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A Multimodal Approach to Analgesia in Anorectal Surgery

Tatiana N. Garmanova[1,*], Daniil R. Markaryan[1], Ekaterina A. Kazachenko[1], Alexander M. Lukianov[1], Marya A. Kazachenko[2], Mikhail A. Agapov[1]

[1] *Medical Research Educational Center, Lomonosov Moscow State University, Moscow, Russian Federation*
[2] *I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation*

Aim: Evaluation of methods for pain prevention and pain reduction after anorectal surgery at all stages of treatment based on publications found in available databases.
Key points. Most anorectal diseases are benign and do not affect life expectancy, meanwhile about 40 % of the population suffer from it. Mainly anorectal disorders affect middle-aged people reducing their life quality. At the same time many articles aimed at studying only postoperative anesthesia. Two researchers independently searched for articles published in Medline, Scopus, Cochrane, Web of Science, E-library databases using keywords. A total of 54 publications were included. A multimodal approach should include the pain prevention during pre-, intra- and postoperative periods. Acetaminophen is recommended for pain reduction according to the dosing protocols. Acetaminophen combined with other systemic analgesics is advisable for patients with severe pain. The opioids use is justified only for moderate-severe postoperative pain. Metronidazole and lidocaine with nitroglycerin ointment/nifedipine/corticosteroids effectiveness has been proven for local postoperative anesthesia. Prophylactic use of antibiotics and bowel preparation do not reduce postoperative pain. Stool softeners are recommended for reducing postoperative pain severity. Additional local anesthesia such as nerve blockade or infiltration anesthesia is recommended for all patients. Modern minimally invasive treatment methods of hemorrhoid are associated with less severe postoperative pain.
Conclusion. The recommended scheme of multimodal anesthesia for patients after anorectal surgery is presented. Further studies are needed to evaluate preoperative anesthesia effectiveness, the feasibility of the perioperative flavonoids use, as well as comparisons of various minimally invasive treatment methods of anorectal diseases.
Keywords: anorectal surgery, hemorrhoidectomy, analgesics, surgery, pain syndrome, analgesia
Conflict of interest: the authors declare no conflict of interest.

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Мультимодальный подход к обезболиванию в хирургии аноректальной области

Т.Н. Гарманова[1,*], Д.Р. Маркарьян[1], Е.А. Казаченко[1], А.М. Лукьянов[1], М.А. Казаченко[2], М.А. Агапов[1]

[1] *Медицинский научно-образовательный центр ФГБОУ ВО «Московский государственный университет имени М.В. Ломоносова», Москва, Российская Федерация*

[2] *ФГАОУ ВО «Первый Московский государственный медицинский университет имени И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

Цель обзора: оценка методов профилактики и уменьшения болевого синдрома после оперативного лечения аноректальных заболеваний на всех этапах лечения на основе найденных в доступных базах данных публикаций.
Основные положения. Заболевания аноректальной области в большинстве являются доброкачественными и не влияют на продолжительность жизни, при этом их распространенность в популяции достигает 40 %, они в основном затрагивают людей трудоспособного возраста, снижая качество жизни. При этом в литературе в большинстве случаев уделяется внимание только послеоперационному обезболиванию. Независимо двумя исследователями был проведен поиск статей в базах данных Medline, Scopus, Cochrane, Web Of Science, E-library с 2000 по 2021 г. по ключевым словам. Всего в обзор было отобрано 54 публикации. Мультимодальный подход должен включать профилактику возникновения боли как на до- и интраоперационных этапах, так и в послеоперационном периоде. Ацетаминофен рекомендуется использовать в качестве стандартной терапии при послеоперационном болевом синдроме, а для пациентов с сильной болью целесообразно сочетать его с другими системными анальгетиками. Применение опиоидов оправдано при умеренной или сильной послеоперационной боли. Препараты с метронидазолом и лидокаином в комбинации с нитроглицериновой мазью, кортикостероидами или нифедипином продемонстрировали свою эффектив-

ность в снижении послеоперационной боли при местном применении. Профилактическое применение антибиотиков и предоперационная подготовка кишечника не влияют на послеоперационный болевой синдром и частоту послеоперационных осложнений. Применение средств для нормализации стула рекомендовано, так как снижает уровень послеоперационной боли. Дополнительное местное обезболивание в виде блокады нервов или инфильтрационной анестезии рекомендовано всем пациентам. Современные минимально инвазивные методы лечения геморроя ассоциированы с менее выраженным послеоперационным болевым синдромом.

