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Abstract

Background Pharmaceutical opioid consumption has been increasing worldwide, but disparities in access to these medications exist. Few countries of the WHO Eastern Mediterranean Region have well defined pain management policies.

Aims This study presents trends in the consumption of pharmaceutical opioids in the 22 countries in the Eastern Mediterranean Region from 2010 to 2019, with comparative intra- and extra-regional analyses; the correlation between pharmaceutical opioid consumption and human development index rankings; and pharmaceutical opioids use in the region.

Methods We calculated the defined daily doses for statistical purposes (S-DDD) per million inhabitants per day of pharmaceutical opioids from 2010 to 2019, and used the mixed effects models to assess changes in consumption. We used regression analyses to establish the strength of associations between human development index level and consumption in the region and elsewhere.

Results Pharmaceutical opioid use has fluctuated in the region since 2010, with a mean sum of S-DDD of 2547 for 2010–2019. Consumption is relatively low in the region irrespective of the human development index. The highest-consuming country reported 369 S-DDD in 2019 and

the lowest reported 1 S-DDD. The most used pharmaceutical opioids in the region were fentanyl, morphine, pethidine, oxycodone, and codeine.

Conclusion Consumption could be considered inadequate in several countries of the region. Supporting these countries to improve collection and reporting of consumption data, and providing humanitarian assistance to enhance access to pain relief, should be a priority for the international community.

Keywords: opioid, analgesia, morphine, fentanyl, human development, Eastern Mediterranean

Citation: Erthal-Williamson J; Clare P; Gisev N; Santoso C; Berterame S. Trends in pharmaceutical opioid consumption in the WHO Eastern Mediterranean Region, 2010–2019. East Mediterr Health J. 2022;28(11):788–797. https://doi.org/10.26719/emhj.22.085
Received: 13/10/21; accepted: 01/08/22

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Introduction

Pharmaceutical opioids are indicated to treat a wide range of moderate to severe pain symptoms, including acute and cancer-related pain, chronic non-cancer pain and pain at the end of life (1). Selected opioids are listed in the WHO Model List of Essential Medicines (2). Ensuring adequate access to opioid analgesics is therefore important, especially as the burden of cancer is increasing rapidly globally (3). Untreated pain may not only reduce a person's quality of life, it may also have physical, psychological and social impacts (4). In turn, these indirect effects may hinder achievement of the Sustainable Development Goals (SDGs) related to poverty and economic growth (5).

Over the past decade, pharmaceutical opioid consumption has been increasing in developed countries, yet disparities in the distribution of, and lack of access to, these medicines in

developing countries continue to exist, and in some instances have increased (6). In 2015, more than 80% of the 61 million individuals who experienced either serious health-related suffering or death, lived in low- and middle-income countries with limited access to palliative care and pain relief (7). Furthermore, every year almost 2.5 million children globally die with serious health-related suffering (8). Access to palliative care is considered a human right as outlined in article 25 of the Universal Declaration of Human Rights (9). Governments around the world have responded to the call by the United Nations General Assembly in 2016 to increase the availability of opioid analgesics for pain relief (10). The reality of the global divide in access to opioid analgesics for medical purposes has been clearly illustrated by the work of the Lancet Commission on Palliative Care and Pain Relief (7). The Commission measured the availability of opioid analgesics for consumption, as reported by competent national authorities to the International Narcotics Control Board, against the estimated amount needed for the health conditions most associated with serious health-related suffering (an indicator developed on the basis of existing health data and statistics). In the Commission's report, an essential package of palliative medicine containing cheap, off-patent morphine (injectable and oral immediate-release) is proposed to be made universally accessible (8). However, in some regions, progress has varied and some countries have seen their levels of consumption of palliative medicines decrease. Even for substances such as morphine, which is relatively cheap and easy to procure, access can be a challenge in low-income countries. Over the past 20 years, on average, only 9.0% of the morphine available globally was used for pain management, and in 2019, 80.4% of the population in low- and middle-income countries consumed only 12.8% of this amount (11).

