS questionnaire ($p < 0.05$). Analyses of specific items showed that tingling and numbness in the DN4 tool, and light touch pain and altered pinprick threshold in the LANSS scale, were the most important features of neuropathic pain.
Conclusions: These results show that although both questionnaires are good screening tools, the DN4 questionnaire is particularly recommended for identifying patients with neuropathic pain in clinical practice and research studies.

1. Introduction

Neuropathic pain has been redefined by the International Association of the Study of Pain as pain arising as a direct consequence of an injury or disease that affects the somatosensory system (Treede et al., 2008). This pain is currently considered a significant health problem that causes suffering to the patient and a huge burden on the health-care provision system (O'Connor, 2009). This type of chronic pain is characterized by the presence of both positive (pain, paraesthesia or dysaesthesia) and negative symptoms and signs (sensory deficiencies) with a plausible neurological distribution (Bouhassira and Attal, 2011). It is often accompanied by co-morbidities, such as anxiety, depression and sleep disorders (Attal et al., 2011), and has a significant negative impact on quality of life (Smith et al., 2007; Attal et al., 2011). Its prevalence is

What's already known about this topic?

- Several questionnaires have been developed for the detection of neuropathic pain.
- The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale and Douleur Neuropathique en 4 questions (DN4) questionnaire have been validated for the Spanish population, but their diagnostic accuracy has not been compared in the same population of patients with neuropathic pain.

What does this study add?

- We compared the diagnostic accuracy of the LANSS pain scale and the DN4 questionnaire in the Spanish population for the diagnosis of peripheral neuropathic versus non-neuropathic pain.
- We also performed a detailed analysis of the diagnostic quality of each item in both questionnaires.

estimated at 6.9–8.2% in the general population (Torrance et al., 2006; Bouhassira et al., 2008), but is much higher (51.9%) among patients treated at pain clinics (Pérez et al., ~~2012~~).

The health issues related to neuropathic pain have not received due attention, and this may have implications for treatment (Bouhassira and Attal, 2011). This is important because the pharmacological treatment of neuropathic pain differs from that of nociceptive pain and can involve the use of anticonvulsants, antidepressants, topical lidocaine and opioid agonists as the first choice for treatment (Dworkin et al., 2007).

In recent years, research groups from different countries have developed and validated several questionnaires for the detection of neuropathic pain. All are based on verbal descriptors used to define the characteristics of neuropathic pain, and also incorporate some assessment of physical signs. The screening tools differ not only in the number of items, layout and structure but also in the fact that validation studies have not been uniform. Thus, validation of the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale included only patients with peripheral pain, whereas validation of the Douleur Neuropathique en 4 questions (DN4) questionnaire included patients with both peripheral and central neuropathic pain. It must also be considered that validation studies of the LANSS questionnaire included patients with mixed pain due to radiculopathy or type I complex regional pain syndrome (CRPS), whereas the DN4 questionnaire was validated only in patients with neuropathic pain. Thus, the LANSS and DN4 tools have not been validated for the same types of pain or pathologies (Bennett, 2001; Pérez et al., 2006, 2007; Bouhassira and Attal, 2011).

Experts have pointed out the need for comparative studies of different pain questionnaires to analyse their discriminative capacity and predict their potential interchangeability (Bouhassira and Attal, 2011). However, to date, such studies have been performed in the Turkish population (Unal-Cevik et al., 2010) and in patients with spinal cord injury from the Swedish population (Hallström and Norrbrink, 2011). The main aim of this study was thus to compare the diagnostic accuracy of the LANSS and DN4 questionnaires for the detection and assessment of peripheral neuropathic pain in the Spanish population. We also compared the discriminative ability of different items in both questionnaires.

2. Methods

2.1 Design and patients

This was an observational, cross-sectional epidemiologic study. We studied 192 consecutive patients suffering from chronic pain, who were recruited among the outpatients attending the Pain Management Unit at the Reina Sofía University Hospital (Córdoba) and Virgen de las Nieves University Hospital (Granada) in Andalusia, Spain, during the period between February and December 2012.

Eligible participants were all adults aged 18 years or over, with a known diagnosis of chronic peripheral pain lasting for more than 3 months, and with an intensity of pain ≥4 on a 10-cm visual analogue scale (VAS) as determined during a face-to-face interview. The exclusion criteria were as follows: inability to understand or speak Spanish, physical or mental impairment, no pain during the previous week, pain of central origin, fibromyalgia as the primary or secondary pathology and type I CRPS. During the study period, 12 patients did not meet the inclusion criteria and were therefore excluded (4 with fibromyalgia and 8 for whom some data needed for the study were not available).

The study was conducted according to the usual standards of care at each participating centre. It was approved by the Provincial Biomedical Research Ethics Committee of Granada (Andalusia, Spain) and was performed in compliance with the Helsinki Declaration for research in humans. All patients provided their informed consent to participate in this research before they were included in the study.

