https://doi.org/10.33878/2073-7556-2026-25-2-65-78

Does PRP therapy affect wound epithelialization time after excision of chronic anal fissure? Results of a randomized trial (NCT07268261)

Ekaterina Yu. Lebedeva[1], Maria A. Ignatenko[1], Evgeny E. Zharkov[1], Aleksey A. Ponomarenko[1], Andrey A. Mudrov[1,2], Ivan V. Kostarev[1,2]

[1]Ryzhikh National Medical Research Center of Coloproctology (Salyama Adilya st., 2, Moscow, 123423, Russia)
[2]Russian Medical Academy of Continuous Professional Education (Barrikadnaya st., 2/1, bld. 1, Moscow, 125993, Russia)

ABSTRACT *OBJECTIVE: to evaluate the efficacy of PRP therapy following excision of chronic anal fissure (CAF) combined with pharmacological relaxation of the internal anal sphincter using 40 units of botulinum toxin type A (BTA).*

PATIENTS AND METHODS: single-center prospective randomized controlled trial (NCT07268261) was held between September 2023 and November 2025comparing outcomes of fissure excision (FE) combined with 40 units of BTA plus platelet-rich plasma injection (FE + BTA + PRP — study group) versus FE with BTA alone (FE + BTA — control group).142 patients were randomized during this period: 70 in FE + BTA + PRP group and 72 in FE + BTA group. 125 patients were included in the final analysis after applying exclusion criteria: 60 in the study group and 65 in the control group. During preoperative and postoperative period patients underwent control examinations, pain intensity assessment using the visual analog scale (VAS), profilometry, and evaluation of transient fecal incontinence using the Wexner scale. The primary end point was the rate of wound epithelialization at 60 days post-surgery.

RESULTS: on the 60th days, wound healing rates were comparable between both groups: 43/60 (71.7%; 95% confidence interval [CI]: 58.6–82.5) in the FE + BTA + PRP group versus 47/65 (72.3%; 95% CI: 59.8–82.7) in the FE + BTA group (p = 0.936). However, on the 15th days, no patients had epithelialized wounds; on the 30th days, wound healing occurred in 11/60 (18.3%) patients in the FE + BTA + PRP group versus none in the FE + BTA group (p = 0.0003); on the 45th days — in 18/60 (30.0%) versus 3/65 (4.6%) patients respectively (p = 0.0001). No postoperative complications developed in any patient. Transient fecal incontinence on the 30th days was observed in 12/60 (20.0%) patients in the studied group and 10/65 (15.4%) in the control group (p = 0.498); on the 60th days — in 5/60 (8.3%) and 2/64 (3.1%) patients, respectively (p = 0.262). Pain intensity during the day and during defecation in the postoperative period was comparable between two groups throughout the observation period, except of day 10 (during defecation, p = 0.049) and day 12 (during the day, p = 0.036; during defecation, p = 0.035), with lower scores in the control group; by day 60, pain was successfully relieved in almost all patients in both groups. According to profilometry data on the 30th days internal anal sphincter (IAS) spasm persisted in 15/48 (31.3%) patients in the study group and 10/51 (19.6%) in the control group (p = 0.183); on the 60th days — in 15/45 (33.3%) and 11/49 (22.4%) patients, respectively (p = 0.239). No statistically significant differences were achieved in favor of the study group regarding the number of days of temporary disability — 15 (11; 22) days in the FE + BTA + PRP group versus 20 (13; 27) in the FE + BTA group (p = 0.079). Female gender was identified as a factor significantly increasing the odds of absence of epithelialization on the 30th days in univariate logistic regression analysis (odds ratio [OR] = 3.95; 95% CI: 1.09–14.37; p = 0.037). On the 45th days, in addition to gender (OR = 3.29; 95% CI: 1.26–8.61; p = 0.015), significant factors were: treatment method in favor of the FE + BTA + PRP group (OR = 0.11; 95% CI: 0.03–0.41; p = 0.0009); age (OR = 1.07; 95% CI: 1.01–1.13; p = 0.015); and presence of constipation (OR = 5.14; 95% CI: 1.43–18.53; p = 0.013). On the 60th days, only female gender was statistically significantly associated with non-healing wound (OR = 3.22; 95% CI: 1.22–6.66; p = 0.019). No factors influencing the presence of transient fecal incontinence were identified.

CONCLUSION: the use of platelet-rich plasma combined with BTA injection and FE in the treatment of CAF does not increase the rate of postoperative wound epithelialization at 2 months after surgery; however, it offers an advantage by increasing the rate of epithelialization at 30 and 45 days. At the same time this method does not affect the incidence of postoperative complications, pain intensity, functional treatment outcomes, or social and occupational rehabilitation of patients.

KEYWORDS: *chronic anal fissure, botulinum toxin type A, BTA, fissure excision, internal anal sphincterspasm, platelet-rich plasma*

CONFLICT OF INTEREST: *the authors declare no conflict of interest*

FOR CITATION: Lebedeva E.Yu., Ignatenko M.A., Zharkov E.E., Ponomarenko A.A., Mudrov A.A., Kostarev I.V. Does PRP therapy affect wound epithelialization time after excision of chronic anal fissure? Results of a randomized trial (NCT07268261). *Koloproktologia.* 2026;25(2):65–78. (in Russ.). https://doi.org/10.33878/2073-7556-2026-25-2-65-78

ADDRESS FOR CORRESPONDENCE: *Lebedeva E.Yu., Ryzhikh National Medical Research Center of Coloproctology, Salyama Adilya st., 2, Moscow, 123423, Russia; 8 (977)-955-89-20; e-mail: lebedeva_ey@gnck.ru*

Received — 23.03.2026 *Revised — 26.03.2026* *Accepted for publication — 13.05.2026*

INTRODUCTION

The pathogenesis of chronic anal fissure (CAF) is associated with hypertonus of the internal anal sphincter (IAS), which determines the need for its elimination as part of treatment [1]. According to the literature, there is a widespread practice of refusing excision of CAF against the background of botulinum toxin (BTA) monotherapy [2,3]. Russian clinical guidelines show cases when excision of an anodermic defect is indicated in patients with fibrous polyp, sentinel tag, accompanied by clinical manifestations [1]. This volume of surgery means the formation of a postoperative wound, the presence of which can increase the period of rehabilitation of patients, and is also associated with severe pain compared to methods where the CAF is not excised.

According to recent studies, excision of a fissure significantly increases the chance of non-healing of the lesion within 30 ($p < 0.0001$) and 45 ($p = 0.003$) days, compared with isolated lateral subcutaneous sphincterotomy (LSS) [4]. The rate of healing of a postoperative wound after excision of a fissure with relaxation of the internal sphincter with BTA type A does not exceed 86%, while a number of authors indicate the use of stimulants of reparative processes in case of non-healing of the wound, which increases the chances of epithelialization of the wound [4–6]. One of the methods that stimulate regeneration is injection of Platelet Rich Plasma (PRP) into the bottom of the lesion. This method is used, among other things, for the treatment of acute and chronic anal fissures and, according to various authors, reduces the healing time of the lesion and the intensity of pain [7–9].

AIM

Evaluation of the effectiveness of PRP therapy after excision of the chronic anal fissure (CAF) in combination with drug relaxation of the internal sphincter with BTA at a dosage of 40 units.

