

<https://doi.org/10.33878/2073-7556-2023-22-2-49-56>



Effectiveness of minimally invasive and surgical methods of treatment of chronic hemorrhoids using phlebotonics

Boris M. Belik¹, Aleksey N. Kovalev^{1,2}

¹Rostov State Medical University (Nakhichevanskii per., 29, Rostov-on-Don, 344022, Russia)

²International Medical Center "URO-PRO" (imeni 40-letia Pobedy st., 108, Krasnodar, 350901, Russia)

ABSTRACT *PURPOSE:* to evaluate the effect of phlebotropic therapy on the results of surgical treatment of hemorrhoids. *PATIENTS AND METHODS:* a comparative analysis of the results of treatment of 406 patients with chronic hemorrhoids of stages III and IV was performed. With surgical treatment of hemorrhoids, standard conservative therapy was performed in 205 patients (group I) and 201 patients (group II) in the perioperative period, as well as at the rehabilitation stage, the standard program of drug treatment was supplemented with phlebotropic therapy using Detralex (1000 mg). *RESULTS:* in group II patients, compared with group I patients, pain syndrome was stopped faster, quality of life and working capacity were restored, and the period of epithelization of the anal canal wound was shortened (21.4 ± 1.7 days versus 26.8 ± 2.1 days). This made it possible to increase the number of good and satisfactory results of surgical treatment of hemorrhoids from 82.4% to 91.5%. *CONCLUSION:* outpatient surgical treatment of hemorrhoids of stages III-IV in combination with phlebotropic therapy can reduce the number of postoperative complications from 17.6% to 8.5% and increase the overall number of good and satisfactory treatment results from 82.4% to 91.5% ($p < 0.005$).

KEYWORDS: hemorrhoids, surgical treatment, prolonged phlebotropic therapy, outpatient treatment

CONFLICT OF INTEREST: the authors declare no conflict of interest

FOR CITATION: Belik B.M., Kovalev A.N. Effectiveness of minimally invasive and surgical methods of treatment of chronic hemorrhoids using phlebotonics. *Koloproktologia*. 2023;22(2):49–56. (in Russ.). <https://doi.org/10.33878/2073-7556-2023-22-2-49-56>

ADDRESS FOR CORRESPONDENCE: Belik B.M., Rostov State Medical University, Nakhichevanskii per., 29, Rostov-on-Don, Russia; тел.: 8-904-500-64-42; e-mail: bbelik@yandex.ru

Received — 01.11.2022

Revised — 09.01.2023

Accepted for publication — 17.05.2023

INTRODUCTION

The modern concept of surgical treatment of chronic hemorrhoids provides for the use of both minimally invasive methods and hemorrhoidectomy [1,2]. In recent years, such minimally invasive methods of surgical treatment of hemorrhoids as desarterization of hemorrhoids with mucopexia and laser submucous destruction of hemorrhoids are becoming more widespread and are used, including in outpatient settings. Minimally invasive surgical methods are used mainly in the I–II stages of hemorrhoids, as well as in the treatment of chronic internal hemorrhoids of stages III–IV without a pronounced external component [2–4]. Most coloproctologists perform Milligan-Morgan hemorrhoidectomy in patients with hemorrhoids of stages III–IV, especially when this disease is combined with

another pathology of the anal canal (polyp, anal fissure) [3–6].

In recent years, such high-tech surgeries as closed seamless hemorrhoidectomy based on such technologies as LigaSure and Harmonica have been actively introduced into clinical practice in the treatment of patients with late stages [1,2,6]. The most significant disadvantages of Milligan-Morgan hemorrhoidectomy and its various modifications include a severe pain syndrome in the early stages after surgery, postoperative bleeding, inflammatory wound complications, which significantly increases the rehabilitation time of patients. In addition, in the long-term period after hemorrhoidectomy, 6–9% of patients develop cicatricial stricture of the anal canal, and 1.8–4% of patients develop sphincter insufficiency [1,2,6]. When choosing a method for the treatment of late-stage chronic hemorrhoids, a combination

of various minimally invasive techniques is used as an alternative to Milligan-Morgan hemorrhoidectomy (for example, a combination of transanal Doppler-controlled ligation of hemorrhoidal arteries with submucous laser destruction). They are often combined with the removal of single hemorrhoidal piles, which does not significantly affect the surgical radicalism, and at the same time it reduces its duration and trauma [3,6–8].