2.2 Assessment

Pain was diagnosed based on the medical history, physical examination and any procedure (laboratory test, electro-

physiology, imaging, etc.) considered appropriate by the pain specialist to establish the diagnosis of the type of pain, which was initially classified as purely neuropathic, non-neuropathic or mixed. The specialist's diagnosis was considered the reference diagnosis. The questionnaires were administered in a blinded and random manner by one of the authors (H.A.) after appropriate training. This investigator did not participate in the previous diagnosis of the nature of pain. The LANSS and DN4 questionnaires were used to obtain information that would verify or refute the neuropathic nature of the pain. Patients in the group with neuropathic pain were asked about and tested in the area involved, and patients with non-neuropathic pain were asked about and tested in the site of their most intense pain. A specially designed case report form was prepared to record clinical information and the results of the LANSS and DN4 pain questionnaires. For all participants, information was recorded for socio-demographic data, type of appointment (first or follow-up), pain type, location, aetiology, duration and intensity (measured with a VAS as described below), underlying disease, associated diagnoses and treatments. All interviews were conducted by the same investigator (H.A.) in the course of a single appointment for each participant. For statistical purposes, two groups of patients were used: group NP comprised patients with neuropathic pain, i.e., patients suffering from pure neuropathic or mixed pain, and group NNP comprised patients whose pain was of non-neuropathic origin.

The LANSS pain scale consists of seven items grouped into two sections. The first section (five items) refers to symptoms and the type of pain. The second section (two items) investigates clinical signs with a sensory test in the painful area to explore allodynia and altered pinprick threshold. Each item requires a binary response. Positive responses are scored differently as 1, 2, 3 or 5 points depending on the item, and negative items are scored 0. The maximum score is 24, and a cut-off score of ≥12 indicates neuropathic pain (Bennett, 2001). The linguistic adaptation and validation for the Spanish population were reported earlier; the discriminative value of this cut-off score was very high, with a sensitivity of 91.1% and a specificity of 89.4% (Pérez et al., 2006).

The DN4 questionnaire consists of a total of 10 binary-response items grouped into four sections. The first section consists of three items related to the type of pain (burning, painful cold, electric shock); the second section consists of four items related to the association of pain with abnormal sensations such as tingling, pins-and-needles sensation, numbness and itching. The other two sections (three items each) are related to clinical signs in the painful area (touch hypoesthesia, pinprick hypoesthesia, tactile allodynia or brushing). A score of 1 is given to each positive (yes) item. The total score is calculated as the sum of the 10 items, and the cut-off value for the diagnosis of neuropathic pain is a total score of ≥4 out of 10 (Bouhassira et al., 2005). This instrument has been validated for the Spanish population, and the psychometric properties analysed were shown to be good with a sensitivity of 79.8% and a specificity of 78.0% (Pérez et al., 2007).

The intensity of pain was measured with a 10-cm VAS anchored at 0 (*no pain at all*) and 10 (*the worst pain imaginable*).

2.3 Data analysis

2.3.1 Validity

The validity (diagnostic accuracy) of the DN4 and LANSS questionnaires was assessed with receiver operating characteristic (ROC) curve analysis by calculating the area under the ROC curve (AUC), and by calculating sensitivity and specificity. Youden's index (Y) was also calculated with the equation Y = sensitivity + specificity − 1. The AUC was calculated with the trapezoid method. Two-sided 95% confidence intervals (95% CI) were also computed.

2.3.2 Statistics

For statistical analysis, Stata v. 11.5 software was used. An initial descriptive analysis was performed for the main variables. All data were expressed as the mean ± standard error of the mean (SEM) when necessary. Unpaired Student's t-tests were used to compare mean values between two groups. Categorical variables were compared with the chi-squared test, or with Fisher's or McNemar's tests. A value of $p < 0.05$ was considered statistically significant. The AUCs of the ROC curve for the DN4 and LANSS questionnaires were compared with Delong's test.

2.3.3 Sample size

Based on the information in the literature, we calculated a sample size to detect a difference between the two AUC of 0.09, assuming values for these areas of 0.97 and 0.88 and a correlation coefficient of 0.4 between the two questionnaires in NP and NNP groups. According to the method of Hanley and McNeil (1982), for an alpha error of 5% and 80% power, a sample size of 71 individuals in each group was calculated (for a total of 142 individuals). However, as patients were enrolled, it became clear that the number of patients in each group differed. Despite the imbalance in the sample, patient recruitment continued until the smaller group had reached a size of $n = 71$ participants, as initially established. The final sample size for both groups combined was 192, which ensured that the analysis was adequately powered in accordance with our original power calculations. In fact, this sample size provided more statistical power than what was used to calculate our initial sample sizes and allowed us to detect a smaller difference between the two AUC.

3. Results

3.1 Patients' characteristics

A total of 192 patients were recruited. There was 39 patients (20.31%) with pure neuropathic pain, 71

Table 1 Demographic and baseline characteristics in patients with neuropathic (NP) and non-neuropathic pain (NNP).