PATIENTS AND METHODS

In the period from September 2023 to November 2025, a single-center prospective randomized controlled trial (NCT07268261) was conducted to compare the effects on wound healing after fissure excision (FE) in combination with BTA at a dosage of 40 units, and platelet-rich plasma injections (FE + BTA + PRP — the main group) with FE in combination with BTA (FE + BTA — control group). Randomization was carried out by generating random numbers in Access (Microsoft Office 2013) 1:1. When a patient was entered into the database, if an even number fell out, he was assigned to the main group, and if an odd number fell out, he was assigned to the control group. During this period, a total of 142 patients were randomized with a diagnosis of CAF — 70 were included in the main group and 72 in the control group. Subsequently, 17 patients were excluded due to intraoperatively detected anal fistula (2 in the main and 3 in the control); non-compliance with postoperative recommendations (2 people in the main and 1 in the control group), as well as due to non-attendance at any of the control points after surgery (6 in the main and 3 in the control group). Thus, the final analysis included 125 patients: 60 in the FE + BTA + PRP group and 65 in the FE + BTA group (Fig. 1).

The diagnosis of “Chronic anal fissure” was verified if the patient had at least 1 of the following characteristics: a medical history of more than 2 months; scar tissue of the lesion margins; fibrous polyp of the anal canal at the proximal edge of the lesion; the presence of a sentinel tag at the distal edge of the anal canal.

Inclusion criteria: established diagnosis of "Chronic anal fissure" with confirmed spasm of the IAS according to profilometry results; age of patients at least 18 years; signed informed consent to participate in the study.

Non-inclusion criteria: individual intolerance and hypersensitivity to BTA; previous anal canal surgery (with the exception of minimally invasive techniques); anal incontinence (AI) of any degree (more than 0 points on Wexner's scale); pectenosis; the presence of inflammatory bowel diseases in the patient; chronic paraproctitis; the presence of severe comorbidities in decompensation; pregnancy and lactation; myasthenia gravis and myasthenia-like syndromes; external and internal hemorrhoids of stages II-IV, requiring combined surgery; allergic reaction to anticoagulants in the life history; blood diseases (thrombocytopenia, splenomegaly, etc.); malignant neoplasms.

Exclusion criteria: detection of a fissure complicated by a fistula during intraoperative revision of the rectum; refusal of the patient to participate at any stage of the study; non-compliance with the protocol of the study.

Methods of examination.

As part of the study, all patients underwent profilometry using a Solar GI HRAM device (the Netherlands) before surgery, as well as on the 30th and 60th days after the surgery.

The spasm of the IAS was confirmed by exceeding the upper limit of the normal value of one of two parameters — the average pressure in the anal canal at rest (normal values: 44.0–60.4 mmHg) or the maximum pressure at rest (normal values: 89.4–112.2 mmHg). As part of the follow-up protocol, patients underwent an assessment of pain syndrome on a visual analog scale (VAS) and an assessment of anal incontinence (AI) during a survey on Wexner's incontinence scale before and daily after surgery.

If anal fistula was suspected, patients underwent transanal ultrasound.

Methods of treatment and management of patients in the postoperative period.

The patients were placed in a supine position with their legs brought to their stomachs. In the main group, the anodermic defect was first excised in accordance with clinical giudelines using a double-leaf mirror [1], after which BTA type A

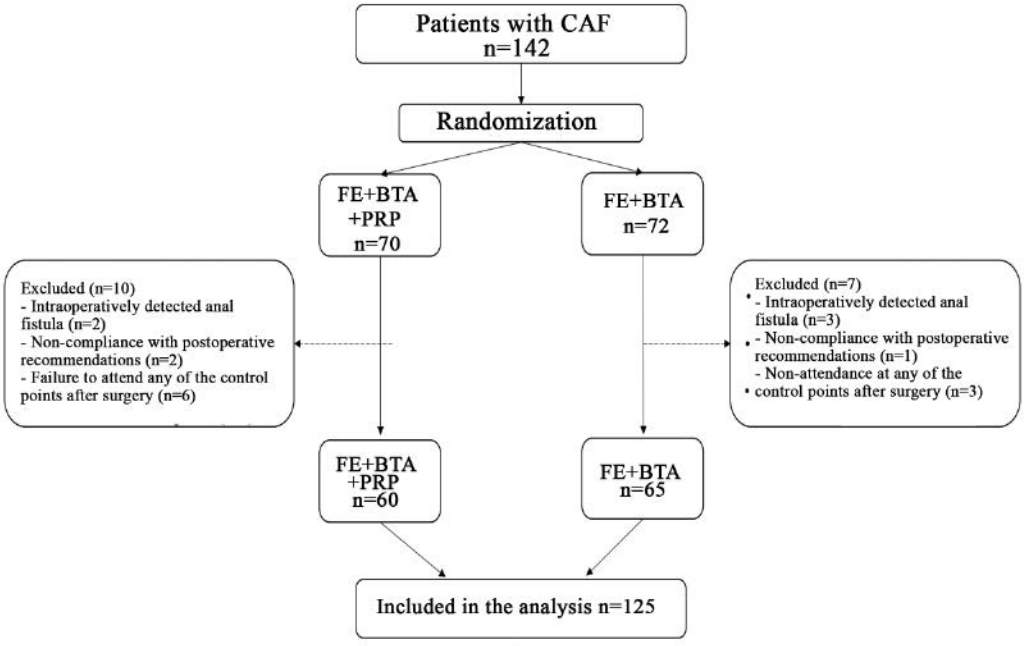

Рисунок 1. *Блок-схема исследования*
Figure 1. *Block chart of the study*

(without complexing proteins) was injected into the IAS. The agent was injected into four anatomical points (1, 5, 7, 11 o'clock of the conventional clock) for 10 units (40 units in total) using an insulin syringe per 100 units, previously the drug was diluted in 1 ml of saline solution. After that, plasma was injected into the bottom of the postoperative wound by injection until the edges of the wound were leveled at 3 points at a distance of 1 cm between the injections, the total volume of plasma was 3 ml. Patients in the control group underwent fissure excision and injection of BTA type A at a dosage of 40 units into the same points of the sphincter. For a period of 60 days, all patients were prescribed local ointment therapy containing dioxomethyltetrahydropyrimidine, aimed at wound healing. Pain relief was carried out with the help of systemic analgesic drugs. The incidence of administration and dosage were determined depending on the intensity of the pain syndrome. In patients who had bowel movements during the periods of preoperative cleansing and postoperative recovery, nutritional correction was recommended, including a sufficient amount of fluid and dietary fiber, to optimize the motor evacuation function of the gastrointestinal tract in order to form a regular shaped stool in the patient. With insufficient effectiveness of diet therapy, osmotic laxatives were prescribed with monitoring of their effectiveness [1].

The primary point of the study:

- Epithelialization of the postoperative wound on the 60th day after surgical treatment.

Secondary examination points:

- Epithelialization of the postoperative wound on the 15th, 30th and 45th days after surgical treatment.
- Incidence and structure of postoperative morbidity.
- Pain intensity during the daytime and during bowel movements for 60 days after treatment.
- Incidence of IAS spasms on the 30th and 60th days after treatment.
- Days of disability.
- Factors presumably influencing the non-healing of the postoperative wound on days 30, 45 and 60.
- Factors presumably influencing the presence of AI on days 30 and 60.

