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Research Article

CONSUMPTION TREND OF OPIOIDS IN AMBULATORY PATIENTS IN ALBANIA 2014-2019

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ABSTRACT

Objective: The aim of this paper is to evaluate 6-year trends in community use of prescribed opioid analgesics in Albania, using the Anatomic Therapeutic Chemical Classification-Defined Daily Dose methodology.

Methods: We collected the data from the database of the Health Insurance Institute (HII). Analysis of the data includes the period 2014–2019; also, we analyzed the data of import and domestic production of drugs, which represent the real consumption of drugs in the country. These data were subsequently involved in a comparative analysis of the utilization data according to the HII.

Results: We report a 2.5 fold increase in opioid utilization over the study period. The maximal rise in consumption refers to fentanyl, oxycodone, and tramadol. Meanwhile, the maximal values of consumption refer to strong opiate, morphine. We note that around 30% of the consumption of this class flows out of the scheme. Furthermore, around 25% of consumption of morphine and oxycodone flows out of scheme too. Meanwhile, the tramadol consumption runs out of the scheme over 200%.

Conclusions: The outcomes indicate that patients in Albania have low access to opioids medications mainly because of low opioids availability. A strong opiophobia among the population and the medical professionals constitutes one of the major impediments for efficient palliative care.

Keywords: Opioids, Morphine, Consumption, Defined daily dose.

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INTRODUCTION

Opioids are a class of drugs naturally found in the opium poppy plant and that work in the brain to produce a variety of effects, including the relief of pain with many of these drugs. Some prescription opioids are a direct product of the plant. Other opioids are synthetized in labs, by using the same chemical structure. Opioids often are used as medicines because they contain chemicals that relax the body and can relieve pain. Opioids can also make people feel very relaxed and "high" - which is why they are sometimes abused even for non-medical reasons. This can be dangerous because opioids can be highly addictive, and overdoses and death are common.

The prevalence of chronic pain is high and affects 12–30% of all Europeans, with a considerable impact on self-reported quality of life, posing a major international healthcare issue [1]. For some patients, opioids are used to treat chronic pain, and the total use of opioids more than doubled from 1999 to 2016 worldwide [2].

Prescription opioids might be used to treat moderate-to-severe pain. Often these are prescribed following surgery or injury, or for health conditions such as cancer. In recent years, there has been a dramatic increase in the acceptance and use of prescription opioids for the treatment of chronic non-cancer pain (CNCP), such as back pain or osteoarthritis, despite serious risks and the lack of evidence about their long-term effectiveness. Studies suggest that regional variation in use of prescription opioids cannot be explained by the underlying health status of the population [3]. More than 191 million opioid prescriptions were dispensed to American patients in 2017 - with wide variation across states [4]. Anyone who takes prescription opioids can become addicted to them. In fact, as many as one in four patients receiving long-term opioid therapy in a primary care setting struggles with opioid addiction [5-7]. Once addicted, it can be hard to stop. In 2016, more than 11.5 million Americans reported misusing prescription opioids in the past year [4]. Taking too many prescription opioids could stop a person's breathing - leading to death.

In USA, Opioid prescriptions per capita increased 7.3% from 2007 to 2012, with opioid prescribing rates increasing more for family practice, general practice, and internal medicine compared with other specialties [8]. Opioids are commonly prescribed for pain. An estimated 20% of patients presenting to physician offices with non-cancer pain symptoms or pain-related diagnoses (including acute and chronic pain) receive an opioid prescription [9].

METHODS

The study aimed to assess the out-of-hospital Opioid drugs use in Albania during the period 2014–2019. The data were obtained from the Health Insurance Institute (HII) [10]. All data were collected for the period 2014–2019 and analyzed. The analysis included the total number of prescriptions made and quantities of drugs used.

The data about the population were obtained from the Institute of Statistics [11]. The data about the consumption of drugs were expressed as a number of Defined Daily Dose (DDDs)/1000 inhabitants/day. All drugs were classified by groups of Anatomic Therapeutic Chemical Classification (ATC).

