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Evaluation of Magnesium Sulphate in the Prevention of Postoperative Pain Syndrome

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Abstract: For chronic postoperative pain syndrome, the neuropathic component is a major component. The use of magnesium sulfate for the prevention of pain syndrome is theoretically based on its ability to block N-methyl-D-aspartate receptors in the spinal cord. Our aim was to evaluate the effect of magnesium sulphate as an adjuvant analgesic in the prevention of postoperative and chronic pain syndrome in patients after surgery using combined general anaesthesia.

Keywords: Pain syndrome, magnesium sulphate, analgesics, chronic pain syndrome.

Introduction: Pain syndrome after surgery remains an important problem in anaesthesiology [1]. The main mechanisms leading to acute and chronic pain syndrome are central and peripheral sensitisation and neuronal hyperexcitability that develop after surgery. Controlling pain syndrome immediately after surgery optimises the recovery period by enhancing daily activities, and reduces the incidence of chronic postoperative pain syndrome (CPPS) and improves patients' quality of life. The incidence of CPPS ranges from 10 to 65%, and some reports suggest up to 80%, depending on the type of surgery undergone [2, 3]. The neuropathic component is the main component of chronic pain formation, but it is also important for the perception of acute pain. A large number of studies have focused on the intraoperative use of adjuvants such as lidocaine, magnesium sulphate or ketamine to prevent acute and chronic pain syndrome, including herniorrhaphy and cholecystectomy [4, 5]. The use of magnesium sulphate for the prevention of pain syndrome is theoretically based on its ability to block N-methyl-D-aspartate (NMDA) receptors in the spinal cord, which alters pain processing and reduces the induction and maintenance of central sensitisation. However, its practical efficacy remains a matter of debate.

The aim of the study was to evaluate the effect of magnesium sulphate as an adjuvant analgesic agent in the prevention of postoperative and chronic pain syndrome in patients after surgery using combined general anaesthesia.

Material and methods 152 patients were included in the study, 112 patients completely completed all study procedures (Table 1). Inclusion criteria: age from 19 to 81 years, physiological status according to ASA II-III scale, scheduled surgical intervention - laparoscopic cholecystectomy or hernioplasty. Exclusion criteria: presence of pain syndrome of any etiology before surgery, bradycardia, AV-blockade, myasthenia gravis, renal failure. Voluntary informed consent was obtained from each study participant for the use of personal data for research purposes. Patients who met the inclusion and exclusion criteria were allocated by the method of stratified randomisation into 2 groups: with intraoperative infusion of magnesium sulphate