Заключение. Представлена комплексная схема мультимодальной анальгезии для пациентов после аноректальных вмешательств. Дальнейшие исследования необходимы для оценки эффективности предоперационного обезболивания, целесообразности периоперационного применения флавоноидов, а также сравнений различных минимально инвазивных методик лечения аноректальных заболеваний.

Ключевые слова: аноректальная хирургия, геморроидэктомия, обезболивание, болевой синдром, хирургическое лечение, анальгетики

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Background

Speaking of the treatment of the benign anorectal diseases in the modern world both patients and coloproctologists are extremely interested in “one-day surgery, outpatient surgery or surgery without pain”. According to some reports, benign anorectal diseases affect more than 50 % of the US population over 50 years old, and 75 % of people have experienced any symptoms of these diseases at least once in their lives [1, 2]. Annually up to 6.5 thousand operations for hemorrhoidal disease are performed in Russia [3]. Being the most painful surgical intervention in anorectal surgery, hemorrhoidectomy remains the most effective and radical operation for hemorrhoidal disease. Prolonged severe pain after surgery significantly affects the patient’s dissatisfaction with the treatment. A large number of studies have been published describing the ways of reducing pain syndrome after surgical treatment of hemorrhoidal disease. Postoperative pain control remains problematic, 12 % of patients after anorectal surgery suffer from severe pain during the recovery period, and in 5 % of cases pain relief can hardly be achieved. In these situations the standard treatment regimen is unlikely to help [4, 5]. Due to relevance of pain relief issues the entire sections in international recommendations have appeared devoted to analgesia after surgical treatment of hemorrhoidal disease [6, 7]. One of the main tasks of anesthesia in surgery is to minimize the opioid consumption or total opioid rejection, as opioid analgesics have a large range of side effects, including stool retention, nausea, vomiting, urinary retention [6, 8]. Now there is a significant increase in opioid consumption in the USA and patients with chronic and acute postoperative pain, dependent on the opioid analgesics. At the same time, the mortality rate due to opioid overdoses is also increasing. [9–12]. The daily activity and life quality of patients can also suffer significantly [1, 13, 14].

The purpose of this literature review was a critical assessment of existing methods of pain prevention and pain reduction after hemorrhoidectomy during preoperative, intraoperative and postoperative periods, based on publications of the last two decades and the development of optimal analgesia scheme for treating pain after anorectal surgery based on the management of patients undergoing hemorrhoidectomy.

Materials and Methods

The search for publications in Russian and English was carried out in the Medline, Scopus, Skype, Web Of Science, E-library, Cochrane Collaboration, EMBASE databases from 2000 to 2022 using the following keywords: ”anesthesia in anorectal surgery”, ”pain syndrome”, ”hemorrhoidectomy and pain syndrome”, ”proctological diseases and anesthesia”, ”Analgesia for Hemorrhoidectomy”, ”Preemptive Analgesia for Hemorrhoidectomy”, ”pain management”, ”posthemorrhoidectomy pain”, ”pain management in proctology”, ”anorectal surgery”, ”obstetric injury”, ”postpartum complications”. The search was not limited to randomized controlled trials (RCTs), since some RCTs are not listed as randomized controlled trials in the databases. The search was carried out independently by two researchers. The main limitations of the selected studies included the small sample size and heterogeneity of the study endpoints. The manual search for relevant studies was also performed in the bibliographic lists of previously selected articles.

Randomized studies devoted to the evaluation of various anesthesia methods during hemorrhoidectomy in adults and providing with data on the pain level according to VAS, verbal or numerical evaluation scale were included in this review, as well as Russian-language recommendations and data from real clinical practice.