Data on real consumption (import and domestic production)

For all the period under study 2014–2019, there were collected and analyzed data from the import and domestic production of the drugs, which represent the real consumption of drugs in the country [12]. To obtain an updated study, there were chosen the data of import and domestic consumption only for the last 4 years, 2016, 2017, 2018, and 2019 and those were involved in a comparative analysis with the equivalent consumption data according to HII. To minimize the effect of variations between consumption and stock inventory balances from 1 year to another, it was calculated and put to analysis the annual average value of the three chosen years (on the one hand, that of the import and domestic consumption, and, on the other hand, that of HII).

Presentation of the results and statistical elaboration

The database of HII was modified in Microsoft Office Excel 2007, whereas the statistical elaboration of the obtained results was conducted with the statistical package StatsDirect (version 2.7.2.). A descriptive statistic was used to report all data on drugs consumption and the results obtained were displayed in tabular form as well as through the histogram method.

Average annual values of consumption in the country level and for each district were used as a basis to generate the overviews and the graphics that illustrate the trends of consumption for each class of drugs during the 6-years period 2014-2019. The linear regression model was used to evaluate the trends of consumption of drugs relative to the time. A value of $p \leq 0.05$ was considered as significant.

RESULTS

The data are expressed as a number of DDDs per 1000 inhabitants/day (DDDs/1000 inhabitants/day).

The consumption of opioid drugs was 2.21–5.44 DDD/1000 inhabitants/day, respectively, in 2014–2019, reflecting a specific increase of approximately 150%. The opioids included in the reimbursement scheme are morphine, fentanyl, oxycodone, pethidine, and tramadol. The most prescribed are morphine and oxycodone; meanwhile, the largest increase in consumption is attributed to fentanyl and oxycodone (Figs. 1 and 2) [13-22].

DISCUSSION

Chronic pain is one of the largest contributors to global disability [23]. Prevention, assessment, and treatment of chronic pain are challenges for health providers and systems. Pain might go unrecognized, and patients, particularly members of racial and ethnic minority groups, women, the elderly, persons with cognitive impairment, and those with cancer and at the end of life, can be at risk for inadequate pain treatment [24]. Patients can experience persistent pain that is not well controlled. There are clinical, psychological, and social consequences associated with chronic pain including limitations in complex activities, lost work productivity, reduced quality of life, and stigma, emphasizing the importance of appropriate and compassionate patient care [24]. Chronic pain has been variably defined but is defined within this guideline as pain that typically lasts >3 months or past the time of normal tissue healing [25]. Chronic pain can be the result of an underlying medical disease or condition, injury, medical treatment, inflammation, or an unknown cause [24].

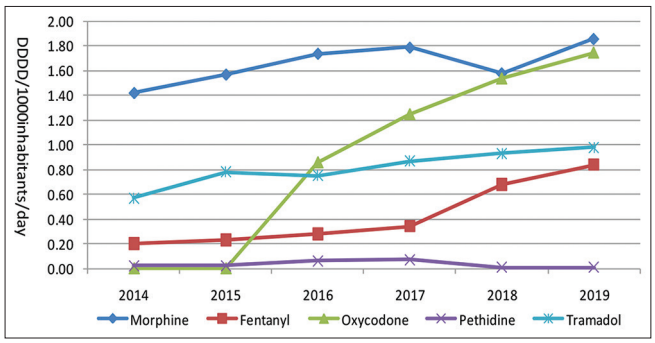

Fig. 1: Consumption of each opioid at national level (Defined Daily Dose /1000 inhabitants/day)

