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Research Article

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Efficacy of Topical Metal Polyacrylates for the Prevention and Treatment of Bleeding After Retrograde Cholangiopancreatography

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RELEVANCE In recent years, local hemostatic agents have become widespread, as their application at the incision area of the major duodenal papilla can stop or prevent bleeding.

AIM OF STUDY To study the efficacy of topical application of incomplete silver salt of polyacrylic acid (PAAg) (Haemoblock) for the prevention and treatment of bleeding from the papillosphincterotomy area.

MATERIAL AND METHODS The prospective study included 211 patients who were hospitalized at the Regional Clinical Hospital in Ryazan from 2020 to 2023. In the main group of patients, for the purpose of hemostasis and prevention of bleeding, the area of the dissected major duodenal papilla was irrigated with 20 ml of an aqueous solution of PAAg. In the control group, irrigation was carried out with 20 ml of 0.9% sodium chloride. The main group included 111 patients (44 men, 67 women, mean age 55.09±20.97), the control group included 100 patients (43 men, 57 women, average age 53.85±20.34).

RESULTS In the main group of patients, bleeding from the MDP incision was observed in 83 cases after papillosphincterotomy, and in 82 cases in the control group. After irrigation with an aqueous solution of PAAg, bleeding from the MDP incision was arrested within 120 seconds in the main group in 70 patients, and in 51 patients in the control group, after irrigation with 0.9% sodium chloride solution. Within 300 seconds from the initiation of irrigation, hemostasis occurred in 12 of the 13 remaining patients in the main group with ongoing bleeding and in 27 of 31 patients in the control group.

In two patients in the control group, bleeding was managed in 300 seconds without additional methods of endoscopic hemostasis. The use of additional methods of endoscopic hemostasis due to ongoing bleeding in the main group was required in one patient; the incision area was injected with an adrenaline solution. In the control group, additional endoscopic hemostasis was performed on two patients: in one case, injection with an adrenaline solution, in the other, diathermocoagulation of the incision area of MDP. In the early postoperative period, delayed bleeding was detected in 3 patients of the main group, which was significantly lower than the same indicator in the control group (7 observations).

CONCLUSIONS Local application of PAAg for the treatment of early bleeding in papillosphicterotomy showed a significantly faster onset of hemostasis.

Keywords: metal polyacrylates, endoscopic papillosphincterotomy, endoscopic retrograde cholecyostopancreatography, bleeding, endoscopic hemostasis
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AAEPST — antegrade-assisted endoscopic papillosphincterotomy
APTT — activated partial thromboplastin time
bERCP — bleeding after ERCP
EPST — endoscopic papillosphincterotomy
ERCP — endoscopic retrograde cholecystopancreatography
FGDS — fibrogastroduodenoscopy
INR — international normalized ratio
MDP — major duodenal papilla
PAPSS — polyacrylic acid partial silver salt (Hemoblock)

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is important in the treatment of benign diseases of the biliary tract. Over several decades, ERCP has evolved from a diagnostic procedure to a primarily therapeutic one. The number of ERCPs performed is steadily growing, and in the Russian Federation alone, more than 34,000 operations were performed in 2022 [1]. Technological advances, increased operator experience, and improved patient selection have improved the safety of ERCP. However, ERCP is still considered an operation with a significant risk of complications [2].

Bleeding after ERCP is usually observed when this procedure is supplemented with endoscopic papillosphincterotomy (EPST). A large systematic review of prospective studies examining complications associated with ERCP, including 16,855 patients, found the incidence of ERCP to be approximately 1.34% [3]. We devide post-ERCP bleeding into early bleeding, which occurs directly during the procedure, bleeding that has a high potential for spontaneous arrest, and delayed bleeding, which manifests itself after completion of the procedure. The frequency of early post-ERCP bleeding can reach 12%, delayed bleeding occur in 2% [4, 5]. An important element of successful papillosphincterotomy is timely prevention of bleeding from the incision area. Taking into account the frequency of occurrence of this complication, in addition to prophylactic hemostasis, it is necessary to resort to the actual bleeding arrest, which is required in 100% of cases of complications arising directly from the manipulation.

