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Article

Treatment of patients with neuropathic pain and provision of drug information by clinical pharmacists

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Patient's satisfaction with healthcare services has an influence on pain management, which can be improved by patient education. Therefore, this study was aimed at identifying primary care health service opportunities in the treatment of neuropathic pain and assessing patients' satisfaction with the provision of drug information by clinical pharmacists. This was a cross-sectional, prospective study conducted at a pain unit during March-May 2017. Patients aged >18 years; diagnosed with neuropathic pain; and who used amitriptyline, gabapentin, pregabalin, or duloxetine were included. They were verbally informed about drug treatment by a clinical pharmacist, and their satisfaction was evaluated after 1 month. In all, 90 patients were included. The median duration for which the patients experienced pain until hospital admission was 3.6 years; furthermore, this duration was longer among women ($p < 0.05$). However, the median time to seeking advice from doctors was 3 months. The patients (15.6%) were less likely to admit pain unit initially and 46.7% had visited different units before being admitted to a pain unit. More than 95% of the patients indicated that they had received information from a pharmacist at a clinic and were satisfied with the provision of information (median duration, 8.5 min). Thus, the involvement of pharmacists in multidisciplinary pain management may help improve health-related outcomes at hospitals and/or in community care settings.

Keywords: Neuropathic pain. Clinical pharmacist. Drug information. Patient satisfaction. Adjuvant analgesics.

INTRODUCTION

Neuropathic pain is defined as "pain caused by a lesion or disease of the somatosensory nervous system" (Jensen *et al*., 2011), which can develop as a direct consequence of disease, pathological dysfunction, or damage affecting the nervous system. It is known that in one in every five patients with chronic pain has neuropathic characteristics and its prevalence is between 6.9 and 10%, accounting for up to 25% of pain clinic visits (Cohen, Mao, 2014; van Hecke *et al.,* 2014; Navarro *et al.,* 2011). Owing to the mechanism and unknown pathophysiology of neuropathic pain, its assessment and treatment continue to be challenging for health professionals and contributes to the global burden of disease (Blyth, 2018). Increased severity of neuropathic pain leads to an increase in the number of drugs used, doctor visits, or hospital admissions, and absenteeism while causing a decrease in productivity, daily functions, and quality of life (Schaefer *et al.,* 2014; Van Acker *et al*., 2009; Smith *et al.,* 2007; Nicholson, Verma, 2004). Therefore, a multidisciplinary approach is required that involves early diagnosis, comprehensive assessment, and close monitoring of patients; provision of effective pharmacological/nonpharmacological treatment; and integration of patient education into the health system (Garven *et al.,* 2011).

The treatment of neuropathic pain includes the choice of monotherapy (such as amitriptyline, duloxetine, gabapentin, or pregabalin) as first-line treatment and other adjuvant analgesics (used as monotherapy or in combination); and invasive procedures are preferred for refractory cases (Tompkins, Hobelmann, Compton, 2017;

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National Institute for Health and Care Excellence, 2019; Finnerup *et al*., 2015; Kamerman *et al.,* 2015; Attal *et al*., 2010; Colloca *et al*., 2017; Dworkin *et al*., 2013). Patients experiencing pain initially seek advice for relief from primary care health professionals once the symptom develops and tend to resort to self-care (Jonsdottir *et al.,* 2013). However, early diagnosis and an initiation of the appropriate treatment could be prolonged due to insufficient knowledge or experience regarding neuropathic pain among primary health care providers. This in turn delays admissions to specialized pain units (Romanelli *et al.,* 2017). Therefore, unintentional delays in diagnosis or analgesic treatment may lead to increased doctor visits and health expenditure, which also contribute to a vicious circle of pain management (van Hecke *et al.,* 2014).

It has been shown that pharmacist-delivered educational interventions for patients with chronic pain reduce adverse effects and increase patient satisfaction and pain-related outcomes (Bennett *et al.,* 2011; Edwards *et al.,* 2019; Coffey *et al.,* 2019). Patients need to balance the knowledge between the necessity of treatment continuation and potential side effects of drugs, differentiate between drug addiction and tolerance, and understand other nonpharmacological and self-care options for pain relief during the treatment process. Physical and psychosocial support and drug information provision will provide a realistic approach and outcomes for pain management in patients with chronic pain (Jones *et al.,* 2019).