The hypothesis of the study: The use of platelet-rich plasma will increase the incidence of wound healing for up to 60 days after excision of a chronic anal fissure in combination with injection of BTA at a dosage of 40 units.

Calculation of the sample size: With a probability of type I error of 5% and a study capacity of 80%, it was necessary to recruit at least 61 patients in each group in order to prove an increase in the incidence of epithelialization of the lesion on day 60 from 86% with a combination of BTA at a dosage of 40 units with fissure excision by 13% [5] (up to 99%, respectively) when combining this treatment method with platelet-rich plasma. Taking into account possible dropouts from the study, the number of patients required for randomization was increased to 142.

The initial characteristics of the included patients in the study are presented in Table 1.

All the patients included in the analysis (60 in the FE + BTA + PRP group and 65 in FE + BTA) underwent a follow-up examination, profilometry, assessment of pain intensity and the presence or absence of transient AI according to Wexner's scale. On day 15, all the included patients underwent a follow-up examination and filled out questionnaires. Attendance at subsequent checkpoints was incomplete. In order to preserve all available data and minimize systematic errors, all randomized patients were included in the analysis. Accordingly, the number of patients in each group who underwent a specific examination method before surgery and at subsequent control points is shown in Figure 2.

Statistical Analysis

The data analyzed in the study was entered into an Access relational database (Microsoft Office 2013); statistical data analysis was performed in RStudio (R v. 4.4.1 (R Core Team, Vienna, Austria))

Table 1. *Baseline characteristics of patients*

Values	FE + BTA + PRP N = 60	FE + BTA N = 65
Age, years, Me (Q1; Q3) Min–Max	39 (29; 44) 21–72	39 (34; 46) 20–75
Gender, *n* (%) Male Female	 18 (30.0%) 42 (70.0%)	 24 (36.9%) 41 (63.1%)
BMI, kg/m^2, Me (Q1; Q3) Min–Max	23.7 (20.7; 29.7) 17.0–50.3	24.5 (22.2; 29.8) 17.7–41.7
Duration of medical history, months, Me (Q1; Q3) Min–Max	15 (6; 47) 3–180	15 (8; 48) 3–240
Childbirth, *n* (%)	14/42 (33.3%)	19/41 (46.3%)
Number of childbirths, *n*/N (%) 1 2 3	 8/14 (57.1%) 5/14 (35.7%) 1/14 (7.1%)	 6/19 (31.6%) 12/19 (63.2%) 1/19 (5.3%)
A history of complicated childbirth, *n*/N (%)	0/14 (0%)	1/19 (5.3%)
Number of anal fissures, *n* (%) 1 2	 50 (83.3%) 10 (16.7%)	 57 (87.7%) 8 (12.3%)
Localization of anal fissure, *n* (%) Anterior Posterior Lateral Anterior and Posterior	 6 (10.0%) 43 (71.7%) 1 (1.7%) 10 (16.7%)	 5 (7.7%) 48 (73.8%) 4 (6.2%) 8 (12.3%)
IH, *n* (%) 1 2 3	 3 (5.0%) 2 (3.3%) 13 (21.7%)	 4 (6.2%) 0 4 (6.2%)
EH, *n* (%) 1 2 3	 4 (6.7%) 2 (3.3%) 13 (21.7%)	 6 (9.2%) 2 (3.1%) 4 (6.2%)
Sentinel tag, *n* (%) 1 2	 9 (15.0%) 0	 9 (13.8%) 2 (3.1%)
Fibrous polyp, *n* (%)	3 (5.0%)	3 (4.6%)

Note: BMI — body mass index; IH — internal hemorrhoids; EH — external hemorrhoids.

using the libraries RODBC, dplyr, gtsummary, ggplot2, GenBinomApps. Qualitative values are given as absolute and relative frequencies (*n* (%) or n/N (%)); quantitative and qualitative ordinal values (with the number of possible values > 5) are given as medians, lower and upper quartiles (Me (Q1; Q3)).

For the primary endpoint of the study (the dichotomous value), a 95% coincidence interval (CI) was calculated using Clopper-Pearson's test. The comparison of groups by qualitative values was performed by χ^2 Pearson's test with expected values of more than 10 for four-field tables and more than 5 for at least 20% of observations for multi-field; in the other cases, two-sided Fisher's exact test was used. When comparing groups by quantitative and qualitative ordinal values (with the number of possible values > 5), Wilcoxon's rank sum test was used. Wilcoxon's continuity-adjusted test was used to assess the differences between two-time observation points within the same group. The search for factors that could be associated with the outcome was carried out using a univariate logistic regression analysis indicating the value of the odds ratio (OR) and its 95% CI using Wald's method. The differences were considered significant at $p < 0.05$. To visualize the results, span

diagrams and a histogram with grouping were also built.

RESULTS

Epithelialization was assessed by anoscopy at each control point. Wounds were considered healed in the case of complete epithelialization of the lesion upon visual control, along with the simultaneous absence of complaints of pain, itching, discomfort, and blood discharge. On day 60, there was a comparable rate of postoperative wound epithelialization: 43/60 (71.7%; 95% CI: 58.6–82.5) cases in the main group and 47/65 (72.3%; 95% CI: 59.8–82.7) in the control group ($p = 0.936$), which did not reach the expected values calculated when calculating the sample size. Nevertheless, the following pattern was noted at earlier follow-up: on the 15th day, there was no epithelialization of the postoperative wound in any case, and on the 30th and 45th days, a significantly higher healing rate was recorded in patients in the group using platelet-enriched plasma. On day 30, in the FE + BTA + PRP group, the postoperative wound healed in 11/60 (18.3%) patients, while in the group without plasma, the wound did not heal in any patient ($p = 0.0001$); on day 45, in 18/60 (30.0%) versus 3/65 (4.6%) patients, $p < 0.0001$ (Fig. 3).

By the 60-day control point, the incidence of non-healing of postoperative wounds in the study group was 17/60 (28.3%) cases and 18/65 (27.7%) in the control group ($p = 0.936$) (Fig. 4).

One patient in the FE + BTA + PRP group and two in the FE + BTA group with a non-healing wound developed intra-sphincter anal fistulas, confirmed by transanal ultrasound. All fistulas were excised on a probe into the lumen of the rectum and healed within up to 60 days after surgery. On the 60th day after surgery, all other patients with non-healing wounds were prescribed local therapy with a drug containing dexpanthenol to stimulate tissue repair. During the therapy in the main group, the wound healed in three patients on day 75, in one on day 85 and in one on day 90 after surgery; in the control group, the postoperative wound epithelized in one patient on day 75, in two on day 80 and in four on day 85. Five patients had unknown treatment outcomes (two in the main group and three in the control group).

