

Therapeutic use of opioids in the elderly patient

Abstract

The continuous use of opioid drugs has its origin best known for analgesia since the discovery of its use as an anesthetic and its therapeutic use nowadays has become relatively high due to elderly patients, mainly with chronic pain of oncological and musculoskeletal origin. However, with the aging process, both drug doses and analgesic effects must undergo new adjustments to obtain the expected results. And, in addition to the concern about drug interactions and maintenance of periodic examinations in the elderly, there are greater risks involving tolerance and pseudo addiction, which may mix physical and psychological dependence. This work intends to elucidate the pharmacodynamics in aging and update dose adjustments and possible effects in the therapeutic use of opioids in the elderly.

Keywords: opioids, elderly, tolerance, aging, dependence

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Brief history

Opiates are drugs derived from Opium, a “milk” (green kind) or “powder” (dry kind) found in the Asia Minor native species called “Papaver”. *Somniferum* known as Papoula The use of opium and its derivatives comes from antiquity, being used first by the Sumerians; in Egypt, the “Papyrus of Ebers”, 1552 BC, states that a mixture of substances containing opium was used to sedate children.¹ In Greece, Hippocrates prescribed poppy juice to treat leucorrhea, also prescribing its use as a purgative and narcotic. Galen, who was the highest expression of Roman Medicine, realized the risks of the exaggerated use of opium through the case of Emperor Antoninus, whose physician he was and who, by all indications, was a victim of addiction to the drug.² Biblical data from the Old Testament refer to the substance as a “punishment” for the people of Israel. The Islamic peoples and also the Chinese came to know opium, Paracelsus called it the “immortality stone” but only in 1721 (London) did the Paregoric Elixir appear, containing opium, honey, camphor, aniseed and wine.¹ In the 19th century, morphine was discovered by Friedrich Sertürner, a German, a pharmacist’s assistant who worked on the isolation of the active principles of opium, but in 1860 this drug became a medical and social problem responsible for one third of all cases of opium addiction and the reports were about fatal poisonings and even committed suicide.³ In this century, the Opium War between England and China took place, as this encouraged the use of opium through smoking. On the battlefields American soldiers showed visible dependence after having used opium orally or subcutaneous morphine to ease the pain caused by wounds⁴ and the same happened to British and German soldiers in the second half of the 19th century.³ Between the 19th and 20th centuries, heroin was used to replace morphine as it relieved its withdrawal symptoms; after 12 years this thought led to the realization that heroin has a much greater potential for addiction.⁵

Purpose

The present work aims to show the reader the developments through the discovery of opium, which may be the main implications for the health of the elderly individual in the therapeutic use of opioids

Contemporary management

The World Health Organization Committee currently defines addiction as “a state of periodic or chronic intoxication, harmful to the individual and society, produced by the repeated use of a drug. Its characteristics are: an absolute need to continue using the drug (compulsion) and to obtain it by any means, and also tolerance,

psychic dependence and, sometimes, physical dependence”. This Committee does not configure the obligation of the last attribute, while the Drug Addiction Committee of the Ministry of Health in the United Kingdom

emphasizes the obligatory presence of physical dependence, with the appearance of the abstinence syndrome, when of drug withdrawal.⁶ In 2016, Brazil was among the countries that least prescribed opioids in the world, with a consumption of 3.09mg/ percapita of morphine, when the average in America was 25.7mg/per capita and, in the world, 5.42mg/ percapita (the access to opioids is one of the indicators of the Human Development Index, HDI, since adequate pain control improves quality of life.⁷

Therapeutic consumption of opioids for analgesia is often the cause of liver aggression as well as an increased risk of respiratory depression (mainly in chronic obstructive pulmonary diseases)⁸ and the administration of opioids, in adequate doses, is rarely responsible for the phenomenon of addiction in patients victimized by chronic pain, however this possibility cannot be excluded as their prolonged use favors physical and psychological dependence as well tolerance and nowadays the literature recommends mainly Methadone and Naltrexone to control withdrawals or dosage decreases, taking into account doses and general condition each patient.⁹

Opioids and pharmacodynamics in aging

Opioids produce analgesia by binding to enkephalin or endorphin receptors in the brain, spinal cord, and peripheral nervous system. They act modulating nociceptive activity through numerous mechanisms. They are divided into agonists (morphine, codeine, heroin, oxycodone, methadone, propoxyphene, meperidine, fentanyl), partial agonists (buprenorphine), agonist/antagonist (pentazocine, nalbuphine) and antagonist (naloxone), according to their ability to sensitize opiate receptors.

