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Narcotic Analgesics: OPIOIDS

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Abstract

Opioids are morphine-like analgesics used for the management of severe pain, such as acute pain and cancer pain. IASP considers the relief of pain in acute or terminal illnesses as a human right, supporting opioid use in patients of all ages. IASP signed the Declaration of Montreal with other parties in 2010, reflecting its point of view. The aim of this study was to describe opioid analgesics and their adverse effects. Outcomes of a current review of the literature were used in this study. Like all analgesics, opioids should be used at the right time, for the right patient, for the right indication, at the right dose, and with the appropriate mode of administration. The acknowledgment of every healthcare worker seeing patients in all branches in medicine will allow for patient access to analgesics via the appropriate approaches.

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Keywords:

Narcotic analgesic, Opioid, Adverse Effects

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INTRODUCTION

McCaffery described pain in 1968 as “whatever the experiencing person says it is, existing whenever and wherever the person says it does”. This definition highlights that pain is a subjective experience (McCaffery, M, 1968). The most reliable indicator of pain is considered to be the feedback given by the pain sufferer (Herr, KA, & Mobily, PR, 1998). Opioids are indispensable treatment agents used in pain centers today (90%) and they are modified morphine derivatives (Yildirim, D, Gulbeyaz, C, 2019). These agents are named as opioids since their effects occur because of their binding to the opioid receptors. They act as agonists at the opioid receptors. The mu1, kappa, sigma and orphanin-nociceptin OFQ/N receptors are the major receptors, to which opioids bind some groups of opioids bind to delta and epsilon receptors, too (Azzam AAH, Mcdonald J, Lambert, DG, 2019). Selecting the type of analgesic medication depends on the severity of the pain. Once the appropriate drug is selected, the route and frequency of administration are determined for treatment. The oral route should always be the first choice. These agents may also be administered intravenously, subcutaneously or transdermally when required (The American Pain Society 2001, Kabalak, A, Ayla O, 2013). Pharmacological approaches are the mainstay of treatment for severe pain affecting the patient's quality of life. Almost half of the individuals having pain-associated impaired quality of lives prefer nonprescription analgesics as the first choice for pain relief. The most preferred analgesics for this type of pain are the opioids (The American Pain Society 2001).

Properties of Opioids and Adverse Effects

Sydenham argued in 1682 that none of the available remedies is as universal and effective as opium to relieve the suffering of man, highlighting the opioid miracle (Andre, J, Karen, O, 1999). The Angelic face of Opium is dazzlingly seductive, but if you look on the other side of it, it will appear altogether a Devil. (*Thomas Willis "Medicine in Man's Body" VII i 128 1848*) (Cyril R, Ballantyne J. 2016).

Opioids have been used since the 1980s. Opioids are chemical agents acting by binding to the opioid receptors, which are mainly located in the central nervous system and the gastrointestinal tract. These receptors mediate both the beneficial and adverse effects of opioids in both organ systems (Katzung, BG, 2004, Berry, PH, 2001).

According to the National Drug Threat Assessment Report (2010), opioids are the most common drugs prescribed incorrectly. Studies demonstrate that opioid-associated deaths have increased by 98% in the period from the year 2001 to 2006. The rate of prescribing opioids for chronic pain relief is reported to be 28% in Europe (Robertson, JA, Purple, RJ, 2016). In a study, mortality and severe adverse effects caused by commonly prescribed opioids were compared according to seven types of opioids. In a 7-year period, 19.480 cases of serious adverse events were identified and it was found that hydrocodone and oxycodone opioids were responsible for 77% of the cases (Murphy, DL, Lebin, JA, Severtson, SG, Olsen, et al., 2018). In recent years, the use of prescription opioid drugs has increased dramatically in the United States, with only 16,651 opioid-related deaths occurring in 2010 (Dart, RC, Surratt, HL, Cicero, TJ, Parrino, MW, et al., 2015). Opioid treatment is mainly applied in pain of severe diseases such as acute pain, cancer pain and AIDS. Denizbasi et al. defined the population of patients, in whom opioid use

should be avoided, as opioid-dependent newborns, cocaine addicts, and poisoned patients with an unidentified stimulant (Altınok, A, Denizbaşı, ÇÖ, Özge O, 2019).