	NP (n = 121)	NNP (n = 71)	p-value
Age (years)	58.9 ± 1.2[a]	69.3 ± 1.3[a]	<0.001
Sex, female/male, n (%)	82/39 (67.8/32.2)	52/19 (73.2/26.8)	0.425
Height (cm)	163.7 ± 0.6[a]	161.4 ± 1[a]	0.067
Weight (kg)	75.9 ± 1.3[a]	75.7 ± 1.7[a]	0.926
BMI (kg/m^2)	28.4 ± 0.5[a]	29.1 ± 0.6[a]	0.444
Educational level, n (%)			0.012
None or elementary studies	26 (21.5)	29 (40.9)	
Primary education	50 (41.3)	29 (40.9)	
Secondary education	22 (18.2)	6 (8.5)	
Vocational training	14 (11.6)	2 (2.8)	
Higher education	9 (7.4)	5 (7)	
Type of appointment, n (%)			0.613
First	35 (28.9)	23 (32.4)	
Follow-up	86 (71.1)	48 (67.6)	
Duration of pain symptoms (months)	65.9 ± 8.2[a]	121.5 ± 15.8[a]	<0.001
VAS (cm)	6.44 ± 0.14[a]	5.87 ± 0.19[a]	0.018

BMI, body mass index; NNP, non-neuropathic pain; NP, neuropathic component pain; VAS, visual analogue scale (0–10 cm).
[a]Data are expressed as the mean ± standard error of the mean.

(36.98%) with nociceptive pain and 82 (42%) with mixed pain. Most patients (121, 63.02%) had a neuropathic pain component. For comparison purposes, the patients were grouped into those with pain associated with a neuropathic component (NP group) and patients with non-neuropathic pain (NNP group).

The demographic and clinical features of the participants are shown in Table 1. There were no differences in sex, height, weight, body mass index or type of appointment. Patients in the NNP group were older ($p < 0.001$) and their pain has lasted longer ($p < 0.001$) than in the NP group. Educational level was significantly associated with neuropathic pain ($p = 0.012$). Patients with neuropathic pain had higher VAS scores than those with non-neuropathic pain ($p = 0.018$).

The aetiology of pain is summarized in Table 2. All patients with pain from radiculopathies, neuralgia, neuropathies, type II CRPS, carpal tunnel syndrome, plexopathies and deafferentation were diagnosed as having a neuropathic pain component. Analysis showed that neuropathic pain was significantly associated with radiculopathies, neuralgias ($p < 0.001$) and neuropathies ($p < 0.05$), whereas there were no significant associations with any of the other aetiologies, perhaps because of the small numbers of patients with each of these pathologies. Patients who experienced pain from degenerative osteoarthritis or osteoporosis were all diagnosed with nociceptive (non-neuropathic) pain. Analysis showed an inverse relationship between neuropathic pain and these two aetiologies ($p < 0.001$).

3.2 Frequencies of positive responses on the DN4 and LANSS questionnaires

The frequencies of positive responses to each item in the LANSS and DN4 questionnaires were compared between the NP and NNP groups (Table 3). Positive responses were significantly more frequent ($p < 0.001$) in the NP group than the NNP group.

Table 2 Aetiology of pain in patients with neuropathic (NP) and non-neuropathic pain (NNP).

Aetiology, n (%)	NP (n = 121)	NNP (n = 71)	p-value
Radiculopathies	67 (55.4)	0	<0.001
Neuralgia[a]	19 (15.7)	0	<0.001
Post-surgical pain	16 (13.2)	5 (7)	0.185
Neuropathies	7 (5.8)	0	0.039
CRPS II	6 (5)	0	0.057
Carpal tunnel syndrome	2 (1.7)	0	0.276
Plexopathies	1 (0.8)	0	0.442
Deafferentation pain	1 (0.8)	0	0.442
Neoplasia[b]	1 (0.8)	1 (1.4)	0.701
Arthritis	1	2 (2.8)	0.283
Osteoporosis and mechanical pain	0	8 (11.3)	<0.001
Osteoarthritis	0	55 (77.5)	<0.001

Frequencies for aetiology are presented as n and the percentage (%) calculated for the total number of patients in each group of neuropathic component pain (NP) or non-neuropathic pain (NNP). CRPS II, complex regional pain syndrome type II.
[a]Includes post-herpetic (n = 9), trigeminal (n = 6) and others (occipital, crural, pudendal) (n = 4).
[b]Includes a case of neoplastic plexopathy in a patient with multiple myeloma (NP group) and pelvic metastases secondary to prostate tumour (NNP group).

Table 3 Frequency of positive items in patients with neuropathic and non-neuropathic pain.

	NP (n = 121)	NNP (n = 71)	p-value
LANSS items, n (%)			
Pricking, tingling, pins and needles	118 (97.52)	36 (50.70)	<0.001
Skin discoloration	29 (23.97)	0	<0.001
Light touch pain	92 (76.03)	7 (9.86)	<0.001
Electric shocks, jumping, bursting	86 (71.07)	28 (39.44)	<0.001
Feeling of altered skin temperature	98 (80.99)	31 (43.66)	<0.001
Allodynia	59 (48.76)	8 (11.27)	<0.001
Altered pinprick threshold	111 (91.74)	18 (25.35)	<0.001
DN4 items, n (%)			
Burning	89 (73.55)	22 (30.99)	<0.001
Painful cold	21 (17.36)	2 (2.82)	0.003
Electric shocks	68 (56.20)	14 (19.72)	<0.001
Tingling	90 (74.38)	2 (2.82)	<0.001
Pins and needles	83 (68.60)	23 (32.39)	<0.001
Numbness	89 (73.55)	7 (9.86)	<0.001
Itching	54 (44.63)	6 (8.45)	<0.001
Touch hypoesthesia	53 (43.80)	5 (7.04)	<0.001
Pinprick hypoesthesia	53 (43.80)	6 (8.45)	<0.001
Brushing	57 (47.68)	9 (12.68)	<0.001

Frequencies are presented as n and the percentage (%) calculated for the total number of patients in each group with neuropathic pain (NP) or non-neuropathic pain (NNP).

