European Journal of Pain 15 (2011) 99–102

Contents lists available at ScienceDirect

European Journal of Pain

journal homepage: www.EuropeanJournalPain.com

Short Communication

Classifying post-stroke shoulder pain: Can the DN4 be helpful?

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ARTICLE INFO

Article history:
Received 9 October 2009
Received in revised form 23 April 2010
Accepted 20 May 2010
Available online 12 June 2010

Keywords:
Stroke
Shoulder pain
Neuropathic pain diagnostic questionnaire
Quantitative sensory testing

ABSTRACT

The etiology of post-stroke shoulder pain (PSSP) is largely unclear and may involve both nociceptive and neuropathic mechanisms. No gold standard is present for PSSP diagnosis. The neuropathic pain diagnostic questionnaire (DN4), was originally developed to identify neuropathic pain in the clinical context. In this study we used the DN4 to categorize PSSP patients and compared symptoms and signs suggestive of either nociceptive or neuropathic pain. Pain complaints and sensory functions were compared between patients with chronic PSSP scoring at least four (DN4+, $n = 9$) or less than four (DN4−, $n = 10$) on the DN4. Pain was assessed using a numeric rating scale and the McGill pain questionnaire. Sensory functions were assessed using clinical examination and quantitative sensory testing combined with a cold pressor test. Patients classified as DN4+ reported constant pain, higher pain intensity, a higher impact of pain on daily living, more frequent loss of cold sensation, reduced QST thresholds at the unaffected side and increased QST thresholds at the affected side. Notably, several symptoms and signs suggestive of either neuropathic or nociceptive pain corresponded to the subgroups DN4+ and DN4− respectively. However, since the pathophysiological mechanisms remain unclear and none of the sensory signs could be exclusively related to either DN4+ or DN4−, PSSP prognosis and treatment should not be solely based on the DN4. Nonetheless, a thorough assessment of neuropathic and nociceptive pain complaints and somatosensory functions should be included in the diagnostic work-up of PSSP.

1. Introduction

Shoulder pain is a common complication after stroke (Dromerick et al., 2008; Lindgren et al., 2007) of which the etiology is largely unclear. Traditionally, post-stroke shoulder pain (PSSP) is considered as a nociceptive pain (Bender and McKenna, 2001; Turner-Stokes and Jackson, 2002). In addition, PSSP has been related to central post-stroke pain, complex regional pain syndrome type 1, depression and sensory abnormalities and may be caused and maintained by various pain mechanisms (Gamble et al., 2002; Lindgren et al., 2007; Lundström et al., 2009; Teasell et al., 2007).

Although prognosis and treatment of PSSP is largely dependent on suspected involvement of nociceptive and/or neuropathic pain mechanisms, there is no gold standard or consensus regarding the diagnostic tools to differentiate PSSP of predominantly neuropathic from that of predominantly nociceptive origin. The use of grading systems for neuropathic pain (Treede et al., 2008) or central post-stroke pain (Klit et al., 2009) is problematic in PSSP. Based on the grading system for neuropathic pain, even patients with pure nociceptive PSSP might be classified as having neuropathic pain, simply because they have a relevant lesion affecting the central somatosensory system and the pain has a distinct neuroanatomically plausible distribution. On the other hand, to be classified as central post-stroke pain, all other causes of pain must have been ruled out, which can be difficult in PSSP (Roosink et al., 2010).

Several neuropathic pain scales have been developed for defining neuropathic pain in clinical practice. One of these is the neuropathic pain diagnostic questionnaire (DN4) comprising pain descriptors and a sensory examination (Bouhassira et al., 2005). Its scale ranges from 0 to 10 and a score of at least four has been suggested to correlate with pain of predominantly neuropathic origin. However, neither the DN4 nor any other neuropathic pain scale has been validated for post-stroke pain.

