PAIN AND THE MAJOR OPIOID DRUGS: PREVENTING POTENTIAL PROBLEMS

Position statement from the Council of Medical Associations of Catalonia (CCMC)

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The World Health Organisation (WHO) recognises pain as an important public health problem. Pain alone is a common reason for visiting a doctor and doctors have a wide range of drug and non-drug treatments available to deal with pain.

Analgesic drugs are used in an escalating way. Pain-relievers like paracetamol are the first step, ranging up to the *strong* or *major opioids* (morphine, methadone, hydromorphone, oxycodone, oxycodone/naloxone, fentanyl, buprenorphine and tapentadol) on subsequent levels.

Over the last few years, a change has been noticed in the use of opioids. Whereas they were once used almost exclusively for patients with cancer pain and for relatively short periods of time, their use is gradually becoming widespread for chronic non-cancer pain.

Opioids are very effective analgesics, but they do have side-effects (hyperalgesia, neurotoxicity, overdose). They must be prescribed with special care, with strict control and only in the appropriate cases. Addiction is one of the most worrying side-effects in the case of major opioids.

Opioid consumption has gradually increased over the last few years, bringing an increase in the risk of inappropriate use, adverse reactions, dependency, abuse, intoxication and death by overdose in several high-income countries. This situation is a cause for concern among international health bodies.

Patients and medical professionals are responsible for making the best and safest possible use of these drugs in order to avoid their abuse or misuse.

2.- The context of the problem: the crisis in the United States of America (USA)

The so-called opioid epidemic crisis in the USA began in the mid-nineties and has notably intensified in the past decade. The death of more than 100 people/day through opioid overdose (mostly fentanyl and heroin) is a national crisis in the USA, affecting public health and economic and social well-being. From 2000 to 2015, the prescribed dose per head of major opioids increased by 300% in Canada and the USA and between 50% and 100% in the European Union (EU).

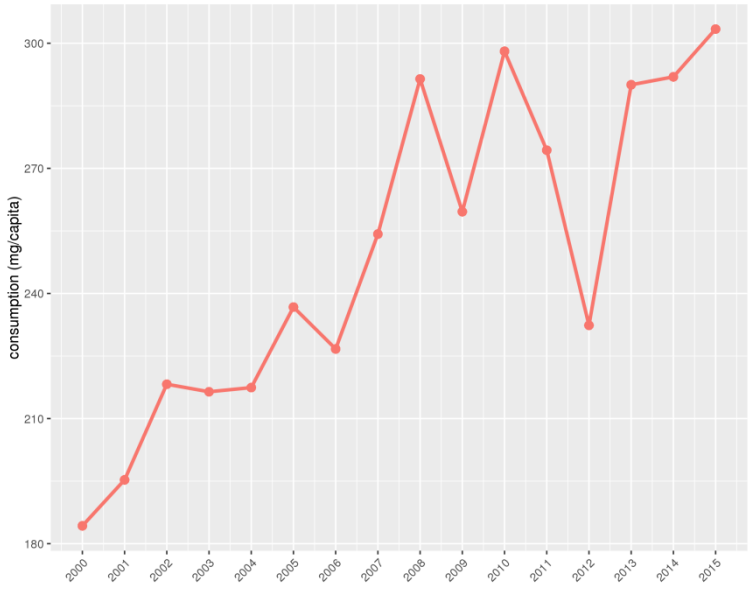
There are many causes of this crisis. The health care structure of the USA, with no coordination between primary medicine and specialist hospital care and without strict prescription control has encouraged the over-indication of these drugs. This is not unconnected with strong advertising, which does not always correspond to reality, and with the inducements to prescribing offered by some drug companies. In the USA, the replacement of these drugs by substances from illegal markets has been observed, with an increase in accident and emergency visits and more cases of mortality for overdoses, particularly of heroin.

This year, 2018, the United Nations (UN) has called the world's attention to this serious public health problem, pointing out that "*the aggressive campaigns to promote drugs containing opioids is making the problem worse*", while highlighting the need to adopt measures to raise users' awareness and to improve the monitoring and control of prescription and distribution systems for the major opioid drugs.

3.- Situation in Catalonia and the European Union (EU)

Despite the fact that the prescription of major opioid pain-relievers and the complications deriving from their improper use and abuse in the EU do not match the figures for the USA, it has significantly increased in the last few years. Besides this, in 2013, the United Kingdom showed a rate of prevalence of the improper use of opioids of 0.3%, followed by the Nordic countries (0.15%), Germany (0.13%) and Spain (0.07%). In 2016, the UK was the EU country with the greatest improper use of opioid pain-relievers.

Opioid consumption in Spain has increased by 84% in the last eight years (2008-2015), moving from 7.25 DID (DID: number of Defined Daily Doses/1000 inhabitants/day) in 2008 to 13.31 DID in 2015.



Total opioid consumption in Spain (equivalence with mg of morphine/capita) 2000-2015. Pain & Policy Studies Group. University of Wisconsin WHO Collaborating Center (2018).

The warning indicators (such as an increase in demand for treatment, acute adverse reactions to drugs and mortality) are continuing to increase, without for the moment generating alarm. However, the under-reporting of these indicators cannot be ruled out.