The quality of the studies was assessed according to the Oxford Centre for Evidence-based Medicine 2011 Levels of Evidence protocol [15]. Studies describing issues of prognostic factors were additionally evaluated using the QUIPS algorithm (Quality In Prognosis Studies tool) [16].

Summary information of the included studies was recorded in data tables. This information included pain assessment, additional use of analgesics, functional outcomes and complications. We assumed that the level of postoperative pain was evaluated at rest, unless otherwise indicated in the study.

A quantitative meta-analysis was not carried out, because of the high heterogeneity of the studies.

After the initial search, 464 studies were identified, totally 54 were included in the review. The most common reasons for exclusion were the following criteria: non-randomized study, repeated study, lack of information about the level of pain. For qualitative analysis, the studies were divided into three large groups: preoperative methods of preventing and reducing pain, intraoperative methods and postoperative features of patient management.

Features of pain syndrome in the anorectal area

The appearance of pain is associated with both the influence of endogenous and exogenous factors on the endings of peripheral nerves as well as pathological excitation of neurons in the central nervous system (CNS). The general state of a person and their psycho-emotional status also play a certain role. Nociceptors can be activated by various stimuli, including mechanical stimuli resulting from tissue puncture or incision, chemical stimuli resulting from the action of inflammatory mediators, and thermal stimuli resulting from tissue heating or cooling. Thus, any surgical intervention is always accompanied by a varying degree of pain syndrome [17].

1. Preoperative methods of prevention and reduction of postoperative pain syndrome

The intensity of pain after surgical interventions in the anal canal and perianal area depends on the spasm in the anal sphincter and puborectal muscles, type of anesthesia, wound healing rate, surgical technique, pre-, intra-, and postoperative pain management scheme, stool consistency, and subjective perception of the patient's condition [18, 19]. The target level of pain, at which the patient's quality of life is unaffected, is currently considered to be 3 or lower according to VAS scale [20].

During the preoperative stage, modifying the following factors may reduce the severity of postoperative pain:

1) Daily intake of dietary fiber or other supplements, adherence to a diet, and normalization of stool consistency (Bristol stool scale types 3 and 4) can reduce the severity of hemorrhoidal disease symptoms [1, 21]. Fiber increases the mass, volume, and softness of stool by retaining more water, thus facilitating passage and reducing mechanical irritation in the affected area (such as anal fissures or postoperative wounds) [22]. It has also been shown that normalizing stool consistency reduces the risk of postoperative bleeding and helps to reduce the severity of hemorrhoidal disease symptoms compared to the placebo group. Basing on these facts normalizing stool consistency and prescribing stool softeners are mandatory in the preoperative stage for all patients [1, 6, 21];

2) Preoperative bowel preparation using laxatives and the use of antibiotics did not show significant results in reducing pain in the postoperative period (evidence level A) [6, 23];

3) Patients with impaired stool evacuation feel 50 % more pain after surgery [24, 25], which should be taken into account when designing postoperative pain management protocols;

4) Preoperative analgesia aims to prevent pain during surgery and targets several points in the "pain cascade". The most commonly used non-opioid analgesics that suppress peripheral pain perception include NSAIDs, corticosteroids, and aspirin. Non-opioid drugs that suppress central sensitization include ketamine, acetaminophen, and some anticonvulsants, such as gabapentin. The preoperative use of even one type of analgesic helps to reduce pain level and the consumption of opioid analgesics after the intervention [4, 13, 14, 26, 27]. In a study by Van Backer et al. [4], preoperative analgesia (acetaminophen and gabapentin) combined with intraoperative ketamine and dexamethasone was found to be effective in reducing pain for the first 8 hours after surgery. Importantly, throughout the entire recovery period, the pain in both groups did not exceed 3 points according to VAS. Preoperative analgesia also significantly reduced the frequency of opioid analgesic prescriptions. Administering only 60 mg of intravenous ketorolac at the beginning of the operation significantly reduced the number of patients with significant pain syndrome on the day of the operation [28]. V. Poylin [13], along with co-authors, demonstrated the effectiveness of 1000 mg of gabapentin administered 1 day before surgery in reducing pain on days 1 and 7 after the intervention. Preoperative analgesic administration may be used to reduce the severity of postoperative pain syndrome (evidence level C).