This pilot study was performed to explore whether the DN4 might be useful for the classification of PSSP subtypes. Therefore, different pain complaints and somatosensory functions as related to either nociceptive or neuropathic pain were compared between

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1090-3801/$36.00
doi:10.1016/j.ejpain.2010.05.012

subgroups of PSSP as classified with the DN4. In brief, movement related pain, pain related to arm function and/or biomechanical changes around the shoulder joint were expected to be associated with nociceptive pain (Gamble et al., 2002). Neuropathic pain after stroke has previously been associated with spontaneous or constant pain, touch and cold allodynia (Klit et al., 2009), impaired spino-thalamo-cortical tract function (Boivie et al., 1989; Widar et al., 2002) and disturbed diffuse noxious inhibitory controls (DNIC) (Tuveson et al., 2009). Although none of these symptoms and signs has been exclusively related to neuropathic pain, the incidence of these symptoms and signs was expected to be higher in the group of patients classified as neuropathic pain.

2. Methods

2.1. Subjects

Patients ($n = 19$) were recruited in two regional rehabilitation centers in the Netherlands (Roessingh Rehabilitation Center in Enschede and Sint Maartenskliniek in Nijmegen). All patients (age > 18 years) sustained a unilateral brain infarction with an onset at least 6 months prior to participation and had daily shoulder pain at the affected side for more than three subsequent months with an onset post-stroke. None fulfilled the diagnostic criteria for central post-stroke pain (Klit et al., 2009). In addition, none of the patients had other concomitant chronic pain complaints, either stroke or non-stroke related. Exclusion criteria were: pregnancy, trauma, infection, signs of any possible concomitant neurological condition. The study was approved by the human ethics committee and all participants gave written informed consent prior to their participation.

2.2. Demographic and medical assessment

Demographics and medication use were registered. Depressive symptoms were assessed using the ZUNG self-rating depression scale (Turner-Stokes and Hassan, 2002). Cognitive impairment was defined using the Mini Mental State Exam (score < 24) (Tombaugh and McIntyre, 1992). Physical examination of the upper extremity included assessment of trophic changes (visual inspection), glenohumeral subluxation (palpation), pain-free range of motion for passive shoulder elevation and external rotation (ratio between sides, affected/unaffected), motor function (Motricity Index, score 0 = no function, score 100 = normal function) (Collin and Wade, 1990) and spasticity of elbow flexors and shoulder internal rotators (Modified Ashworth Scale, score $\geqslant 1$) (Bohannon and Smith, 1987).

2.3. Subjective pain evaluation

Shoulder pain was evaluated at rest and during movement using a numeric rating scale (0 = no pain, 10 = maximum conceivable pain), the McGill Pain Questionnaire (Van der Kloot et al., 1995) and the neuropathic pain diagnostic questionnaire (DN4) (Bouhassira et al., 2005; Van Seventer et al., 2009).

2.4. Somatosensory assessment

Modality specific somatosensory assessment is important for the diagnosis of neuropathic pain (Cruccu et al., 2004). A clinical examination and quantitative sensory testing (QST) was performed at both the affected and unaffected side at upper and lower part of the middle deltoid (C5 dermatome). Differences between sides (sensation) and evoked pain (allodynia) were recorded in response to the application of a cotton wool stick (light touch), a cold metal object (cold sensation) and a Semmes Weinstein filament size 6.65 (sharpness). Proprioception was tested at the thumbs. The tactile detection threshold was determined using Semmes Weinstein filaments (Touch-Test Hand Kit, North Coast Medical, Inc., UK). The pressure pain threshold was determined using a Somedic pressure algometer (1 cm^2, 50 kPa/s). In addition, patients were trained to determine electrical sensation, pain and pain tolerance thresholds using an ambulant stimulator (settings: 0.2 ms, 100 Hz, 0.4 mA/s). For QST, the method of limits was used and the start side of stimulation was randomized. For analysis, absolute thresholds (average of three recordings) were used for the unaffected side and relative thresholds (affected/unaffected) for the affected side.