Currently, the pathogenetic validity of the use of phlebotropic therapy in the conservative treatment of acute hemorrhoids has been proven, and data on the positive effect of phlebotonics on the effectiveness of minimally invasive surgeries in patients with chronic hemorrhoids have been presented [9,10,11].

The long clinical practice of using Detralex (micronized purified flavonoid fraction) has clearly shown the high efficacy and safety of using this phlebotonic in the treatment of patients with various forms of hemorrhoidal disease [10–12]. At the same time, there are no studies justifying and clearly regulating the regimen of phlebotropic therapy during the entire perioperative period, as well as at the stage of rehabilitation in patients with stages III-IV of the disease after surgical treatment. This prompted us to develop a rational strategy for phlebotropic therapy before and after surgical treatment of patients with chronic hemorrhoids of stages III-IV and to evaluate its clinical effectiveness.

AIM

To evaluate the effectiveness of surgical treatment of hemorrhoids of stages III-IV in outpatient settings with the use of phlebotropic therapy in the perioperative period.

PATIENTS AND METHODS

The present study included 406 patients with chronic hemorrhoids of stages III and IV who were on outpatient treatment at the MMC “URO-PRO” in Krasnodar in the period of 2018–2022. There were 179 men (44.1%) and 227 women (55.9%). The age of the patients ranged from 18 to 73 years. Most of

the patients were of working age. The average age of the patients was 45.5 ± 3.7 years. All patients underwent checkup on an outpatient clinic with conventional clinical, laboratory and instrumental tests. Colonoscopy was performed in patients aged over 40 years. All patients underwent surgical treatment of hemorrhoids, including the use of traditional and minimally invasive technologies.

Depending on the variant of drug treatment in the perioperative period and at the stage of rehabilitation, two groups were created. In 205 (50.4%) patients of the I (control) group, generally accepted drug therapy was performed in the perioperative period, including the use of topical combined agents. In 201 (50.6%) patients of group II (main) in the perioperative period, as well as at the rehabilitation stage, the standard program of drug treatment was supplemented with prolonged phlebotropic therapy using Detralex (1000 mg).

When choosing a phlebotropic drug prescribing scheme, the severity of the inflammatory process in the area of hemorrhoids was taken into account. In patients with chronic hemorrhoids with mild symptoms of exacerbation of the disease, Detralex 1000 mg was prescribed 1 tablet 2 times a day for 7 days before surgery. In the presence of clear signs of exacerbation of chronic hemorrhoids (edema, node soreness), in addition to topical remedies, in order to stop the inflammatory component before surgery, patients received Detralex 1000 mg 1 tablet 3 times a day for 4 days, then 1 tablet 2 times a day for 3 days. After surgery, the drug was prescribed to patients of group II according to the same scheme as in case of exacerbation of the disease (1 tablet 3 times a day for 4 days, then 1 tablet 2 times a day for 3 days). Subsequently, patients received the drug 1 tablet 1 time a day for 2 months. After that, they took a break from taking the drug for 60 days, and then a second course of phlebotropic therapy (1 tablet per day) was carried out for 2 months.

At the start of the treatment, the groups of patients were comparable in clinical manifestations of chronic hemorrhoids in accordance with the stage of the disease (Table 1).