There are no studies in the databases that examine the effectiveness of reducing postoperative pain with coxibs (selective COX-2 inhibitors) in the context of pre- and postoperative analgesia in anorectal surgery. However, there are results from large studies demonstrating a comparable analgesic effect to non-selective NSAIDs, as well as a lower incidence of complications such as gastrointestinal reactions, allergic reactions, and other side effects after surgical interventions [29].

2. Intraoperative prevention of pain syndrome

The choice of anesthesia in anorectal surgery is quite wide. It includes general anesthesia, epidural anesthesia, nerve blocks, and local infiltration anesthesia. The effectiveness of pudendal nerve block in reducing postoperative pain has been demonstrated in many studies. [6,30] Peripheral nerve blocks (sciatic nerve block, pudendal nerve block, perianal infiltration anesthesia) can be used as the main method of intraoperative pain relief; these techniques have a low frequency of complications, are technically simple, and provide analgesic effects for up to 12 hours after surgery. Of all possible methods of peripheral nerve blocks, the pudendal nerve block showed greater efficacy (Evidence A). Additional use of local anesthetic injections significantly reduces pain during the first 96 hours after surgery and reduces the total amount of administered analgesics [6].

In open hemorrhoidectomy with only local nerve block without general anesthesia, a correlation was observed with greater pain immediately after surgery, but on the 8th day ($p = 0.05$), the pain was significantly less. Comparing general anesthesia with preoperative perianal block, there was no significant difference in pain intensity between the groups [6].

In addition to the pharmacological reduction of pain, attention should also be paid to the surgical technique. Damage to a larger amount of tissue, especially with a large number of nerve endings, leads to increased swelling and inflammation, and consequently, to significant postoperative pain intensity [31, 32]. The use of minimally invasive techniques allows for a reduction in the amount of damaged tissue, which gives these techniques a significant advantage.

According to some studies, pain syndrome after closed hemorrhoidectomy is less intense during the first 24 hours. However, according to other studies, there is no significant difference in pain intensity between closed and open hemorrhoidectomy. Nevertheless, a higher frequency of postoperative complications, including those related to pain, is observed after closed technique [1, 6, 31] (evidence level B).

To minimize damage from heating when using power tools, bipolar devices can be used [31, 32]. When using an ultrasonic dissector compared to electrosurgery, pain syndrome and complication frequency were lower during the first 24 hours and at 7 days post-operation. When using bipolar coagulation, pain intensity was also significantly lower [1, 6, 31] (evidence level A).

The results of intraoperative sphincterotomy are contradictory [33, 34]. D. Giuseppe et al [34] found that a dosed sphincterotomy could reduce pain from 28.8 % to 10.45 % without a significant increase in incontinence frequency, but other studies still do not recommend this technique [1, 6]. Comparable analgesic effect can be achieved through medication-induced sphincter relaxation [6]. Sphincterotomy to reduce pain syndrome is not recommended due to the high risk of complications.

3. Postoperative possibilities of pain reduction

There are many protocols available for treating postoperative pain, including both medication and non-medication therapies. Sitting in warm water (40–42 degrees Celsius) baths can be classified as a non-medication therapy and is considered to promote relaxation of the internal sphincter, reducing the intensity of pain [1].

One of the most commonly prescribed analgesics are non-steroidal anti-inflammatory drugs (NSAIDs), which have a significant analgesic effect, allowing for a reduction in opioid analgesic doses by up to 18.3 % even with acute pain [8]. The combination of NSAIDs and paracetamol enables the dosage of both drugs to be reduced and provides a better effect [35].