Aim of the study: to study the effectiveness of topical application of polyacrylic acid partial silver salt (PAPSS) for the prevention and treatment of post-ERCP bleeding.

MATERIAL AND METHODS

The prospective study included 211 patients aged 18 to 80 years who were hospitalized in the department of surgery of the Ryazan Region Regional Clinical Hospital from 2020 to 2023.

Inclusion criteria were indications for performing ERCP with EPST:

1. Choledocholithiasis, confirmed by instrumental diagnostic methods (ultrasound examination of the abdominal organs or magnetic resonance imaging).
2. Stenosing papillitis of the major duodenal papilla.

Non-inclusion criteria:

1. Refusal of the patient to participate in the study.
2. Age under 18 or over 80 years old.
3. The diameter of common bile duct stones is more than 12 mm.
4. Severe concomitant disease, which is a contraindication to ERCP.
5. Disorders of the hemostasis system (international normalized ratio INR above 1.5, or activated partial thromboplastin time aPTT above 40 sec, or blood platelets less than 100×10^9/l).
6. Impossibility of performing ERCP, revealed during a preliminary examination of the patient (parafaterial diverticulum, history of gastric resection according to Billroth II).

Exclusion criteria:

1. Refusal of the patient to participate in the study.
2. The inability to perform EPST, established directly during the attempt to perform it, due to the peculiarities of the anatomical structure of the major duodenal papilla (MDP).
3. The length of EPST is less than 5 mm.
4. EPST complicated by perforation of the duodenum.
5. ERCP complicated by entrapment of the endoscopic basket during lithoextraction.
6. Malignant neoplasm of the biliopancreaticoduodenal zone diagnosed upon ERCP.

Patients included in the study were randomized into two groups: the main group and the comparison group. In the main group of patients, for the purpose of hemostasis and prevention of bleeding, the area of the abdominal joint dissected during EPST was irrigated with 20 ml of an aqueous solution of PAPSS through the papillotome channel. In the comparison group, irrigation was carried out with 20 ml of 0.9% sodium chloride.

PAPSS is registered in the Russian Federation as a topical hemostatic agent under the trade name “Hemoblock”.

The main group included 111 patients, the comparison group included 100.

Both groups were identical to each other in terms of demographic indicators; there were no statistically significant differences between the groups in gender and age (Table 1).

Table 1

Age and gender characteristics of patients in the main and comparison groups

Index	Main group	Comparison group
Men	44	43
Women	67	57
Age, years (*M*±*m*)	55.09±20.97	53.85±20.34

Both groups of patients were identical in terms of initial laboratory parameters; there were no statistically significant differences between the groups in the levels of hemoglobin, bilirubin, blood alkaline phosphatase, INR and APTT (Table 2).

Table 2

Baseline laboratory parameters of patients included in the study

Index	Main group (*M*±*m*)	Comparison group (*M*±*m*)
Red blood cells, $\times 10^{12}$/l	4.15±0.75	4.2±0.74
Hemoglobin, g/l	129.32±23.02	131.65±22.77
Bilirubin total, μmol/l	41.53±20.98	39.05±17.11
Direct bilirubin, μmol/l	30.37±16.61	30.02±15.9
Alkaline phosphatase, U/l	131.72±40.58	133.14±43.01
INR, UNITS	1.16±0.15	1.17±0.16
APTT, sec	29.83±19.2	29.37±18.95

Notes: APTT — activated partial thromboplastin time; INR – international normalized ratio

All interventions were performed under general sedation (Intravenous Propofol). During ERCP, the following principles were observed: selective cannulation of the ducts with mandatory aspiration test; use only diluted non-ionic contrast agent (Ultravist); dosed administration of a contrast agent under mandatory x-ray control; use of electrodiathermy for papillosphincterotomy in *Cut* mode. Surgical interventions were performed with endoscopic device ˝*Olympus CV* 190 *Plus*˝.

Directly during ERCP, the following parameters were assessed: arrest of bleeding from the MDP incision within 120 seconds after irrigation; arrest of bleeding from the MDP incision within 300 seconds after irrigation; the need to use other methods of local endohemostasis (needling of the MDP area with an adrenaline solution, additional electrocoagulation of the incision area).