3.3 Comparison of the validity of the DN4 and LANSS questionnaires

In the LANSS questionnaire, the mean score (±SEM) for patients with NP was 15.7 ± 0.41, with a range from 5 to 24, whereas in patients with NNP the mean score was of 5.3 ± 0.39, with a range from 0 to 11. In the DN4 questionnaire, the mean score (±SEM) for patients with NP was 5.5 ± 0.13 with a range from 1 to 9, whereas in patients with non-neuropathic pain, the mean score was 1.4 ± 0.12 with a range of 0–4. Overall, the mean score on both the LANSS and the DN4 questionnaires was significantly higher in patients with neuropathic pain compared with the NNP group ($p < 0.001$).

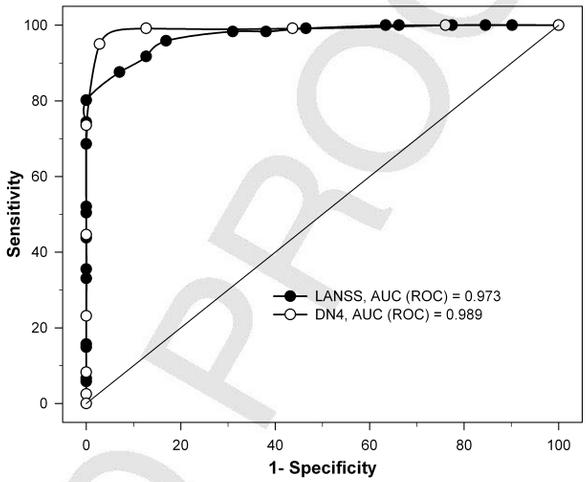

Figure 1 Receiver operating characteristic (ROC) curves and area under the ROC curve (AUC) values for the Spanish version of the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) and Douleur Neuropathique en 4 questions (DN4) questionnaires for the differential diagnosis of peripheral neuropathic versus non-neuropathic pain.

In the group of patients with neuropathic pain, a cut-off value of ≥12 to diagnose neuropathic pain with the LANSS pain scale had a sensitivity of 80.17% and a sensitivity of 100%. A cut-off point value of ≥4 with the DN4 questionnaire yielded a sensitivity of 95.04% and a specificity of 97.18% (see the confidence intervals in Table 4). These results indicate a good relationship between the clinical diagnosis and scores on the LANSS and DN4 questionnaires with their accepted cut-off values of ≥12 and ≥4, respectively.

The estimated area under the ROC curves (95% CI) was 0.973 (0.956–0.991) for the LANSS pain scale and 0.989 (0.977–1) for the DN4 questionnaire (Fig. 1). The AUC for the DN4 questionnaire was significantly greater than for the LANSS tool ($p < 0.05$). Youden's index was 0.80 for the LANSS tool and 0.92 for the DN4 questionnaire.

Mean administration time (±SEM) was 2.5 ± 0.08 min for the DN4 tool and 5.3 ± 0.11 min for the LANSS pain scale.

Table 4 Comparison of the validity of the LANSS and DN4 questionnaires in patients with peripheral neuropathic pain.

	LANSS (score ≥ 12)	DN4 (score ≥ 4)	p-value
Sensitivity, % (95% CI)	80.17 (71.9–86.9)	95.04 (89.5–98.2)	—
Specificity, % (95% CI)	100 (94.9–100)	97.18 (90.2–99.7)	—
AUC (CI 95%)	0.973 (0.956–0.991)	0.989 (0.977–1.00)	0.048[a]

AUC, area under the curve (ROC analysis); CI, confidence interval; DN4, Douleur Neuropathique en 4 questions; LANSS, Leeds Assessment of Neuropathic Symptoms and Signs.
[a]Delong's test.

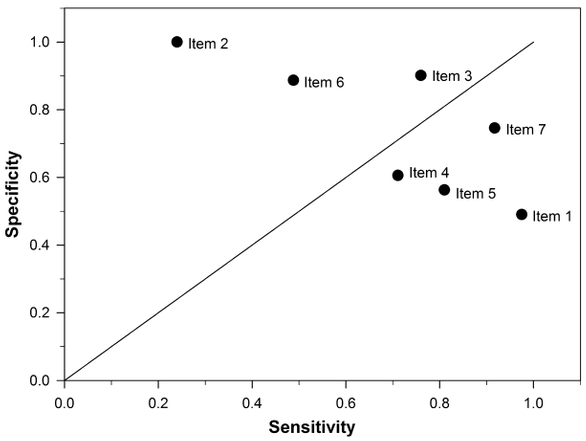

Figure 2 Analysis of the validity of each item in the Spanish version of the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale based on a cut-off value of ≥12. The specificity for each item was plotted against its sensitivity. LANSS items: item 1, pricking, tingling, pins and needles; item 2, skin discoloration; item 3, light touch pain; item 4, electric shocks, jumping, bursting; item 5, burning, hot; item 6, allodynia; item 7, altered pinprick threshold.