Corticosteroids (CS) reduce the synthesis of inflammatory mediators, reducing edema, tissue infiltration, and inhibiting vascular dilatation. Therefore, using locally products containing glucocorticosteroids is effective in reducing pain [21]. A combination of CS and local anesthetics has been shown to significantly reduce the severity of symptoms and improve the quality of life for patients. Additionally, the effectiveness of the two drugs used simultaneously is greater due to the potentiation of their actions [21]. CS should not be used for more than 2–4 weeks due to the risk of complications such as skin atrophy, teleangiectasia, and delayed wound healing. The use of oral corticosteroids is also effective for pain relief caused by inflammation, especially when there are contraindications to the use of NSAIDs (pregnancy or lactation) [21].

Glycerol trinitrate (nitroglycerin) helps reduce spasm of the internal sphincter, leading to a reduction in pain and tension, and promotes wound

healing [1, 6, 19, 36–38]. According to some studies, a significant effect is achieved only on the 7th day after surgery [36]. However, the high and dose-dependent frequency of side effects, particularly headache (10–50 % of patients), limits its use [19, 36–38]. Nitroglycerin ointment, however, allows for a reduction in the dosage of narcotic analgesics, but increased consumption of NSAIDs and paracetamol due to the appearance of headaches [36]. To prevent this side effect, intraanal nitroglycerin ointment application is used, which significantly less frequently causes headaches compared to perianal application. To enhance the analgesic effect, nitroglycerin ointment is used in combination with lidocaine, which also allows for a reduction in the dose of both drugs [6]. The combination of local 2 % lidocaine and 0.2 % or 0.4 % nitroglycerin ointment is recommended after surgery (level of evidence A).

Metronidazole is capable of suppressing bacterial flora and also has immunomodulatory effects and reduces the risk of cell damage by oxygen free radicals, but the specific mechanism in relation to pain is not fully understood [6, 39–41]. At the same time, effectiveness is observed only with local application, while oral administration remains ineffective. Metronidazole significantly reduces pain syndrome on the 1st, 2nd, 7th and 14th days, as well as during the first bowel movement [1, 6, 42–44]. Also noted is effectiveness in reducing edema and rapid healing [24]. However, the level of evidence remains low (D).

Flavonoids have a phlebotonic effect and inhibit the production of inflammatory mediators, while also improving lymphatic drainage, and are safe for use [1, 45–47]. They significantly reduce the frequency of bleeding in the early postoperative period, as well as reduce the severity of postoperative changes such as edema and itching [45–48]. The ability of flavonoids to provide pain relief remains uncertain, but the use of non-narcotic analgesics after 6 days post-surgery was lower in patients taking flavonoids [45]. Side effects are quite common (headache, gastrointestinal symptoms). Flavonoids can be used as part of multimodal analgesia after hemorrhoidectomy in addition to NSAIDs (level of evidence A).

The use of lidocaine ointment and other local anesthetics allows for rapid achievement of an analgesic effect. Its repeated application is permissible in case of insufficient effectiveness, which is safe since it does not lead to significant changes in the blood and does not have a systemic effect on the body [21, 49].

The local application of diltiazem (a selective blocker of class III calcium channels, a benzothiazepine derivative) did not show sufficient effectiveness in reducing pain after surgical intervention [50]. According to the results of a multicenter randomized controlled trial, local application of nifedipine (a selective blocker of class II calcium channels, a dihydropyridine derivative) with lidocaine allows for a reduction in pain syndrome for a short time after surgery (at 6 hours and on day 7 after intervention $p < 0.011$ and $p < 0.054$, respectively) [51].

According to the results of a randomized controlled trial with a placebo group, a 15 % ointment with colestyramine demonstrated a significant reduction in the severity of pain at rest and during defecation after open hemorrhoidectomy [52]. There is also data on the effectiveness of local application of Baclofen 5 % and Atorvastatin 2 % for postoperative pain syndrome after hemorrhoidectomy [53, 54]. However, based on these data, it cannot be unequivocally stated about the effectiveness of the mentioned drugs since the research data were conducted on groups that were relatively small, and no similar articles were found in the available databases.