Additional interventions in the FE + BTA + PRP group were performed to the following extent:

Examination methods	Before surgery	Day 15	Day 30	Day 45	Day 60
Control inspection	FE+BTA+PRP N=60 FE+BTA N=65	FE+BTA+PRP N=60 FE+BTA N=65	FE+BTA+PRP N=60 FE+BTA N=65	FE+BTA+PRP N=60 FE+BTA N=64	FE+BTA+PRP N=60 FE+BTA N=64
Assessment of pain intensity	FE+BTA+PRP N=60 FE+BTA N=65	FE+BTA+PRP N=60 FE+BTA N=65	FE+BTA+PRP N=60 FE+BTA N=65	FE+BTA+PRP N=60 FE+BTA N=64	FE+BTA+PRP N=60 FE+BTA N=64
Profilometry	FE+BTA+PRP N=60 FE+BTA N=65	Not conducted	FE+BTA+PRP N=48 FE+BTA N=51	Not conducted	FE+BTA+PRP N=49 FE+BTA N=45
Assessment of transient AI	FE+BTA+PRP N=60 FE+BTA N=65	Not conducted	FE+BTA+PRP N=60 FE+BTA N=65	Not conducted	FE+BTA+PRP N=60 FE+BTA N=64

Figure 2. *The number of patients in the main and control groups who underwent examinations (follow-up, assessment of pain intensity, profilometry, assessment of transient AI) before surgery, on the 15th, 30th, 45th and 60th days after surgery*

- Two patients received an additional injection of platelet-rich plasma (healing was achieved on days 75 and 90 after the first surgery);
- Excision of scar tissue was performed in two patients without IAS spasm — healing on days 90 and 180;
- Four patients with IAS spasm were prescribed conservative therapy with an ointment containing nifedipine and lidocaine (healing was achieved on days 90 and 102, in two patients the outcomes are unknown);
- One patient underwent medical relaxation in IAS — BTA 80 units.

Subsequently, the patient's spasm was not detected, the lesion healed on the 60th day after the isolated injection of BTA. However, on the 90th day, a recurrence of CAF was noted, an isolated lateral subcutaneous sphincterotomy was performed, healing was achieved on the 15th day.

Additional interventions in the FE + BTA group:

- Three patients received an injection of platelet-rich plasma, and healing was achieved on day 75;
- In one patient, due to the ineffectiveness of the therapy and the absence of IAS spasm, scar tissue was excised in the area of the lesion, the outcome of treatment is unknown;
- Two patients with IAS spasm were prescribed conservative therapy with an ointment containing nifedipine and lidocaine, the outcomes are unknown.

Despite the randomization before surgery, the intensity of pain during the day was slightly lower in the FE + BTA + PRP group and amounted to 3 (2; 4) points versus 4 (3; 5) points in the FE + BTA group ($p = 0.039$). However, on day 1 after surgery, the severity of pain syndrome leveled off and amounted to 4 (2; 6) points in the main and control groups ($p = 0.577$). Further, the groups continued to remain comparable in this indicator at all control points, with the exception of 12 days (1 (0;3) points in the FE + BTA + PRP group versus 2 (1; 4) points in the FE + BTA group ($p = 0.036$)).

By day 60, almost all patients in both groups managed to relieve pain during the day ($p = 0.242$) (Fig. 5).

During defecation, the changes in the pain severity was similar to that during the day (Fig. 6). Before surgery, the pain intensity was 5 (4; 7) points in the main group versus 6 (4; 7) points in the control group ($p = 0.394$). The groups continued to remain comparable for two months, with the exception of 10 days (3 (1; 4) points in the FE + BTA + PRP group versus 4 (2; 6) in the FE + BTA group ($p = 0.049$))

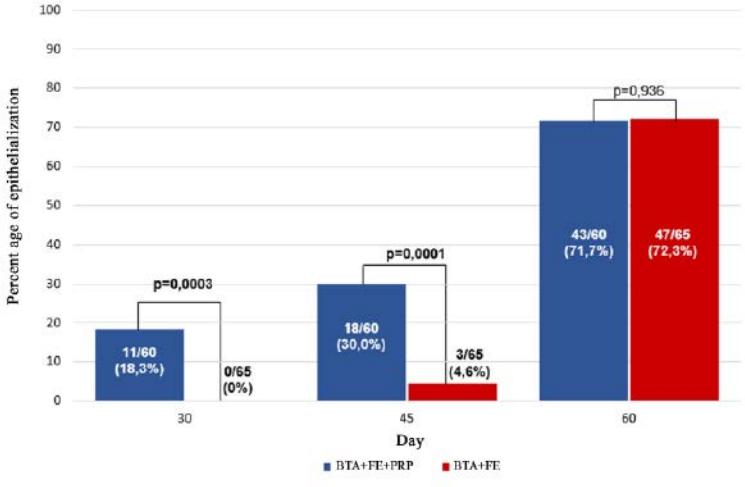

Figure 3. *Rate of epithelialization of the postoperative wounds on days 30, 45 and 60*
Note: If patient initially had two CAFs, the fact of epithelialization was considered only after healing of both postoperative wounds.

and 12 days (2 (1;4) points against 3 (2;4) points (p = 0.035)). By day 60, almost all patients in both groups had no pain during bowel movements (p = 0.635).

Despite the almost complete absence of differences between the groups in pain intensity during 2 months of follow-up after surgery, the number of patients using painkillers was slightly lower in the group where intraoperative injection of platelet-rich plasma was used. However, significant differences were noted only on day 15 — 4/60 (6.7%) patients took painkillers in the main group, versus 18/65 (27.7%) in the control group (p = 0.002). On day 30, the groups were comparable in this parameter (p = 0.681) (Fig. 7).

Before surgery, the maximum pressure in the anal canal at rest was 121 (117; 136) mmHg in the main group and 129 (118; 143) mmHg — in the control group (p = 0.035). On day 30, both groups showed a significant decrease to the baseline data (both p < 0.0001): up to 90 (79; 113) mmHg in the FE + BTA + PRP group and 87 (78; 101) mmHg in the FE + BTA group. (p = 0.565). On day 60, there were no significant changes in the maximum pressure in the anal canal at rest compared to day 30 (p = 0.759 for the main group and p = 0.578 for the control group), while the groups remained comparable — 88 (76; 118) mmHg in the FE + BTA + PRP group and 96 (75; 107) mmHg were in the FE + BTA group (p = 0.766), respectively (Fig. 8).

The mean pressure in the anal canal at rest before surgery was 64 (59; 69) mmHg in the main group and 63 (62; 65) mmHg in the control group (p = 1.0). On day 30, both groups showed a significant decrease in the values of the indicator (both p < 0.0001): 47 (40; 60) mmHg in the group where platelet-rich plasma was used, versus 44 (39; 49) mmHg in the group without the use of stimulants