2.5. DNIC function

Following QST, patients immersed their unaffected hand in a polystyrene box filled with ice water (0–0.5 °C). Subjects were instructed to keep their hand in the water as long as possible (maximum 3 min). Immersion time was recorded using a digital stopwatch. After removing their hand from the water, patients rated the cold pressor induced pain using a numeric rating scale (0 = no pain, 10 = maximum conceivable pain), immediately followed by another determination of the electrical pain threshold and pressure pain threshold at the affected upper arm. A ratio (post/pre) was calculated for the pain thresholds determined before and after cold pressor testing.

2.6. Data analysis

Subgroups were formed based on the DN4 score: $\geqslant 4$ (DN4+) or <4 (DN4−). All ratios were log-transformed prior to statistical analysis. Due to the small sample sizes, only the differences in abnormal sensation (chi-square tests), QST thresholds (independent *t*-tests) and cold pressor parameters were statistically tested. Statistical significance was assigned at the $p < 0.05$ level.

3. Results

3.1. Demographics and medical examinations

All demographic and medical data are presented in Table S1.

3.2. Subjective pain evaluation

Pain characteristics are presented in Table 1. Pain intensity was somewhat higher in DN4+ patients. Moreover, only DN4+ patients

Table 1
Pain characteristics.

		DN4+ ($n = 9$)	DN4− ($n = 10$)
DN4 score, median (range)		5 [4–6]	2 [0–3]
Pain onset (months post-stroke), mean ± SD		5 ± 8	2 ± 3
Pain duration (months), mean ± SD		20 ± 9	18 ± 17
Pain intensity (0–10), mean ± SD	Rest	4.7 ± 2.9	2.5 ± 2.4
	Movement	7.3 ± 1.8	4.4 ± 3.2
Pain distribution, *n* (%)	Localized	8 (90%)	10 (100%)
	Radiating	5 (56%)	2 (20%)
	Shooting	1 (11%)	0 (0%)
Pain incidence, *n* (%)	Attacks	0 (0%)	5 (50%)
	Intermittent	5 (56%)	5 (50%)
	Constant	4 (44%)	0 (0%)
Impact on daily life (0–27), mean ± SD		5.9 ± 4.8	2.0 ± 2.6

Abbreviations: DN4+: patients with DN4 score $\geqslant 4$, DN4−: patients with DN4 score < 4, *n*: number of patients, SD: standard deviation.

Table 2
Abnormal sensation (diminished/increased) and allodynia at the affected upper arm.

		DN4+ (n = 9)	DN4− (n = 10)
Touch	Diminished	7 (78%)	6 (60%)
	Increased	0 (0%)	0 (0%)
	Allodynia	1 (11%)	0 (0%)
Cold	Diminished	7 (78%)*	2 (20%)
	Increased	1 (11%)	5 (50%)
	Allodynia	1 (11%)	2 (20%)
Proprioception	Diminished	6 (67%)	7 (70%)
	Increased	0 (0%)	0 (0%)
	Allodynia	0 (0%)	0 (0%)
Sharpness	Diminished	5 (56%)	5 (50%)
	Increased	1 (11%)	3 (30%)
	Allodynia	2 (22%)	3 (30%)

Abbreviations: DN4+: patients with DN4 score ⩾ 4, DN4−: patients with DN4 score < 4, n: number of patients.
* $p < 0.05$.

reported constant pain, whereas only DN4− patients reported pain attacks. In all patients with pain attacks, pain was primarily related to movement. However, of the patients with intermittent pain, all but one (DN4 score: 0) also reported an increase in pain intensity (range: 1–5) during movement. In patients with constant pain, pain was only minimally exacerbated upon movement.

3.3. Somatosensory assessment

Results are presented in Table 2 and Fig. S1AB. Diminished cold sensation was significantly more frequently observed in DN4+. With respect to QST, no significant differences were found comparing DN4+ and DN4−. However, in patients classified as DN4+ there was a trend towards lower pain thresholds at the unaffected side, and a trend towards higher sensation and pain thresholds (all thresholds) at the affected side.