In the early postoperative period, the following parameters were assessed:

— the occurrence of delayed bleeding from the MDP area with an assessment of its severity according to *P. Cotton* and *C. Williams* [13];

— blood hemoglobin level in 24 hours and on the 5th day after surgery;

— development of acute pancreatitis in the early postoperative period;

— macroscopic characteristics of MDP during fibrogastroduodenoscopy (FGDS) on the 5th day after EPST.

Cotton–Williams classification of the severity of post-ERCP bleeding provides for the identification of three degrees of bleeding severity:

Mild: clinical (non-endoscopic) signs of bleeding, a decrease in Hb level by less than 30 g/l within 24 hours after the intervention. Blood transfusion is not indicated.

Moderate: transfusions (4 doses or less) are indicated; surgery and angiographic embolization are not indicated.

Severe: transfusions (5 doses or more) or intervention (surgery or angiographic embolization) are indicated.

To characterize the condition of the MDP, we used an assessment of signs of the severity of the inflammatory process in the incision area (Table 3).

Table 3

Criteria for assessing inflammatory changes in the area of the MDP incision on day 5

Points	Edema	Hyperemia	Fibrin plaque
0	Moderate: boat-shaped incision, the edges of the incision are smoothed	Moderate: the color of the edges is close to the color of the duodenal mucosa	No fibrin
1	Significant: the incision looks slit-like, the edges of the mucosa almost close and are slightly turned outward due to edema	Significant: the edges of are noticeably brighter than the color of the duodenal - mucosa	Fibrin deposits

The assessment was carried out in a “blind” manner: during FGDS, photographic recording of the MDP area was performed, photographic materials of each patient were numbered, after which an independent expert scored the severity of inflammation based on the photographic image, without information to which group the patient belonged to. With the most pronounced inflammatory changes, the maximum total score is 3, with the least significant it is 0.

Statistical processing of the study results was carried out on a personal computer using the *STATISTICA* 12.0 software package (*StatSoft Inc.*). Data were presented as the mean value and arithmetic mean error ($M \pm m$). Comparisons between groups were made using the Student's t test, which is used when analyzing samples with a normal distribution. To assess the significance of differences between the actual number of outcomes or qualitative characteristics of the sample and the theoretically expected, if the null hypothesis is true, the Pearson criterion (χ^2) was used. Differences were considered significant at *p values* $\leqslant 0.05$, which is the standard for biomedical research. The type of distribution was determined using the Shapiro–Wilk test. If the *p value* was >0.05, the sample was considered to have a normal distribution.

RESULTS

The study, which included 209 patients, 108 in the main group, 99 in the comparison group, was completed. All patients underwent EPST of adequate

length; the length of the MDP incision in the main and comparison groups did not differ significantly (Table 4).

Table 4

Comparative characteristics of endoscopic interventions in patients of the main and control groups

Index	Main group	Comparison group
EPST (including AAEPST), patients	108 (36)	99 (37)
EPST length, mm (*M*±*m*)	13.25±4.11	13.32±4.08
Choledocholithiasis, patients	93	94
Choledocholithiasis was eliminated during the first ERCP, patients	64	61
Choledocholithiasis was eliminated during repeat ERCP, patients	29	33
Eliminated stenosing papillitis, patients	60	59

Notes: EPST – endoscopic papillosphincterotomy (EPST); AAEPST – antegrade-assisted EPST; ERCP – endoscopic retrograde cholecystopancreatography

In some patients, EPST was performed in the antegrade-assisted version (AAEPST), i.e. An endo-string was used as a guide for the papillotome, inserted into the MDP antegradely, either directly during laparoscopic surgery, or through a percutaneous transhepatic cholangiostomy placed under ultrasound guidance.

