Comparative analysis of methods of prevention of drug- ERCP-induced pancreatitis

I. H. Aminov, M. V. Churkin, E. J. Plotnikova, V. I. Podoluzhny, K. A. Krasnov, O. A. Krasnov

Key words: acute pancreatitis, endoscopic retrograde cholangiopancreatography, Wirsung's duct, Oddi's sphincter, endoscopic papillosphincterotomy, proton pump inhibitors, premedication retrograde cholangiopancreatography

Introduction. Retrograde cholangiopancreatography (ERPHG) allows to visualize the biliary and pancreatic ducts, assess their anatomical relationship and choose the best type of treatment. Endoscopic retrograde cholangiopancreatography is considered to be a "gold standard" in the diagnosis of pathology of the biliary tract. Diagnostic value of ERCP in detecting of biliary disease is 79-98% of cases [2]. In some cases this fluoroscopic intervention is accompanied by various complications. However, as with all invasive, diagnostic and therapeutic transpapillary intervention causes serious and life-threatening patient complications such as endoscopic acute pancreatitis, acute cholangitis, bleeding during endoscopic papillosphincterotomy (EPST), perforation of the pancreatic-biliary ductal and 12 duodenal ulcer, etc. These complications occur in 1,3-9,0% of cases, and the mortality rate reaches 0.5-1.5%. Among the possible complications of ERCP n he most commonly observed occurrence of ERCP-induced pancreatitis hours pilots at that development, according to different authors. It ranges from 1.3% to 40%, while its effective prevention measures to be developed and to date [6, 26, 30].

Despite the experience on this problem, many issues remain unresolved, in particular, issues of selection of radical methods of early diagnosis of complications of endoscopic and reliable measures to prevent their [14].

Regardless of etiology, the criteria for the diagnosis of ERCP-induced acute pancreatitis requires two of the following three criteria [8]: 1) abdominal pain (symptoms) in the appropriate diagnosis; 2) increased serum amylase and/or lipase is more than 3 times the upper limit of normal; 3) characteristic tomographic features

(CT and/or MRI) in accordance with the diagnosis. Inconsistencies of pain in stomach and transient elevation of amylase and/or lipase as a marker post-ERCP pancreatitis may explain why reports of cases of acute pancreatitis after ERCP varies from 4% to 31% in different studies [9, 23, 24 45].

Due to the lack of specificity of pain and increase of serum amylase/lipase in patients who underwent ERCP, CT or MRI is becoming the most important criterion in determining the diagnosis of post-ERCP acute pancreatitis. Post-ERCP acute pancreatitis should be suspected in any patient in whom pain occurs within 6 hours after the procedure and is much less likely to develop 12 hours after ERCP. Abdominal pain after ERCP with a pronounced increase in serum amylase and/or lipase, especially when the value of more than 1000 IU/L, leads to the assumption of pancreatitis. In the case of diagnostic doubt, especially with predicted severe pancreatitis radiological research should confirm the diagnosis [19, 43, 49].

Identifying risk factors — a necessary measure of prevention of pancreatitis after ERCP. According to F. Donnellan and Michael F. Byrne [14] they divided the factors related to the characteristics of the patient and factors related to the ongoing procedure. The first group includes: female gender, suspected sphincter of Oddi dysfunction, ERCP-induced pancreatitis in history, absence of chronic pancreatitis, young age (less than 60 years), normal levels of bilirubin (for the period of ERCP). In the second group highlighted: the existence of difficulties in cannulation BDS, papillosphincterotomy preliminary dissection of the mouth of the BDS (precut sphincterotomy), contrast introduction of the pancreatic duct, balloon dilatation of unchanged sphincter of Oddi (biliary sphincter), dissection of the sphincter of the mouth Wirsung's duct, dissection of the small duodenal papilla [46] The third group includes inadequate training and/or experience of the doctor conducting the study [38, 44] which showed that patients at risk for post-ERCP pancreatitis — a woman with suspected choledocholithiasis, with unexpanded common bile duct, normal levels of bilirubin, undergoing sphincterotomy, but no stone found. In this patient population, more than a quarter (27%), there is a post-ERCP acute pancreatitis. Magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound, which are not complicated by acute pancreatitis, can provide useful information,

duplicate ERCP and are the preferred methods of visualization in the initial assessment of pathology pancreatic-biliary zone in such patients.