Sixty-one (15.0%) patients were diagnosed with posthemorrhagic anemia, which required hemotransfusions and the administration of

Table 1. Distribution of patients by clinical signs and stages of chronic hemorrhoids

Clinical signs/stages of chronic hemorrhoids	Number of patients			
	I Group (n = 205)		II Group (n = 201)	
	Abs.	%	Abs.	%
Piles prolapse from the anal canal (stage III)	33	16.1	38	18.9
Piles prolapse (stage III) + bleeding	73	35.6	71	35.3
Piles prolapse (stage IV)	3	1.5	3	1.5
Piles prolapse (stage IV) + bleeding	96	46.8	89	44.3

Table 2. Surgeries performed in patients with chronic hemorrhoids of stages III-IV in groups I and II

Surgeries	Number of patients			
	I Group (n = 205)		II Group (n = 201)	
	Abs.	%	Abs.	%
Hemorrhoidectomy by Milligan-Morgan + HAL-RAR	9	4.4	13	6.5
Hemorrhoidectomy by Milligan-Morgan + LHP	26	12.7	21	10.4
Hemorrhoidectomy by Milligan-Morgan + HAL-RAR + LHP	14	6.8	16	8.0
Hemorrhoidectomy with LigaSure + HAL-RAR	22	10.7	18	8.9
Hemorrhoidectomy with LigaSure + LHP	21	10.2	24	11.9
Hemorrhoidectomy with LigaSure + HAL-RAR + LHP	33	16.1	29	14.4
Hemorrhoidectomy with harmonic + HAL-RAR	26	12.7	19	9.4
Hemorrhoidectomy with harmonic + LHP	30	14.6	29	14.4
Hemorrhoidectomy with harmonic + HAL-RAR + LHP	24	11.7	32	15.9

iron-containing drugs at the stage of preoperative preparation.

When choosing the method of surgical treatment of chronic hemorrhoids, individual clinical and anatomical features of the pathological process were taken into account (the size and “stage of development” of each individual node, its location in relation to other hemorrhoids, as well as the relationship between the external and internal components). Guided by this principle, two or more hemorrhoidal node removal techniques were

used in a personalized manner for each patient, including a combination of traditional surgeries and minimally invasive methods. The types of surgeries performed in both groups of patients are presented in Table 2.

Traditional hemorrhoidectomy according to Milligan-Morgan in various combinations with minimally invasive methods was performed in 49 (23.9%) patients of group I and 50 (24.9%) of group II. At the same time, as minimally invasive methods of treatment, dearterisation of hemorrhoids

with mucopexia (HAL-RAR technology) using the A.M.I. "HAL-Doppler II" device (Austria) and laser submucous destruction of hemorrhoids (Laser Hemorrhoid Plasty, LHP) with the LAKHTA-MILON device ("Touch screen" model, Russia) were used. Closed seamless hemorrhoidectomy by LigaSure apparatus (ValleylabFT10, USA) in various combinations with HAL-RAR and LHP techniques was performed in 76 (37.1%) patients of group I and 71 (35.3%) patients of group II. Closed seamless hemorrhoidectomy with Covidien ultrasound scalpel (USA) in combination with minimally invasive methods was performed in 80 (39.0%) patients of group I and 80 (39.8%) patients of group II. A rational combination of traditional operations and minimally invasive techniques in the surgical treatment of patients with chronic hemorrhoids of stages III-IV, without generally affecting the radicality of the surgery, significantly reduced the level of its traumatism, as it allowed avoiding excessive excision of the anoderm when removing internal hemorrhoids with uneven degree of their loss.

In both groups of patients, we compared the degree of pain syndrome after surgery (according to the numerological evaluation scale, NRS: from 0 to 10 points), as well as the severity of postoperative inflammatory changes in the anal area (pain in the anus and discomfort during exercise and defecation, perianal edema, blood spotting during defecation). The comparison parameters in the study groups took into account the healing time of wounds in the anal area, the number of postoperative complications and recurrences of the disease. We considered the complete elimination of the main manifestations of the disease to be good results; satisfactory results — preservation of perianal edema, a feeling of discomfort in the anal area during defecation; unsatisfactory results — the presence of postoperative complications and/or recurrence of the disease. The quality of life of patients after surgery was assessed using the SF-36 questionnaire.

Statistical analysis was performed using Statistica 7.0 for Windows. To check the normality of the distribution of values in the samples, the Kolmogorov-Smirnov and Shapiro-Wilk criteria were used. The statistical significance of the differences between the groups was assessed using the Mann-Whitney

criterion (U). When assessing changes in parameters within one group of patients in the dynamics of observation, the Wilcoxon rank criterion of paired comparisons was used. The differences were considered statistically significant at $p < 0.05$.

