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Medication and treatment use in primary care patients with chronic pain of predominantly neuropathic origin

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Background. Neuropathic pain is widely recognized as one of the most difficult pain syndromes to treat and presents a significant challenge for pain clinicians and GPs.

Methods. The Self-complete Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire, recently validated for identifying pain of predominantly neuropathic origin (POPNO), was sent to 6000 adults identified from general practices in the UK. The questionnaire also contained items about chronic pain identification, medications and treatments received for pain and the pain relief these provided.

Results. In total, 1420/3002 (48%) of respondents indicated that they suffered with any chronic pain. These were further categorized as those with chronic pain who were S-LANSS negative ['chronic pain (non-POPNO)' group, $n = 1179$] and those with chronic pain who were S-LANSS positive, indicating the presence of POPNO ('chronic POPNO' group, $n = 241$). Questions relating to treatments and medications were completed by 88% of the respondents (1244/1420). The chronic POPNO group was more likely to receive multiple pain medications (37% versus 21% took two or more pain medications, $P < 0.001$) and stronger painkillers [e.g. opioids odds ratio 1.94; 95% confidence interval 1.10, 3.42]. Despite this, they reported less effective pain relief than the non-POPNO chronic pain group.

Conclusion. Patients in primary care reporting chronic pain were found generally to obtain incomplete relief from their medication with chronic POPNO patients reporting less relief. It is important that patients with any chronic pain are identified and managed appropriately according to their distinct treatment needs.

Keywords. Chronic pain, neuropathic pain, primary care, S-LANSS, treatment.

Introduction

Neuropathic pain is defined as 'pain initiated or caused by a primary lesion or dysfunction in the nervous system'.[1] Traditionally patients were diagnosed as suffering from neuropathic pain using a disease-centred approach, for example in patients with diabetes, herpes zoster, HIV, cancer and post-operative pain[2] (Box 1). A recent study found, however, that only 37% of patients with peripheral neuropathy and neuropathic pain had been given a definitive underlying diagnosis.[4]

Regardless of the initiating condition, neuropathic pain is widely recognized as one of the most difficult pain syndromes to treat and presents a significant challenge to clinicians as it often does not respond to conventional analgesic therapies.[2,5] Treatment with non-conventional painkillers including anti-epileptics (such as carbamazepine and gabapentin) or antidepressants (particularly amitriptyline) can be effective in neuropathic pain.[6,7]

Patients with neuropathic pain often report symptoms to their GP, are subsequently managed in primary

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BOX 1 *Some common causes of neuropathic pain*[3]

Peripheral nerve lesion or dysfunction

- Painful diabetic neuropathy
- Post-herpetic neuralgia
- Post-surgical pain (including post-mastectomy and phantom limb pain)
- Complex regional pain syndrome
- Trigeminal neuralgia
- Chemotherapy-induced neuropathy
- Neuropathy secondary to tumour infiltration

Central nerve lesion or dysfunction

- Central post-stroke pain
- Multiple sclerosis pain
- Spinal cord injury pain

care, and are not necessarily referred to secondary care.[8] It has been suggested that neuropathic pain is often under-diagnosed and suboptimally managed in primary care,[4,8] for example by failing to provide specific treatments such as anti-epileptics or antidepressants.

The Self-complete Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire identifies patients with pain of predominantly neuropathic origin (POPNO), by a score of 12 or more out of a maximum of 24, and has been validated for use in community-based research.[9] Chronic POPNO was found to affect 8% of people in the general population.[10] If neuropathic pain is indeed under-diagnosed and suboptimally managed, this suggests a high prevalence of unnecessary suffering that could be reduced by appropriate prescribing. Using data from this recent primary care-based community survey [10], we tested the hypothesis that chronic pain with distinct neuropathic components is under-treated in primary care, particularly in comparison with other types of chronic pain.

Methods

The study was conducted in three UK cities (Aberdeen, Leeds and London) in 2004.[10] Two GP practices in each city generated a random sample of 1000 registered patients aged 18 years or over. Therefore, the study sample comprised 6000 individuals who were posted a questionnaire which contained demographic items, chronic pain identification questions, the S-LANSS questionnaire and validated questions asking about treatments or medications received for pain and the pain relief provided, extracted from the Brief Pain Inventory.[11]

Individuals with chronic pain were identified by affirmative answers to two questions (i) Are you currently troubled by pain or discomfort, either all the time or on and off? and (ii) Have you had this pain or discomfort for >3 months?[1] Chronic POPNO was identified by the S-LANSS questionnaire.[9] This is a seven-item questionnaire, including five questions about pain characteristics and two self-examination items, with responses weighed to provide a maximum score of 24.