3.4. DNIC function

No significant differences were found for the duration of hand immersion (71 ± 55 vs. 80 ± 70 s), cold pressor pain intensity (5.7 ± 1.7 vs. 7.2 ± 1.5) or QST threshold ratios (post/pre, EPT: 1.71 ± 0.63 vs. 1.36 ± 0.43, PPT: 1.20 ± 0.19 vs. 1.13 ± 0.23) comparing DN4+ to DN4−.

4. Discussion and conclusions

The aim of this pilot study was to explore whether the DN4 can be used to define subgroups of PSSP, differentiating between PSSP of predominantly neuropathic or nociceptive origin. Since no gold standard is available for the diagnosis of post-stroke pain, patients with PSSP were classified using the DN4 and subgroups were compared regarding well known symptoms and signs suggestive of either nociceptive or neuropathic pain.

Several symptoms and signs suggestive of neuropathic pain were observed in DN4+, such as the higher incidence of abnormal cold sensation suggesting impaired spino-thalamo-cortical tract function (Boivie et al., 1989; Widar et al., 2002), spontaneous (constant) pain (Klit et al., 2009) and a higher degree of sensory loss at the affected side (Widar et al., 2002). In addition, patients classified as DN4+ showed a trend towards reduced thresholds for pain at the unaffected side, suggestive of central sensitization. The primary sign suggestive of nociceptive pain in DN4− was that half of the patients reported pain attacks primarily related to movement (Gamble et al., 2002). In addition, the incidence of subluxation was somewhat higher and arm function somewhat lower in these patients, which is in line with the traditional biomechanical view of PSSP (Teasell et al., 2007). On the other hand, touch or cold allodynia at the affected side, regarded as supportive criteria for the diagnosis of central post-stroke pain (Klit et al., 2009), were not clearly associated with either DN4+ or DN4−. DNIC function appears to be normal in PSSP.

Unfortunately, the actual pathophysiological mechanisms leading to these pain complaints and sensory abnormalities in PSSP remain unclear. In chronic PSSP, symptoms and signs of central sensitization may be induced by both neuropathic as well as (ongoing) nociceptive pain mechanisms which may coexist in individual patients. Indeed, a large group of patients presented with mixed pain complaints (e.g. spontaneous *and* movement related pain). In addition, similar to previous findings, none of the sensory abnormalities could be exclusively related to either DN4+ or DN4− (Rasmussen et al., 2004). The majority of PSSP patients may therefore not be classifiable as having *either* neuropathic *or* nociceptive pain.

Although the interpretation of this study is limited by the relatively low number of subjects in each subgroup, this study showed that the DN4 can be used to classify PSSP subgroups that differ with respect to pain complaints and sensory abnormalities. Notably, several symptoms and signs indicative of either neuropathic or nociceptive pain corresponded to the DN4 classification, suggesting that the DN4 may indeed be helpful in classifying PSSP. However, since the pathophysiological mechanisms remain unclear and none of the sensory signs could be exclusively related to either DN4+ or DN4−, classification using the DN4 should not be the sole basis for PSSP prognosis and treatment. Nonetheless, by showing that neuropathic pain complaints are common in PSSP this study provides a firm rationale to abandon the traditional view of PSSP as being a purely nociceptive, biomechanical pain problem. The diagnostic work-up of PSSP should involve a thorough assessment of both nociceptive and neuropathic pain complaints and somatosensory functions, similar as described for central post-stroke pain (Klit et al., 2009). This may help to further identify markers of nociceptive and neuropathic pain mechanisms in PSSP which, in the future, could lead to the development a (set of) tool(s) that specifically deal(s) with classifying and treating pain in the post-stroke pain population.

Acknowledgements

Medical doctors Frits Lem, Nanny Steinmeijer and Marion Verhulsdonck assisted in patient recruitment at the Sint Maartenskliniek in Nijmegen. This study was supported by a grant from the AMPHoraest foundation. None of the authors have any conflict of interest.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ejpain.2010.05.012.

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