A large number of studies have evaluated the effectiveness of the pharmacological prevention of post-ERCP acute pancreatitis. However, some studies have shown that there are drugs worthy of further study. Studied drugs can be divided into five groups: 1) reducing inflammation of the pancreas, 2) reducinge spasm of the sphincter of Oddi, 3) reducing the systemic inflammation, 4) depressing the pancreatic function; 5) activity of protease inhibitors.

For drugs that reduce inflammation of the pancreas, are antioxidants, antibiotics, corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs). Infectious complications contribute to morbidity and mortality in acute pancreatitis, but there are almost no studies to assess the potential role of antibiotics in the prevention of post-ERCP acute pancreatitis. Only one study was found that antibiotic therapy has the advantage of in the prevention of post-ERCP acute pancreatitis in patients treated with 2 g of ceftazidime 30 minutes before ERCP versus placebo (2,6% vs. 9,4%. P=0,009) [37].

Seven studies were conducted involving 3308 patients estimating the influence of corticosteroids to reduce the frequency and severity of pancreatitis after ERCP. Retrospective study [57] showed a reduction in the incidence of post-ERCP acute pancreatitis patients. Later, 5 large studies (four and one randomized, double-blind) using various corticosteroids including prednisolone and hydrocortisone and intravenous methyl-prednisolone, did not reveal the advantages in reducing the frequency and severity of pancreatitis after ERCP [15 17, 39]. It should be noted that two studies using corticosteroids for prevention of post-ERCP pancreatitis demonstrated decrease in amylase level (2 to 2.5 times) [29].

The conditions inducing inflammatory reaction, most promising results have been observed with NSAIDs. Two clinical trials have been published evaluating the role of diclofenac in reducing the incidence of post-ERCP acute pancreatitis [16, 47]. In both studies, patients received 100 mg of diclofenac rectal suppository. With the incidence of acute pancreatitis reductions it was observed in 6.4% of patients in the diclofenac group compared with 15.5% in the placebo group (p=0,049).

Satoudehmanesh and et al. [27] showed similar positive results with indomethacin.
Of the drugs, removing a spasm of the sphincter of Oddi, of particular interest is nitroglycerin. We have 3 randomized study to assess the use of nitroglycerin were examined during ERCP. Sudhindran et al. [51] compared the prophylactic administration of 2 mg sublingual nitroglycerin with placebo in patients undergoing ERCP. They found that the incidence of acute pancreatitis after the procedure was significantly lower in patients treated with nitroglycerin (7.7% vs. 17.8%, $p < 0.05$). In the following study Moretó et al. [53] was used in 144 patients 15 mg of nitroglycerine in a transdermal patch and identical placebo. A significant reduction in post-ERCP acute pancreatitis It was demonstrated in nitropatch group (4% vs. 15%, p=0,03). In the last and the largest of the three studies [1] Unfortunately, in 318 patients with a low risk of pancreatitis after ERCP, there was no difference in the development of post-ERCP acute pancreatitis between the active nitroglycerin and placebo.

Two other studies to assess the drugs to reduce spasm of the sphincter of Oddi for the prevention of post-ERCP pancreatitis, including whether a use of nifedipine and [33, 48], but one study on irrigation of sphincter of Oddi lidocaine and another study using botulinum toxin [52]. Unfortunately, none of these studies demonstrated a positive role in reducing the severity and incidence of acute pancreatitis after ERCP.

The development of acute pancreatitis depends on the activation and proliferation of proteases, which leads to a theoretical advantage of protease inhibitors in reducing the frequency and severity of the disease after ERCP. In the non-randomized, prospective study involving 815 patients, heparin was associated with a statistically significant decrease in m pancreatitis after ERCP (3,4% vs. 7,9%, P=0,005) [13]. However, despite these encouraging results of the first two years later t as well as groups of researchers conducted a randomized, double-blind study using heparin, which is not showing reducing development of the post-ERCP acute pancreatitis in patients with high risk [31].