The reporting of pain-related medications was categorized using the analgesic and musculoskeletal and joint classifications found in the British National Formulary (http://www.bnf.org/bnf/). Anti-epileptics and antidepressants were categorized separately because of their known effectiveness in neuropathic pain. Medications we categorized as 'other' pain medications included anti-migraine drugs, proton pump inhibitors and antispasmodics. The reported use of physiotherapy and alternative practitioners was also recorded.

To compare reported medication and treatment use between the pain groups, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Chi-square tests were used to test for associations between categorical variables. Data were analyzed using SPSS for Windows (version 13.0).

Results

The corrected response rate was 52% ($n = 3002$) and varied with age and gender. Non-responders were more likely to be younger than responders [mean (SD): 43.2 years (17.2) versus 50.3 years (17.1), $P < 0.001$] and women were more likely to respond than men [55.6% ($n = 1669$) versus 44.4% ($n = 1333$), $P < 0.001$].[10] Three groups of respondents were identified: those with 'No chronic pain' ($n = 1537$), those with chronic pain who were S-LANSS positive, indicating the presence of 'chronic POPNO' ($n = 241$) and those with 'chronic pain (non-POPNO)' i.e. were S-LANSS negative ($n = 1179$).

The questions relating to medications and treatments were completed by 88% of respondents who indicated that they suffered from any chronic pain (1244/1420). Of these, 65% (662/1025) of the chronic pain group and 67% (147/219) of the chronic POPNO group specified the medications they were receiving for their pain (Table 1). A further 83 (8%) and 23 (11%), respectively, indicated that they took 'painkillers' although they did not specifically name these drugs. There were no significant differences in response to the medication question between the chronic pain and chronic POPNO groups, in terms of age or gender [mean (SD) age was 48.7 years (16.9) versus 49.6 (17.1) years, $P = 0.942$; 51.3% versus 53.9% females, $P = 0.491$]. The chronic POPNO respondents were marginally more likely to receive 'any' pain-related medication [76.4% versus 82.5% (OR 1.46, 95% CI 0.99, 2.15)]. The chronic POPNO group were significantly more likely to receive antidepressants and stronger analgesic medication such as

TABLE 1 *Reported treatments or medications received for chronic pain, n (%)*

	Chronic pain (n = 662)	Chronic POPNO[a] (n = 147)	OR (95% CI)
Anti-epileptics	2 (0.3)	2 (1.4)	4.55 (0.64, 32.58)
Antidepressants (tricyclic and selective seratonion re-uptake inhibitor)	12 (1.8)	8 (5.4)	3.11 (1.25, 7.77)
Non-steroidal anti-inflammatory drugs/salicylates/ COX-2 inhibitors	288 (43.5)	70 (47.6)	1.18 (0.83, 1.69)
Corticosteriods	22 (3.3)	3 (2.0)	0.61 (0.18, 2.05)
Opioids	47 (7.1)	19 (12.9)	1.94 (1.10, 3.42)
Compound preparations	126 (19.0)	52 (35.4)	2.32 (1.58, 3.44)
Paracetamol only	160 (24.2)	33 (22.4)	0.91 (0.59, 1.39)
Other medications (e.g. benzodiazepines, antispasmodics, etc.)	86 (13.0)	10 (6.8)	0.49 (0.25, 0.97)
Physiotherapy	75 (11.3)	13 (8.8)	0.76 (0.41, 1.41)
Complementary and alternative therapy	94 (14.2)	18 (12.2)	0.84 (0.49, 1.45)
Number of pain medications reported			P-value[b]
None	107 (16.2)	20 (13.6)	<0.001
One	416 (62.8)	73 (49.7)	
Two	103 (15.6)	44 (29.9)	
Three or more	36 (5.4)	10 (6.8)	
	Chronic pain (n = 975)	Chronic POPNO (n = 206)	OR (95% CI)
Any pain-related medication[c]	745 (76.4)	170 (82.5)	1.46 (0.99, 2.15)
No pain-related medication	230 (23.6)	36 (17.5)	

[a]POPNO, ascertained by a score of 12 or more on the S-LANSS questionnaire.
[b]From chi-square test for trend.
[c]Includes all respondents who named specific medications plus those who entered 'painkillers'.

opioids and compound preparations (paracetamol plus opioid, Table 1). These differences between the two groups remained after adjustment for age and gender (antidepressants OR 2.96, 95% CI 1.18, 7.41; opioids OR 1.99, 95% CI 1.13, 3.54; compound preparations OR 2.45, 95% CI 1.63, 3.67). The chronic POPNO group also reported less pain relief in the previous 24 hours (P = 0.005, Fig. 1) despite greater use of multiple pain medications (Table 1).