Therefore, this study was aimed at identifying primary care health service opportunities in the treatment of patients with neuropathic pain and evaluating patients' satisfaction with the provision of drug information by a clinical pharmacist in a hospital pain unit. The findings of this study may help clinicians, health authorities, or policy makers learn more about patient's experiences in the treatment process and to reveal potential opportunities for pharmacists (in hospitals or the community) to be involved in the management of various chronic pain syndromes.

MATERIAL AND METHODS

This cross-sectional, prospective study was conducted at the outpatient pain unit of a university research and training hospital between March and May 2017. The procedures followed in the study were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and the Declaration of Helsinki. Ethical approval was obtained from the University Non-Clinical Trials Ethics Committee.

At the hospital pain unit, doctors and nurses provide pain management services (diagnosis, treatment, and monitoring) for approximately 25 patients per day, of which approximately 20 are patients with neuropathic pain, between 8.30 am and 4.30 pm. There is no (clinical) pharmacist involved in the routine service of the unit. The commonly used adjuvant analgesics at the unit are amitriptyline, gabapentin, pregabalin, and duloxetine. Drug information for patients is delivered by nurses who mainly focus on drug usage and provide limited information on drug side effects, drug interactions, and storage conditions. For the purpose of the study, a clinical pharmacist was integrated into the pain unit during the study period, and drug information was provided by the pharmacist.

The study inclusion criteria were as follows; age higher than 18 years; a diagnosis of neuropathic pain (screened using Douleur Neuropathique en 4 Questions [DN4]) and monitoring at the unit; use of amitriptyline, gabapentin, pregabalin, or duloxetine; ability to communicate and purchase medicines from a community pharmacy independently; and provision of written consent for participation. Patients who did not meet the inclusion criteria and were monitored for cancer pain at the unit were excluded from the study.

Eligible patients were referred to a clinical pharmacist after consultation with a doctor at the pain unit. The clinical pharmacist invited patients to participate in the study and requested their written consent for participation. Once the patients agreed to participate, they were individually interviewed (face-to-face) by a clinical pharmacist about their existing adjuvant analgesic drug treatment at an appropriate location in the pain unit. During the interview, the pharmacist questioned the patients about demographic characteristics, history of neuropathic pain and its management, and current drug treatment. Additionally, relevant data were retrieved

and collected from patients' medical records. Standard information was provided to the patients on drug usage, storage conditions, side effects, and precautions; what to do if a dose is missed or extra dose is taken; time required for the analgesic effect; alert symptoms for which a doctor should be approached urgently; and other special circumstances for the use of amitriptyline, gabapentin, pregabalin, or duloxetine. The patients were followed up after 1 month by a nurse or a secretary at the unit over the telephone and asked about their satisfaction with the provision of information by the clinical pharmacist. Follow-up at 1 month was considered appropriate since 2-4 weeks are required to achieve the desired analgesic effects of adjuvant drug treatments started recently.

Thus far, no study has assessed patient satisfaction in this scenario. Therefore, the calculation of the sample size for the study was based on the number of patients cared for at the pain unit, which resulted in the inclusion of 100 patients during the study period. A control group was not considered for the study because, previously, drug information was provided by nurses previously at the unit, which might have influenced the perceptions of the patients and other healthcare professionals.

Study data were analyzed using the Statistical Package for Social Science (SPSS) v22.0 program, and a descriptive analysis was performed for demographic data. Quantitative data were normalized using the Kolmogorov-Smirnov test. Relationships between quantitative variables were analyzed using the Mann-Whitney U test, and qualitative variables were analyzed using the Chi-square test. The Kruskal-Wallis test was used for the comparison of three or more groups. A p-value of <0.05 was considered significant.

RESULTS

During the study period, 100 patients were included and interviewed by a clinical pharmacist. However, 10 patients were not followed up after 1 month, and were excluded from the analysis. Therefore, 90 patients (64 women; median age [25^{th}-75^{th} percentile]: 52.5 [45-62] years) were interviewed by a clinical pharmacist and followed up (Table I). Of these 90 patients, 89% were married and 31% were employed. Furthermore, 20 and 5 patients reported being smokers and social drinkers, respectively, while 11 and 48 patients reported having drug allergies and no history of surgery, respectively. Twenty-six percent of the patients (n = 23) had been recently (newly) diagnosed with neuropathic pain at the time of study participation, whereas 74% (n = 67) were already being monitored at the pain unit.