Gabexate maleate is a protease inhibitor with anti-inflammatory properties. Its ability to inhibit trypsin is significantly higher than that of most other and protease

inhibitors. In 1995, A. Messori et al. [22] published the results of a meta-analysis of 5 studies that showed a statistically significant reduction in the incidence of complications in patients receiving Gabexate maleate after development of acute pancreatitis. More double-blind study of G. Cavallini et al. [25] subsequently showed a significant decrease in the incidence (2,4% vs. 7,6%, p=0,03) and the severity of acute pancreatitis in patients receiving Gabexate maleate compared to placebo. The original meta-analysis of 6 studies by A. Andriulli et al. [35] showed a statistically significant reduction in the development of post-ERCP acute pancreatitis (OR: 0.27, 95% CI: 0.13-0.57, p=0.001). But in another publication meta-analysis A. Andriulli et al. [40], conflicting results have been presented after additional testing. Despite conflicting data, infusion preparation for 1-2 hour and to ERCP, and then for 12 hours after ERCP, showing good statistically significant effect [50].

Protease inhibitor ulinastatin has long been used in the prevention and treatment of acute pancreatitis in Japan and China. [11] In a randomized, m, placebo-controlled study [55], ulinastatin, administered bolus before ERCP significantly reduced the incidence (2.9% vs. 7.4%; p=0.041), but not the severity of acute pancreatitis. Two subsequent randomized controlled trials comparing ulinastatin in gabexate, found no difference between the drugs in the prevention of acute pancreatitis [12, 56]. Further study of protease inhibitors is justified in the high-risk group.

Theoretically, inhibition of pancreatic exocrine secretion can prevent post-ERCP pancreatitis by "tripping" the damaged gland. Despite the attractiveness of the concept, there is no enough scientific basis to support such an approach. Somatostatin and its synthetic analogue, octreotide octapeptide, are potent inhibitors of pancreatic secretion. Although some somatostatin studies demonstrated effectiveness in reducing the speed of ERCP acute pancreatitis [10, 28], the majority of these studies do not support the routine use of this drug [34, 58]. In a meta-analysis in 2007, A. Andriulli et al. [41] studied 16 investigations with the use of somatostatin and concluded that this drug had statistically significant effect on decrease of hyperamylasemia after ERCP (OR: 0.67, 95% CI: 0.57-0.81).

In 2000 A. Andriulli et al. [36] conducted a meta-analysis of 10 studies on the

use of octreotide in the prevention of pancreatitis after ERCP. They came to the conclusion that, as somatostatin, octreotide is only effective in reducing hyperamylasemia after ERCP, but does not reduce the incidence of acute pancreatitis after ERCP. However, two later studies [21, 54] reported a statistically significant effect of octreotide in reducing acute pancreatitis after ERCP (2% vs. 8.9%, p=0.03) and (2.4% vs. 5.3.%; p=0.046), respectively. Drugs like somatostatin, calcitonin [20], inhibit the secretion of the pancreas, but none of them have been identified and the effect of reduction of acute pancreatitis after ERCP. It is worth noting that one study showed beneficial effects of beta-carotene in reducing the severity of pancreatitis after ERCP (2.22% vs. 0%; p <0.01) [32].

In Russia, the prevention of complications after ERCP engaged a number of researchers [1, 3, 4, 5], whose work questions the prevention of acute pancreatitis during ERCP were covered. A.A. Ilchenko offers a number of recommendations for ERCP, including the prevention of acute pancreatitis, based on its review of foreign studies and his own observations. In his work A.A. Ilchenko said that each case should be considered by the ratio of risk of various complications and diagnostic value of this study, which should be performed by an experienced professional, very carefully, and as far as possible with the minimum amount of contrast agent. The validity and accuracy of ERCP performance are of particular importance, since the analysis of the extensive literature does not allow to make an unambiguous conclusion about the effectiveness of prevention of ERCP-induced pancreatitis by means of a pharmacological agent. The best prevention ERCP-induced pancreatitis is possible as to this procedure [3] can often be avoided.