A total of 15% (122/809) of respondents reported receiving medications that have recently been withdrawn due to concerns about their safety. These drugs were Vioxx (n = 23), Celebrex (n = 25) and co-proxamol (n = 74) and their usage was equally distributed between the pain groups.

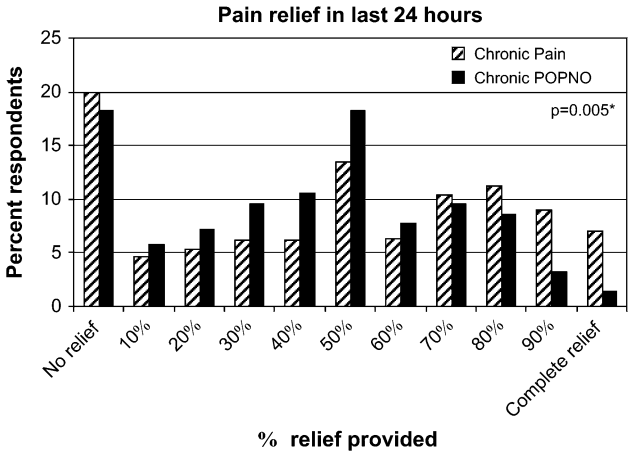

FIGURE 1 *Pain relief reported from treatments or medications in the previous 24 hours. *Chi-square test for trend*

Discussion

This study describes treatment and medication use in a large community sample of patients with chronic pain, including POPNO. The overall prevalence of chronic pain was the same as that found in a previous community-based study using an identical case definition.[12] Patients with chronic POPNO reported greater use of pain-related medications, particularly opioid and compound preparations. Although, they were more likely to report the use of antidepressants, the total numbers reporting these were very small, and the great majority who might benefit did not report their use. Anti-epileptics were also used infrequently, and no more often than by those without POPNO. Chronic POPNO tends to be more severe and of longer duration than other chronic pain[10] which may partly explain the higher levels of pain medication use. However, we found a relatively low frequency of medications specific to neuropathic pain: in chronic POPNO, more is therefore not necessarily better.

Furthermore, people with chronic pain were found generally to obtain incomplete relief from their medication and chronic POPNO patients reported less relief than other chronic pain patients in this study. Similar findings of inadequate relief have been reported in other chronic pain conditions, such as

migraine which affects ~12% of the adult population, but only 40% of whom receive effective treatment.[13] It appears likely, therefore, that chronic pain patients in general are under-treated, but that patients with neuropathic pain are particularly disadvantaged.

Fifteen per cent of respondents reported receiving pain medications that have subsequently been withdrawn due to concerns about their safety. At the time this survey was conducted (2004), these drugs were still available. The subsequent withdrawal of these drugs may represent a challenge for GPs, patients and others in effectively managing an already under-treated condition.

We found a similar proportion of patients receiving 'any pain-related medication' compared with patients registered with a large US health insurance company database who were diagnosed with a selected list of painful neuropathic disorders.[14] In the UK, we found similar levels of prescribing of paracetamol-based 'compound preparations' compared with primary care patients with specified neuropathic pain conditions.[8] However, we found lower prescribing levels of anti-epileptics and antidepressants in our sample compared with both these studies. There was significantly greater use of opioid analgesics by patients with chronic POPNO, although the overall use was relatively low, with only 13% of POPNO patients reporting receiving opioid treatment. In a systematic review, Eisenberg *et al*. [15] concluded that opioids are ineffective in the short-term treatment of neuropathic pain in clinical trials; however, these drugs produced significant reductions in pain intensity with intermediate term use. The greater number of pain medications reported by patients with chronic POPNO compared with non-POPNO pain may reflect the complex nature of the former in terms of the involvement of several pain mechanisms, and hence differential response to different treatment modalities.