TABLE I - The demographics of study patients (n=90)

	n (%)
Age	
24-29	4 (4.4)
30-39	9 (10.0)
40-49	25 (27.8)
50-59	21 (23.3)
60-69	24 (26.7)
70-79	6 (6.7)
80-85	1 (1.1)
Education	
Primary & Secondary school	65 (72.2)
High school & College	16 (17.7)
University	9 (10)
Comorbidities	
Hypertension	37 (41.1)
Diabetes Mellitus	18 (20.0)
Intervertebral disc disorders	15 (16.7)
Hypothyroidism	9 (10.0)
Asthma	7 (7.8)
Peptic Ulcer	7 (7.8)
Dyslipidemias	6 (6.7)
Gastroesophageal reflux	5 (5.6)
Osteoporosis	3 (3.3)
Affective disorders	3 (3.3)
Number of comorbidities	
0	22 (24.4)
1	22 (24.4)
2	25 (27.8)
3	10 (11.1)
4	6 (6.7)
>4	5 (5.5)
Number of drugs used	
0	21 (23.3)
1	24 (26.7)
2	13 (14.4)
3	15 (16.7)
4	8 (8.9)
>4	9 (10.0)

Medical history of neuropathic pain (diagnosis and treatment) in the patient population

According to the data from the interviews; the median (25^{th}-75^{th} percentile) duration for which the patients experienced pain until the admission to the pain unit was 3.6 (1-10) years. This duration was significantly longer in women (4.5 [1.1-10] years) than in men (2.0 [0.7-6] years) ($p < 0.05$). However, the median time to seeking advice from doctors was 3 months (0-2 years).

Sixty-six percent of the patients reported pain in more than one area of the body, and the common areas in which pain was reported were the lower back (n = 59), legs (n = 33), and neck (n = 18). There was no significant difference between the number of painful areas (≤2 vs. ≥3) and age (≥40 vs. <40 years) or sex ($p > 0.05$).

The patients were likely to seek initial advice from hospitals (72%), primary care settings (doctors or community pharmacy) (28%), a primary care doctor (8.9%), or a community pharmacist (4.4%); 57.8% of the patients reported using analgesics before consulting a doctor (Table II). The median (25^{th}-75^{th} percentile) wait time for consultation with a doctor was longer among the patients who had previously used analgesics (6.6 [1-34.5] months vs. 0.4 [0-5.1] months in non-users) ($p < 0.05$); in women (5.1 [0-34.5] months vs. 1 [0-8.2] months in men) ($p > 0.05$); and in non-employed patients (6 [0.4-31.5] months vs. 0.4 [0-2.8] months in employed) ($p < 0.05$). Further, the time for admission to the pain unit was longer among college graduates. However, there was no association between the educational background of the patients and the time for admission ($p > 0.05$).

Most patients (83.3%) reported visiting a community pharmacy once a month or less to purchase their medicines, but reported not receiving any drug information. Only 15.6% (n = 14) of the patients were admitted to a pain unit initially (Table III), and 46.7% (n = 42) visited at least two different hospital units before their admission to the pain unit (35.6% of patients visited the physical therapy and rehabilitation unit). The relatives and friends influenced the referral to the pain unit (36.7%), and only 8.9% of the patients sought admission independently.

TABLE II - Patients' self-treatment preferences for analgesics before a doctor visit

Analgesics	n (%) (n=number of patients)
NSAID	25 (48.1)
NSAID + myorelaxant	7 (13.5)
NSAID + Paracetamol	7 (13.5)
Paracetamol	6 (11.5)
Myorelaxant	3 (5.8)
NSAID + Paracetamol + myorelaxant	3 (5.8)
Paracetamol + myorelaxant	1 (1.9)
Total	52 (100)

NSAID: Non-Steroidal Anti-Inflammatory Drug

TABLE III - Utilized health units for diagnosis and treatment of neuropathic pain

	n (n=number of patients)		
Units at hospital	First admission n (%)	Diagnosis n (%)	Treatment n (%)
Algology (Pain Unit)	14 (15.6)	75 (83.3)	77 (85.6)
Orthopedics	16 (17.8)	4 (4.4)	4 (4.4)
Neurology	4 (4.4)	4 (4.4)	3 (3.3)
Physical treatment	32 (35.6)	3 (3.3)	3 (3.3)
and rehabilitation	13 (14.4)	2 (2.2)	2 (2.2)
Neurosurgery	3 (3.3)	1 (1.1)	-
Rheumatology	1 (1.1)	1 (1.1)	1 (1.1)
Oncology	7 (7.8)	-	-
Others[a]			