Russian authors' group has formulated standards for ERCP, which reflect all the main features of this procedure are clearly defined indications, contraindications, and premedication scheme postmanipulyatsionnye procedure. Also in these standards are the degree of risk and severity ERCP-induced pancreatitis (Ranson criteria) [7]. These recommendations should be used during ERCP in clinical practice.

Proceeding from the above-described methods of prevention, we conducted a study of their own versions of the prevention of acute pancreatitis after ERCP.

The aim of research is to compare different methods of drug prevention of

ERCP-induced pancreatitis.

Material and methods. We studied two groups of patients who underwent ERCP. In both groups, there were 120 persons. In one group 26 men (21.7%), 94 women (78.3%). The average age of patients — 62,2 ± 1,25, by age group was divided into subgroups: 20-40-years-old — 9 people; 41-60-years-old — 39; 61-80-years-old — 68; more than 80 years — 4 patients. In group 2 there were 29 men (24.2%), 91 women (75.8%). The average age of patients — 61,4 ± 1,45, by age group was divided into subgroups: 20-40-years-old — 13 people; 41-60-years-old — 45; 61-80-years-old — 50; more than 80 years — 12 patients. By sex and age groups were comparable.

The indications for ERCP were complications for cholelithiasis (choledocholithiasis, BDP stenosis, obstructive jaundice). The criterion for non-inclusion in the study was the cancer pathology (tumor of the gallbladder, liver, biliary tract, BNS, duodenal ulcer).

All patients received pharmacological prophylaxis of ERCP-induced acute pancreatitis. In order to study the patient was transported to the X-ray room lying on a gurney. Patients in group 1 for 30 minutes before the intervention received premedication: Atropine sulfate 0.1% — 1.0 ml/m, Diphenhydramine, 1% — 1.0 ml/m, Promedol 2% — 1.0 ml i/m. In group 2, in addition to the above premedication, used Droperidol 0.25% — 2.0 ml/m — 30 minutes prior to the intervention, and 10 mg of sublingual Nitrosorbid — 60 minutes prior to ERCP. The time of manipulation (ERCP) was 10-20 minutes. In case of difficulty the common bile duct cannulation was undertaken (3-5 attempts). Location of catheter was controlled by aspirate (receipt of bile or pancreatic juice), or, in difficult cases, the contrast with the subsequent introduction of RO-graphy. In the absence of results (isolated choledochal cannulation) was an attempt to access atypical choledoch (in particular, papillotomy from the mouth of BDP, suprpapillar dissection of BDP) followed by an attempt to common bile duct cannulation. If there is no result, carrying out the intervention was completed (i.e. patient was prescribed to have a cavity surgery). After the manipulation, patient was transported back to the ward lying on a gurney. During the day the patient was prescribed to have a rest. After

ERCP infusion therapy was prescribed: Papaverine 2% — 2.0 ml + 400 ml — 0.9% solution of NaCl, No-spa 2.0 ml + 400 ml — 0.9% solution of NaCl, Potassium Chloride 4% — 30 ml 400 ml + 5% glucose solution. At 18.00 on the day of the study was administered the control of blood amylase; in the presence of clinical manifestations of acute pancreatitis — control blood amylase was carried out before. If during the study used an atypical access choledoch or pancreatic duct was contrasted (i.e. the probability of increasing development of acute pancreatitis), then the above therapy increased 5-fluorouracil 10 ml + 400 ml — 0.9% solution NaCl, the inhibitor of proton pump (omeprazole or esomeprazole) 40 mg 200 ml + 0.9% solution of NaCl, 0.01% Octreotide — 1.0 ml of s/c, Platifillin 0.2% — 1.0 ml s/c; additionally conducted hypothermia of epigastric region (ice pack). According to the methods, we received priority in the application of the invention "Method of premedication of retrograde cholangiopancreatography in the treatment of pain jaundice" number 2012117882 from 27.04.2012.

We assess the level and duration of hyperamylasemia dynamics before and after ERCP. The difference between the reference parameters was considered statistically different at $p \leq 0.05$.