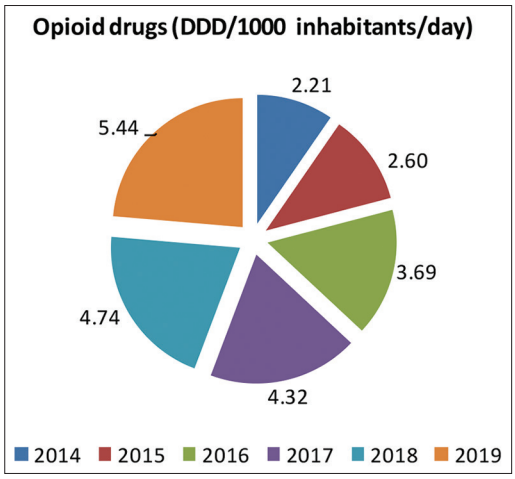

Fig. 2: Opioid consumption at national level (Defined Daily Dose /1000 inhabitants/day) p=0.0089; strength (with significance level ≤0.05)=93.84%; correlation coefficient statistically significant

Evidence supports short-term efficacy of opioids for reducing pain and improving function in non-cancer nociceptive and neuropathic pain in randomized clinical trials lasting primarily ≤12 weeks [26,27], and patients receiving opioid therapy for chronic pain report some pain relief when surveyed [28-30]. However, few studies have been conducted to rigorously assess the long-term benefits of opioids for chronic pain (pain lasting >3 months) with outcomes examined at least 1 year later [31]. Opioid pain medication use presents serious risks, including overdose and opioid use disorder. In the past decade, while the death rates for the top leading causes of death such as heart disease and cancer have decreased substantially, the death rate associated with opioid pain medication has increased markedly [32].

In the past two decades, various opioids, including oxycodone, hydromorphone, buprenorphine and fentanyl, have been registered and subsidized for the treatment of CNCP in many health care settings around the globe. These changes brought dramatic growth in opioid prescribing and use, despite uncertainty about their efficacy in the long-term treatment of this indication [33,34].

This paper provides an evaluation of Albanian trends in prescribed opioid analgesic dispensing. Opioids are essential medicines for the treatment of pain and have been included in the 2007 Essential Medicines in Palliative Care by International Association for Hospice and Palliative Care. The list includes 34 medications of which 14 are already included in the WHO list as essential in the treatment of several conditions, some of which are common in palliative care from which 27 drugs or 75% are available in Albania. In the reimbursement drug list of Fund of Health Care Insurance, 17 drugs are included or 48%. Meanwhile, 20% of this group of drugs (reimbursed for palliative care) has limitations on their use and quantity [35].

We report a 2.5 fold increase in opioid utilization over the study period. The maximal rise in consumption refers to fentanyl, oxycodone, and tramadol. Meanwhile the maximal values of consumption refers to strong opiate (morphine), Figs. 1-3 show clearly that consumption of opioids have an increasing trend, especially from 2016 onward.

Attempting to obtain a deeper understanding of what has really happened we included in the analysis the import data (which represent the real consumption), by comparing the average annual value of consumption of opioids drugs from imports with the equivalent value reported by the HII. Fig. 4 presents the comparison import-HII in the consumption of opioids the whole class, and some representatives like morphine, tramadol, and oxycodone. We note that around 30% of the consumption of this class flows out of the scheme. Furthermore, around 25% of consumption of morphine and oxycodone flows out of scheme too. Meanwhile, the tramadol consumption runs out of the scheme over 200%. The distribution of opioids in the pharmaceutical market relies in accordance to a well-determined regulation. Only a small number of pharmacies do have the right to sell opioids. These pharmacies apply for a special license with the Ministry of Health and Social Welfare. They can start selling opioids only after being equipped with such license and ensuring a separate place for opioids – a safe deposit box/cabinet. On the other hand, to have the right to purchase opioids, a patient should obtain a special medical prescription, duly signed and stamped by three doctors.