In most cases, EPST was used to eliminate stenosing papillitis of the MDP. In 33 patients of the main group and in 35 of the comparison group, EPST was performed in the absence of stenosis of the common bile duct orifice in order to perform lithoextraction from the common bile duct using a Dormia loop. In the vast majority of cases in the main and comparison groups, lithoextraction was performed after EPST. In 59% of patients in the main group and in 62% of the comparison group, choledocholithiasis was eliminated during the first ERCP. In some patients, choledocholithiasis for various reasons could not be eliminated during the first ERCP. In such cases, on the 3rd–4th day of the postoperative period, a control ultrasound examination of the abdominal organs was performed to identify signs of residual choledocholithiasis (stones in the lumen of the common bile duct or persistent signs of biliary hypertension). In these patients, FGDS on the 5th day was performed using an operating fibroduodenoscope with the aim of re-inspecting the common bile duct using a Dormia basket. With repeated ERCP, choledocholithiasis was eliminated in 27% of patients in the main group and in 33% of patients in the comparison group. There were no cases of unresolved choledocholithiasis in patients included in the study.

In the main group of patients, visible bleeding from the MDP incision after EPST was observed in 83 observations, in the comparison group it was observed in 82 cases. The fact of bleeding was recorded when fresh blood was released from the incision, regardless of its volume and intensity of flow.

After irrigation with an aqueous solution of PAPSS, arrest of bleeding from the MDP incision within 120 seconds in the main group was observed in 70 patients; in the comparison group, after irrigation with a 0.9% sodium chloride solution, it was observed in 51 patients (Table 5).

Table 5

Comparative characteristics of hemostasis efficacy in the main and comparison groups

Index	Main group	Comparison group
Bleeding from the MDP incision	83	82
Hemostasis within 120 seconds	70*	51
Hemostasis within 300 seconds	12*	27
Hemostasis over 300 seconds without methods of additional endohemostasis	0	2
The need for additional endohemostasis methods	1	2

Notes: * — $p<0.05$ compared to the control group. MDP – major duodenal papilla

The frequency of observations of bleeding arrest within 120 seconds in the main group significantly exceeds that of the comparison group.

Within an additional 180 seconds (300 seconds) from the moment of irrigation, hemostasis occurred in 12 of 13 patients in the main group who remained with ongoing bleeding and in 27 of 31 patients in the comparison group.

In 2 patients of the comparison group, bleeding ceased after 300 seconds, but without the use of additional methods of endoscopic hemostasis.

The use of additional methods of endoscopic hemostasis due to ongoing bleeding in the main group was required in one patient; the incision area was injected with an adrenaline solution. In the

comparison group, additional endoscopic hemostasis was performed on two patients: in one case, injection with an adrenaline solution, in the other, diathermocoagulation of the incision area of the MDP.

In the early postoperative period, delayed bleeding was detected in 3 patients of the main group, which was significantly lower than that of the comparison group, 7 cases (Table 6).

Table 6

MComparative characteristics of the efficacy of prevention of delayed post-ERCP bleeding in the main and control groups

Index		Main group	Group comparisons
Post-ERCP bleeding (*Cotton–Williams* mild/moderate/severe), patients		3* (3/0/0)	7 (5/2/0)
Red blood cells, $\times10^{12}$/l (*M±m*)	1st day	4.16±0.73	3.94±0.8
	5th day	4.18±0.75	3.91±0.82
Hemoglobin, g/l (*M±m*)	1st day	125.5±21.83	116.46±21.94
	5th day	122.93±21.65*	110.65±23.77
Assessment of inflammatory changes in the area of the MDP incision, score (*M±m*)		1.26±0.55*	1.7±0.63

Notes:* — p<0.05 compared to the control group. MDP – major duodenal papilla

At the same time, two cases of delayed post-ERCP bleeding in the comparison group were considered to be of moderate severity and required massive blood transfusion and conservative hemostatic therapy. There was a significant increase in blood hemoglobin levels in patients of the main group compared to the comparison group by 9.2% on the 5th day of observation after ERCP.

When visually assessing the severity of inflammatory changes in the area of the MDP incision, significantly less significant signs of inflammation were noted in patients of the main group on the 5th day after surgery.