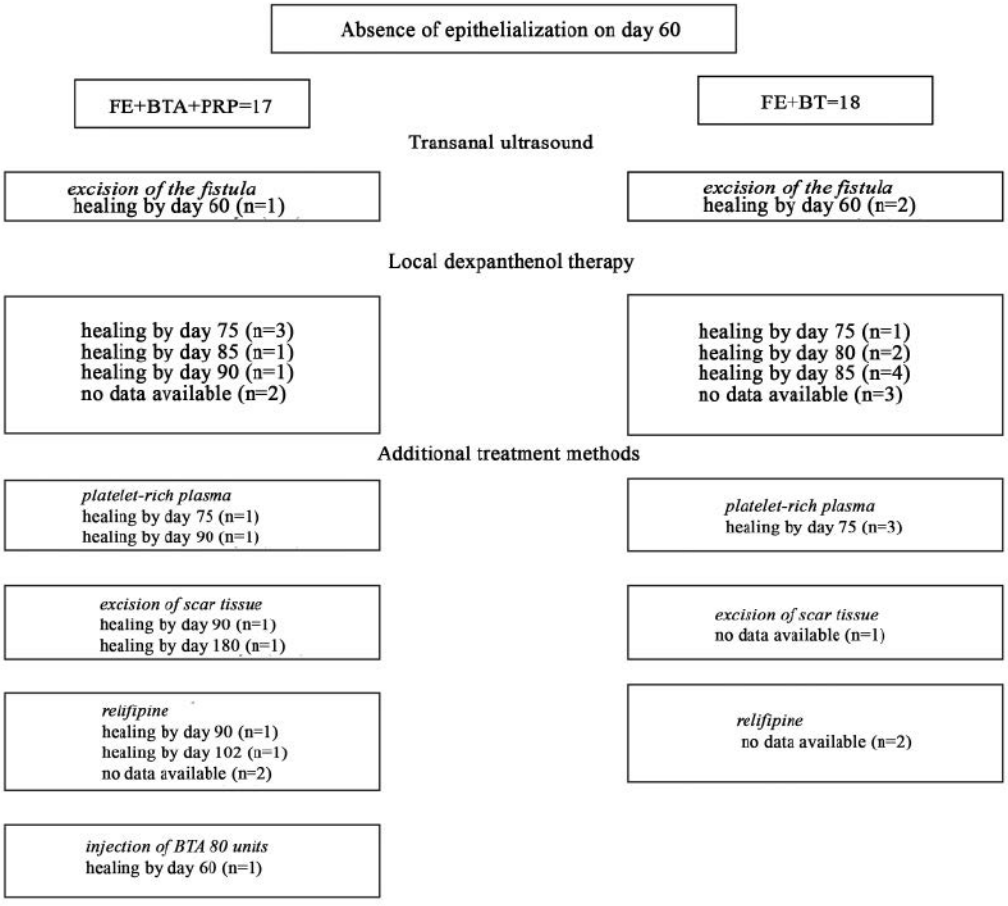

Figure 4. *Treatment methods for patients with long-term non-healing wounds*

of reparative processes (p = 0.042); on day 60, the values remained approximately at the same level (p = 0.509 in the main group and p = 0.080 in the control group), amounting to 46 (40; 54)

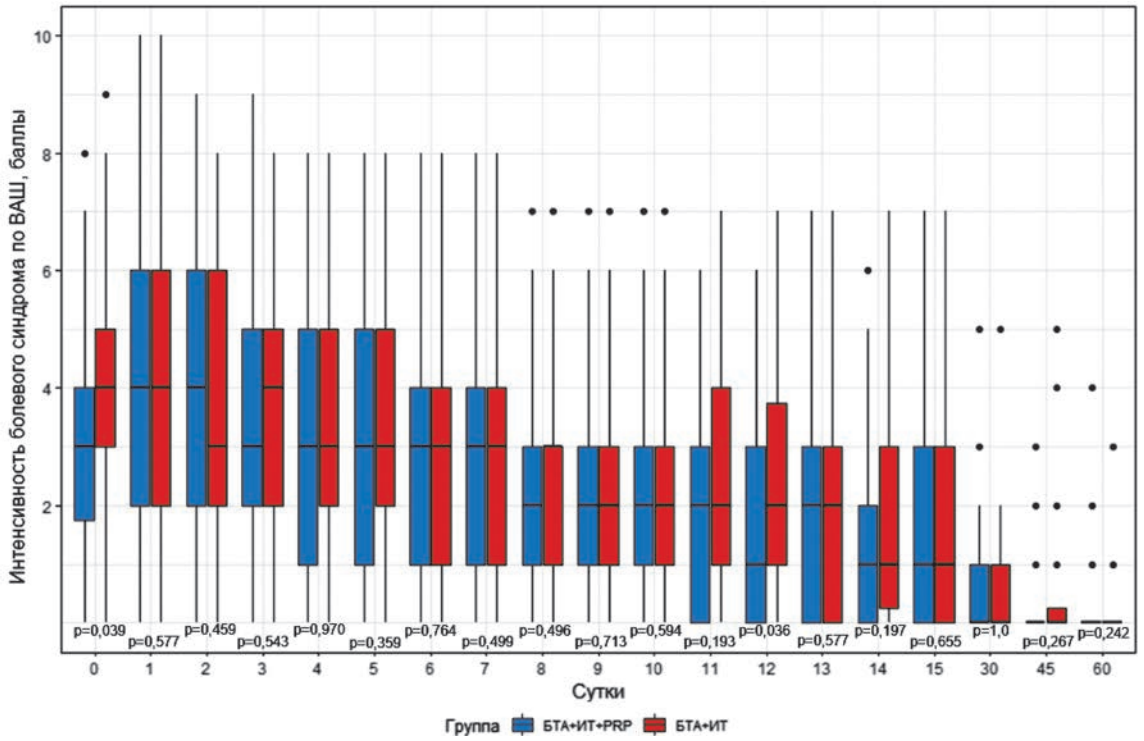

Figure 5. *Change of the intensity of pain syndrome (according to the VAS) during the day in main and control groups on 0–15, 30, 45 and 60 days*

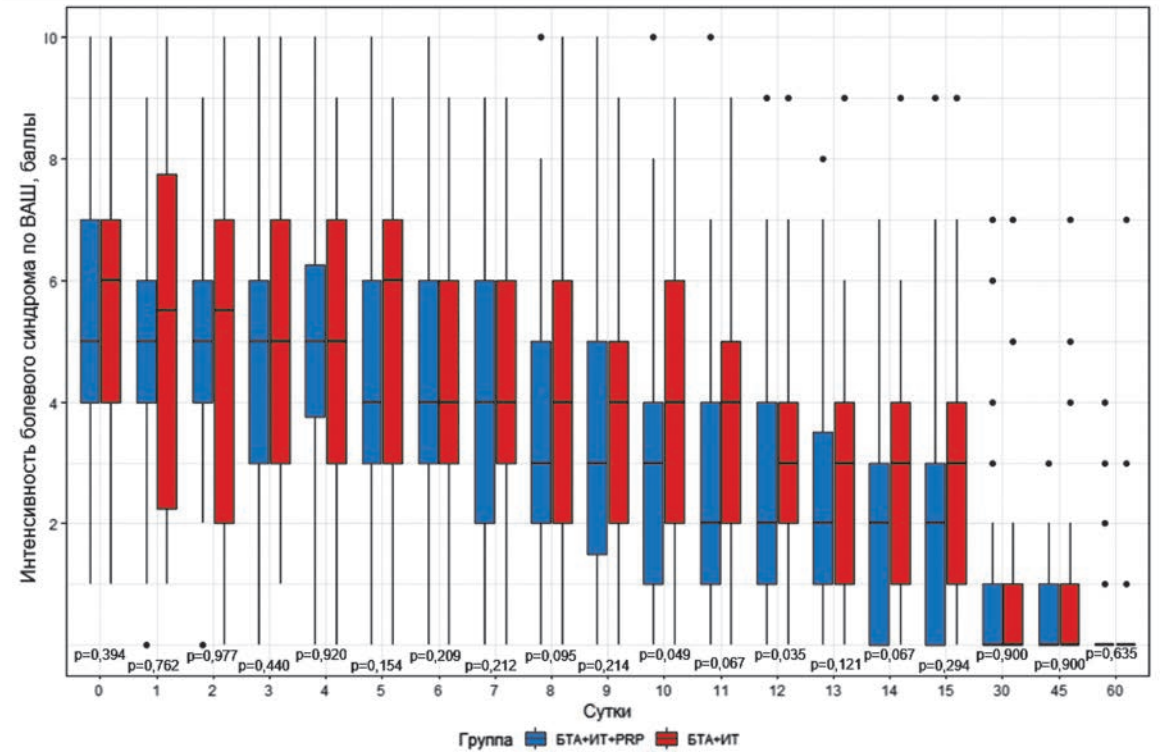

Figure 6. *Change of the intensity of pain syndrome (according to the VAS) during the defecation in main and control groups on 0–15, 30, 45 and 60 days*

mmHg. — in the FE + BTA + PRP group and 44 (40; 50) mmHg — in the FE + BTA group (p = 0.370), respectively (Fig. 9).

