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USING DEXMEDETOMIDINE FOR THE RELIEF OF PAIN IN THE POSTOPERATIVE PERIOD AFTER SPINAL INJURY

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Pain syndrome in spinal surgery is an urgent problem far from a final solution. After extensive surgical interventions on the spine, a pronounced postoperative pain syndrome is observed, comparable in intensity to pain after thoracic operations, limb amputations, and extensive interventions on the hip joint**.** Expansion of knowledge about the pathogenesis of pain formation has led to a revival of interest in the use of drugs such as antidepressants, glucocorticoids, magnesium sulfate, dexmedetomidine for postoperative analgesia. However, data on the effectiveness of their use in spinal trauma surgery are extremely limited. We used dexmedetomidine to optimize perioperative pain management in patients with spinal cord injuries.The study was conducted in the surgical clinic of the AMU. The study included 59 patients who underwent decompression and fixation of the spine at the lumbar and thoracic levels due to spinal cord injury. The patients were divided into 2 groups. In patients of group I, surgical interventions were performed only under general anesthesia, and in group II, dexmedetomidine was included in the general anesthesia regimen. The use of multimodal analgesia protocols, including dexmedetomidine and general anesthesia after decompression of neural structures and fixation of the spine in patients with spinal cord injury, provides adequate pain control throughout the entire postoperative period. In patients operated on for spinal canal stenosis, the use of this scheme does not provide adequate pain control only during the first two hours after surgery.

Key words: postoperative spinal injuries, dexmedetomidine, multimodal analgesia.

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ЗАСТОСУВАННЯ ДЕКСМЕДЕТОМІДІНА ДЛЯ КУПУВАННЯ БОЛЮ В ПІСЛЯОПЕРАЦІЙНОМУ ПЕРІОДІ ПІСЛЯ ТРАВМИ ХРЕБТА

Больовий синдром у хірургії хребта є актуальною проблемою далекою від остаточного вирішення. Після проведення великих хірургічних втручань на хребті спостерігається виражений післяопераційний больовий синдром, який можна порівняти за інтенсивністю з болем після торакальних операцій, ампутацій кінцівок, великих втручань на тазостегновому суглобі. Розширення знань про патогенез формування болю призвело до відродження інтересу до застосування для післяопераційної аналгезії таких препаратів: антидепресантів, глюкокортикоїдів, сульфату магнію, дексмедетомідину. Однак дані про ефективність їх застосування в хірургії травми хребта вкрай обмежені. Ми використовували дексмедетомідин для оптимізації періопераційного знеболювання у пацієнтів із травмами хребта. Дослідження було проведено у хірургічній клініці АМУ. У дослідження було включено 59 хворих, яким проводилася декомпресія та фіксація хребта на поперековому та грудному рівні з приводу хребетно-спинномозкової травми. Хворі були поділені на 2 групи. У хворих I групи оперативні втручання проводилися лише під загальною анестезією, а у II групі до схеми загальної анестезії включали дексмедетомідин. Використання протоколів мультимодального знеболювання, що включають дексмедетомідин та загальну анестезію після декомпресії невральних структур та фіксації хребта у пацієнтів з хребетно-спинномозковою травмою, забезпечує адекватний контроль болю протягом усього післяопераційного періоду.

Ключові слова: післяопераційні травми хребта, дексмедетомідин, мультимодальне знеболення.

Pain syndrome in spinal surgery is an urgent problem far from a final solution. After extensive surgical interventions on the spine, a pronounced postoperative pain syndrome is observed, comparable in intensity to pain after thoracic operations, limb amputations, and extensive interventions on the hip joint. An analysis of numerous literature sources shows that the administration of analgesics “on demand” does not provide an adequate level of analgesia for 56 days after decompression of neural structures and fixation of the spine at the lumbar or thoracic levels in patients with spinal canal stenosis or spinal cord injury [6, 15]. This problem can be solved by using a preventive multimodal analgesia regimen including non-steroidal anti-inflammatory drugs and dexmedetomidine.

It should be recognized that, despite a significant improvement in the understanding of the pathophysiological mechanisms of pain, the emergence of new analgesics and technologies for their delivery, modern dosage forms, as well as the development of minimally invasive surgery, the quality of treatment of postoperative pain syndromes remains insufficiently satisfactory. Inadequate postoperative analgesia after surgical interventions on the spine leads to an increase in the number of cardiovascular and pulmonary complications, changes in the psyche, and difficulty in early rehabilitation of patients. When conducting pain relief for patients with diseases and spinal injuries, at present, the specifics of operations, individual pain threshold and pain tolerance, socio-demographic and psychological characteristics of the patient are often not taken into account, the multimodal approach to analgesia and the concept of rapid recovery surgery are not fully implemented in practice.