Results and discussion. All patients were performed ERCP. Based on the results obtained, 94 patients of group 1 (78.3%) underwent endoscopic papillotomy, 59 (49.2%) cases, noted the complexity of the cannulation of BDP, 24 (20%) patients required the implementation of the pre-dissection of BDP mouth. 89 patients of group 2 (74.2%) underwent endoscopic papillotomy, 66 (55%) cases had difficulty with cannulation of BDP, 30 (25%) patients at the same time carried out a preliminary dissection of the mouth of the BDP for the purpose of common bile duct cannulation. Following the intervention in 13 (10.8%) patients in group 1 development of ERCP-induced pancreatitis was marked, in 4 (3,3%) cases with the subsequent development of pancreatic necrosis. After ERCP in 4 (3.3%) patients in group 2 was recorded ERCP-induced pancreatitis (in 1 (0.8%) cases with the development of pancreatic necrosis). The development of ERCP-induced pancreatitis was significantly lower in patients in group 2 compared with patients in group 1 ($p < 0.05$). In addition, there is a statistically significant decrease in mean values of duration of hyperamylasemia of

patients of group 2, conducting ERCP who were accompanied by difficulties in cannulation of BDP (Tab. 1) and the preliminary dissection of the mouth of the BDP (Tab. 2).

When contrasting Wirsung's duct (as well as in its absence) the application of the extended medical prophylaxis (patients of group 2) resulted in a statistically significant reduction in the mean values of the duration of hyperamylasemia (Tab. 3).

Conclusions. Knowledge of the possible complications of ERCP, their expected frequency and risk factors for their occurrence can help suggest and minimize the frequency and severity of these complications. There must be careful patient selection for appropriate intervention. The specialist carrying out the study must be very well acquainted with the planned procedure and available technologies, and also be ready to treat any adverse complications that may arise. Early detection of complications and timely intervention can minimize morbidity and mortality, associated with these complications. Our proposed complex of extended premedication allowed reduce significantly the incidence of ERCP-induced pancreatitis.

References

1. Дискуссионные вопросы хирургических вмешательств на большом сосочке двенадцатиперстной кишки / Лебедев С. В., Еремеев А. Г, Балалыкин А. С. [и др.] // Анналы хирургической гепатологии. — 2007. — № 4. — С. 45–53.
2. Ильченко А. А. Желчнокаменная болезнь / А. А. Ильченко. — М. :Анахарсис, 2004. — 200 с.
3. Ильченко А. А. Эндоскопическая ретроградная холангиопанкреатикография: возможна ли эффективная профилактика ЭРХПГ-индуцированного панкреатита / А. А. Ильченко// Экспериментальная и клиническая гастроэнтерология. — 2008. — № 3. — С. 62–71.
4. Лосев С. В. Применение «Октреотида» для профилактики панкреатита при проведении ЭРХПГ [Электронный ресурс] / С. В. Лосев, В. В. Феденко. — Электрон. текстовые дан. — Режим доступа: http://octreotide.Pharm-sintez.ru/issue/octr107.htm.
5. Манцеров М. П. Реактивный панкреатит после эндоскопических манипуляций на большом дуоденальном сосочке / Манцеров М. П., Мороз Е. В. // Рос. журн. Гастроэнтерол., гепатол., колопроктол. — 2007. — Т. XVII, № 3. — С. 14–23.
6. Ханевич М. Д. Транспапиллярные методы лечения механической желтухи / М. Д. Ханевич, А. М. Гробовый // Российский журнал гастроэнтерологии, гепатологии, колопроктологии. — 2005. — № 3. — С. 57–61.
7. Эндоскопическая ретроградная холангиопанкреатография. Стандарт проведения / Щербаков П. Л., Парфенов А. И., Ильченко А. А. [и др.] // Экспериментальная и клиническая гастроэнтерология. — 2009. — № 3. — С. 150–155.
8. Banks P. A. Practice Parameters Committee of the American College of Gastroenterology. Practice Guidelines in Acute Pancreatitis / P. A. Banks, M. L. Freeman // Am. J. Gastroenterol. — 2006. — Vo. 101. — P. 2379–2400.
9. Banks P. A. Practice Parameters Committee of the American College of

Gastroenterology. Practice Guidelines in Acute Pancreatitis / P. A. Banks, M. L. Freeman // Am. J. Gastroenterol. — 2006. — Vol. 101. — P. 2379–2400.