Opioids are classified as below (Erden, ÖF, 2018):

a) Natural opioids

Phenanthrenes (Morphine and Codeine)

Benzyl Quinolines (Papaverine)

b) Synthetic Opioids

Morphine derivatives

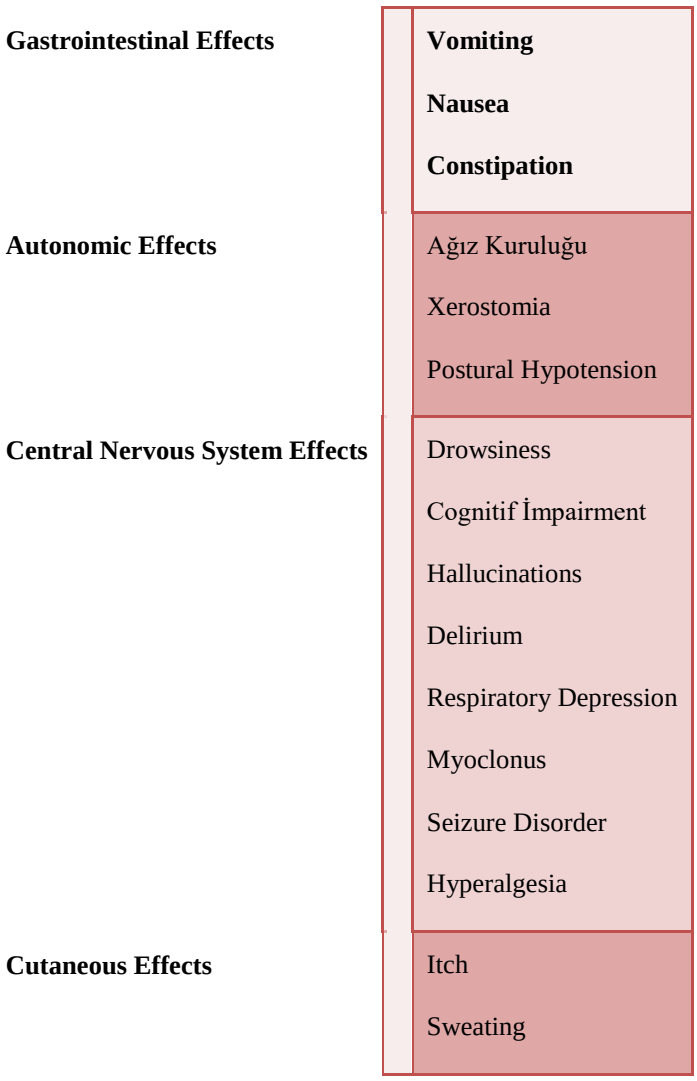
Diphenyl or methadone derivatives

Benzomorphans and phenylpiperidine derivatives.

c) Semisynthetic Opioids

Examples of opioid drugs include codeine, fentanyl morphine, hydromorphine, oxycodone, methadone, meperidine, and hydrocodone. The most commonly prescribed drugs at health care centers are the opioids. The psychological and physical side effects of opioid drugs are considerable. Doctors do profit and lost analysis according to the patient's priorities and the prognosis of the disease. Therefore, they may sometimes ignore, possible adverse effects when giving prescribe (Pathan, H, Williams, J. 2012).

Figure 1. The Common Effects of Opioids (Swegle, JM, Logemann, C. 2006).



Selected side effects of opioids are described below:

Psychological and Physical Side Effects of Opioids: Opioids taken before and after surgery may affect recovery and outcomes. Patients receiving opioids prior to back surgery have been shown to have unfavorable outcomes including pain, impaired functioning, and depression (Dambisya, YM. and Lee, TI, 1995). Patients receiving opioids before knee replacement surgery gave negative feedback about pain (Pivec R, 2014).

Opioid use in the postoperative period is known to delay the recovery. Modern surgical and postoperative procedures are designed to reduce the use of opioids besides other factors in order to accelerate the recovery. However, excessive pain has a negative effect on the recovery processes. Therefore, it is imperative to use a multimodal approach to alleviate the pain and to minimize the use of oral and long-acting opioids (Varadhan, K.K, Lobo, DN., 2010).

Cognitive impairment: The effect of opioid drugs on cognition is still a complex issue.

As it is known, the use of larger doses of opioids can cause drowsiness, lethargy, and even death. Study results about the effects of doses commonly used in the outpatient treatment of pain are more complex because the pain itself may compromise the cognitive functions. A prospective study, evaluating the effects of opioids on cognitive functions, has shown that opioid treatment in patients with chronic pain caused a reduction in the spatial memory capacity and resulted in impairments in the working memory (Schiltenwolf, M, Akbar, M, Hug, A, Pfuller, U, et al. 2014). In another study, urine and hair samples were collected and analyzed from 23 individuals who applied to a trauma center and who were using non-prescription opioids. Neuropsychological tests were also applied to these individuals. As a result of this study, chronic opioid users showed poor performance in recognizing emotions primarily from faces (gesture and facial expression), prosody and complex scenes (Kroll, SL, Nikolic, E, Bieri, F, Soyka, M, et al., 2018). Marco et al. conducted a study of 64 patients who admitted to the emergency department with severe pain and agreed to receive opioid treatment. In this study, the patients who had a mean age of 36 were evaluated with mini mental examination before and after the examination with montreal cognitive assessment scale. At the end of the study, mini mental examination scale scores revealed a relationship between opioid use and decrease in cognitive performance (Marco, CA, Mann, D, Rasp, J, Ballester, M, et al. 2018).