[a]: Urology (2 patients), emergency (1 patient), dentistry (1 patient), internal medicine (1 patient), gastroenterology (1 patient), psychiatry (1 patient)

Treatment pattern of neuropathic pain

A pattern of drug treatment in neuropathic pain revealed that patients were on dual or triple analgesic combinations (43 patients in NSAIDs and adjuvant analgesics, seven in opioids and adjuvant analgesics, and nine in NSAID + opioid + adjuvant analgesics). In addition, invasive treatment options (57.8%, n = 52) such as intra-articular or trigger point injections, somatic/intraspinal nerve blocks, and radiofrequency thermoregulations,

were preferred in combination with drug treatment. Most patients (60%) were either on pregabalin, gabapentin, amitriptyline, or duloxetine (monotherapy) or dual combination therapy (40%) (Table IV).

TABLE IV - Analgesic drug treatments in patients with neuropathic pain

(n=number of patients)	n (%)
Adjuvant analgesics;	
Monotherapy (n=54);	
Duloxetine	24 (26.7)
Pregabalin	23 (25.5)
Amitriptyline	5 (5.6)
Gabapentin	2 (2.2)
Combination therapy (n=36);	
Pregabalin + Duloxetine	27 (30.0)
Pregabalin + Amitriptyline	5 (5.6)
Gabapentin + Duloxetine	3 (3.3)
Gabapentin + Amitriptyline	1 (1.1)
NSAIDs (alone or in combination)	52 (57.8)
Opioids (alone or in combination)	16 (17.8)

Patient satisfaction regarding the provision of drug information by a clinical pharmacist

Although drug information was provided by nurses at the pain unit previously, 76.7% (n = 69) and 7.7% (n = 7) of the patients reported "not received" and "partly received", respectively, when asked about the provision of drug information at the unit previously. Furthermore, the responses did not differ significantly between patients who were newly diagnosed and those who were followed up (Chi-square test, p = 0.084). Only 14 patients reported having received information previously from nurses (n = 7), doctors (n = 4), pharmacists (n = 1), doctors/nurses (n =1), and pharmacists/nurses (n = 1). The most preferred and reliable source of drug information according to the patients (n = 76) was the internet (n = 72), followed by doctors (n = 67), nurses (n = 54), and pharmacists (n = 47).

Patient satisfaction was assessed by posing four questions and using the 5-point Likert scale, and 95% of the patients were "satisfied" or "very satisfied" with the service provided by a clinical pharmacist (Table V). Most of the patients (91.1%, n = 82) indicated that they would like to have this information service continuously at the hospital for each prescribed drug and 90% (n = 81) preferred to have this service at the community pharmacy. The median (25^{th}-75^{th} percentile) duration for provision of information was 8.5 (7-10) minutes, which was found to be adequate by 91.1% of the patients. A clinical pharmacist identified and solved problems related to drug-drug interactions in eight out of 16 patients who used pregabalin and proton pump inhibitors and inappropriate storage of drugs in six patients. Three patients for whom analgesic treatment was started at the unit discontinued the treatment because of concerns about side effects. However, they decided to continue with analgesic treatment after their interview with a clinical pharmacist.

TABLE V - Patient satisfaction about drug information provided by a clinical pharmacist

(n=number of patients)	n (%)				
Opinions on;	**Very satisfied**	**Satisfied**	**Indecisive**	**Not satisfied**	**Not satisfied at all**
the service provision in general	84 (93.3)	5 (5.6)	1 (1.1)	0 (0)	0 (0)
the format and content of the information	69 (76.7)	19 (21.1)	2 (2.2)	0 (0)	0 (0)
the clinical pharmacist's responses to your questions	82 (91.1)	7 (7.8)	1 (1.1)	0 (0)	0 (0)
the comprehensibility of clinical pharmacist's responses	78 (86.7)	12 (13.3)	0 (0)	0 (0)	0 (0)

DISCUSSION

This study aimed to evaluate patient satisfaction achieved by provision of drug information by a clinical pharmacist at an outpatient pain unit. Revealing the treatment pathways of patients with neuropathic pain could also help identify strategic steps for other healthcare professionals (such as pharmacists) to have an active role in the pain management process.