After decompression of neural structures and fixation of the spine, as well as after traumatic injuries of the spine, a number of patients continue to experience pain in intensity comparable or even greater than that felt before surgery. Also, pain sensations, changing their nature and intensity, can persist for a very long time, which leads to structural changes in the central nervous system, the formation of a chronic pain syndrome. The reasons for the development of such a syndrome of "failed spinal surgery" may be errors in preoperative diagnosis, iatrogenic damage to neural structures during surgery, as well as insufficient pain relief and rehabilitation measures, and the progression of degenerative disease of the spine. The result of prolonged pain impulse after extensive operations on the spine, in which sometimes unintentional damage to neural structures also occurs, may be the development of central sensitization, that is, an extreme increase in the excitability of the neurons of the posterior horns of the spinal cord. This leads to the appearance of allodynia (the occurrence of pain when exposed to non-painful stimuli) and hyperalgesia (intense pain with mild nociceptive stimulation) in the surgical area and surrounding tissues [2]. As a result of the ongoing recovery process, or (more often) the restructuring of neuronal connections in the central nervous system, chronic postoperative pain can develop, which is usually defined as the persistence of pain for three or more months after surgery for a spinal injury [1]. The urgency of the problem is great, as the number of spinal surgeries in the world is increasing every year. At the same time, the frequency of chronic pain formation in patients after such operations does not change significantly and ranges from 20 to 60 %.

Thus, taking into account the foregoing, it should be noted that there is an urgent need to improve perioperative anesthesia in patients operated on for spinal injuries. Expansion of knowledge about the pathogenesis of pain formation has led to a revival of interest in the use of drugs such as antidepressants, glucocorticoids, magnesium sulfate, dexmedetomidine for postoperative analgesia. However, data on the effectiveness of their use in spinal trauma surgery are extremely limited.

The purpose of the study was to research the use of dexmedetomidine to optimize perioperative pain management in patients with spinal injuries.

Materials and methods. The study was conducted in the surgical clinic of the AMU. The study included 59 patients who underwent decompression and fixation of the spine at the lumbar and thoracic levels due to spinal cord injury. Written informed consent was obtained from all patients participating in the study. Inclusion criteria were age 15–75 and American Society of Anesthesiologists (ASA) class I–II physical condition. The exclusion criteria were as follows: arrhythmia, heart failure, and severe liver or kidney disease.

After the patient was admitted to the operating room, a standard electrocardiographic monitor and non-invasive devices for measuring blood pressure and peripheral oxygen saturation were connected to the patient. All patients underwent general anesthesia. The patients were divided into 2 groups. In patients of group I, surgical interventions were performed only under general anesthesia, and in group II, dexmedetomidine was included in the general anesthesia regimen. In group II, patients received decmedetomidine at a dose of 1 μg/kg for 10 minutes (loading dose), and then 0.2–0.7 μg/kg/hour for a maintenance dose. Hypotension (median blood pressure reduction greater than 20 % of baseline) was treated with intravenous phenylephrine 100 μg, and bradycardia (heart rate less than 50 bpm) with atropine 0.5 mg.

Postoperative supplemental analgesia was standardized. Pain severity was determined using a numerical rating scale (VAS) from 0 (no pain) to 10 (worst pain). If the patient reported pain in the surgical area as more than 3, then an intravenous mixture was started, which included 50 μg of fentanyl in 50 ml of 0.9 % saline at a rate of 1 ml/hour with a bolus dose of 1 ml. The time to the first complaint of pain was recorded, and patients with a VAS score of more than 3 were administered the narcotic analgesic trimeperidine 20 mg. Once oral administration became tolerable, all patients received oral ketorolac every 6 hours. Despite this protocol for the administration of analgesics, if the patient complained of more pain, such as a VAS pain score of more than 4 points, trimeperidine was administered intravenously at a dose of 20 mg. Pain quality was assessed 8, 16 and 24 hours after surgery and included in the table. When postoperative nausea and vomiting appeared, metoclopramide 10 mg was administered intravenously to patients.

Results of the study and their discussion. 59 patients were divided into 2 study groups. Patient characteristics were comparable between the two groups. The postoperative cumulative dose of intravenous trimeperidine was significantly lower in the group of patients in whom dexmedetomidine was included in the anesthesia regimen (0.01 [0.01–8.0 mg]) than in the group without dexmedetomidine (10.3 [6.5–12.5 mg]) at 16 hours (median difference 7.83 [5.2–11.6 mg]) and at 24 hours 5.72 mg. Postoperative consumption of non-opioid analgesics was comparable between the two groups (p=0.542).

The time to first complaint of surgical pain was 556 minutes (492–863 minutes) in the dexmedetomidine group and 402 minutes in the non-dexmedetomidine group.

The incidence of common postoperative complications did not differ significantly between the two groups.