RESULTS

In patients of group II, in whom surgical treatment of hemorrhoids of stages III-IV in the perioperative period and at the stage of rehabilitation was accompanied by phlebotropic therapy, the degree of pain syndrome after surgery was significantly lower compared to patients of group I. At the same time, in patients of group II, the pain syndrome was largely stopped by 5.6 ± 1.2 days after surgery, while in group I patients — only by 8.3 ± 1.3 days (Fig. 1).

Along with a decrease in pain syndrome in patients of the main group, there was a more distinct regression of clinical signs due to postoperative inflammatory changes (Table 3).

In patients of the main group, reduction of perianal edema and cessation of bloody discharge during the act of defecation were noted earlier after surgery, and at the same time, a decrease in pain and discomfort in the anus during defecation and during physical exertion. In the majority of cases in patients of group II, the elimination of acute inflammatory changes in the surgery site was noted on the 6.1 ± 1.2 days after surgery, and in a large number of patients of group I, these manifestations regressed only on the 10.2 ± 1.7 postoperative days. In patients of the main group, the healing time of postoperative wounds of the anal area decreased (respectively, 21.4 ± 1.7 days versus 26.8 ± 2.1 days in patients of the control group). In patients of the main group, the ability to work was restored at an earlier time after surgery (respectively 4.2 ± 1.1 days versus 6.9 ± 1.4 days in patients in the control group). Group II patients with prolonged phlebotropic therapy showed a decrease in the total number of postoperative complications by more than 2 times compared with group I patients (8.5% vs. 17.6%) (Table 4). First of all, it concerned a significant reduction in the number of wound inflammatory complications (early eruption of the anoderm

Table 3. Postoperative inflammatory changes in the perineum in groups I and II ($P \pm m$) %

Clinical signs	Group of patients	Day after surgery ($n = 406$)				
		1st	3rd	5th	7th	10th
Pain in the anal canal during the act of defecation, %	I Group	98.6 \pm 1.3	84.8 \pm 3.1	62.6 \pm 3.7	44.8 \pm 2.2	11.2 \pm 1.6
	II Group	98.1 \pm 1.4*	75.6 \pm 2.8	37.3 \pm 4.4	15.9 \pm 3.3	4.6 \pm 1.4
Pain and discomfort in the anus during exercise, %	I Group	97.5 \pm 2.7	60.1 \pm 3.3	43.4 \pm 3.8	22.4 \pm 4.1	8.7 \pm 2.3
	II Group	93.2 \pm 2.1*	54.3 \pm 2.7*	18.5 \pm 3.1	9.1 \pm 2.2	3.4 \pm 1.2
Perianal edema, %	I Group	89.5 \pm 2.1	78.4 \pm 2.7	57.8 \pm 3.3	34.1 \pm 4.2	12.3 \pm 3.2
	II Group	85.3 \pm 2.6*	45.4 \pm 4.2	24.3 \pm 2.1	13.5 \pm 1.3	3.1 \pm 1.9
Blood spotting during the act of defecation, %	I Group	97.5 \pm 1.2	85.6 \pm 2.8	72.1 \pm 2.7	56.1 \pm 3.9	40.9 \pm 4.3
	II Group	97.1 \pm 1.4*	78.1 \pm 3.5	49.2 \pm 3.8	35.3 \pm 3.0	21.3 \pm 3.4

Note: * — Statistically unreliable differences between groups ($p > 0.05$)

sutures and suppuration of wounds). In the main group of patients, postoperative thrombosis of residual cavernous tissue developed significantly less frequently in the projection of cutaneous-anodermal bridges (2.5% versus 5.8% in the control group), which required additional therapeutic measures, including excision of this tissue together with excess perianal skin and segment of the anoderm.

In addition, in 2 (0.5%) cases, postoperative bleeding from anal canal wounds was noted in patients requiring emergency surgical hemostasis.

Stricture formation of the anal canal was observed in 6 (2.9%) patients of group I and 5 (2.5%) patients of group II due to cicatricial retraction of the mucous layer and anoderm later after surgery. Of these, 7 patients had stricture eliminated conservatively (multiple finger augmentation) and 4 patients required reconstructive surgery (stricturoplasty). There were no recurrences of the disease during the entire follow-up period in patients in both groups.