3.4 Diagnostic quality of each item in the Spanish version of LANSS and DN4 questionnaires

The diagnostic quality of each item in the LANSS pain scale (cut-off value of ≥12) and DN4 questionnaire (cut-off value of ≥4) was analysed for the differential diagnosis of neuropathic pain versus non-neuropathic pain. In each questionnaire, we compared the sensitivity and specificity as the area under the ROC curve for each item. On the basis of the variability we observed, we grouped the items into three diagnostic quality categories: high, intermediate and low.

For the LANSS scale (Fig. 2), the first group (high diagnostic quality) contained items 3 'light touch pain' and 7 'altered pinprick threshold', for which the area under the ROC curve was significantly larger ($p < 0.05$) than for the other items (item 3, 0.831; item 7, 0.832). The second group (intermediate diagnostic quality) contained items 1 'pricking/tingling/pins and needles', 4 'electric shocks, jumping, bursting', 5 'burning, hot' and 6 'allodynia', for which the area under the ROC curve was significantly smaller ($p < 0.05$) than for the first group but greater ($p < 0.05$) than for the third group (item 1, 0.734; item 4, 0.658; item 5, 0.687; and item 6, 0.687). The third group (low diagnostic quality) contained item 2 'skin discoloration', for which the area was significantly smaller ($p < 0.05$) than for the intermediate group (0.620).

In the DN4 questionnaire (Fig. 3), the first group (high diagnostic quality) contained items 4 'tingling' and 6 'numbness', with an area under the ROC curve significantly greater ($p < 0.05$) than the area for the remaining items (item 4, 0.858; item 6, 0.818). The intermediate diagnostic quality group contained items 1 'burning', 3 'electric shocks', 5 'pins and needles', 7 'itching', 8 'touch hypoesthesia', 9 'pinprick hypoesthesia' and 10 'brushing'. The area under the ROC curve for these items was significantly smaller ($p < 0.05$) than for the first group and significantly greater than for the third group (item 1, 0.713; item 3, 0.682; item 5, 0.681; item 7, 0.681; item 8, 0.684; item 9, 0.677; item 10, 0.672). The low diagnostic quality group contained item 2, with an area under the ROC curve significantly smaller ($p < 0.05$) than that of all other items (0.573).

4. Discussion and conclusions

This study reports the first comparison of the validity of the DN4 and LANSS questionnaires to assess neuropathic pain in the Spanish population. Overall, we confirm the high discriminative value of the Spanish versions of both tools and provide evidence that the DN4 questionnaire is even better than the LANSS pain scale. We also provide the first analysis of the diagnostic accuracy of the different items in each questionnaire in the Spanish population.

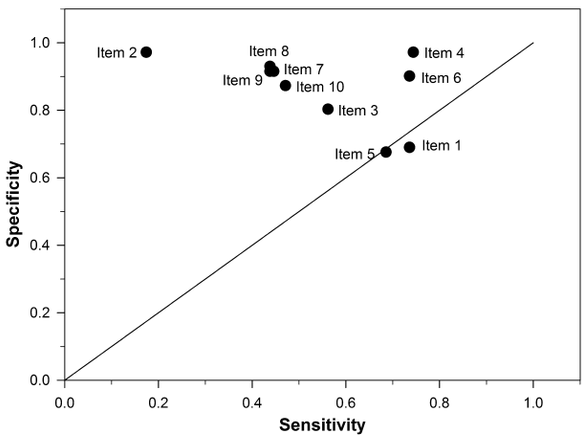

Figure 3 Analysis of the validity of each item in the Spanish version of the Douleur Neuropathique en 4 questions (DN4) questionnaire based on a cut-off value of ≥4. The specificity for each item was plotted against its sensitivity. DN4 items: item1, burning; item 2, painful cold; item 3, electric shocks; item 4, tingling; item 5, pins and needles; item 6, numbness; item 7, itching; item 8, hypoesthesia to touch; item 9, hypoesthesia to prick; item 10, pain caused or increased by brushing.

The diagnosis of neuropathic pain is still challenging, and one way to detect it is with a series of specific descriptors that have been used to prepare different scales and questionnaires. Because of the specific clinical characteristics of neuropathic pain, a combination of selected symptoms and signs, as used in the questionnaires we compared, is assumed to have a high discriminative value for the identification of this category of pain. The DN4 questionnaire was originally validated in the French population (Bouhassira et al., 2005) and subsequently in the Spanish population (Pérez et al., 2007), and was more recently tested in Turkish (Unal-Cevik et al., 2010), Portuguese (Santos et al., 2010) and Moroccan Arabic dialect populations (Harifi et al., 2011). It is consists of items related to both symptoms and clinical signs. It is easier to administer (taking an average of 2.5 min) and to score (each positive item is scored 1 and each negative item is scored 0) than the LANSS tool. The LANSS scale was originally validated in an English population (Bennett, 2001), and later in Turkish (Yucel et al., 2004) and Spanish populations (Pérez et al., 2006). This tool also has two parts: a patient-completed section and a brief physical assessment. Five questions in the patient-completed section (maximum score 16) identify those who are experiencing phenomena associated with neuropathic pain, such as paraesthesia (pricking, tingling, pins and needles), autonomic changes (skin discolorations), evoked dysaesthesia (sensitive skin or light touch pain) and spontaneous dysaesthesia (electric shock pain, jumping, bursting, burning pain). Positive responses for different items are scored differently, with the highest score of 5 points for items 1 (pricking, tingling, pins and needles) and 2 (skin discolorations) and the lowest scores for items 4 (electric shocks, jumping, bursting; 2 points) and 5 (burning, hot; 1 point). The cut-off score for neuropathic pain is ≥12 for the LANSS scale.