(magnesium sulphate group, n=37) and with infusion of 0.9% sodium chloride solution (control group, n=75). Intraoperative magnesium sulfate infusion involved intravenous administration of the drug at a dose of 40 mg per 1 kg body weight per hour from the start of induction and 20 mg per 1 kg body weight per hour throughout the operation. Patients in the control group were administered a 0.9% sodium chloride solution 10 ml/h throughout the operation. The drugs were administered using a perfuser. After induction of anaesthesia, for which propofol 2 mg per 1 kg body weight and fentanyl 1-2 mcg per 1 kg body weight were used, tracheal intubation was performed. Anaesthesia was maintained by inhalation of isoflurane at a concentration of 0.8-1.0 MAC, and analgesia was maintained by intravenous injection of fentanyl 3-4 mg per 1 kg body weight per hour. Myorelaxation was maintained by administration of pipecuronium bromide - loading dose 0.03 mg per 1 kg body weight, maintenance dose 0.01 mg per 1 kg body weight every 20-40 min. On the 1st day after surgery for preventive analgesia all patients were administered ketorolac 30 mg intramuscularly immediately after the end of the intervention, regardless of the presence or absence of pain syndrome. Repeated administration was performed routinely in 6 h and 12 h after the end of the operation. In case of persisting pain syndrome, tramadol 100 mg intramuscularly was administered. On the 2nd and 3rd day ketorolac was used for analgesia at the patient's request only in the presence of pain. The Brief pain inventory (BPI) was chosen to assess the pain syndrome in the postoperative period on the 1st and 3rd day. The questionnaire is one of the most widely used tools for clinical assessment of pain syndrome. It allows patients to assess the severity of their pain and the extent to which it interferes with their daily life. The questionnaire was originally developed for oncology practice, but it has since been shown in a wide range of clinical studies to be a universal methodology for the study of pain syndrome of any origin and is now a recognised standard. The consensus consensus on the study of chronic pain recommended the use of BPI in all studies devoted to this problem, as well as in the assessment of physical activity and pain (IMMPACT, D.C. Turk et al., 2008) [6,7]. "Brief Pain Questionnaire" allows to assess the sensory and reactive influence of pain on the patient's condition. It contains 13 questions in 2 groups that determine the strength of pain (sensory component): worst pain, mild pain, average pain and pain at the time of interview, as well as the impact of pain on daily activity. The latter, in turn, includes two sub-dimensions of pain - the affective component: attitude towards people, enjoyment of life, mood, and the active component: work, motor activity, general activity and sleep. Thus, the use of the questionnaire allows us to assess the emotional component of the pain syndrome. Each parameter is assessed on a 10-point scale. In addition, the administration of analgesic drugs and the effectiveness of pain relief afterwards (%) are taken into account. To analyse the data obtained from the Brief Pain Questionnaire, in this study, pain index was calculated as the ratio of the sum of "pain impact" score to the pain relief score (%) after administration of non-steroidal anti-inflammatory drugs. Pain was assessed at 3, 6, and 12 months after surgery using the McGill questionnaire developed by Melzack and Casey. The questionnaire includes 3 pain measurement scales: sensory-discriminative (characterisation of pain sensation), motivational-affective (emotional) and cognitive-evaluative (pain intensity). The first scale includes word groups 1-10, 17-19 of the questionnaire and describes temporal and spatial characteristics of pain, point pressure, traction pressure, sensory variety, temperature sensitivity and other properties. The motivational-affective (emotional) scale includes word groups 11-15, 20 of the questionnaire and describes tension, fear, and autonomic reactions. The cognitive-evaluative scale includes word groups 16, 20 of the pain questionnaire. The descriptor words are arranged in order of increasing pain intensity. The patient should select those descriptors that correspond to their sensations. In the study, the McGill questionnaire data were analysed according to two indicators: the index of the number of selected descriptors - the total number of words that the patient indicated, and the overall pain ranking index - the sum of the numbers of selected words. Past 4.0, Sytel Studio software was used for statistical processing of the data. Pairwise comparisons of the pain index according to the Brief Pain Questionnaire were performed using the Wilcoxon criterion, statistical analysis of the McGill questionnaire results using the Fisher and Mann-Whitney tests.

Results The study randomised 152 people, of whom 123 people completed the study 3 months after surgery and 112 people completed the study 6 months after surgery. Data analysis of the "Brief Pain Questionnaire" The mean values of pain index in the groups are presented in Table 2. Statistical analysis did not reveal statistically significant differences between the groups by this index neither on the 1st nor on the 3rd day. The average level of pain syndrome on the 1st day was 3.5±0.5, on the 3rd day - 1.8±0.3. Thus, the use of magnesium sulphate as an adjuvant does not affect the development of acute postoperative pain.

Analysis of the McGill questionnaire data The index of the number of selected descriptors. In 3 months after the operation according to the results of the analysis of the index of the number of selected descriptors the chronic pain syndrome was detected in 13% of patients in the magnesium sulphate group and in 17,5% - in the control group (p=0,3). After 6 months the proportion of patients with signs of chronic pain in both groups slightly decreased and was 12.4% in the magnesium sulphate group and 15.7% in the control group (p=0.09). It should be noted that there was no statistically significant difference between the indices both after 3 and 6 months, i.e. the development of chronic pain syndrome did not depend on intraoperative administration of magnesium sulphate. General rank index of pain. The analysis of the total rank index of pain by categories allows us to assess the structure of chronic pain syndrome. According to the sensory scale, which gives a description of sensations associated with pain, 3 months after surgery, most patients did not experience pain. From the clinical point of view, a high level of pain (≥7 points) is of particular interest, which indicates the need for immediate resolution of the problem. The frequency of severe pain in patients in the control group was 10.2%, in the magnesium sulphate group - 4.3% (p=0.11). At 6 months after surgery, this indicator in the control group was 3.9%, in the magnesium sulphate group - 8.7%, p=0.43 . There was no statistically significant difference between the indices in both groups, which means that the total rank index on the sensory scale at 3 and 6 months after surgery was almost the same. The affective scale allows us to assess the emotional component of the pain syndrome. At 3 months after surgery, the incidence of chronic postoperative pain was 25.9% in the control group and 17.4% in the magnesium sulphate group, (p=0.68). At the same time the level of pain was insignificant - 1-3 points, more than 4 points were not observed in patients of magnesium sulphate group, and in the control group such level was noted only by 2.8% of patients. However, this did not constitute a statistically significant difference . At 6 months after surgery, according to emotional characteristics, the chronic pain syndrome was practically not detected, it made up an insignificant proportion, as well as the level of intensity: 9.1% of patients in the control group at insignificant intensity, 0% in the magnesium sulphate group at insignificant intensity and 4.3 - at moderate intensity (p=0.2).). The minor severity of chronic pain syndrome had no effect on the emotional component either 3 or 6 months after surgery. When analysing the evaluative scale, which gives an indication of how the patient himself assesses the impact of pain syndrome on quality of life, at 3 months after surgery, most patients did not report any impact. However, there were slightly fewer such patients in the control group, 72.2%, than in the magnesium sulphate group. In addition, a significantly smaller proportion of patients in the magnesium sulphate group assessed the impact of pain syndrome on the quality of life at its insignificant level, and none of this group had more severe pain. At the same time, the difference in this indicator in both groups was statistically significant, p=0.022 .At 6 months after surgery, according to the evaluative scale, this indicator in the control group was 11.7%, in the magnesium sulphate group - 4.3%, (p=0.45) . Thus, despite the relatively large difference in all categories of indicators in both the early and late postoperative period, the study did not reveal statistically significant differences between the groups. The exception was the evaluation of chronic pain syndrome using the evaluative scale. The presence of a statistically significant difference between the groups on this scale reflects the actual effect of magnesium sulphate in preventing the development of chronic pain syndrome, as the obtained indicators represent an integral assessment of the patient's quality of life. Discussion Currently, the main attention of researchers in the search for adjuvants for the treatment and prevention of pain syndrome is