Good and satisfactory outcomes of surgical treatment were obtained in 184 (91.5%) patients in

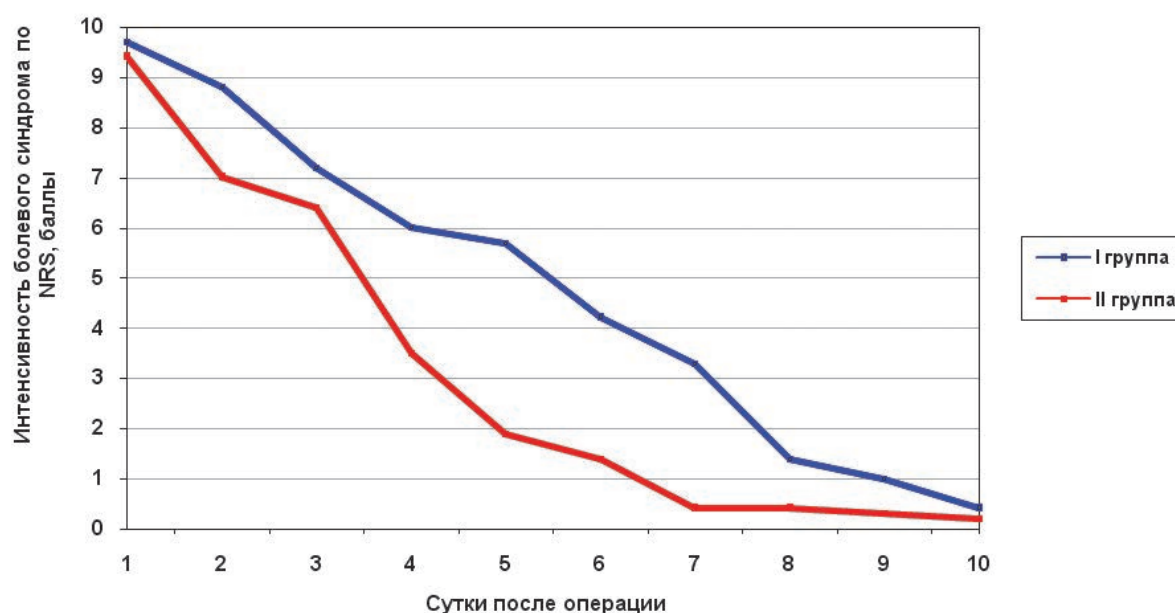
**Figure 1.** The intensity of pain syndrome according to a 10-point numerological evaluation scale in patients with chronic hemorrhoids of stages III–IV in groups I and II after surgery

Table 4. Structure of postoperative complications in patients of groups I and II

The nature of complications	Number of patients			
	I Group (n = 205)		II Group (n = 201)	
	Abs.	%	Abs.	%
Bleeding from anal canal wounds	1	0.5	1	0.5
Thrombosis of residual cavernous tissue	12	5.8	5	2.5
Eruption of the anoderm sutures	6	2.9	2	1.0
Purulent-inflammatory wound complications	11	5.4	4	2.0
Stricture of the anal canal	6	2.9	5	2.5
Total patients with complications	36	17.6	17	8.5

Table 5. Comparative characteristics of the quality of life of patients of groups I and II after surgery

Follow-up periods after surgery	I Group		II Group	
	PH (M ± m)	MH (M ± m)	PH (M ± m)	MH (M ± m)
Day 5	64.2 ± 2.7	68.2 ± 2.2	76.2 ± 3.1	74.2 ± 2.8
Day 10	67.2 ± 3.2	72.2 ± 2.9	78.2 ± 3.3	80.2 ± 3.4
Day 20	74.2 ± 2.6	78.2 ± 3.0	81.2 ± 2.9	86.2 ± 2.7
Day 30	81.2 ± 3.1	84.2 ± 2.1	87.9 ± 2.4	89.. ± 3.1
3 months	85.1 ± 2.7	87.1 ± 2.8	91.5 ± 3.1	93.8 ± 3.0
6 months	92.1 ± 2.5	89.3 ± 2.4	96.5 ± 3.2*	95.8 ± 2.7

Note: * — Statistically unreliable differences between groups ($p > 0.05$)

the main group and in 169 (82.4%) patients in the control group.