According to one expert panel, the main clinical strength of questionnaires as screening tool lies in their ability to identify patients with possible neuropathic pain, but they cannot replace clinical judgement (Haanpää et al., 2010). Clinical judgement has been considered a valid standard to test the diagnostic accuracy of questionnaires for neuropathic pain (Bennett et al., 2005). In our study population, the agreement between the clinical diagnosis of neuropathic pain and the diagnosis based on the questionnaire results was high, as reflected by AUC values higher than 0.97.

Our study population consisted of 192 patients with peripheral pain. The demographic characteristics of the patients included in our study were similar to those of other studies (Bouhassira et al., 2005; Harifi et al., 2011; Unal-Cevik et al., 2010; Perez et al., 2007, ~~2012~~), except for the age of the patients, which was lower in studies of the Turkish (Unal-Cevik et al., 2010) and Moroccan populations (Harifi et al., 2011) than in European studies (Bouhassira et al., 2005, Perez et al., 2007, ~~2012;~~ this study). The aetiologies of peripheral neuropathic pain in the Spanish patients in the present study were consistent with other studies (Bouhassira et al., 2005; Sommer et al., 2007; Unal-Cevik et al., 2010; Bouhassira and Attal, 2011; Harifi et al., 2011; De Andrés et al., 2012).

In our study population, the average age of patients with neuropathic pain was lower than in patients with non-neuropathic pain, which is consistent with the findings in the initial description by Bennett (2001) of the LANSS scale. There were no differences between the two groups of patients in sex, height, weight, body mass index or type of appointment, which agrees with other published series (Pérez et al., 2006, 2007; Unal-Cevik et al., 2010). The existence of a neuropathic pain component is associated with a higher level of education, as reported by Perez et al. (2007). This could be interpreted as a sign that patients with low literacy levels have difficulty understanding some of the language or terms used in neuropathic pain questionnaires.

In the population we studied, pain intensity was greater in patients with a neuropathic component than in those with non-neuropathic pain, which agrees with the data reported by other authors (Unal-Cevik et al., 2010; Attal et al., 2011; Harifi et al., 2011). On the other hand, the duration of pain was longer in the NNP group than that in the NP group, which agrees with the findings reported by Harifi et al. (2011) but not with the results published by Bouhassira et al. (2005). Non-neuropathic pain is due, in most cases, to processes of osteoarthritis and osteoporosis, which are long-lasting. This factor, together with the advanced age of the patients, may explain the longer duration of chronic pain in the NNP group.

The sensitivity (95.04%) and specificity (97.18%) we found for the DN4 questionnaire are close to the figure reported in previous studies (Santos et al., 2010; Unal-Cevik et al., 2010) but are higher than those reported by others (Bouhassira et al., 2005; Perez et al., 2007; Spallone et al., 2012; Hallström and Norrbrink, 2011). Regarding the LANSS scale, sensitivity (80.17%) was within the range of previously reported values (Bennett, 2001; Yucel et al., 2004; Perez et al., 2006), and specificity was very high, at 100%. Recently, a study of Swedish patients with spinal cord injury documented a similar specificity but

lower sensitivity for the LANSS scale (Hallström and Norrbrink, 2011). Differences in study populations and in the classification of neuropathic pain may explain the variability among different studies. Moreover, the diagnosis in the patients included in the present study was made by medical specialists affiliated with pain clinics, based on their clinical judgement, prior tests or imaging studies; thus, the quality of the clinical diagnosis of neuropathic pain would be expected to be high. In our comparison of the validity of the DN4 and LANSS tools, we found that although both are highly discriminative, the predictive ability of the DN4 questionnaire was better, because the AUC in ROC analysis was significantly larger ($p < 0.05$) than the area obtained for the LANSS scale. The study by Hallström and Norrbrink (2011) also showed that the AUC for the DN4 questionnaire was higher than that of other screening tools in patients with spinal cord injury.

We also analysed the sensitivity and specificity of each item in both tools, and found differences that merit attention. In the DN4 questionnaire, the items with the highest diagnostic quality were numbness (item 6) and tingling (item 4), which agrees with the findings of Unal-Cevik et al. (2010), Santos et al. (2010) and Hallström and Norrbrink (2011). However, in the LANSS scale, tingling, which is listed along with other descriptors in the same item (item 1), had an intermediate level of diagnostic quality. A provisional conclusion that can be drawn from this finding is that it is preferable to use simple descriptors rather than complex ones. In contrast, the items with the lowest diagnostic quality in the present study were skin discoloration (item 2, LANSS) and painful cold (item 2, DN4). Among the different descriptors of physical signs that both questionnaires use, altered pinprick threshold in the LANSS scale showed the best diagnostic quality, which was even better than allodynia despite the fact that a positive response for allodynia (item 6, 5 points) is scored more highly than a positive response for altered pinprick threshold (item 7, 3 points).