In Catalonia during the period 2012-2016, opioid consumption increased by 45%, moving from 6.73 DID in 2012 to 9.74 DID in 2016. The consumption of major opioids increased by 33% in the same period, moving from 2.69 DID in 2012 to 4.01 DID in 2016. Fentanyl is the most consumed opioid and the one whose use has increased most (49%), although in absolute terms this increase is due to transdermal fentanyl use. The consumption of quick-release fentanyl has recorded the highest relative increase (80%). This growth pattern is similar to that recorded in Spain, although Spain shows slightly higher consumption figures than those in Catalonia.

4.- What prospects and possible scenarios must be considered concerning the prescription, misuse and abuse of opioids and what elements allow us to reduce or control these risks?

There are elements differentiating the environment in the USA with that in Catalonia. In Catalonia, health professionals have access to precise, up-to-date information about opioid prescription. Meanwhile, there is no significant black market in major opioid prescription like the one in the USA.

The main tool for detecting patients at risk of abusive behaviour with major opioids is their clinical history. A background of consumption of abusive substances (opioids, alcohol, benzodiazepines, cocaine, cannabis and other drugs) should alert a doctor to this risk and prevent various prescriptions being made by different doctors.

In the Catalan context, the new technologies, specifically the e-prescription and the corresponding digital certificate, make it possible, in line with the aims of the prescription itself, to identify drug prescriptions very reliably with respect to their volume and suitability as treatment. They also allow good coordination between prescribing doctors and pharmacies throughout the territory.

Different scientific associations draw up and regularly update clinical practice guidelines for medical prescriptions, including the indications for which each type of drug is recommended, how to use them and when they must be withdrawn. These guides are often jointly drawn up by associations from different specialisms, allowing all professionals to work together in the same direction and make good use of medicines. The **Medicines Division of CatSalut and the Health Quality and Evaluation Agency of Catalonia** (AQuAS) periodically review the consumption of certain drugs (including opioids) and their suitability, while providing data to detect possible problems associated with their excessive consumption.

5.- Proposals to be considered to improve the prevention and monitoring of this situation

Opioid analgesics have been used for decades for treating moderate to intense pain and they are an essential weapon in a doctor's armoury for treating high-intensity chronic pain. We must not forget, however, that the management of chronic non-cancer pain must also combine other multimodal, integrated and interdisciplinary strategies. An integrated assessment of the pain and the impact it has on everyday life must be made and realistic targets set depending on the diagnosis.

When a doctor, with knowledge and expertise in the management of these major opioid drugs, decides to prescribe them, he/she must bear different recommendations in mind. Correct patient selection is essential to achieve the best results and reduce the associated risks, including possible abuse or addiction. Special care must be taken with elderly patients and/or those with comorbidity, in whom the frequent presence of associated diseases and polypharmacy can intensify the adverse effects and complications of pain relievers. It is possible that among some health professionals there could be a certain (false) perception of low risk in the use of these major opioids.

The patients and their families must always be provided with detailed, understandable information on the benefits, possible side effects and risk of addiction. Certain common concepts that are sometimes wrongly interpreted must be explained and clarified: addiction is not a synonym for physical dependence and tolerance; addiction is not the sum of bad personal choices; pain is no protection against developing opioid addiction; the long-term use of certain types of opioids is not the only cause of addiction and, finally, despite differences in vulnerability, and no patients are immune to opioid addiction.

Once the type of major opioid has been chosen, a pattern of regular use must be established with fixed times and doses. On-demand prescriptions must be avoided. Individualised treatment must be begun with continuous monitoring, making stricter checks on the patient during the first month of treatment and assessing the effectiveness of the drug, the appearance of side-effects and risk

behaviours. After 3-6 months of treatment, the patient must be reassessed to evaluate whether it is appropriate to continue the prescription, reduce the dose or offer other treatment strategies.

We have tools to identify the patients most susceptible to the risk of addiction to major opioids. Among these are monthly checks by the prescribing doctor on the treatment, including any evolution and possible side effects. Using a set of guided questions and specific questionnaires, we can detect addiction to major opioids. If a patient becomes addicted, we must remember that our health departments have specialised addiction units to deal with this problem and the patient must be referred to one of them as soon as possible.

Final reflections

The major opioids are a very good tool for treatment if used on people following suitability criteria, taking the recommended precautions.

Safe, effective treatment with opioids begins with the right selection of the patients who could benefit from them. The origin type, duration and intensity of the pain determine the optimum treatment approach.

Despite this, we must always remain prudent when it comes to deciding to prescribe these drugs and watch out for possible side-effects, especially in elderly or fragile people. They should always be subject to close monitoring to detect tolerance and possible side-effects that can even lead to hospital admission.

Continuing the treatment longer than necessary must always be avoided.

To ensure good use of opioid drugs, it is important to follow the indications and recommendations of the scientific associations and medicine regulation agencies.

When opioids are prescribed, the patient and their family must always be clearly informed of the expected benefits, possible side-effects and risk of addiction. We must not be afraid to prescribe them, but we must never lose respect for them.

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Catalan and Balearic Internal Medicine Association

Catalan Psychiatric Association

Catalan Rheumatology Association

Catalan and Balearic Palliative Treatment Association

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