In case of an acute pain attack after intervention on the background of multimodal analgesia, it is permissible to use narcotic analgesics: low doses of opioids can be used for pain scores up to 5, and for severe pain (VAS above 5), opioids are recommended in higher doses [6].

Thus, to achieve an acceptable level of pain, it is necessary to apply a strategy of multimodal analgesia, which will allow to affect all mechanisms of its occurrence, reduce the dosage of drugs used, and minimize the use of opioids [1, 6, 55].

Conclusion

This review presents objective data on the effectiveness of various methods aimed at minimizing postoperative pain syndrome in patients undergoing interventions in the anorectal area. A multimodal approach should include the use of techniques for preventing the emergence of pain during pre- and intraoperative stages, as well as reducing it in the postoperative period.

Given the safety and proven effectiveness of acetaminophen, it is recommended to use it as the standard pain relief scheme for patients after surgical interventions in the anorectal area. However, considering its insufficient effectiveness in patients with severe pain, it is advisable to combine it with other systemic analgesics, such as nonsteroidal anti-inflammatory drugs, the effectiveness of which has also been proven. The use of opioids for postoperative pain relief is limited, including due to the side effects they can cause. The use of strong opioids is justified at the level of postoperative

pain from moderate to severe (more than 5 points on the VAS scale).

The effectiveness of metronidazole and lidocaine with nitroglycerin ointment, corticosteroids, or nifedipine has been proven for local postoperative pain relief. The prophylactic use of antibiotics and preoperative bowel preparation does not reduce postoperative pain. The use of stool normalizing agents is recommended as it reduces the level of postoperative pain.

Additional local pain relief in the form of nerve blocks or infiltration anesthesia is recommended for all patients planning interventions in the anorectal area. However, at present, the block of the pudendal nerve is considered the most effective, rather than perianal administration of anesthetics. Despite positive results of studies comparing liposomal bupivacaine with the regular form and placebo, liposomal bupivacaine cannot yet be recommended for routine use due to the lack of comparison with recommended pain relief methods and cost issues. Moreover, this type of anesthesia is preferable to spinal anesthesia due to longer analgesia and fewer side effects.

The modern literature presents a large number of publications on high-tech, minimally invasive treatment of hemorrhoidal disease. Thus, open hemorrhoidectomy with electrocoagulation of the vascular pedicle gives a less pronounced pain syndrome after the operation compared to ligation of the vascular pedicle, there is no convincing evidence that closed hemorrhoidectomy is less painful than open hemorrhoidectomy.

Thus, the recommended comprehensive scheme of multimodal anesthesia for patients after performing operations in the anorectal area is presented on Pic. Further research is needed to assess the effectiveness of preoperative pain relief, the advisability of perioperative use of flavonoids, as well as comparisons of different minimally invasive methods for treating diseases of the anorectal area.