A limitation of this study is the imbalance of the sample sizes of the two groups due to the different rates of recruitment of patients in each group. However, the final sample retained sufficient power to detect statistically significant differences between groups. The main strength of this study lies in our comparison of the diagnostic accuracy of pain questionnaires in the same population of patients, i.e., in patients with neuropathic pain (pure and mixed) of peripheral origin.

In conclusion, this study documents the high discriminative value of the Spanish version of the LANSS pain scale and the DN4 questionnaire for the detection of peripheral neuropathic pain. The DN4 questionnaire is particularly recommended for identifying patients with neuropathic pain in clinical practice and in research studies. Our analysis of specific items shows that tingling and numbness in the DN4 questionnaire, and light touch pain and altered pinprick threshold in the LANSS scale, are the most important features of neuropathic pain.

Author contributions

A.H. was responsible for interviewing the patients and collecting the data. He also participated in the data analysis, discussion of the results and manuscript revision.

J.D.L. was responsible for the statistical analysis of the data. He also participated in the discussion of the results and manuscript revision.

E.D.P. was responsible for writing and preparing the manuscript. She also participated in the study design, data analysis and interpretation, and discussion of the results.

R.G. was responsible for the study design and supervising data collection. He also participated in the data analysis, discussion of the results and manuscript revision.

Acknowledgement

We thank K. Shashok for improving the use of English in the manuscript.

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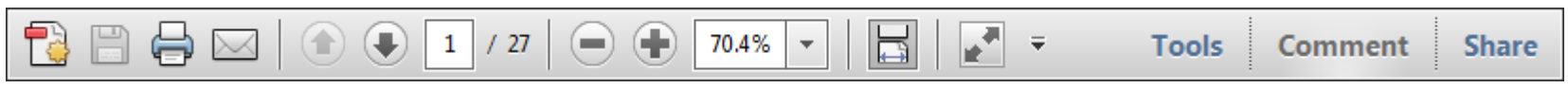

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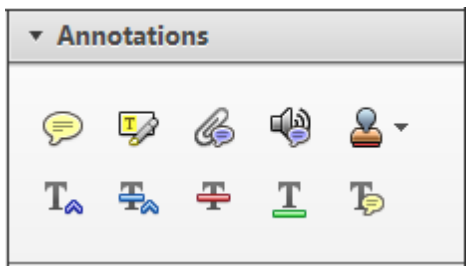

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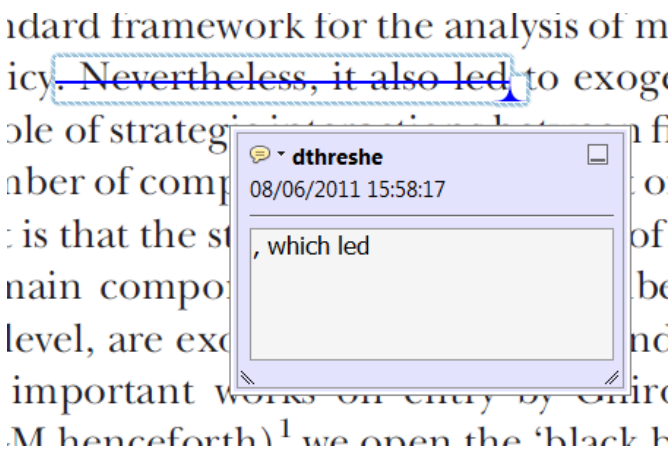

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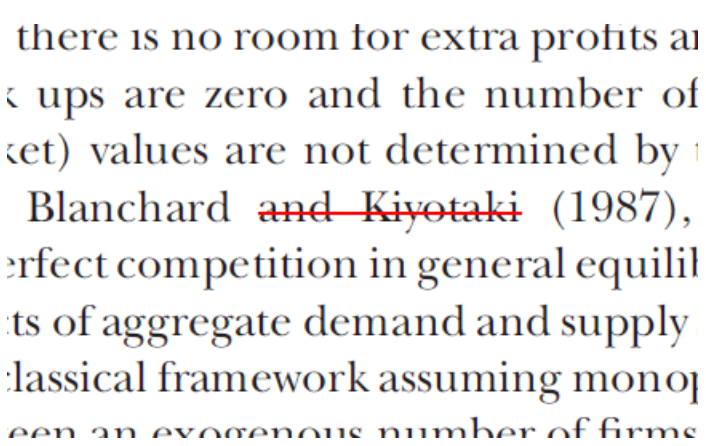

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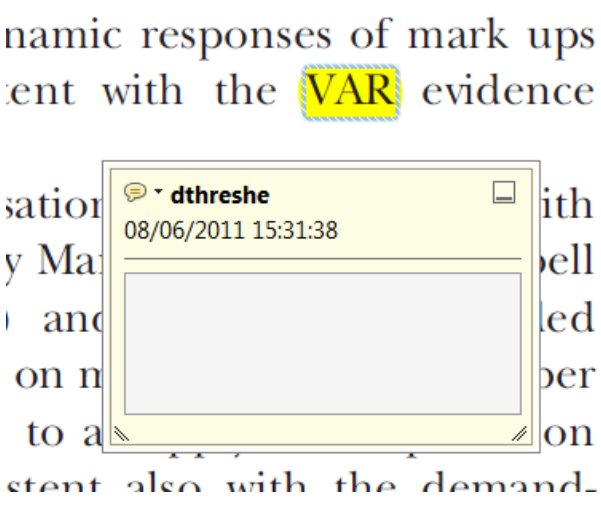