The characteristics of pain duration and affected localization in neuropathic pain in this study were comparable with those in previous studies (Torrance *et al.,* 2006; Bouhassira *et al*., 2008; Moulin *et al.,* 2015). This finding confirms that neuropathic pain commonly observed in the lower back (65.6%) and legs (36.7%), develops in more than one body locations (65.6%), and lasts for approximately 3 years. We found that women experienced neuropathic pain lasted significantly longer than did men (4.5 vs. 2 years), which was consistent with the report by The International Association for the Study of Pain; the report indicated that women experience repetitive and intense pain (International Association for the Study of Pain, 2007). These findings highlight the patient groups requiring particular attention of healthcare professionals so as to ensure early referrals to specialists and appropriate initiation of pain treatment.

Patients with pain are likely to treat themselves initially by using analgesics before they seek advice from healthcare professionals, which may lead to delayed diagnoses and initiation of effective drug treatment. It was demonstrated in this study that patients who were previously self-treated with analgesics waited significantly longer to seek advice from a doctor (6.6 months vs. 0.4 months, $p < 0.05$). Although primary care doctors and community pharmacists are appreciated as easily accessible healthcare professionals in primary care settings, 72.2% of the patients were directly admitted to a hospital when they experienced pain symptoms, and 46.7% visited at least two different units before admission to the pain unit. A lack of awareness about the availability of pain units at hospitals and increased patient willingness to self-manage for pain relief may lead to unnecessary medicine use and increased the risk of side effects and medical costs. Therefore, healthcare professionals in primary care settings should play an active role in pain management by informing and educating patients about self-management strategies, closely monitoring drug treatment (responses vs. side effects), and referring patients to pain specialists when necessary.

Besides healthcare professionals, relatives and friends seemed to have a major influence on patients' perceptions of pain management. In this study, 36.7% of the patients were referred to the pain unit by relatives and friends. This finding highlights the potential for undertaking public educational activities to emphasize the importance of early diagnosis and initiation of treatment for neuropathic pain.

One of the interesting findings of this study was that although drug information is usually provided by nurses/doctors at the pain unit, 76.7% of the patients reported not receiving any information on drugs previously. The most preferred source of drug information indicated by the patients was the internet, which should be critically assessed. Because of the widespread use of the internet, television and social media, patients can easily obtain health information. However, this information may not be always accurate and the sources may be unreliable. Considering that the patient satisfaction with drug information service provided by a clinical pharmacist was higher than 90% in our study, the involvement of pharmacists in educational activities may help decrease the workload of other healthcare professionals at the pain unit and allow patients to focus on their drug treatment and assume responsibility in pain management. Therefore, comprehensive and long-term studies are required to demonstrate the impact of pharmacists' involvement in neuropathic pain management and health-related outcomes at hospitals and/or in community care settings.

The limitations of this study include well-known constraints in research in hospital settings and are as follows: a relatively short study duration and follow-up period, the inclusion of a convenient number of patients (however, a control group was lacking), interview of the patients in an inconvenient (non-private) area at the pain unit, and lack of an employed clinical pharmacist at the hospital. The relatively small number of participants may limit the impact of the results of this study. Furthermore, provision of the drug information service by nurses/

doctors in routine care at the pain unit resulted in the lack of a control group in this study, which could have led to misinterpretation of the findings. Finally, standard drug information was provided verbally by a clinical pharmacist once at the unit, and information leaflets or any other written materials were not provided for reinforcement. However, the authors believe that the findings of this study will guide researchers in evaluating the impact of a multidisciplinary healthcare team on the management of neuropathic pain.

Thus far, treatment success in neuropathic pain has been less than desirable, although a variety of treatment options are available for its management. However, it is acknowledged that effective treatment can be achieved by multidisciplinary and collaborative approaches in primary and/or secondary care settings through the involvement of patients by education and counseling in the care process.

Adjuvant analgesics are the main treatment options for neuropathic pain. However, the onset of their analgesic effects is late and patients are not familiar with their indications, dose schedule and increments, drug interactions, and side effects, which may negatively affect patients' attitudes towards symptom management. Given that pharmacists are easily accessible health professionals for patients to gain information on drugs and symptom management, the establishment of pharmacist-patient relationships in community or hospital settings would further help identify any drug-related problems in the management of neuropathic pain.

It is promising that patients were satisfied with the drug information provided by a clinical pharmacist in this study, however, a precise style (verbal or written), adequate content, sufficient duration, and appropriate location for the provision drug information should be established in pain units. Active and deliberate involvement of community pharmacists in the patient referral process to pain units would decrease the time required for admission and unnecessary analgesic use in the management of neuropathic pain.

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