General physicians are able to prescribe opioids, but only after an oncological consultancy. The authority for prescribing opioids is limited to palliative

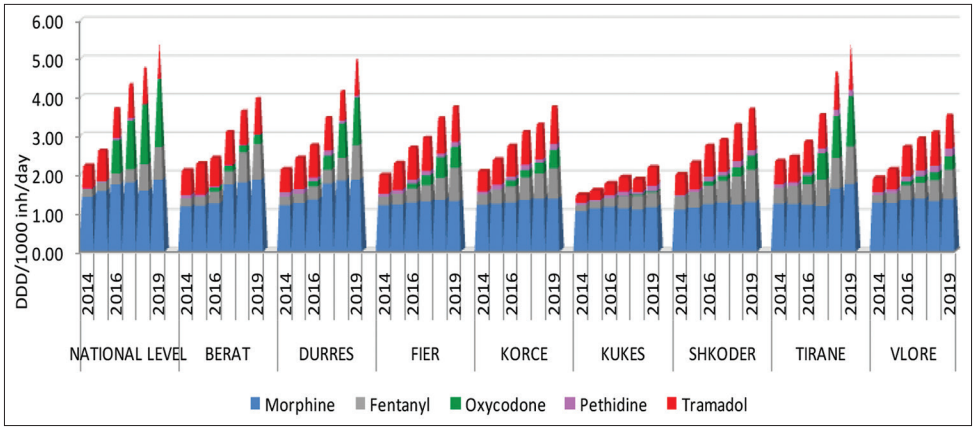

Fig. 3: Consumption of opioids in different regions and at the national level (defined daily dose/1000 inhabitants/day)

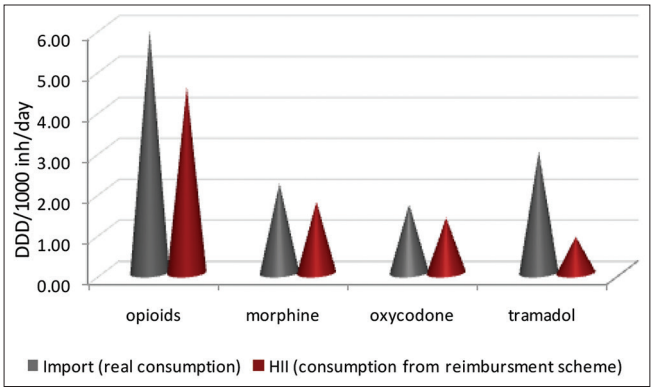

Fig. 4: Annual average value of consumption of Opioids: Consumption based on import (real consumption) (*) versus Consumption based on Health Insurance Institute. (*) The "Import" item includes the consumption based on import data as well as the consumption based on domestic production: This represents the factual consumption

care physicians and oncologists. There are four palliative care services operating in Albania. The length of a prescription has been limited to 7 days, but because of the new legal stipulations, it was expanded to a maximum of 28 days [35]. For many years the only opiate available, was morphine 10 mg injection and 10 mg slow-release tablet. In 2014, patch fentanyl was also included in the scheme. Whereas, in 2016, the scheme extended further by including morphine oral solution (oral drops) and oxycodone 10 mg tablet.

In Albania, prescription opioids are used almost entirely to treat cancer associated moderate-to-severe pain. They are prescribed in isolated cases also by an orthopedist or endocrinologist for the treatment of diabetic foot ulcer, or for pains from multiple fractures. On the contrary, in European countries opioids are commonly prescribed for pain. An estimated 20% of patients presenting to physician offices with non-cancer pain symptoms or pain-related diagnoses (including acute and chronic pain) receive an opioid prescription [9].

One reason for this prescription disparity is ophidiophobia, a closed mentality amongst the medical staff and throughout the population. Another possible reason may be their significantly high price in our country as compared to in other European countries. When comparing the scheme data with the customs import figures, where the latter indicate the real consumption in the country, we note that around 30% of opioids flow out of the scheme. We need to consider here that the customs import figures include also the hospital consumption of opioids. When analyzing item by item, we note consumption values out of the scheme at the level of 26% for morphine and 25% for oxycodone. An explanation for this finding may be the informal trading of these drugs (under the counter), or alternatively, their residual stock inventory may be an explanation. Between the two of them, oxycodone is more easily accessible.