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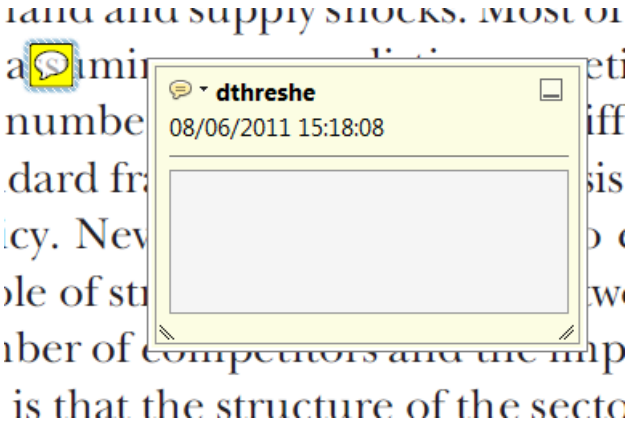

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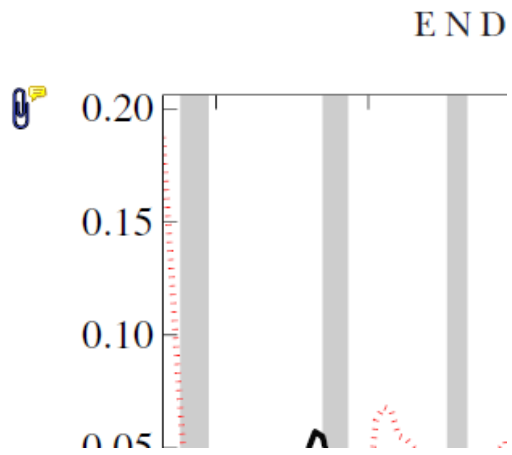

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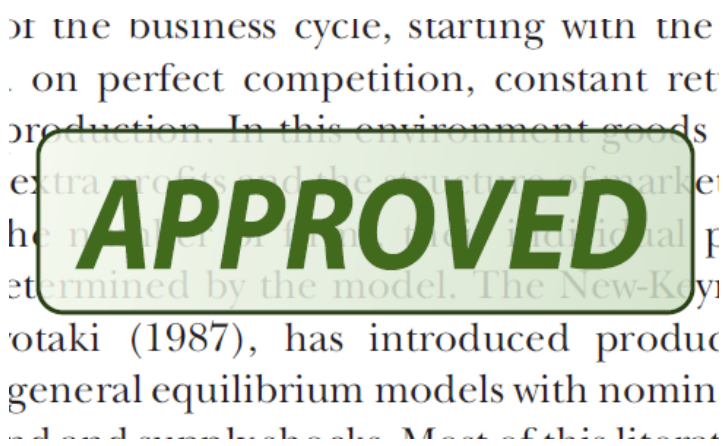

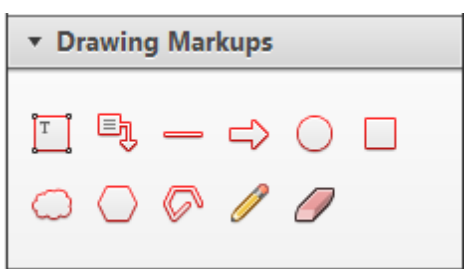

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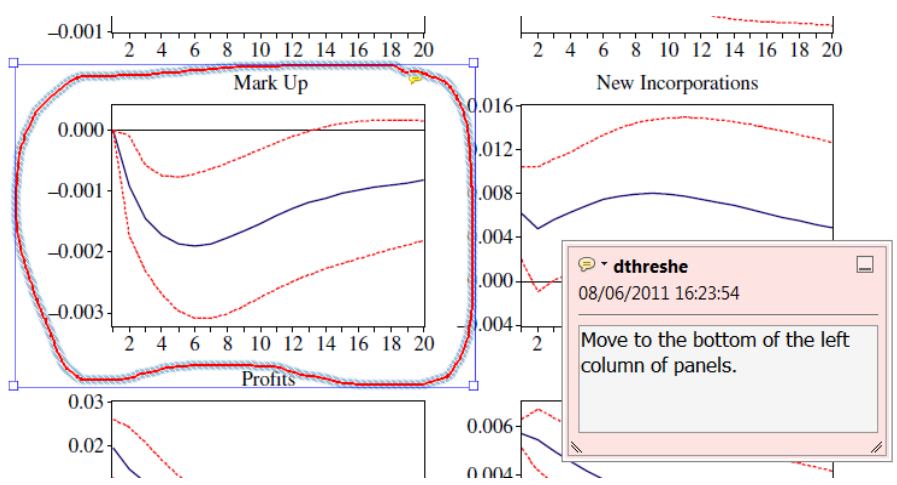

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