Respiratory depression: Opioids adversely affect the respiratory system. Carbon dioxide (CO2) levels in the blood affect breathing negatively. When the respiratory rate slows down, the levels of CO2 increase. Opioids affect the CO2 and O2 feedback loop (Shenoy, SS, Lui, F, 2018). When the patient receives a high dose of an opioid, wakefulness will be decreased due to the high levels of the opioid. In particularly, mu (m) -opioid peptide agonists with high affinity and good selectivity are obviously excellent analgesics, but in general cause ventilator depression (Azzam AAH, Mcdonald J, Lambert, DG, 2019).

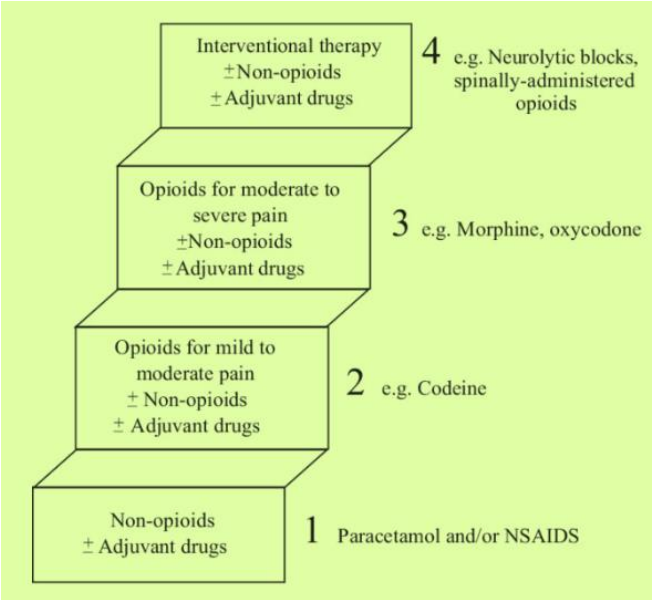
Endocrine-hypogonadism: Chronic use of opioid drugs can cause many endocrine problems. The most obvious problem is the decrease in the released levels of gonadotropin-releasing hormone (GnRH), which promotes the synthesis of sexual hormones (estrogen and testosterone) by our bodies. These low hormone levels can be seen in 50% of individuals receiving chronic opioid treatment (Reddy, RG., 2010).

Constipation: Constipation usually occurs with opioid medication use. Opioids inhibit gastrointestinal peristalsis and slow gastric emptying. They also increase the tone of the anal sphincter, disrupting the defecation reflex and making defecation difficult (Sizar O, Gupta M, 2019). In the other resource the incidence of constipation due to reported opioids is highly variable between 15% and 81% (Tafelski S, Beutlhauser T, Bellin F, Reuter E, et al., 2016). Constipation due to opioids may occur as soon as opioid use begins or in any of the use processes. Problems such as nausea, vomiting, abdominal tension in this type of constipation may not heal despite the use of laxatives. In this case, most patients may discontinue opioid use (Sizar O, Gupta M, 2019).

Nausea and vomiting: Nausea and vomiting are common side effects of opioid drugs and they, too, occur due to the reduced peristaltic activity of the stomach and small intestine (Swegle, JM, Logemann, C. 2006). İncidence of nausea and vomiting between 10% and 50%. Opioids have an emetogenic effect

with many mechanisms. These are; direct stimulation of the chemoreceptor-triggering zone, prevention of peristaltism, mechanisms related to vestibulum. It is very difficult to control these prblems (Porreca, F, Ossipov, MH, 2009).

Figure 2. The "Analgesic Ladder" of the World Health Organization for analgesic use (Kabalak, A, Ayla O, 2013).



Conclusion

The recommendations of the World Health Organization on the following analgesic use principles (Figure 2) need to be considered when using opioids (The American Pain Society, 2001).

Principles of analgesic use

a) Selection of the analgesic should be based on the pain-analgesic ladder principle according to the severity of the pain.

b) The cause and the nature of the pain should be taken into consideration when selecting analgesics.

c) The oral route should be the first choice for the mode of analgesic administration.

d) The dose of a particular analgesic medication should be determined individually for each patient.

e) Analgesics should be given at regular intervals before the onset of pain.

f) Prophylaxis and treatment for side effects should be provided.

g) Ungrounded concerns of patients and their relatives should be ruled out.

h) Adjuvant drugs should not be used unless necessary (WHO 1996, Colleau SM, 2006, Aydınlı, I, 2002, Royal College of Anaesthetists, 1998).

It is considered vital that health professionals follow guidelines on opioids in line with the principle of "Don't give harm firstly".

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