

Original Article

Irrational drug use in neuropathic pain treatment: a two-year data analysis

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ABSTRACT

Background: Neuropathic pain (NeP) manifests as chronic pain and causes significant medical and economic burden for both the individual and the society. Treatment of NeP is often symptomatic and includes single or combination drug therapy. Many drugs that are not recommended in the guidelines are also widely used. **Aim:** The present study was aimed at determining the annual cost of NeP treatment in Turkey and to assess the amount of resource loss due to irrational drug use and its associated complications. **Methods:** Each item in NeP prescriptions and their relevant costs between July 2007 and June 2009 was retrospectively analyzed. **Results:** The number of prescriptions for NeP was 8646358 and 9650641 for the first and second years, respectively. The irrational items were 7513299 in the first year and 8360754 in the second year. The proportion of irrational treatment cost was 48.5% for the first year and 48.6% for the second year. Total cost of these prescriptions was estimated to be 47924534 Turkish Liras and 60715905 Turkish Liras for the first and second years, respectively. The estimated irrational treatment cost of NeP together with the additional burden exceeded half of the total cost. **Conclusions:** Further studies on health economics perspective are needed to confirm these results. Better education of healthcare professionals and better regulations in reimbursement will help to improve this problem.

Key words: Neuropathic, pain, treatment, irrational, cost, burden

INTRODUCTION

Neuropathic pain (NeP) is defined by the International Association for the Study of Pain (IASP) as pain initiated or caused by a primary lesion or dysfunction in the nervous system.^[1] Recently, Treede *et al.* presented a more precise definition of NeP as pain arising as a direct consequence of lesion or disease affecting the somatosensory system.^[1] This revised definition fits into the nosology of neurologic disorders.^[1] Neuropathic pain include diabetic peripheral neuropathy, postherpetic neuralgia, trigeminal neuralgia, post-stroke pain, neuropathic back and leg pain, and complex regional pain syndrome.^[2,3] Although NeP is acute in nature, it is persistent (or refractory) in most patients and manifests as chronic pain in clinical practice.^[3]

The prevalence of NeP in developed countries is estimated to range from 1.5% to 3%.^[3,4] The prevalence is reported to be higher in particular patient groups. A multicenter cross-sectional study in Turkey revealed that NeP prevalence in diabetic patient population was 14.0%.^[5] Although data concerning the prevalence of NeP is limited, it is thought to be more common than assumed. Due to the progressive increases in the elderly population and in the diseases associated with NeP such as diabetes and cancer, the prevalence is expected to increase further in the future.^[6] As NeP is a common chronic problem associated with reduction in quality of life and loss of manpower, NeP causes significant medical and economic burden for both the individual and the society.^[3,7]

In most of the patients, treatment of NeP is often symptomatic rather than targeting the cause or being curative.^[8] Management of NeP requires an interdisciplinary approach.^[2,8] Many types of drugs including calcium channel alpha-2-delta ligands (pregabalin, gabapentin) and tricyclic antidepressants (nortriptyline and desipramine), serotonin–norepinephrine reuptake inhibitors, and topical lidocaine are used in the treatment of NeP.^[2] Tramadol and controlled-release opioid analgesics or combined regimens are recommended as the second-line treatment.^[9-11] A group of other drugs including non-steroidal anti-inflammatory drugs (NSAIDs) and vitamin B₆ were recommended as agents to avoid (never

use).^[12] However, these are currently not recommended, as there is no evidence supporting their benefits in the treatment of NeP.^[9] The guidelines by the American Society of Pain Educators (ASPE) and Neuropathic Pain Platform (SNAPS) have a special warning as “agents to avoid” for these medications.^[12,13] Hence, these medications are considered as “irrational treatment” for NeP.

The aim of the present study was to determine the annual cost of NeP treatment in Turkey and to assess the amount of resource loss due to irrational drug use and its associated complications.

METHODOLOGY

Each item in NeP prescriptions and their relevant costs between July 2007 and June 2009 were retrospectively analyzed. Data retrieved from the Information Medical Statistics (IMS) and PROMED Healthcare Consultancy database were used for prescription calculations, and the database of Turkish Ministry of Health was used for cost analysis.^[14-16]

Number of patients receiving NSAID treatment was estimated for the analysis regarding NSAIDs. Adverse effects of NSAIDs on the gastrointestinal (GI) system were determined based on the treatment guidelines and literature data.^[12,17-20] Classification and treatment approaches to patients admitted to hospitals due to these adverse effects were formed according to patient flow charts recommended by current treatment guidelines. This process included assessment of data from previous studies conducted in our country and contribution of expert opinion-leaders. Treatment-related costs were calculated based on Turkish Ministry of Health Price List 2007.^[16]

RESULTS

Analysis of IMS data revealed that, in addition to antiepileptics (anticonvulsants) and antidepressants that are indicated for use in NeP in Turkey, medications including NSAIDs, centrally-acting muscle relaxants, vitamins, and non-narcotic analgesics were frequently prescribed based on NeP diagnosis. This second group of drugs was regarded within the context of irrational drug use as they are

not effective and are not indicated for most types of NeP.