According to profilometry data, on the 30th day after surgery, IAS spasm persisted in 15/48 (31.3%) patients of the main group and in 10/51 (19.6%) patients of the control group (p = 0.183); on the 60th day — in 15/45 (33.3%) and 11/49 (22.4%) patients (p = 0.239), respectively.

At the same time, on day 60 in the main group, despite the healed postoperative wound, IAS spasm persisted in 9/31 (29.0%) patients, whereas in the control group, a similar pattern was observed in 5/33 (15.2%) patients (p = 0.232). In the absence

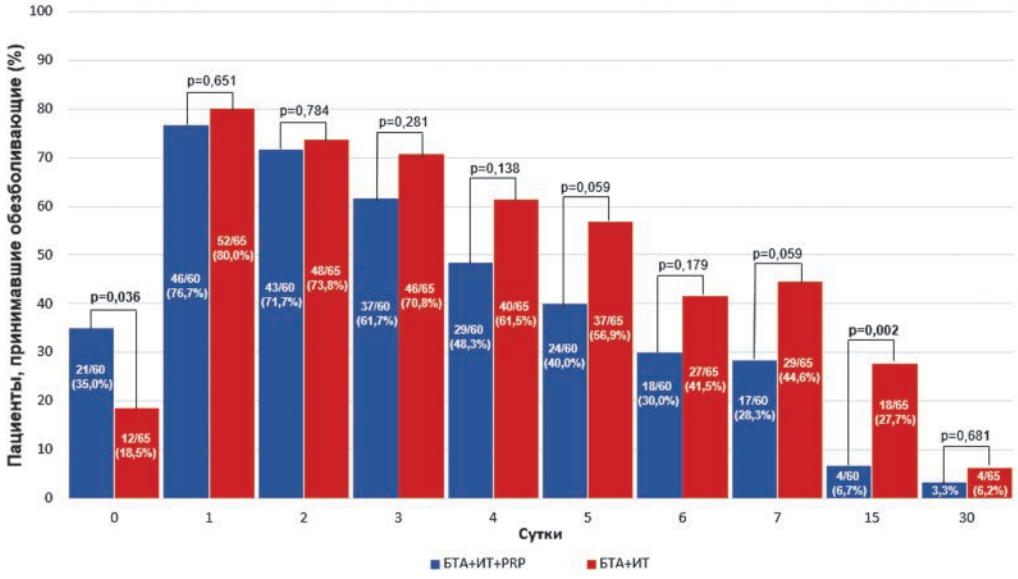

Figure 7. *Frequency of use of painkillers on days 0–7, 15 and 30*

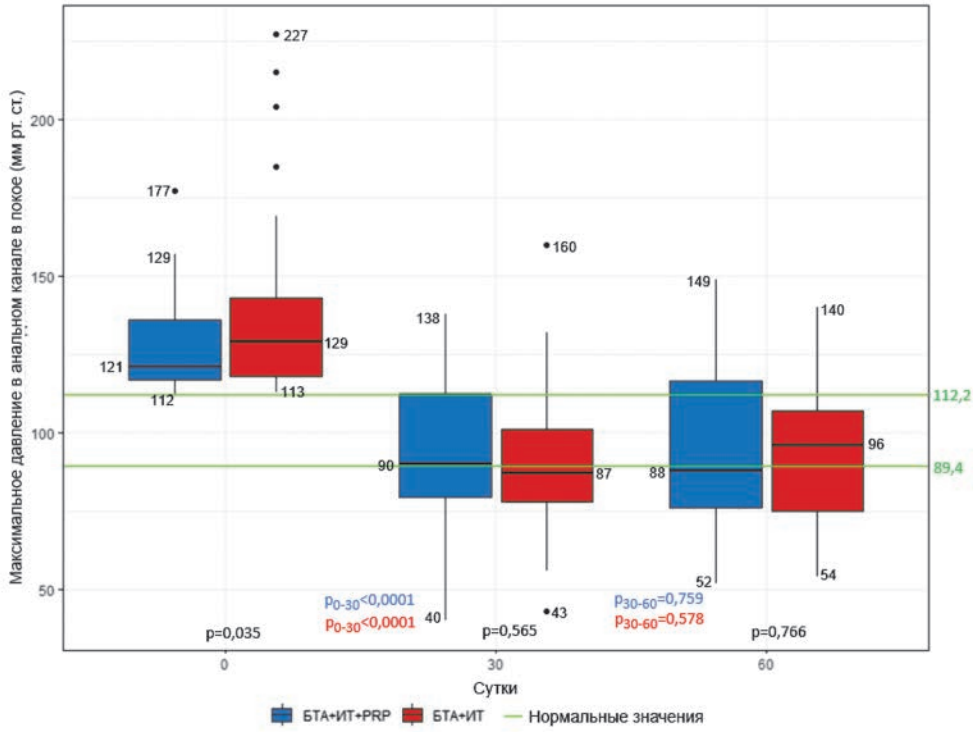

Figure 8. *The maximum pressure in the anal canal at rest in the main and control groups according to profilometry results on 0, 30 and 60 days*

Table 2. *Comparison of the fact of healing of the postoperative wound and the presence of IASspasm on the 60th day after surgery in the main and control groups*

Value	Postoperative wound healing by day 60					
	Yes			No		
	FE + BTA + PRP N = 31	FE + BTA N = 33	p-value	FE + BTA + PRP N = 14	FE + BTA N = 16	p-value
IAS spasm	9 (29.0%)	5 (15.2%)	0.232	6 (42.9%)	6 (37.5%)	1.0

of epithelialization, spasm was not eliminated in some patients: in the FE + BTA + PRP group — in 6/14 (42.9%) patients, in the FE + BTA group — in 6/16 (37.5%) patients, $p = 1.0$ (Table 2).

Transient AI on day 30 was observed in 12/60 (20.0%) patients of the main group and in 10/65 (15.4%) patients of the control group ($p = 0.498$); on day 60 — in 5/60 (8.3%) and 2/64 (3.1%) patients, respectively ($p = 0.262$).

When assessing social and labor after rehabilitation in the postoperative period, the duration of temporary disability in the groups did not differ — 15 (11; 22) days in the FE + BTA + PRP group and 20 (13; 27) days in the FE + BTA group ($p = 0.079$).