The results of the survey of patients based on the SF-36 questionnaire showed that after surgery, patients of the main group assessed their physical health (PH) and mental status (MH) higher than patients of the control group (Table 5).

DISCUSSION

The results of the study showed that when the clinic is equipped with modern high-tech equipment, it is quite possible to provide high-quality surgical treatment of patients with chronic hemorrhoids of stages III-IV in the “one-day hospital” mode. In this category of patients, it is most rational to use high-tech hemorrhoidectomy (LigaSure, Harmonica) in combination with modern minimally invasive methods of treatment (desarterization of hemorrhoids, LHP). This combination does not significantly affect the surgery radicality, but significantly reduces the degree of its traumatism. At the same time, a personalized approach should be applied taking into account the individual clinical and anatomical features of the pathological process, including the size and “stage of development” of each individual node, the presence of boundaries

between internal nodes, as well as external and internal nodes.

The inclusion of phlebotropic therapy (Detralex 1000 mg) in the program of comprehensive drug support in this category of patients throughout the entire perioperative period and the rehabilitation stage is pathogenetically justified. In this case, prolonged phlebotropic correction using micronized purified flavonoid fraction is primarily aimed at reducing vein distension and limiting the inflammatory reaction in the venous wall, eliminating increased microvascular permeability, improving venous outflow and lymphatic drainage in the area of altered tissues. At the same time, the scheme of prescribing the drug assumes an individualized approach to choosing the mode of prolonged phlebotropic correction, depending on the severity of the initial inflammatory changes in the area of hemorrhoids.

The best results of surgical treatment obtained by us in patients of the main group who additionally underwent phlebotropic therapy were achieved mainly due to a decrease in the severity of postoperative perianal edema, which, in turn, contributed to a decrease in the number of inflammatory wound complications. It is noteworthy that the early eruption of the anoderm sutures against the background of inflammatory perianal edema, as a rule, was accompanied by

the development of persistent sphincterospasm and severe pain syndrome. The effectiveness of surgeries using phlebotropic drugs is confirmed by a large number of good and satisfactory treatment results in patients of the main group, as well as a higher assessment of the quality of life after surgery (compared with patients of the control group).

CONCLUSION

Thus, conducting targeted phlebotropic drug therapy in the perioperative period during surgical treatment of chronic hemorrhoids and at the stage of postoperative rehabilitation of patients is pathogenetically justified and is primarily aimed at reducing the severity of perianal edema and pain syndrome, as well as preventing inflammatory wound complications. In this case, surgical treatment of hemorrhoids of stages III–IV on an outpatient basis in combination with phlebotropic therapy contributes to the relief of pain syndrome earlier after surgery, regression of inflammatory changes in the surgery area,

acceleration of the healing rate of postoperative wounds, improvement of the quality of life of patients and improvement of their social rehabilitation. This makes it possible to reduce the number of postoperative complications from 17.6% to 8.5% and increase, in general, the number of good and satisfactory results of surgical treatment of hemorrhoids from 82.4% to 91.5%.

AUTHORS CONTRIBUTION

Concept and design of the study: *Boris M. Belik, Aleksey N. Kovalev*

Collection and processing of the material: *Boris M. Belik, Aleksey N. Kovalev*

Statistical processing: *Boris M. Belik, Aleksey N. Kovalev*

Writing of the text: *Boris M. Belik, Aleksey N. Kovalev*

Editing: *Boris M. Belik, Aleksey N. Kovalev*

INFORMATION ABOUT THE AUTHORS (ORCID)

Boris M. Belik — Head of department of general surgery, Rostov State Medical University, Rostov-on-Don, Russia

Aleksey N. Kovalev — coloproctologist of the Medical Center “URO-PRO”, Krasnodar, Russia