Despite the importance of having opioid analgesic available for medical purposes, in 2015, about 71.0% of the global population lived in countries with extremely low consumption of these medicines (6), indicating potential barriers to access. The Eastern Mediterranean Region was among the WHO regions that had inadequate consumption of pharmaceutical opioids, which was a defined daily doses for statistical purposes (S-DDD) of less than 200 in 2001–2003. Although pharmaceutical opioid use increased in 2011–2013, the majority of countries in the region still reported consumption of less than 200 S-DDD (12). The WHO Eastern Mediterranean Region consists of several countries that have experienced social and political unrest, humanitarian crises and conflicts. Very few countries have well-defined policies on cancer management or palliative care (13). Pain management in the region has been hindered by unscientific cultural beliefs, stigma and bias (13,14). While economic and healthcare developments have occurred in some countries of the region in the past few years (13,15), it is unclear whether these developments were accompanied by increased pharmaceutical opioid consumption. A previous study indicated that contextual factors, such as the human development index (HDI), influenced the use of pharmaceutical opioids (12), but more recent studies (16,17) have suggested that contextual factors such as HDI may not be the only decisive factors. A study in 2013 described the trends in pharmaceutical opioid consumption specifically in the Middle East from 1980 to 2010, but it did not investigate the determinants of any changes (13). No up-to-date literature currently exists on the trends in pharmaceutical opioid consumption in the Eastern Mediterranean Region. Information on such changes and associated determinants of pharmaceutical opioid consumption in this region is essential to aid

the development of policies that can ensure availability of and adequate access to opioids for medical purposes.

Objectives

We aimed to present trends in the consumption of pharmaceutical opioids in countries of the WHO Eastern Mediterranean Region (Afghanistan, Bahrain, Djibouti, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates and Yemen) from 2010 to 2019, with a comparative intra- and extra-regional analysis. We analyse the correlation between pharmaceutical opioid consumption and HDI rankings, and identify the opioids used in the region.

Methods

Data sources

All countries that are parties to the Single Convention on Narcotic Drugs of 1961 are mandated to provide data to the International Narcotics Control Board on the annual consumption of controlled opioid analgesic medicines for medical and scientific purposes (18). The Convention has been ratified by 186 States. All countries of the Eastern Mediterranean Region except Palestine are parties to the Convention. The Convention understands consumption as the full amount of each substance that is available for use in each country each year, thus it refers to the amount available for consumption, rather than the quantities actually dispensed to patients in each country in a given year. Countries are also mandated to submit estimates of their annual requirements of controlled substances for medical and scientific purposes, which are the basis for their annual imports and manufacture of controlled opioids. Opioids for which countries submit data and estimates are the ones scheduled under the Convention (19). This information was verified by the International Narcotics Control Board using data from export and import notifications. These data are expressed in terms of the S-DDD to establish the extent of use. The S-DDD is a technical unit of measurement established and used by the International Narcotics Control Board (20). This unit does not represent a recommended prescription dose. Because no internationally agreed standard doses exist for opioid analgesics, the S-DDD is used to provide a comparable measure to rank pharmaceutical opioid use across countries. S-DDD for a drug is calculated using the following formula: annual use of the pharmaceutical opioid divided by 365 days, divided by the population in millions of the country or territory during the year, divided by the defined daily dose for the opioid. Data for population to calculate the S-DDD were taken from the Human Development Reports published by the United Nations Development Programme (UNDP) for the period 2010–2019 (21).

While S-DDD relate to countries and territories, when reporting on regions we used regional S-DDD (sum of annual use in all countries and territories divided by 365 days, divided by the

sum of the population in all countries and territories in millions during the year, divided by the defined daily dose) or sum of all individual S-DDD for each year in all countries and territories.

We used UNDP's HDI categorical version for each country for each year rather than the HDI score. HDI categories are low, medium, high and very high. HDI data were also taken from UNDP Human Development Reports for 2010–2019 (21).

The pharmaceutical opioids considered in this analysis include: codeine, dextropropoxyphene, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, ketobemidone, morphine, oxycodone, pethidine, tilidine and trimeperidine. Methadone and buprenorphine were excluded from these analyses because their use for pain relief cannot be distinguished from their use in treatment of opioid use disorder. The reported codeine use is limited to its use as a monotherapy for pain management and not for preparations containing codeine for the treatment of cough. Our analysis covered the period 2010–2019 and examined trends over this time. In particular, we examined consumption of the five most consumed pharmaceutical opioids in the region.

Statistical methods

We analysed the trends in pharmaceutical opioid consumption across the Eastern Mediterranean Region, by sum of S-DDD from 2010 to 2019. We analysed trends in pharmaceutical opioid consumption for all of the 22 countries in the region, and the five most consumed pharmaceutical opioids in the region, by S-DDD, for the same period. We analysed annual S-DDD data from 2010 to 2019 using mixed effects models to control for within-country correlations (i.e. to adjust for non-independence between the repeated observations of each country). Because the outcome data (S-DDD) were skewed and over-dispersed, we used negative binomial models. We conducted two mixed effects models. The first model compared countries of Eastern Mediterranean Region with the rest of the world, and included a three-way interaction with time and HDI category, allowing for change over time to vary based on the Eastern Mediterranean Region and HDI categories. The second model separated countries into broader geographical regions that do not correspond with the WHO regions, except for countries in the Eastern Mediterranean Region. This model included a region by time interaction. Both mixed effects models included a random slope for HDI category. The significance level was set at P