focused on NMDA receptors, which are involved in the formation of sensitisation, expansion of receptive fields, neuroplastic changes in the central nervous system and the phenomenon of "excitement". Activation of NMDA receptors by glutamate is the first step in initiating the process of central sensitisation, and blocking this process, including magnesium, may offer promising perspectives in the treatment and prevention of pain syndrome. Some studies have shown the role of magnesium in peripheral sensitisation and the formation of visceral pain . These findings explain the interest in blockers of such receptors in terms of treatment and prevention of postoperative pain. Early studies noted that magnesium sulfate acts as a blocker of NMDA calcium channels, reduces neuropathic pain, increases analgesia, and reduces tolerance to morphine. Moreover, hypomagnesaemia leads to hyperalgesia, which can be relieved by the use of NMDA receptor antagonists, possibly serving as one explanation for magnesium's effects in the postoperative period. In addition, magnesium is a weak alpha-adrenoreceptor antagonist and suppresses neuroendocrine secretion. Magnesium deficiency can provoke hyperalgesia, which can be stopped by NMDA antagonists. Attempts to use magnesium for the prevention and treatment of pain syndrome have been made for quite a long time. Some studies show pronounced efficacy, while others cannot confirm this result. Thus, according to a meta-analysis performed by G.S. De Oliveira et al. the use of magnesium leads to a decrease in postoperative narcotic consumption and pain syndrome in the first 4 hours after surgery, which means that the drug works, but this effect is not always achieved and not in all patients. Another meta-analysis based on 25 studies showed that magnesium slightly reduces pain at rest and during movement, reduces morphine consumption by 24.4% in the first 24 h after surgery. In a meta-analysis of 22 studies, the effect of magnesium on morphine consumption was noted, but the effect on pain in the first 20-24 h on a visual analogue scale was minimal. The effect of magnesium on chronic pain syndrome is more controversial. A number of studies on chronic pain syndrome, including several meta-analyses, have evaluated the use of magnesium in migraine, and the results cannot be described as successful. The use of magnesium in complex regional pain syndrome and in various variants of neuropathic pain has also not shown high long-term efficacy. It should be noted that the studies used oral administration of magnesium and plasma magnesium concentration was not measured. Was an effective concentration of the drug achieved and could this have affected the outcome?