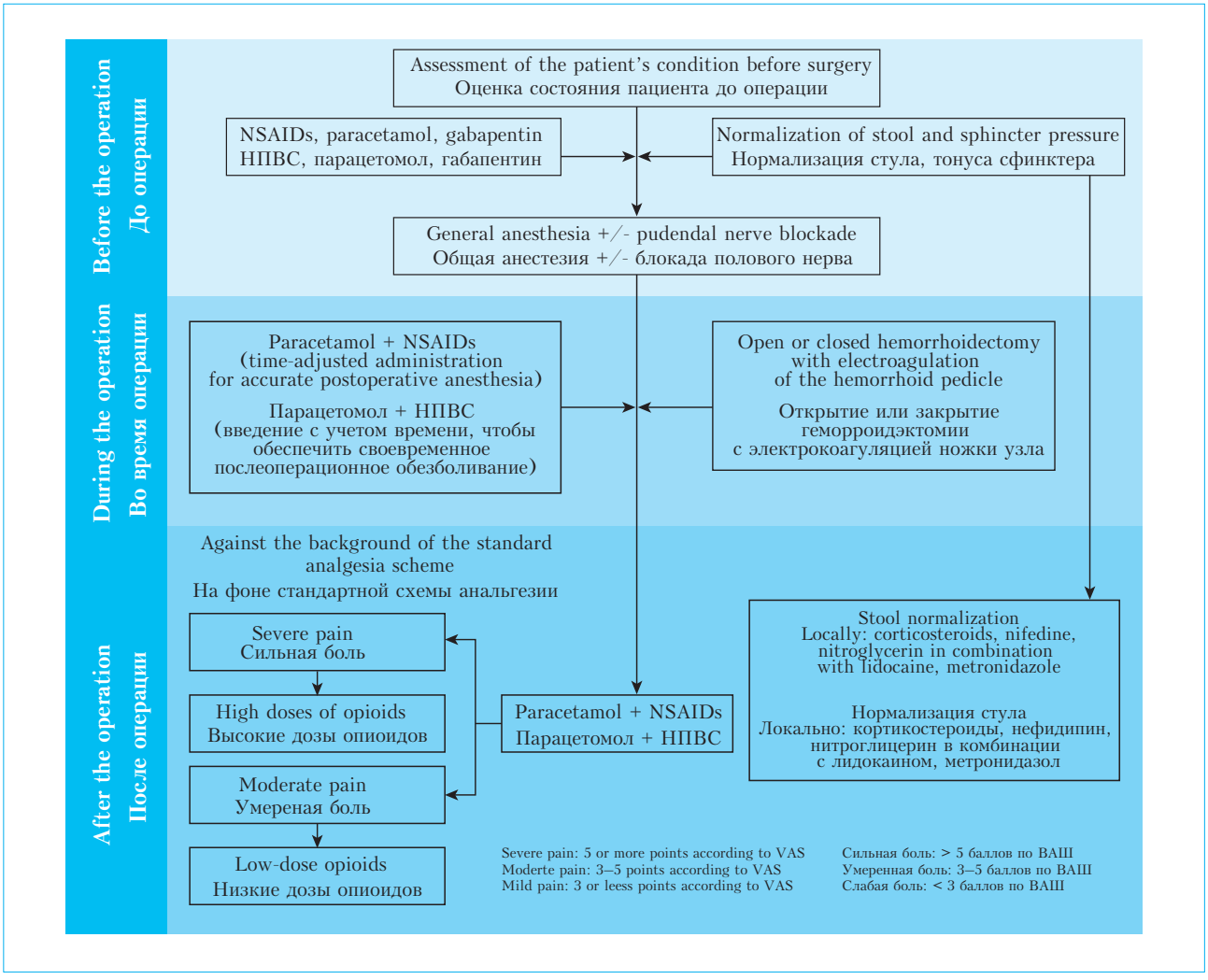

Fig. A scheme of multimodal analgesia for anorectal interventions

Рис. Комплексная схема мультимодальной анальгезии при аноректальных вмешательствах

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Information about the authors

Tatiana N. Garmanova* — Cand. Sci. (Med.), coloproctologist of the Surgery Department of the Moscow Scientific and Educational Center, Lomonosov Moscow State University, Associate Professor of the Surgery Department of the Fundamental Medicine Faculty, Lomonosov Moscow State University.
Contact information: tatianagarmanova@gmail.com;
119192, Moscow, Lomonosovsky ave., 27/10.
ORCID: http://orcid.org/0000-0003-2330-4229

Daniil R. Markaryan — Cand. Sci. (Med.), coloproctologist of the Surgery Department of the Moscow Scientific and Educational Center, Lomonosov Moscow State University.
Contact information: dmarkaryan@gmail.com;
119192, Moscow, Lomonosovsky ave., 27/10.
ORCID: http://orcid.org/0000-0003-2711-2400

Ekaterina A. Kazachenko — 1st-year resident of the Surgery Department of the Fundamental Medicine Faculty, Lomonosov Moscow State University.
Contact information: ekaterina.k.97@mail.ru;
119192, Moscow, Lomonosovsky ave., 27/10.
ORCID: https://orcid.org/0000-0001-6322-7016