The number of prescriptions for NeP was 8646358 and 9650641 for the first and second years, respectively. The irrational items were 7513299 and 8360754 for the first and second years, respectively.

The proportion of irrational treatment cost was 48.5% for the first year, and it was 48.6% for the second year (Table 1). Total cost of these prescriptions was estimated to be 47924534 Turkish Liras and 60715905 Turkish Liras for the first and second years, respectively.

Table 1: Two-year financial burden of neuropathic pain treatment based on drug prescriptions (TL = Turkish Liras)

	First year		Second year	
	Prescription (n)	Cost (TL)	Prescription (n)	Cost (TL)
Neuropathic pain prescriptions	8646358	98689633	9650641	124955285
Drugs indicated in the treatment of neuropathic pain				
Antidepressants	153698	688714	97048	888424
Antiepileptics	979360	50076384	1192839	63350956
Total	1133058	50765098	1289887	64239380
Drugs that are not indicated in the treatment of neuropathic pain				
Nonsteroidal anti-inflammatory drugs	3208244	17824521	3561401	22001268
Centrally acting muscle relaxants	2591334	20072965	2849771	26543947
Non-narcotic analgesics	396218	944602	553203	1543426
Vitamins	1317503	9082446	1396379	10627264
Total	7513299	47924534	8360754	60715905

There is also an additional burden from prevention and treatment of GI complications of NSAIDs used for NeP treatment. Proton-pump inhibitor (PPI) related cost was calculated to be 4456130 Turkish Liras for the first year and 5500317 Turkish Liras for the second year. The cost

of NSAIDs associated adverse effects was calculated to be 3244576 Turkish Liras for the first year and 2447355 Turkish Liras for the second year. The estimated irrational treatment cost of NeP together with the additional burden exceeded half of the total cost (Table 2).

Table 2: Two-year financial burden of neuropathic pain treatment after including costs associated with treatment of complications

	First year		Second year	
	Proportion in total	Cost (TL)	Proportion in total	Cost (TL)
Total rational	47.7%	50765098	48.3%	64239380
Total irrational	52.3%	55625240	51.7%	68663578
Total cost	100%	106390339	100%	132902958

DISCUSSION

The economic burden of chronic diseases on individuals and society is a significant

problem throughout the world, particularly in moderate- and low-income countries.^[21] One of the essential steps that should be taken to reduce healthcare costs is to

develop and standardize treatment approaches.^[22] As experienced in many other disorders, use of medications that are not indicated in NeP treatment creates additional financial burden on healthcare costs.^[23] Standard treatment guidelines should be prepared and used to prevent and overcome this problem. Treatment guidelines for NeP are available in many countries.^[4,9,12,13,17,24] Moreover, determining the current status by cost-analysis studies will provide further guidance in establishing strategic preventative measures.^[23]

In the present study, we investigated the two-year treatment cost of NeP in Turkey and found that the estimated irrational treatment cost of NeP together with the additional burden exceeded half of the total cost. To our knowledge, few studies have addressed this issue. McDermott *et al.*^[25] investigated NeP treatment patterns in 602 patients with NeP from six European countries. They noted that nearly all patients (93%) were prescribed medications for NeP; of these medications, 71% were analgesics, 51% were anti-epileptics, 29% were antidepressants, and 15% were sedatives/hypnotics.^[25] They also reported that 43% of the patients were prescribed for NSAIDs, this percentage was higher based on the patient-reported information, and that 22.6% of patients used herbal drugs, vitamins and supplements.^[25] In their study, Berger *et al.*^[26] identified 55586 patients with NeP using a large US health insurance claims database in the calendar year 2000; they also formed an age- and sex-matched control group without NeP in the same year. They found the cost of total medications to be \$1167 in the NeP group and \$461 in the control group and reported annual health care cost of NeP patients to be three-fold higher than that of the control group (\$17355 vs. \$5715); indirect costs due to loss of manpower were not included in these calculations.

The present study has certain limitations. The adverse effects of drugs other than NSAIDs and their associated costs were not analyzed. The mortality rate of approximately 10% in patients admitted to the hospital with gastrointestinal hemorrhage was not taken into account. Similarly, our cost analysis did not include other indirect costs such as loss of manpower due to adverse effects, its

burden on the society, and costs related to prolonged unsuccessful treatments.

CONCLUSION

Findings of the present study demonstrated the significant burden of irrational drug use in NeP. Further studies on health economics perspective are needed to confirm these results. Better education of healthcare professionals and better regulations in reimbursement will help to improve this problem.

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Conflict of Interest: None declared



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