10. Can somatostatin prevent post-ERCP pancreatitis? Results of a randomized controlled trial / Arvanitidis D., Anagnostopoulos G.K., Giannopoulos D. [et al.] // J Gastroenterol Hepatol. — 2004. — Vol. 19. — P. 278–282.
11. Chen S.Y. Ulinastatin in the treatment of acute pancreatitis : a multicenter clinical trial / Chen S.Y., Wang J.Y. // Chin J Dig Dis. — 2002. — Vol. 3. — P. 70–75.
12. Comparison between ulinastatin and gabexate mesylate for the prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis : a prospective, randomized trial / Ueki T., Otani K., Kawamoto K. [et al.] // J Gastroenterol. — 2007. — Vol. 42. — P. 161–167.
13. Complications of endoscopic sphincterotomy: Can heparin prevent acute pancreatitis after ERCP? / Rabenstein T., Roggenbuck S., Framke B. [et al.] // Gastrointest Endosc. — 2002. — Vol. 55. — P. 476–483.
14. Complications of ERCP by the American Society for Gastrointestinal Endoscopy // Gastrointestinal Endoscopy. — 2012. — Vol. 75, No 3. — P. 467–472.
15. De Palma G. D. Use of corticosteriods in the prevention of post-ERCP pancreatitis : results of a controlled prospective study / G. D. De Palma, C. Catanzano // Am. J. Gastroenterol. — 1999. — Vol. 94. — P. 982-5.
16. Diclofenac reduces the incidence of acute pancreatitis after endoscopic retrograde cholangiopancreatography / B. Murray, R. Carter, C. Imrie [et al.] // Gastroenterology. — 2003. — Vol. 124. — P. 1786–1791.
17. Does prophylactic administration of corticosteroid reduce the risk and severity of post-ERCP pancreatitis : a randomized, prospective, multicenter study / S. Sherman, U. Blaut, J. L. Watkins [et al.] // Gastrointest Endosc. — 2003. — Vol. 58. — P. 23–29.
18. Donnellan F. Prevention of Post-ERCP Pancreatitis / F. Donnellan, M. F. Byrne. // Gastroenterology Research and Practice. — 2012. — Article ID 796751. — 12 p.

19. Early recognition of post-ERCP pancreatitis by clinical assessment and serum pancreatic enzymes / K. Gottlieb, S. Sherman, J. Pezzi [et al.] // Am. J. Gastroenterol. — 1996. — Vol. 91. — P. 1553–1561.
20. Effect of calcitonin on the serum amylase levels after endoscopic retrograde cholangiopancreatography / Odes H.S., Novis B.N., Barbezat G.O., Bank S. // Digestion. — 1977. — Vol. 16. — P. 180–184.
21. Effect of octreotide administration in the prophylaxis of post-ERCP pancreatitis and hyperamylasemia : a multicenter, placebo-controlled, randomized clinical trial / Li Z.S., Pan X., Zhang W.J. [et al.] // Am J Gastroenterol. — 2006. — Vol. 102. — P. 46–51.
22. Effectiveness of gabexate mesilate in acute pancreatitis. A metaanalysis / Messori A., Rampazzo R., Scroccaro G. [et al.] // Dig Dis Sci. — 1995. — Vol. 40. — P. 734–738.
23. Endoscopic pancreatic sphincterotomy: indications, outcome, and a safe stentless technique / E. Elton, D. A. Howell, W. G. Parsons [et al.] // Gastrointest. Endosc. — 1998. — Vol. 47. — P. 240–249.
24. Freeman M. L. Prevention of post-ERCP pancreatitis : a comprehensive review / M. L. Freeman, N. M. Guda // Gastrointest Endosc. — 2004. — Vol. 59. — P. 845–864.
25. Gabexate for the prevention of pancreatic damage related to endoscopic retrograde cholangiopancreatography. Gabexate in digestive endoscopy--Italian Group / Cavallini G., Tittobello A., Frulloni L. [et al.] // N Engl J Med. — 1996. — Vol. 335. — P. 919–923.
26. Guidewire Cannulation Reduces Risk of Post-ERCP Pancreatitis and Facilitates Bile Duct Cannulation / L. A. Everson, P. Sakai [et al.] // American Journal of Gastroenterology. — 2007. — Vol. 102. — P. 2147–2153.
27. Indomethacin may reduce the incidence and severity of acute pancreatitis after ERCP / R. Sotoudehmanesh, M. Khatibian, S. Kolahdoozan [et al.] // Am. J. Gastroenterol. — 2007. — Vol. 102. — P. 978–983.
28. Intravenous bolus somatostatin after diagnostic cholangiopancreatography reduces the incidence of pancreatitis associated with therapeutic endoscopic

