Pain Control In Patients Undergoing Orthopedic Surgery: A Narrative Review Study On The Role Of Anesthetics

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Abstract:

Introduction: Prevention and control of pain after orthopedic surgery is of great importance to achieve appropriate outcomes after surgery. However, the right medication that is being chosen for this should have few side effects for patients. Therefore, the aim of this study was to evaluate pain control in patients undergoing orthopedic surgery as a review study on the role of anesthetics.

Methods: The present study was a narrative review study. In this study, to find related studies, the researchers performed in SID, Magiran, and Google Scholar databases with Persian keywords including “orthopedics”, “lower extremity, “pain”, and “upper extremity”. Inclusion criteria for the present study were Persian articles that dealt with pain in patients undergoing orthopedic surgery (lower and upper), as well as original research articles of clinical trial design.

Results: Our review showed that different studies used various drugs to control pain in patients undergoing orthopedic surgery. Postoperative pain in patients undergoing orthopedic surgery has been the subject of numerous studies with clinical trial design. Interventions in this regard include the use of intrathecal or intravenous injection of drugs such as magnesium sulfate, morphine, ketamine, ketorolac, paracetamol, ibuprofen, pregabalin, gabapentin, tramadol; Methadone, Dexmedetomidine, fentanyl, sufentanil, piroxicam, memantine, and nitroglycerin.

Conclusion: Several studies reviewed in our study claimed that interventions with different drugs can reduce pain in patients undergoing orthopedic surgery. This suggests that the routine use of these drugs in these patients should be considered and that multiple drug options can be used to control pain in patients undergoing orthopedic surgery. However, the choice of these drugs is based on the patient's condition and the decision of the anesthesiologist. Future meta-analytic studies can determine the best possible intervention.

Keywords: Pain, Orthopedics, Lower Extremity, Upper Extremity.

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Introduction

Pain is one of the most common causes of delayed discharge after surgery (1). More than 70% of patients experience moderate to severe pain after surgery and more than 25% of patients experience side effects following the use of analgesics (2). Orthopedic surgery is one of the surgeries that is associated with relatively severe pain during and after surgery (3-4). Orthopedic surgery is one of the most painful surgeries; chronic pain after this type of surgery is reported to be 28% (5). Postoperative pain control is one of the major concerns of physicians and patients undergoing surgery (1) and inadequate postoperative pain control increases the risk of chronic pain (6-8). Mechanism of postoperative pain includes inflammation of tissue due to trauma and surgical incisions, rupture of tissues, burning, and nerve damage (cut or stretch or pressure on a nerve) (9). Postoperative pain with adverse consequences and affecting various mechanisms causes fundamental changes in the body's metabolism in susceptible individuals and can cause hypertension, heart ischemia, respiratory, gastrointestinal, and renal problems and even increase patient mortality. Pain delays the patient's movement and walking, increases the length of hospital stay and treatment costs of patients (10-12). Proper control of postoperative pain is still an important issue in postoperative care. Although narcotics are one of the major treatments for postoperative pain, their widespread use is not without side effects. For this reason, extensive efforts have been made to reduce the need for narcotics to improving postoperative pain by prescribing other drugs or using other methods. There are several mechanisms recommended in postoperative pain, and based on each, different classes of drugs have been proposed for treatment or prevention. Other medications used to treat postoperative pain include corticosteroids, tricyclic antidepressants, and more. Therefore, in order to evaluate a narrative review study, the present study investigates drugs that are effective in controlling pain after orthopedic surgery.

Methods

The present study was a narrative review. In this study, to find related studies, researchers conducted a search in the SID, Magiran, and Google Scholar databases with Persian keywords including pain anesthesia, lower limb orthopedics and upper limb. Inclusion criteria for the present study included: Persian articles that examined pain in patients undergoing orthopedic surgery, as well as original research articles of clinical trial type. Exclusion criteria also included not having access to the full text of the article, abstracts of congressional papers, or conferences, and review or meta-analysis papers. Finally, the findings related to drugs effective in reducing pain in patients undergoing orthopedic surgery were reviewed.