A significant factor increasing the chances of absence of epithelialization on day 30 was female sex (OR = 3.95; 95% CI: 1.09–14.37; $p = 0.037$), as well as on day 45 (OR = 3.29; 95% CI: 1.26–8.61; $p = 0.015$), and on day 60 (OR = 3.22; 95% CI: 1.22–8.54; $p = 0.019$). At the same time, there were several significant factors on day 45, one of which was the treatment method (OR = 0.11; 95% CI: 0.03–0.41; $p = 0.0009$). As the age of patients increases, the chances of non-healing also increase (OR = 1.07; 95% CI: 1.01–1.13; $p = 0.015$). According to the other signs considered by us: the duration of the history, body mass index, localization of CAF, the presence of a sentinel tag, there was no significant association with the absence of epithelialization (Table 3). The remaining formations of the anal canal were not taken into account in the analysis due to their small number.

When assessing the factors potentially affecting the presence of AI on the 30th and 60th days after surgery, none of the parameters under consideration demonstrated an effect on the risk of developing transient anal incontinence (Table 4).

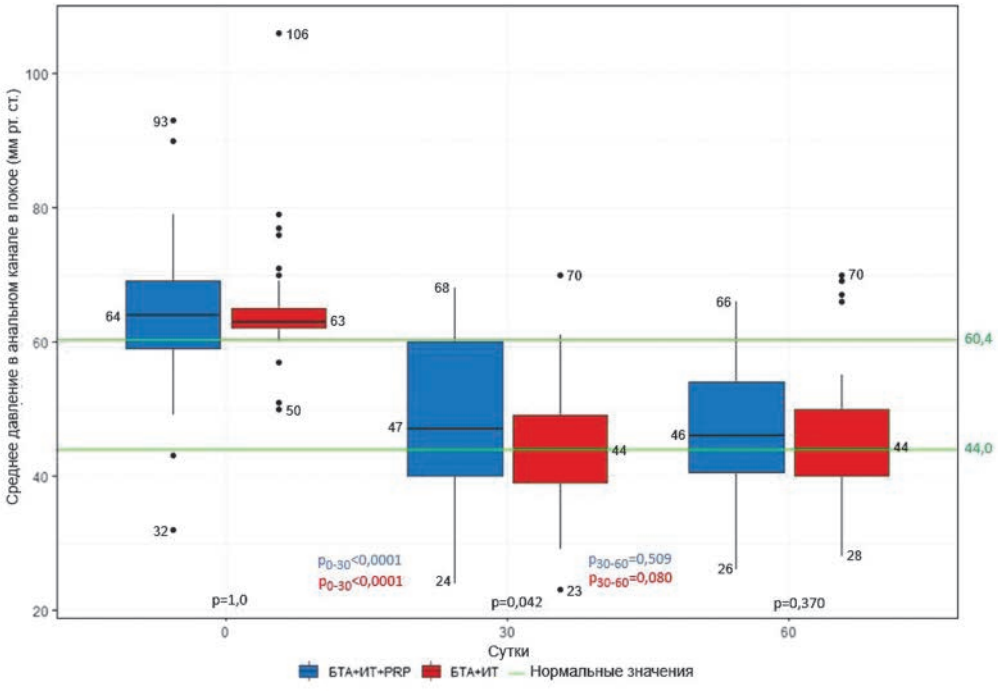

Figure 9. *The mean pressure in the anal canal at rest in the main and control groups according to profilometry results on 0, 30 and 60 days*

Table 3. *Factors presumably influencing the non-healing of the postoperative wound on the 30th, 45th and 60th days after surgery*

Values	On day 30		On day 45		On day 60	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Treatment method		–		**0.0009**		0.936
FE + BTA	1		1		1	
FE + BTA + PRP	0		0.11 (0.03–0.41)		1.03 (0.47–2.25)	
Gender		**0.037**		**0.015**		**0.019**
Male	1		1		1	
Female	3.95 (1.09–14.37)		3.29 (1.26–8.61)		3.22 (1.22–8.54)	
Childbirth	2.04 (0.20–20.5)	0.544	6.09 (0.72–51.2)	0.096	1.38 (0.55–3.46)	0.490
Age, years	1.03 (0.97–1.10)	0.300	1.07 (1.01–1.13)	**0.015**	1.01 (0.98–1.05)	0.463
Medical history, months	1.00 (0.99–1.01)	0.767	1.01 (0.99–1.02)	0.389	1.00 (0.99–1.01)	0.573
BMI, kg/m^2	1.02 (0.92–1.13)	0.769	1.03 (0.95–1.12)	0.481	1.01 (0.95–1.07)	0.797
The presence of constipation	–	–	5.14 (1.43–18.53)	**0.013**	1.83 (0.83–4.03)	0.134
IAS spasm	3.25 (0.39–27.12)	0.277	–	–	1.03 (0.40–2.69)	0.945
CAF Localization		0.968		0.981		0.679
Anterior	1		1		1	
Posterior	1.03 (0.27–4.00)		0.99 (0.33–2.92)		0.82 (0.33–2.08)	
Presence of EH	0.52 (0.14–1.90)	0.321	1.01 (0.34–3.04)	0.982	0.92 (0.36–2.31)	0.852
Presence of a sentinel tag	2.00 (0.24–16.56)	0.544	4.47 (0.56–35.4)	0.156	0.40 (0.11–1.47)	0.169

Table 4. *Factors presumably influencing the presence of incontinence on the 30th and 60th days after surgery*

Values	On day 30		On day 60	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Treatment method		0.500		0.277
FE + BTA	1		1	
FE + BTA + PRP	1.38 (0.55–3.46)		2.82 (0.53–15.11)	
Gender		0.845		0.607
Male	1		1	
Female	1.10 (0.41–2.95)		1.50 (0.32–7.04)	
Childbirth*	1.40 (0.43–4.54)	0.575	–	–
Age, years	1.01 (0.97–1.05)	0.618	0.96 (0.88–1.04)	0.301
Medical history, months	1.00 (0.99–1.01)	0.760	0.99 (0.96–1.02)	0.359
BMI, kg/m^2	1.00 (0.93–1.08)	0.937	1.00 (0.89–1.13)	0.950

*Note: * The calculation was carried out among women.*

DISCUSSION

In recent years, attention has been attracted by the introduction into clinical practice of one of the methods of cell therapy: the use of autologous plasma enriched with platelets (PRP), due to its alleged proangiogenic and regenerative properties. Laboratory studies on cell models (HDMEC and hASC) have shown that PRP prevents damage to endothelial and stromal cells, stimulates angiogenesis, increases the expression of bFGF, the main fibroblast growth factor, which plays a key role in the growth and regeneration of tissues in the body and modulates the inflammatory response through IL-6 [10–13]. This indicates the ability of PRP to overcome microvascular deficiency and trigger reparative processes in conditions of chronic ischemia, which makes this technique particularly promising in the treatment of CAF.

According to Belik B.M., et al. (2022), the use of platelet-rich plasma in the CAF area made it possible to achieve epithelialization of the lesion in 100% of patients by day 29. This is probably due to the mechanism of action of plasma, which initiates a cascade of tissue repair processes [10,14]. The author also notes a decrease in the number of days of disability to 2 days [11].