retrograde cholangiopancreatography procedures : a randomised controlled trial / Poon R.T., Yeung C., Liu C.L. et al. // Gut. — 2003. — Vol. 52. — P. 1768–1773.

29. Kwanngern K. Can a single dose corticosteroid reduce the incidence of post-ERCP pancreatitis? A randomized, prospective control study / K. Kwanngern, P. Tiyapattanaputi, M. Wanitpukdeedecha // J. Med. Assoc. Thai. — 2005. — Vol. 88. — Suppl.4. — S. 42–45.

30. Lazaraki G. Prevention of post ERCP pancreatitis : an overview / G. Lazaraki, P. Katsinelos // Annals of gastroenterology. — 2008. — Vol. 21, No 1. — P. 27–38.

31. Low-molecular-weight heparin does not prevent acute post-ERCP pancreatitis / Rabenstein T., Fischer B., Wiessner V. [et al.] // Gastrointest Endosc. — 2004. — Vol. 59. — P. 606–613.

32. Natural beta-carotene for the prevention of post-ERCP pancreatitis / Lavy A., Karban A., Suissa A. et al. // Pancreas. — 2004. — Vol. 29. — P. e45–e50.

33. Nifedipine for prevention of post-ERCP pancreatitis : a prospective, double-blind randomized study / F. Prat, J. Amaris, B. Ducot [et al.] // Gastrointest. Endosc. — 2002. — Vol. 56. — P. 202–208.

34. Octreotide versus hydrocortisone versus placebo in the prevention of post-ERCP pancreatitis: a multicenter randomized controlled trial / Manolakopoulos S., Avgerinos A., Vlachogiannakos J. [et al.] // Gastrointest Endosc. — 2002. — Vol. 55. — P. 470–475.

35. Pharmacologic treatment can prevent pancreatic injury after ERCP : a meta-analysis / Andriulli A., Leandro G., Niro G. [et al.] // Gastrointest Endosc. — 2000. — Vol. 51. — P. 1–7.

36. Pharmacologic treatment can prevent pancreatic injury after ERCP : a meta-analysis / Andriulli A., Leandro G., Niro G. et al. // Gastrointest Endosc. — 2000. — Vol. 51. — P. 1–7.

37. Post-ERCP pancreatitis: reduction by routine antibiotics / S. Räty, J. Sand, M. Pulkkinen [et al.] // J. Gastrointest. Surg. — 2001. — Vol. 5. — P. 339–345.

38. Predictors of post-ERCP complications in patients with suspected

choledocholithiasis / S. N. Mehta, E. Pavone, J. S. Barkun [et al.] // Endoscopy. — 1998. — Vol. 30. — P. 457–463.

39. Pretreatment with methylprednisolone to prevent ERCP-induced pancreatitis: a randomized, multicenter, placebo-controlled clinical trial / J. A. Dumot, D. L. Conwell, J. B. O'Connor [et al.] // Am. J. Gastroenterol. — 1998. — Vol. 93. — P. 61–65.

40. Prophylactic administration of somatostatin or gabexate does not prevent pancreatitis after ERCP: an updated meta-analysis / Andriulli A., Leandro G., Federici T. [et al.] // Gastrointest Endosc. — 2007. — Vol. 65. — P. 624–632.