Paracetamol (intravenous acetaminophen):

Paracetamol is injectable acetaminophen that falls into the category of para amino phenol derivatives and the non-narcotic and antipyretic analgesic therapy. Its active ingredient is known as paracetamol. It is used in the short-term treatment of moderate pain following surgery and short-term treatment of fever (13). The mechanism of action of this drug is inhibition of prostaglandin synthesis. The first enzyme in the prostaglandin production cycle is cyclooxygenase, which paracetamol inhibits its production by entering the cycle and exerts its analgesic effect (14-15). Side effects of this drug have been shown to be rare and have placebo-like immunity, as well as no obvious interactions with other drugs. Intravenous use with its therapeutic dose (up to 4 g per day) (16) is rarely associated with liver damage and has been shown to be safe even for use in some patients with underlying liver disease (17).

Ibuprofen:

Ibuprofen is classified into nonsteroidal anti-inflammatory drugs, non-narcotic analgesics and antipyretics (18). Its peak plasma concentration is 1-2 hours after consumption. 90% binds to plasma proteins. Its plasma half-life is about 2 hours. It is metabolized in the liver and excreted mainly in the urine. The effects of ibuprofen include inhibition of prostaglandin synthesis, inhibition of inflammatory cell chemotaxis, and reduction in the release of free radicals (19-20). This drug prevents the formation of thromboxane A2 by platelets and reduces platelet aggregation (19).

Buprenorphine:

Buprenorphine, a partial opioid receptor agonist, is a semi-synthetic opioid analgesic derived from thebaine (21). It exerts both agonist and antagonist properties on its receptors (22). The use of low-complication and easy-to-use drugs such as

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buprenorphine, if effective, can help improve the quality of surgery (23). Compared to morphine, it is about 33 times stronger and more soluble in fat (21), which in addition to giving it a higher analgesic power, makes it an attractive molecule for application in different directions (24). Buprenorphine has been studied by numerous researchers to control postoperative pain (31-25). Also, due to the easy administration of this drug, its use for analgesia after surgery is important and significant (34-32)

Ketorolac:

Ketorolac is a non-steroidal anti-inflammatory drug with analgesic properties that inhibits both lipoxygenase and cyclooxygenase enzymes. It is available orally and by injection. Prophylaxis with preoperative analgesia can reduce the need for intraoperative analgesia and reduce postoperative pain (35-38). The analgesic effects of nonsteroidal anti-inflammatory drugs (NSAIDs) are due to the inhibition of prostaglandins, which in turn reduce vasodilation, increase their permeability, have diuretic effects on the kidneys, increase pelvic pressure, and increase the urinary system (39). No complications of respiratory depression, no dependence, and longer sedative effects are the most important advantages of ketorolac ampoules over opioids (40-42).

Morphine:

Opioid-based medications, especially morphine, are among the drugs of choice that have the ability to reduce and inhibit pain transmission. The analgesic effects of narcotics are due to their ability to inhibit the transmission of nociceptive information from the posterior horn of the spinal cord and also their ability to activate pain control mechanisms in higher nerve centers (43). Morphine has low-fat solubility and its penetration into and out of the brain is slower than other drugs and is mainly metabolized in the liver, but the kidneys play a key role in extrahepatic metabolism (44). Morphine is used as an analgesic in heart diseases, sickle cell disease, postoperative pain, and severe chronic pain (45-47).

Pregabalin:

Pregabalin is a synthetic gamma-aminobutyric acid analog that was originally used as an anticonvulsant. It reduces the entry of calcium into the terminals of the central and peripheral nervous systems and lowers levels of basal levels, glutamate, and noradrenaline, which play a major role in causing pain. Today, pregabalin is used to reduce neuropathic and even inflammatory pain, tissue irritation, neurology, and fibromyalgia (48-51). The function of pregabalin on acute postoperative pain is to reduce the stimulation of posterior spinal cord neurons due to tissue damage (52-53).

Gabapentin:

Gabapentin is a gamma aminobutyric acid (GABA) analogue. The mechanism of their action is the pre-synaptic attachment to the (α2-δ) part of voltage-dependent calcium channels, which are abundant in the central and peripheral nervous systems. The effect of these two drugs on calcium channels reduces the secretion of excitatory neurotransmitters such as glutamate, norepinephrine, substance P, and calcitonin gene-dependent peptide (54-55). In addition to its analgesic effect, gabapentin reduces the need for opioids and reduces their dosage, as well as their side effects (56-57).