Answers may be obtained by further research. The best results of chronic postoperative pain syndrome relief were obtained by T.K. Oh et al. Oh et al.: after knee arthroplasty against the background of intraoperative magnesium infusion, a 62% reduction in postoperative pain syndrome was observed. In the work of V. Ghezel-Ahmadi et al. patients who received magnesium sulphate during surgery, within 24 h after surgery noted a lower level of postoperative pain and less consumption of narcotic analgesics. The use of prolonged magnesium infusion for 48 h has an effect on the early postoperative period, but does not affect the risk of developing chronic pain syndrome pressurises neuroendocrine secretion. Magnesium deficiency can provoke hyperalgesia, which can be stopped by NMDA antagonists. Attempts to use magnesium for the prevention and treatment of pain syndrome have been made for quite a long time. Some studies show pronounced efficacy, while others cannot confirm this result. Thus, according to a meta-analysis performed by G.S. De Oliveira et al. the use of magnesium leads to a decrease in postoperative narcotic consumption and pain syndrome in the first 4 hours after surgery, which means that the drug works, but this effect is not always achieved and not in all patients. Another meta-analysis based on 25 studies showed that magnesium slightly reduces pain at rest and during movement, reduces morphine consumption by 24.4% in the first 24 h after surgery. In a meta-analysis of 22 studies, the effect of magnesium on morphine consumption was noted, but the effect on pain in the first 20-24 h on a visual analogue scale was minimal. The effect of magnesium on chronic pain syndrome is more controversial. A number of studies on chronic pain syndrome, including several meta-analyses, have evaluated the use of magnesium in migraine, and the results cannot be described as successful. The use of magnesium in complex regional pain syndrome and in various variants of neuropathic pain has also not

shown high long-term efficacy. It should be noted that the studies used oral administration of magnesium and plasma magnesium concentration was not measured. Was an effective concentration of the drug achieved and could this have affected the outcome? Further study may provide answers. The best results for the management of chronic postoperative pain syndrome were obtained by T.K. Oh et al.: after arthroplasty of the knee joint against the background of intraoperative infusion of magnesium, a 62% decrease in postoperative pain syndrome was observed . In the work of V. Ghezel-Ahmadi et al. patients who received magnesium sulphate during surgery, within 24 h after surgery noted a lower level of postoperative pain and less consumption of narcotic analgesics. The use of prolonged magnesium infusion for 48 h has an effect on the early postoperative period, but does not affect the risk of chronic pain syndrome by maintaining the effective concentration of the drug for a long time. In conclusion, the following should be noted. Magnesium is believed to cause blockade of NMDA receptors in the spinal cord. However, in the work of M. Mercieri et al. found that the concentration of magnesium in the liquor did not depend on the intravenous administration of the drug; this casts doubt on the generally accepted point of view on the mechanism of the analgesic effect of magnesium. Due to the fact that the presumed point of application of magnesium is the spinal cord, attempts were made to administer the drug epidurally, but there was no effect on chronic pain syndrome. Another potential mechanism is the inhibition of calcium current into the cell via potential-dependent channels, which is associated with the antinociceptive effect of the drug, and a statistically significant reduction in muscle fibre membrane excitability has been shown. From a prospective study point of view, it would be interesting to determine the magnesium concentration in serum and liquor at different doses and modes of administration.

Conclusion The main result of the study is the demonstration of the effect of intraoperative administration of magnesium sulphate on the incidence of acute pain in the postoperative period and chronic pain at 3, 6, 12 months after surgery. The study revealed a statistically significant difference between the groups on the evaluative scale 3 months after surgery, i.e. the use of magnesium sulphate causes a higher quality of life in patients in this group compared to patients in the control group.

List of references

1. Medvedeva LA, Zagorul'ko OI, Belov YuV. Chronic post-operative pain: current state of evidence and prevention. Anesteziologiya i reanimatologiya. 2017;62(4):305-309.
2. Haroutiunian S, Nikolajsen L, Finnerup NB, Jensen TS. The neuropathic component in persistent postsurgical pain: a systematic literature review. Pain. 2013;154(1):95-102.
3. Ovechkin AM. Chronic postoperative pain syndrome — «a pitfall» of modern surgery. Regionarnaya anesteziya i lechenie ostroy boli. 2016;10(1):5-18.
4. Efremenko IV, Ovechkin AM, Krasnoselskiy MYa. The analysis of effectiveness of isolated and combined prescription of non-opioid analgesics and adjutants during different surgery. Regionarnaya anesteziya i lechenie ostroy boli. 2015;9(3):19-28.
5. Lee JH, Yang WD, Han SY, Noh JI, Cho SH, Kim SH, Chae WS, Jin HC. Effect of epidural magnesium on the incidence of chronic postoperative pain after video-assisted thoracic surgery. Journal of Cardiothoracic and Vascular Anesthesia. 2012;26(6):1055-1059.
6. Lipnitski AL. Safety of magnesium sulphate introduction as adjuvant before general anesthesia. Anesteziologiya i reanimatologiya. 2015;60(4S):78. (In Russ.).