These data were obtained from a postal questionnaire survey and consequently are dependent on the accuracy of patients' self-report. We have no means of confirming the reliability of reporting. Because of the relatively low response rate and the acknowledged tendency of patients with chronic pain to respond to chronic pain questionnaires[16], we cannot claim representativeness of the sample. However, the main objective of this analysis was to compare medication and treatment use in the chronic pain (non-POPNO) and chronic POPNO groups, and we have no reason to suppose that the study was prone to bias with imbalanced reporting by these groups. In addition, no data were collected on the dosages used; therefore, we are unable to assess whether individual were receiving therapeutic doses to maximize pain relief

Chronic pain can be regarded a primary care condition, with most sufferers not receiving specialist medical attention.[17] It is particularly important that patients with POPNO are identified in primary care and managed appropriately according to their distinct treatment needs. If these findings are confirmed by future, more specific research using data sets large enough to allow detailed subgroup analysis, further work should focus on the targeting of resources and education to manage neuropathic pain effectively in primary care.

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Declaration

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Ethical approval: The study was approved by the National Health Service Research Ethics Committees for Grampian, Leeds (East), and St Thomas' Hospital, London.
Conflicts of interest: There are no conflicts of interest.

References

[1] International Association for the Study of Pain. Classification of chronic pain. *Pain* 1986; **3:** S1–S226.
[2] Dworkin RH, Backonja M, Rowbotham MC *et al*. Advances in neuropathic pain. Diagnosis, mechanisms, and treatment recommendations. *Arch Neurol* 2003; **60:** 1524–1534.
[3] Dworkin RH. An overview of neuropathic pain: syndromes, symptoms, signs, and several mechanisms. *Clin J Pain* 2002; **18:** 343–349.
[4] Booker CK, Keen A. *Illness and Treatment Experiences of Patients with Peripheral Neuropathy and Neuropathic Pain*. Poster Presented at Pain Society Annual Scientific Meeting, Manchester, April 2004.
[5] Rice ASC, Hill RG. New treatment for neuropathic pain. *Annu Rev Med* 2006; **57:** 535–551.
[6] Saarto T, Wiffen PJ. Antidepressants for neuropathic pain. *Cochrane Database Syst Rev* 2005; **3:** 1–48.
[7] Wiffen P, Collins S, McQuay H, Carroll D, Jadad A, Moore A. Anticonvulsant drugs for acute and chronic pain. *Cochrane Database Syst Rev* 2005; **3:** 1–24.
[8] Hall GC, Carroll D, Parry D, McQuay HJ. Epidemiology and treatment of neuropathic pain: the UK primary care perspective. *Pain* 2006; **122:** 156–162.
[9] Bennett MI, Smith BH, Torrance N, Potter J. The S-LANSS score for identifying pain of predominantly neuropathic origin: validation for use in clinical and postal research. *J Pain* 2005; **6:** 149–158.
[10] Torrance N, Smith BH, Bennett MI, Lee AJ. The epidemiology of chronic pain of predominantly neuropathic origin. Results from a general population survey. *J Pain* 2006; **7:** 281–289.
[11] Cleeland C, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singapore* 1994; **23:** 129–138.
[12] Elliott AM, Smith BH, Penny KI, Smith WC, Chambers WA. The epidemiology of chronic pain in the community. *Lancet* 1999; **354:** 1248–1252.

[13] Diener HC, Steiner TJ, Tepper SJ. Migraine—the forgotten epidemic: development of the EHF/WHA Rome Declaration on Migraine. *J Headache Pain* 2006; **7:** 433–437.
[14] Berger A, Dukes EM, Oster G. Clinical characteristics and economic costs of patients with painful neuropathic disorders. *J Pain* 2004; **5:** 143–149.
[15] Eisenberg E, MacNicol ED, Carr DB. Efficacy and safety of opioids agonists in the treatment of neuropathic pain of nonmalignant origin. Systematic review and meta-analysis of randomized controlled trials. *J Am Med Assoc* 2005; **293:** 3043–3051.
[16] Smith BH, Hannaford PC, Elliott AM, Smith WC, Chambers WA. The 'number needed to sample' in primary care research. Comparison of two primary care sampling frames for chronic back pain. *Fam Pract* 2005; **22:** 205–214.
[17] Smith BH. Chronic pain: a challenge for primary care. *Br J Gen Pract* 2001; **51:** 524–526.