In the study, by day 60, we managed to achieve epithelialization of the lesion in 71.7% of patients in the main group and 72.3% in the control group. However, on day 30 in the FE + BTA + PRP group,

the postoperative wound healed in 11/60 (18.3%) patients, while in the group without plasma, the wound did not heal in any patient ($p = 0.0001$); on day 45, in 18/60 (30.0%) versus 3/65 (4.6%) patients, $p < 0.0001$.

When assessing the intensity of postoperative pain syndrome, there were practically no differences between the groups from the 1st to 60th days. At the same time, in the group where platelet-rich plasma was used, the number of patients using painkillers was significantly lower, which is most likely due to the anti-inflammatory effect of plasma.

Despite the decrease in the need for anesthesia, when assessing social and labor rehabilitation in the postoperative period, the number of days of temporary disability in the groups did not differ statistically significantly, which was most likely due to the presence of a postoperative wound. According to Bordakov P.V. et al. (2019), the use of autoplasm in the bottom of the anodermic defect without excision helped to reduce the recovery time to 6 days [15]. Among the other things, it was found that the healing process was negatively affected by factors such as female sex, old age, and a history of chronic constipation. However, there is no clear pathophysiological justification for this case in the modern literature.

CONCLUSION

A single injection of platelet-rich plasma as an adjunct to the surgery for CAF, which includes excision of the fissure in combination with drug relaxation of the IAS by injection of BTA, does not lead to an increase in the frequency of epithelialization of the postoperative wound when assessed 2 months after surgery, but has a statistically significant advantage in the frequency of epithelialization on days 30 and 45. Administration of platelet-rich plasma has no effect on the frequency of postoperative complications, pain intensity, functional treatment outcomes, and social and labor rehabilitation of patients.

AUTHORS CONTRIBUTION

Concept and design of the study: *Evgeny E. Zharkov, Ekaterina Yu. Lebedeva, Aleksey A. Ponomarenko*

Collection and processing of the material: *Ekaterina Yu. Lebedeva, Evgeny E. Zharkov, Maria A. Ignatenko*

Text writing: *Ekaterina Yu. Lebedeva, Maria A. Ignatenko*

Statistical processing: *Maria A. Ignatenko, Ekaterina Yu. Lebedeva*

Editing: *Evgeny E. Zharkov, Aleksey A. Ponomarenko, Andrey A. Mudrov, Ivan V. Kostarev*

INFORMATION ABOUT THE AUTHORS (ORCID)

Ekaterina Yu. Lebedeva — 0000-0002-3590-112X
Maria A. Ignatenko — 0009-0005-1182-419X
Evgeny E. Zharkov — 0000-0003-3403-9731
Aleksey A. Ponomarenko — 0000-0001-7203-1859
Andrey A. Mudrov — 0000-0002-1207-5988
Ivan V. Kostarev — 0000-0002-1778-0571

REFERENCES

1. Anal fissure. Clinical guidelines. Moscow; 2024. URL: https://cr.minzdrav.gov.ru/preview-cr/172_3 (In Russ.).

2. Trzpis M, Klaase JM, Koop RH, et al. Fissurectomy combined with botulinum toxin A: a review of short- and long-term efficacy of this treatment strategy for chronic anal fissure; a consecutive proposal of a treatment algorithm for chronic anal fissure. *Coloproctology*. 2020;42:400–408. doi: 10.1007/s00053-020-00480-7

3. Lindsey I, Cunningham C, Jones OM, et al. Fissurectomy-botulinum toxin: a novel sphincter-sparing procedure for medically resistant chronic anal fissure. *Dis Colon Rectum*. 2004;47(11):1947–52. doi: 10.1007/s10350-004-0693-x

4. Goloktionov N.A., Titov A.Yu., Ponomarenko A.A., et al. Early outcomes of chronic anal fissure treatment using the lateral internal sphincterotomy method without excision (randomized trial NCT05117697). *Koloproktologia*. 2023;22(3):50–61. (in Russ.). doi: 10.33878/2073-7556-2023-22-3-50-61

5. Khryukin R.Yu., Zharkov E.E., Goloktionov N.A., et al. Treatment of chronic anal fissure using botu-

linum toxin type A at a dose of 40 U compared with lateral subcutaneous sphincterotomy (NCT03855046). *Koloproctologia*. 2022;21(1):60–70. (In Russ.). doi: 10.33878/2073-7556-2022-21-1-60-70

6. Sagidova K.I., Ignatenko M.A., Zharkov E.E., et al. Results of chronic anal fissure treatment with botulinum toxin type A at a dose (dosage) of 80 units without its incision (single-center prospective randomized controlled trial NCT05598164). *Koloproktologia*. 2025;24(3):35–47. (In Russ.). doi: 10.33878/2073-7556-2025-24-3-35-47

7. Solovyev D. The use of Platelet-rich-plasma in the treatment of patients with chronic anal fissure. Budapest Proctology Meeting: How We Do It? November 24–26, 2016. Budapest: Hungary. 2016;13. Ac cessed November 2016. Available at: www.proctologybpmeeting.hu; www.convention.hu.

8. Yilmaz G, Tanrikulu Y. Short-term Results of Platelet-Rich Plasma in the Treatment of Chronic Anal Fissure: Randomized Controlled Clinical Study. *Dis Colon Rectum*. 2021;64(6):714–723. doi: 10.1097/DCR.0000000000001903 PMID: 33399410.

9. Krylov N.N., Lyatifova L.V. Autoplasmotherapy in coloproctology. *Pirogov Russian Journal of Surgery*. 2017;(7):61–64. (In Russ.). doi: 10.17116/hirurgia2017761-64

10. Leitner GC, Gruber R, Neumüller J, et al. Platelet content and growth factor release in platelet-rich plasma: A comparison of four different systems. *Vox Sang*. 2006;91(2):135-9. doi: 10.1111/j.1423-0410.2006.00815.x

11. Belik B.M., Kovalev A.N. The use of autologous platelet-rich plasma in the complex treatment of anal fissure combined with anal sphincter spasm in non-hospital settings. *Koloproktologia*. 2022;21(1):50-59. (In Russ.). doi: 10.33878/2073-7556-2022-21-1-50-58

12. Gunin AG, Petrov VV, Golubtzova NN, et al. Age-related changes in angiogenesis in human dermis. *Experimental Gerontology*. 2014;55:143-151, ISSN 0531-5565. doi: 10.1016/j.exger.2014.04.010

13. Lecce L, Lam YT, Lindsay LA, et al. Aging impairs VEGF-mediated, androgen-dependent regulation of angiogenesis. *Mol Endocrinol*. 2014 Sep;28(9):1487-501. doi: 10.1210/me.2013-1405 Epub 2014 Jul 24. PMID: 25058601; PMCID: PMC4154238.

14. Hoch M, Eberle AN, Peterli R, et al. LPS induces interleukin-6 and interleukin-8 but not tumor necrosis factor-α in human adipocytes. *Cytokine*. 2008;41(1):29–37.

15. Bordakov P., Gain Yu. Tissue Engineering in Complex Treatment of Chronic Anal Fissures Using Minimally Invasive Technologies. *Hematology. Transfusiology. Eastern Europe*. 2019;5(4):437–449. (In Russ.).