Meanwhile, when we compare consumption values for tramadol, we note that the real consumption exceeds by far the consumption under the scheme, by around 3.4 times. Probable reasons are the fact that tramadol is available in all pharmacies, can be obtained through a simple prescription issued by only one doctor and its cost is much low. In fact it represents the only alternative in the opioids group that is prescribed extensively also in non-cancer chronical pains.

The consumption of opioids undergoes an increasing trend more conspicuous from 2016 onwards (this year oxycodone and oral drops morphine solution were introduced to the reimbursement list). Minimum consumption is noted in Kukës throughout all years under study. High values of consumption for this class are noted in Tiranë and Durres. The first palliative care service provider in Albania, the Ryder Albanian Association (RAA) from 1993, operate precisely in Tirana and Durres. RAA's focus is the provision of home care, palliative care, advocacy, and fundraising [35].

Worth mentioning is though that from 2015, in addition to the four nongovernment organizations providing palliative care, there are seven new palliative care units in the regional hospitals of Albania: In Shkodra, Elbasan, Durrës, Fieri, Berat, Korça, Kukësi, and Vlora offering inpatient and home care services for patients [35].

Comparisons of consumption at the international level

Opioids have become the cornerstone therapy for treatment of moderate to severe pain in many high-income countries. For prescription opioids, while there is insufficient access in many low- and middle-income countries, the reality in OECD countries is quite different, where the availability of analgesic opioids has been steadily growing. The United States has the highest availability of analgesic opioids among OECD countries, followed by Germany and Canada, while Mexico, Chile, and Colombia show the lowest numbers [36].

In 2019, we report dispensing of opioid analgesics at a rate of 5.44 DDD/1000 inhabitants/day; this is much lower than rates in Canada (22 DDD/1000 inh/day in 2010) and Scandinavia (approximately 20 DDD/1000 inh/day in 2006), who are among the leading consumers of opioid analgesics globally. However, the use of opioids in the treatment of CNCP is controversial [37,38]. While randomized-controlled trials have demonstrated efficacy of opioids for the short-term treatment of chronic pain [39-41], there is no high-quality evidence for their long-term efficacy [42-44]. Other contributors to the increase in opioid utilization may include the ageing population; improvements in pain management and physician education; recognition of the serious side effects of NSAIDs and Cox-2 inhibitors; and growth in opioid misuse and diversion [45-49]. In Fig. 5, we may again conclude that in Albania, these drugs are consumed a few times less as compared to the majority of other countries, leaving room

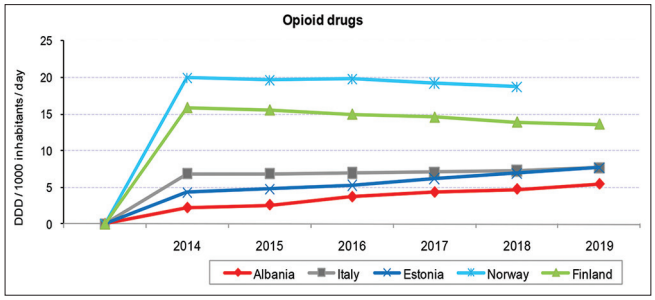

Fig. 5: International comparison in the consumption of opioid drugs class (defined daily dose/1000 inhabitants/day): Albania, Italy [13], Estonia [14], Norway [15-18], Finland [19-22]

to assume that there is under-treatment of pain disorder, and under provision of palliative care services throughout the country.

CONCLUSIONS

The outcomes indicate that patients in Albania have low access to opioids medication, mainly because of low opioids availability. A strong opiophobia among the population and the medical professionals constitutes one of the major impediments for efficient palliative care. To remove this barrier to the treatment of pain, there is a need for a better awareness and education of clinicians, so to avoid exaggerated fear from side effects or addiction, while using this highly efficacious pain-relieving type of medication.

AUTHORS' CONTRIBUTIONS

LK wrote the introduction; LK and GV wrote the methodology and results; LK, SX and LD wrote the discussion section. All authors reviewed the references and approved the final version.

CONFLICT OF INTEREST

Nothing to declare.

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