A key strategy for improving the management of persistent perioperative pain and reducing the patient's time in intensive care is provided by the inclusion of a multimodal approach to pain management and reduction in the use of opioids [3, 4]. Dexmedetomidine is an important component of a multimodal approach to pain management. A large number of studies have demonstrated the superiority of dexmedetomidine over other drugs in the perioperative setting [7, 9]. Dexmedetomidine has a high selectivity for α2:α1 at a ratio of 1620:1 [10], a potent α2-adrenergic receptor agonist, but its molecular mechanism of action is not completely clear. This is likely due to the activation of inhibitory G proteins and the cGMP nitric oxide pathway. Dexmedetomidine has an agonistic effect after binding to G proteins, which have three subtypes (α-2A, α-2B, α-2C). The α-2A and α-2C receptors are mainly found in the CNS, while the α-2B receptors are found on smooth vessels. Dexmedetomidine selectively binds to α-2A receptors through all three receptors, which inhibits adenylcyclase, reducing adenosine monophosphate levels and leading to hyperpolarization of noradrenergic neurons. This leads to the suppression of nerve conduction by inhibiting the supply of calcium necessary for the fusion of neurotransmitter vesicles. This negative feedback loop results in an attenuated sympathetic response and a decrease in both heart rate and blood pressure [11]. By acting on α2 receptors, dexmedetomidine causes inhibition of noradrenaline release from presynaptic neurons, causes centrally induced sedation via α2 receptors in the locus coeruleus, and centrally mediated pain modification via the posterior horns [11].

Numerous meta-analyses demonstrate the efficacy of dexmedetomidine in the control of postoperative pain [8]. In a 2012 meta-analysis, 1792 patients experienced a 30 % reduction in opioid consumption 24 hours after surgery [12]. Dexmedetomidine has a stronger analgesic effect than clonidine and acetaminophen, but weaker than ketamine or non-steroidal anti-inflammatory drugs [15]. In a 2015 meta-analysis, although dexmedetomidine reduced pain intensity, opioid consumption, and postoperative nausea and vomiting, it had no effect on recovery time [12]. Notably, a Cochrane review of the use of dexmedetomidine in abdominal surgery had too many diverse data for a meta-analysis [12]. Dexmedetomidine is an effective analgesic for pediatric patients and has the added benefit of reducing anxiety and resulting agitation [10, 11, 13]. There is variability in the timing of administration of dexmedetomidine, with no consensus on the optimal timing of administration. Preoperative administration of a single dose of 1 μg/kg dexmedetomidine 10 minutes prior to induction of anesthesia has been shown to reduce postoperative narcotic analgesic use [12, 14]. Numerous studies demonstrate the efficacy of intraoperative dexmedetomidine and have also been shown to be superior to intraoperative remifentanil in providing better postoperative pain relief with fewer side effects [15]. In two recent meta-analyses, patients treated with postoperative dexmedetomidine infusion and patient-controlled intravenous opioid analgesia had lower rates of postoperative pain and lower opioid consumption in the first 24 hours postoperatively, with a reduction in nausea and vomiting, compared with patients receiving only opioids.

Our study at AMU showed that patients who received dexmedetomidine during spinal injury surgery needed significantly less opioids during the first 24 hours after surgery, and the time to first pain in the area of the operation was increased. After the analgesic wears off, patients undergoing surgery after a spinal injury experience moderate to severe pain for several days, and inadequate pain relief can lead to negative consequences such as worsening lung function, cardiac overload, and vascular resistance, which in turn, can cause ventricular arrhythmias or serious heart problems. Clinically, intravenous opioids are the first-line drugs used to control postoperative pain, but they may be associated with various side effects such as nausea and vomiting.

Recently, many studies have shown that intravenous administration of dexmedetomidine during surgery significantly reduces postoperative opioid consumption [14, 15]. The analgesic effects of dexmedetomidine are not fully understood, but it may bind to α2 receptors in the central system, probably the locus coeruleus and spinal cord, blocking pain signal propagation and inducing analgesic effects. Studies show that α2-adrenergic receptors of the blue spot mediated the antinociceptive effect after injection of dexmedetomidine in rats [12, 15]. Consistent with this result, we found that intravenous dexmedetomidine sedation significantly reduced postoperative opioid consumption and prolonged the duration of pain relief. Thus, dexmedetomidine may provide effective postoperative pain control. In our study, we found that rapid induction (within 10 minutes) of the initial loading dose of dexmedetomidine was associated with a higher rate of bradycardia than infusion over 20 minutes. In addition, although dexmedetomidine-induced bradycardia is transient and can be easily managed with anticholinergic drugs.

But patients taking drugs that can cause hemodynamic instability should be carefully examined before administering dexmedetomidine.

Based on the above, the following conclusion can be drawn:

Accelerated recovery after surgery is an approach to patient care aimed at optimizing the postoperative period. This includes the implementation of protocols designed to reduce postoperative complications, patient discomfort, and length of hospital stay.

Dexmedetomidine, a highly selective α2-adrenergic agonist, has become a valuable addition to the multimodal approach to anesthesia. Its sedative, anxiolytic and analgesic properties are useful in potentiating postoperative analgesia. These features make it a useful addition to the anesthesia protocol, especially in the context of accelerated recovery after spinal injury surgery.

Conclusions

1. Intravenous administration of dexmedetomidine significantly reduces postoperative opioid use during the first 24 hours after surgery and increases the duration of postoperative pain relief in patients undergoing surgery for spinal injury.

2. The use of multimodal analgesia protocols, including dexmedetomidine and general anesthesia after decompression of neural structures and fixation of the spine in patients with spinal cord injury, provides adequate pain control throughout the entire postoperative period. In patients operated on for spinal canal stenosis, the use of this scheme does not provide adequate pain control only during the first two hours after surgery.

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