The need for better access to pain treatment: learning from drug consumption trends in the USA

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Summary

The Authors of this letter look at consumption of opioids and α2-δ ligands, also known as “gabapentinoids”, in Italy, and specifically in the Provincial Health District of Cosenza, as compared with USA trends of recent decades. Access to analgesic drugs since the introduction of Italian law 38/2010 is also evaluated and possible future measures for better management of chronic pain are proposed.

KEY WORDS: α2-δ ligands (“gabapentinoids”), chronic pain, opioids, pharmacovigilance.

Dear Editors,

Opioids are fundamental to provide relief from cancer pain; however, evidence is lacking for their effectiveness when used for the treatment of chronic non-cancer pain, and these drugs are associated with a number of serious side effects (see Morrone et al., 2017). During the opioid epidemic, from 1999 to 2014, the rate of opioid prescription increased fourfold (Prevention CDCa, MMWR 2011) and it has been calculated that from 2007 to 2012 one in five patients with non-cancer pain or with a pain-related diagnosis received an opioid prescription for the management of acute and chronic pain (Daubresse et al., 2013). In view of the high health risk posed by opioid use, including the high rate of drug abuse-linked deaths (Evoy et al., 2017), the Centers for Disease Control and Prevention recently published recommendations on the prescription of these drugs for chronic pain outside the conditions of active cancer, palliative care and end-of-life care (Dowell et al., 2016).

However, since moderate to severe chronic non-cancer pain, such as rheumatoid arthritis or osteoarthritis pain and low back pain, is resistant to NSAIDs and first-line opioids (codeine, etc.), there has been a shift in the prescription trend towards α2-δ ligands, also known as “gabapentinoids”, i.e. gabapentin and pregabalin. Indeed, a recent report highlighted an increase in the prescription of α2-δ ligands in response to the “opioid epidemic”, likely in community as well as hospital settings, for the management of several types of pain, with gabapentin becoming the 10th most prescribed drug in the USA in 2016 (Goodman et al., 2017). However, these drugs, too, are not devoid of serious side effects and they are mostly used off-label, since both gabapentin and pregabalin have been approved by the US Food and Drug Administration and by the European Medicines Agency for the treatment of neuropathic pain, such as post-herpetic neuralgia (Evoy et al., 2017).

Albeit with a considerable delay with respect to the USA time frame, a qualitatively similar pattern of opioid consumption has been seen in Italy. In fact, data on drug spending on opioids in the three-year period 2012-2014, presented to the Italian Parliament by the country’s Ministry of Health, demonstrate that there was, at national level, a trend towards an approximately 15% increase in spending on opioid use following the implementation in March 2010 of a law (n° 38/2010) designed to facilitate access to pain treatment; these data showed a wide variation among regions (a 41% increase was recorded in Calabria) (Table I). This trend towards increased prescription of opioids was subsequently downsized, with other drugs, namely α2-δ ligands, emerging as the first-ranked category in terms of National Health Service spending, based on the 2016 OsMed (AIFA, Rome) report. The increased prescription of α2-δ ligands will likely be a hotly debated issue because of the potential for abuse of these drugs, previously underestimated (Evoy et al., 2017). Pregabalin, for instance, is indicated for the treatment of fibromyalgia, and it is conceivable that, in the search for drugs safer than opioids, general practitioners and clinicians could feel it is justified to issue off-label prescriptions of pregabalin for not well diagnosed pain with features similar to fibromyalgia, under the fibromyalgia indication (Goodman et al., 2017). However, it should be noted that there is not enough clinical evidence for the effectiveness of α2-δ ligands to reasonably support their use in pain conditions outside the ap-

Table I - Invoiced spending on opioids in Calabria in the three-year period 2012-2014.

<table>
<thead>
<tr>
<th>YEAR</th>
<th>INVOICED SPENDING</th>
<th>Δ &gt; 2014/2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>3,762,010.32</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>4,620,470.63</td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>5,312,269.87</td>
<td>41%</td>
</tr>
</tbody>
</table>
proved indications (Goodman et al., 2017). For instance, they are no better and have more side effects than placebo in sciatica, and should not be used in this common condition (Mathieson et al., 2017). Furthermore, these drugs are not that much safer than opioids, since their use is frequently associated with dizziness, sedation and cognitive deficits, and it has been established that these occur more often when they are administered in multi-drug therapy regimens with psychotropic drugs (Goodman et al., 2017). Importantly, this latter scenario is particularly relevant to comorbid patients mostly suffering from chronic age-related as well as metabolic and cardiovascular diseases. In fact, the continuously growing elderly population is often affected by disorders that have a serious impact on health-related quality of life (HRQL), such as cognitive impairment and chronic pain, since aging predisposes to the development of dementia [which may or may not be Alzheimer’s disease (AD) related], as well as to osteoarthritis, traumas, and post-herpetic and post-diabetic neuropathies. Accordingly, it was supposed that the prescription scenario outlined above might, to an extent, be reflected in the results of a preliminary survey by the Calabrian Pharmacovigilance Territorial Service of the health district of Cosenza (Italy). Prescription data relating to demented patients assisted in the community (general practitioners) or in nursing homes over the two-year period 2014-2015 in the province of Cosenza (Calabria, Italy) were collected in June 2017. The results showed that only 86 of the 2166 patients (2078 of them aged over 65) receiving a prescription of acetylcholinesterase inhibitors and memantine were also prescribed opioid analgesics, such as morphine, fentanyl, codeine and associations, tramadol, tapentadol, buprenorphine, hydromorphone, and oxycodone associations, or acetylsalicylic acid. Accordingly, it is reasonable to conclude that chronic pain, known to occur in some 40-60% of patients affected by AD living in nursing homes (Margallo-Lana et al., 2001; Ballard et al., 2013), is undertreated in the demented elderly in the province of Cosenza. This undertreatment may stem from a lack of pain assessment and measurement. In the population studied no prescription of ≤2-δ ligands was reported and this is at variance with the national and USA data reported above. Although the latter is not per sé good news, it is a situation that warrants in-depth monitoring. Taken together, the findings described above point to a lack of drug prescription appropriateness and a limited level of access to pain treatment according to rigorous criteria of diagnosis and outcome evaluation, in spite of what law 38/2010 dictates; furthermore, the data also underscore the failure of the public investment (at least in the province of Cosenza) in the implementation of educational programs linked to the introduction of law 38/2010. Potentially inappropriate medications are responsible for inadequate management of pathological conditions and for increased occurrence of adverse drug reactions, especially in the elderly (Fick et al., 2008; Dedhiya et al., 2010; Davidoff et al., 2015). Educational programs are of the utmost importance, in order to achieve better control of pathological conditions and to improve patients’ HRQL. Interestingly, the “COMMunication, Systematic assessment and treatment of pain, Medication review, Occupational therapy, Safety (COSMOS)” effectiveness-implementation hybrid trial (ClinicalTrials.gov NCT02238652) (Husebo et al., 2015) suggested that the staff belonging to the intervention group, who underwent a two-day educational program, might be able to ensure more suitable management of patients and improve the quality of life of nursing home patients. Hence, the data gathered so far should prompt the development of training programs for the diagnosis and evaluation of pain by general practitioners, neurologists and geriatric physicians, in order to improve the prescription of analgesic drugs for moderate to severe pain and to guarantee the best use of opioid drugs, which must not be forsaken since they represent a very useful treatment tool when used by skilled hands.

References