Alexander M. Lukianov — 1st-year resident of the Surgery Department of the Fundamental Medicine Faculty, Lomonosov Moscow State University.
Contact information: alexmaxl@mail.ru;
119192, Moscow, Lomonosovsky ave., 27/10.
ORCID: https://orcid.org/0000-0002-2768-4305

Marya A. Kazachenko — 6th-year student of the Institute of Clinical Medicine of the I.M. Sechenov First Moscow State Medical University.
Contact information: mmari1998@mail.ru;
119021, Moscow, Rossolimo str., 11/2.
ORCID: https://orcid.org/0000-0001-9125-1312

Mikhail A. Agapov — Dr. Sci. (Med.), Professor of the Surgery Department of the Fundamental Medicine Faculty, Lomonosov Moscow State University, the Head of the Surgery Department of the Moscow Scientific and Educational Center, Lomonosov Moscow State University.
Contact information: getinfo911@mail.ru;
119192, Moscow, Lomonosovsky ave., 27/10.
ORCID: http://orcid.org/0000-0002-6569-7078

Сведения об авторах

Гарманова Татьяна Николаевна* — кандидат медицинских наук, врач-колопроктолог Медицинского научно-образовательного центра ФГБОУ ВО «Московский государственный университет имени М.В. Ломоносова», доцент кафедры хирургии факультета фундаментальной медицины (ФФМ) ФГБОУ ВО «Московский государственный университет имени М.В. Ломоносова».
Контактная информация: tatianagarmanova@gmail.com;
119192, Москва, Ломоносовский проспект, д. 27, к. 10.
ORCID: http://orcid.org/0000-0003-2330-4229

Маркарьян Даниил Рафаэлевич — кандидат медицинских наук, врач-колопроктолог Медицинского научно-образовательного центра ФГБОУ ВО «Московский государственный университет имени М.В. Ломоносова», доцент кафедры хирургии факультета фундаментальной медицины (ФФМ) ФГБОУ ВО «Московский государственный университет имени М.В. Ломоносова».
Контактная информация: dmarkaryan@gmail.com;
119192, Москва, Ломоносовский проспект, д. 27, к. 10.
ORCID: http://orcid.org/0000-0003-2711-2400

Казаченко Екатерина Александровна — врач-ординатор 1-го года по специальности «общая хирургия» кафедры хирургии факультета фундаментальной медицины (ФФМ) ФГБОУ ВО «Московский государственный университет имени М.В. Ломоносова».
Контактная информация: ekaterina.k.97@mail.ru;
119192, Москва, Ломоносовский проспект, д. 27, к. 1.
ORCID: https://orcid.org/0000-0001-6322-7016

Лукьянов Александр Максимович — врач-ординатор 1-го года по специальности общая хирургия кафедры хирургии факультета фундаментальной медицины (ФФМ) ФГБОУ ВО «Московский государственный университет имени М.В. Ломоносова».
Контактная информация: alexmaxl@mail.ru;
119192, Москва, Ломоносовский проспект, д. 27, к. 1.
ORCID: https://orcid.org/0000-0002-2768-4305

Казаченко Мария Александровна — студентка 6-го курса Института клинической медицины ФГАОУ ВО «Первый Московский государственный медицинский университет имени И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации.
Контактная информация: mmari1998@mail.ru;
119021, Москва, ул. Россолимо, д. 11, стр. 2.
ORCID: https://orcid.org/0000-0001-9125-1312

Агапов Михаил Андреевич — доктор медицинских наук, профессор, профессор кафедры хирургии ФФМ ФГБОУ ВО «Московский государственный университет имени М.В. Ломоносова», заведующий хирургическим отделением МНОЦ ФГБОУ ВО «Московский государственный университет имени М.В. Ломоносова».
Контактная информация: getinfo911@mail.ru;
119192, Москва, Ломоносовский проспект, д. 27, к. 1.
ORCID: http://orcid.org/0000-0002-6569-7078

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* Corresponding author / Автор, ответственный за переписку