However, with aging, many biological changes occur, thus altering the behavior of medications in the face of chronic pain. The World Health Organization created the third step in the guidelines for treating the elderly, which refers to the use of Opioids. In addition to the pharmacodynamic and pharmacokinetic alterations that interfere with the metabolism of opioids, factors inherent to senile elderly people should also be considered as comorbidities of chronic and psychological diseases. Drug absorption is influenced by increased stomach acidity, decreased passive transport and altered circulation in the intestinal region. Metabolization by the liver decreases by up to

40% and renal elimination has become slower. With the increase in fat mass and decrease in lean mass, liposoluble drugs tend to accumulate in adipose tissue, making their elimination even more difficult.^{10,11} Thus, water-soluble drugs will have a decrease in their distribution volume, thus increasing their serum levels, as a result of the use of morphine.¹² Chronic pain in the elderly tends to be more severe than in young individuals: the response to analgesia promoted by opioid derivatives becomes smaller. Drugs and their agonists interact with receptors that, through enzymatic connections, amplify specific responses in tissue structure, thus altering homeostasis.¹³ During the aging, the Peripheral Nervous System loses myelin and its terminal structures become densified (process of structural deterioration) and with a decrease in the “turnover” of the Central Nervous System of (neurotransmitters involved in nociception), there will be changes in the interaction among drug, its respective receptor and the response waited¹⁴⁻¹⁶. Thus, throughout the existence of an addict for beginning therapeutic use or for having already started the use of opium-derived substances with the intention of “adult use”, he will have a decreasing sensitization in the structures of the Nervous System, requiring larger doses for the effects of analgesia before achieved. Dowell et al bring some observations about the selection of opioids that involve approaches at the beginning of therapy, when immediate-release rather than long-acting opioids should be prescribed to avoid the risk of overdose, such as sedation and slurred speech. In addition, opioids should preferably be prescribed at the lowest effective dosage, always weighing the risks and benefits, and, if necessary, considering increasing the dosage.¹⁷

Opioids and their use in the elderly

All risks must be taken into account, so follow-up with tests must be part of the treatment so that risks are controlled.

The increase in infectious risks resulting from the formation of bacterial plaque (biofilm) in the oral cavity¹⁸ must be taken into account, since the lethargic state induced by depression in the Central Nervous System leads the individual to show little interest in his personal care (a condition aggravated by xerostomia), oral hygiene and therapy with antimicrobial chemical agents should also be advocated.¹⁹

Table 1 Therapeutic recommendations of opioid medications for the elderly

Hydromorphone	Ext rel tablet, 8, 16 and 32 mg	8-32 mg/24 hours	6 to 8 hours/24 hour
Fentanyl	Patches 5, 10 and 20 mg 10 and 30 mg Oral solution	5–20 mg/7 days 5–200 mg/4 hours (oral dose)	24 hours/72 hours 15 min/2 hours/4 hours
Morphine Capsules	10 mg/mL Caps Ampoules, 1 mL-10 mg/mL		
*Morphine LC	Capsules, 30, 60 and 100 mg	30–100 mg/8 to 12 hours	1 hour/6 hours/14 hours
Methadone	Capsules, 5 and 10 mg Ampoules, 10 mg/mL	10 a 50mg /6 to 12 hours	1 hour/12 hours/25 hours
Buprenorphine	Patches, 5, 10 and 20 µg	5–20 µg/7 days	18 to 24 hours/72 hours
Oxycodone	Capsules, 10, 20 and 40 mg	10–40 mg/12 hours	1 hour/8 hours/25 hours

Source: Brazilian Society of Geriatrics and Gerontology (2018)²⁶

Conclusion

The aging process, in addition to the tolerance and sometimes pseudoaddiction developed, have metabolic modifications that alter the entire distribution of the drug, also modifying its form of absorption and elimination and with advancing age, plasmatic levels tend to be higher and the response to analgesia tends to be less and less, which generally seems to only increase the risks for maintaining the individual's health balance. For addicts of solely therapeutic

Non-addict chronic pain patients treated with low doses of opioids may develop complaining and hostile behavior similar to the behavior of drug/dependent patients, and this behavior is called pseudoaddiction.²⁰ The prescription of opioids for chronic and oncological pain duly controlled²¹ and monitored by the prescribing professional cannot be held responsible for the development of pseudoaddiction; the deviant behavior of certain patients is due in part to the susceptibility of some individuals who “pressure” the professional in the search for prescriptions, thus developing tolerance and dependence, escaping the normal course of treatment. Tolerance, as defined by either a need for markedly increased amounts of opioids to achieve desired effect (this can cause intoxication), or a markedly diminished effect with continued use of the same amount of an opioid. In these cases, within the 7 Diagnostic Criteria for Opioid Dependence (DSM-V), deviation from use, loss of control and compulsive use must be present.²² Two criteria from the 2019 version of the Beers criteria (use of potentially inappropriate medications in the elderly) were incorporated in response to the growing concern about the abusive use of opioids for they are not to be prescribed in association with Benzodiazepines or Gabapentin.²³ There is controversy regarding the use of opioids to control non-cancer chronic pain. There are academic opinions divided between the effectiveness of using these drugs outside of neoplastic pain; the control of neuropathic and musculoskeletal pain can lead to the occurrence of organic toxicity to the increase in the magnitude of the desired effects.²¹

There are many health implications when using opioids even therapeutically, highlighting: increased risk of delirium in prolonged hospitalization of elderly patients.^{24,25}

We understand that the use of opioids in the elderly requires adjustments regarding dosage, choice of medication, taking into account its half-life in the body and interaction with other medications. The table below lists a suggested therapeutic use, dosages, half-life in the body, and may facilitate the choice of medication²⁶ as well as analysis of interactions and adverse effects can be minimized by meeting the needs of the elderly with a little more assertiveness (Table 1).

use for chronic pain, there is a consensus with the professional in order to minimize the deleterious effects accentuated by the aging process, since with low dosages of continuous use it will also provoke therapeutic responses below expectations, leading to more and more attempts increases in dosages and little change in analgesia response.

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Conflicts of interest

Author have no conflict of interest.

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