When analyzing the frequency of post-manipulation pancreatitis in patients of the main group, 4 cases of mild pancreatitis were observed, all of them had an abortive course. In the comparison group, mild pancreatitis developed in 5 patients, and severe pancreatitis in one patient, requiring long-term hospital treatment and drainage surgical interventions under ultrasound guidance (Table 7).

Table 7

Complications of ERCP, papillosphincterotomy

Complication	Share in the main group, %	Group share comparisons, %
Bleeding from the MDP incision	76.5	82.8
Delayed bleeding	2.8	7.07
Post-manipulation pancreatitis	3.7	5.05

Notes: MDP – major duodenal papilla; PST – papillosphincterotomy; ERCP – endoscopic retrograde cholecystopancreatography

DISCUSSION

Endoscopic hemostasis is the method of choice for the treatment and prevention of post-ERCP bleeding, and various methods are available, including local injection, clipping, balloon compression and coagulation, each with its own advantages and disadvantages [6, 7].

In recent years, local hemostatic agents have become widespread, the application of which to the incision area of the major duodenal papilla can stop or prevent bleeding [8].

In medicine, metallopolyacrylates are widely used as a local hemostatic agent. At the first stage of action of drugs of this group, a polyacrylic matrix structure is formed, which contains albumin molecules in the cells of the polyacrylic matrix and is the primary link of the film formed on the surface of the application. At the next stage, silver ions are reduced by albumin molecules, forming a stable complex. Polyacrylate anions form strong bonds with positively charged protein molecules. This structure forms several microlayers, creating a durable polymethacrylate film over the application area. At the same time, reduced metallic silver in combination with proteins has a bactericidal effect, which promotes faster and more effective repair. Subsequently, the surface structure is replaced by fibrin.

The hemostatic effect is achieved within 1–2 minutes [9–13].

The successful use of drugs with the described mechanism of action in practical surgery is confirmed in the works of A.V. Plotkin et al. [14], A.I. Andreyev et al. [15], N.G. Tereshchenko et al. [16].

Taking into account their chemical and biological properties, metallopolyacrylates are of great interest for topical use during EPST for the treatment and prevention of bleeding.

CONCLUSION

The study proved that the local use of polyacrylic acid partial silver salt for the treatment of early bleeding after endoscopic papillosphincterotomy allows for a significantly faster onset of hemostasis, this is achieved due to the forming polymethacrylate film, which was identified in the works of other authors when studying the possibility of using the data drugs in surgical practice of endoscopic manipulations.

The preventive effect of local application of polyacrylic acid partial silver salt of on delayed bleeding is expressed in a significant reduction in the frequency and severity of delayed bleeding. This is achieved by the fact that the drug used has properties favorable for accelerated repair in the incision area during endoscopic manipulations.

The work proved the effectiveness of using an polyacrylic acid partial silver salt for the prevention and treatment of bleeding from the area of dissection of the major duodenal papilla during endoscopic retrograde cholangiopancreatography.

FINDING

1. In the main group, the arrest of bleeding from the incision of the major duodenal papilla within 120 seconds was observed in 70 patients (84.3%), in the comparison group it was observed in 51 patients (62.2%), which is a statistically significant difference (p <0 .05).

2. In the main group, the arrest of bleeding from the incision of the major duodenal papilla within 300 seconds was observed in 12 patients (14.4%), in the comparison group it was observed in 27 patients (32.9%), which is a statistically significant difference (p <0 .05).

3. In the comparison group, in 2 patients bleeding stopped after 300 seconds without additional methods of endoscopic hemostasis (2.4%).

4. Continued bleeding requiring additional methods of endohemostasis was required in one patient (0.01%) in the main group, and in 2 patients (2.4%) in the comparison group.

5. In the early postoperative period, delayed bleeding was observed in 3 patients of the main group (2.7%), which is significantly lower than that of the comparison group, 7 cases (7.07%).

6. Upon re-examination and macroscopic assessment of the severity of inflammatory changes in the area of the MDP incision 5 days after - papillosphincterotomy, significantly less pronounced signs of inflammation were noted in patients of the main group.

7. Polyacrylic acid partial silver salt is effective in the prevention and treatment of post-manipulation bleeding from the area of the major duodenal papilla.

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