Tramadol:

Tramadol is a synthetic opioid from the amino cyclohexane group. It is a central analgesic with weak opioid agonist properties and its effects on serotonergic and noradrenergic neurotransmissions (58). Tramadol is an analog of 4-phenylpiperidine codeine and acts by acting on hair receptors and the serotonergic system (59). Tramadol is used to treat moderate to severe pain (60-61).

Magnesium sulfate:

The role of magnesium sulfate in causing analgesia is known for its effect in inhibiting NMDA receptors. NMDA receptors play an important role in transmitting pain sensation in the central and peripheral nervous system and causing acute pain in the body. Therefore, magnesium sulfate is also effective in relieving the feeling of severe pain after surgery. Magnesium sulfate acts as a calcium channel blocker and NMDA receptor antagonist. When the magnesium ions are separated from the NMDA receptors, the pain sensation process begins. After major surgery, with the onset of acute pain in the patient, clinical use of magnesium can reduce postoperative pain by blocking the central sensation of pain by blocking NMDA receptors (62).

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Dexmedetomidine:

Dexmedetomidine is a specific alpha-two agonist. Dexmedetomidine provides properties such as analgesia, sedation, and anti-anxiety effects without respiratory depression (63). This drug has hypnotic and analgesic effects (64). By acting on these receptors in the central nervous system, dexmedetomidine inhibits the release of norepinephrine through the function of G proteins, thus inducing hypnotic and analgesic effects in a dose-dependent manner (65). Potassium channels play an important role in the analgesic mechanism of alpha 2 adrenergic receptor agonists (66). The results of studies showed that BK potassium channels are associated with pain (67-69). A randomized trial have shown its benefits and effectiveness in reducing pain in patients undergoing orthopedic surgery (70).

Fentanyl:

Fentanyl is the most common short-acting drug used intrathecal in combination with local anesthetics. Fentanyl has synergistic effects with local anesthetics and improves postoperative analgesia (71)

Sufentanil:

Sufentanil is a strong synthetic sedative and analgesic drug that is 5 to 10 times stronger than fentanyl and 500 times stronger than morphine, which can be used for analgesia alone or in combination with other drugs orally, intravenously, intramuscularly and also is being used intrathecal and intranasal (72). Numerous studies have shown the analgesic effects of sufentanil in reducing pain in patients undergoing orthopedic surgery (73-74).

Ketamine:

Ketamine is an anesthetic drug used for anesthesia, sedation and analgesia and with the antagonistic effect of NMDA that causes the reversal of central nerve sensitivity to painful stimuli and reduces pain after surgery (75).

Methadone:

Methadone is one of the drugs of choice for drugs that have the ability to reduce and inhibit pain transmission. The analgesic effects of opioids are due to their ability to inhibit the transmission of nociceptive stimuli from the posterior horn of the spinal cord as well as their ability to activate pain control mechanisms in higher nerve centers (76). The main use of methadone is in the prevention of withdrawal symptoms and it is also used in the treatment of chronic pain (77).

Piroxicam:

Piroxicam is a potent inhibitor of cyclooxygenase. This enzyme converts arachidonic acid to prostaglandins. Piroxicam reduces the production of prostaglandins by inhibiting cyclooxygenase Cox-1 and Cox-2 and thus shows its analgesic and anti-inflammatory effects (78).

Memantine:

Memantine is a low to moderate NMDA antagonist with a direct affinity for this receptor and a direct effect on the location of phencyclidine on the NMDA receptor channel. The use of memantine in the treatment of chronic pain is relatively new. The main mechanism of action is the flow block through the NMDA receptor channels (79).

Nitroglycerin:

Nitroglycerin is metabolized to NO in the cell and increases the concentration of cyclic guanosine monophosphate, which regulates pain in the central nervous system. In addition, NO exerts its analgesic effects by inhibiting hyperalgesia and its anti-inflammatory effects by inhibiting neurogenic inflammation. NO also leads to analgesia through direct stimulation of peripheral fibers. In addition, painful stimulation increases the production of free radicals. Antioxidants such as nitroglycerin can reduce the need for analgesics by inhibiting the production of free radicals (80-84).

Conclusion:

Several studies reviewed our study claiming that interventions with different drugs can reduce pain in patients undergoing orthopedic surgery. This suggests that the routine use of these drugs in these patients should be considered and that multiple drug options may be used to control pain in patients undergoing orthopedic surgery. However, the choice of these drugs is based on the patient's condition and the decision of the anesthesiologist. Future meta-analytic studies can determine the best possible intervention.

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