REFERENCES

- Shelygin Yu.A., Blagodarny L.A. Clinical recommendations. Coloproctology. Edited by a corresponding member of RAS Shelygin U.A. Moscow: GEOTAR-Media. 2020; p. 30–52. (in Russ.).
- Shelygin Yu.A., Titov A.Yu., Achkasov S.I. Hemorrhoids. Diagnosis and treatment. Moscow: GEOTAR-Media, 2022; 216 p. (in Russ.).
- Crea N, Pata G, Lippa M, et al. Hemorrhoid laser procedure (HeLP) for second- and third-degree hemorrhoids: results from a long-term follow-up analysis. *Lasers in Medical Science*. 2022;37(1):309–315. PMID: 33439376 doi: [10.1007/s10103-021-03249-6](https://doi.org/10.1007/s10103-021-03249-6)
- Poskus T, Danys D, Makunaite G, et al. Results of the double-blind randomized controlled trial comparing laser hemorrhoidoplasty with sutured mucopexy and excisional hemorrhoidectomy. *International Journal of Colorectal Disease*. 2020;35(70):481–490. doi: [10.1007/s00384-019-03460-6](https://doi.org/10.1007/s00384-019-03460-6)
- Brusciano L, Gambardella C, Terracciano G, et al. Postoperative discomfort and pain in the management of hemorrhoidal disease: laser hemorrhoidoplasty, a minimal invasive treatment of symptomatic hemorrhoids. *Updates Surg*. 2020;72(3):851–857. PMID: 31760588, doi: [10.1007/s13304-019-00694-5](https://doi.org/10.1007/s13304-019-00694-5)
- Mikhailichenko V.Yu., Drevetnyak A.A., Gavrilenko S.P., et al. Modern methods of surgical treatment of chronic hemorrhoids. Modern problems of science and education. 2021;1. [Electronic resource]. Access mode: <https://science-education.ru/ru/article/view?id=30533> (accessed: 31.07.2022). (in Russ.).
- Lakmal K, Basnayake O, Jayarajah U, Samarasekera D. Clinical Outcomes and Effectiveness of Laser Treatment for Hemorrhoids: A Systematic Review. *World Journal of Surgery*. 2021;45(4):1222–1236. PMID: 33469736, doi: [10.1007/s00268-020-05923-2](https://doi.org/10.1007/s00268-020-05923-2)
- Ram E, Bachar GN, Goldes Y, et al. Modified Doppler-guided laser procedure for the treatment of second- and third-degree hemorrhoids. *Laser Therapy*. 2018;27(2):137–142. PMID: 30087534, doi: [10.5978/islsm.18-OR-14](https://doi.org/10.5978/islsm.18-OR-14)
- Zagryadsky E.A. Modern treatment of acute haemorrhoids. *Ambulatornaya hirurgiya*. 2019;1-2:112–117. (in Russ.). doi: [10.21518/1995-1477-2019-1-2-112-117](https://doi.org/10.21518/1995-1477-2019-1-2-112-117)
- Belik B.M., Kovalev A.N., Khatlamadzhyan A.L. Administration of phlebotropic drugs during com-

plex treatment of acute hemorrhoids. *Koloproktologia*. 2018;2(64):48–53. (In Russ.). doi: [10.33878/2073-7556-2018-0-2-48-53](https://doi.org/10.33878/2073-7556-2018-0-2-48-53)

11. Groshilin V.S., Cherkasov M.F., Mirzoev L.A., Shvetsov V.K. Improving the efficiency of minimally invasive treatment of hemorrhoids using phlebotonics. *Koloproktologia*. 2016;3(57): 18-23. (in Russ.).

doi: [10.33878/2073-7556-2016-0-3-18-23](https://doi.org/10.33878/2073-7556-2016-0-3-18-23)

12. Gerges SH, Wahdan SA, Elsherbiny DA, El-Demerdash E. Pharmacology of Diosmin, a Citrus Flavone Glycoside: An Updated Review. *Eur J Drug Metab Pharmacokinet*. 2022;47(1): 1-18. PMID: 34687440. doi: [10.1007/s13318-021-00731-y](https://doi.org/10.1007/s13318-021-00731-y)