41. Prophylactic administration of somatostatin or gabexate does not prevent pancreatitis after ERCP: an updated meta-analysis / Andriulli A., Leandro G., Federici T. [et al.] // Gastrointest Endosc. — 2007. — Vol. 65. — P. 624–632.

42. A prospective, randomized, placebo-controlled trial of transdermal glyceryl trinitrate in ERCP : effects on technical success and post-ERCP pancreatitis / A. J. Kaffes, M. J. Bourke, S. Ding [et al.] // Gastrointest Endosc. — 2006. — Vol. 64. — P. 351–357.

43. Relationship between post-ERCP pancreatitis and the change of serum amylase level after the procedure / K. Ito, N. Fujita, Y. Noda [et al.] // World J. Gastroenterol. — 2007. — Vol. 13. — P. 3855–3860.

44. Risk factors for post-ERCP pancreatitis : a prospective multicenter study / Am. J. Gastroenterol. — 2006. — Vol. 101. — P.139–147.

45. Risk factors for post-ERCP pancreatitis : a prospective, multicenter study / M. L. Freeman, J. A. DiSario, D. B. Nelson [et al.] // Gastrointest. Endosc. — 2001. — Vol. 54. — P. 425–434.

46. Risk factors for post-ERCP pancreatitis : a prospective, multicenter study / M. L. Freeman, J. A. DiSario, D. B. Nelson [et al.] // Gastrointest. Endosc. — 2001. — Vol. 54. — P. 425–434.

47. Role of diclofenac in reducing post-endoscopic retrograde cholangiopancreatography pancreatitis / M. Khoshbaten, H. Khorram, L. Madad [et al.] // J Gastroenterol Hepatol. — 2008. — Vol. 23. — P. 11–16.

48. Sand J. Prospective randomized trial of the effect of nifedipine on pancreatic

irritation after endoscopic retrograde cholangiopancreatography / Sand J., Nordback I. // Digestion. — 1993. — Vol. 54. — P. 179–184.

49. Serum amylase measured four hours after endoscopic sphincterotomy is a reliable predictor of postprocedure pancreatitis / P. A. Testoni, F. Bagnolo, S. Caporuscio, F. Lella // Am. J. Gastroenterol. — 1999. — Vol. 94. — P. 1235–1241.

50. Somatostatin and gabexate for post-endoscopic retrograde cholangiopancreatography pancreatitis prevention : meta-analysis of randomized placebo-controlled trials / Rudin D., Kiss A., Wetz R.V. [et al.] // J Gastroenterol Hepatol. — 2007. — Vol. 22. — P. 977–983.

51. Sudhindran S. Prospective randomized double-blind placebo-controlled trial of glyceryl trinitrate in endoscopic retrograde cholangiopancreatography-induced pancreatitis / S. Sudhindran, E. Bromwich, P. R. Edwards // Br. J. Surg. — 2001. — Vol. 88. — P. 1178–1182.

52. The effect of lidocaine sprayed on the major duodenal papilla on the frequency of post-ERCP pancreatitis / Schwartz J.J., Lew R.J., Ahmad N.A. [et al.] // Gastrointest Endosc. — 2004. — Vol. 59. — P. 179–184.

53. Transdermal glyceryl trinitrate for prevention of post-ERCP pancreatitis : a randomized double-blind trial / M. Moretó, M. Zaballa, I. Casado [et al.] // Gastrointest. Endosc. — 2003. — Vol. 57. — P.1-7.

54. Twenty-four hour prophylaxis with increased dosage of octreotide reduces the incidence of post-ERCP pancreatitis / Thomopoulos K.C., Pagoni N.A., Vagenas K.A. [et al.] // Gastrointest Endosc. — 2006. — Vol. 64. — P. 726–731.

55. Ulinastatin for pancreatitis after endoscopic retrograde cholangiopancreatography : a randomized, controlled trial / Tsujino T., Komatsu Y., Isayama H. [et al.] // Clin Gastroenterol Hepatol. — 2005. — Vol. 3. — P. 376–383.

56. Ulinastatin shows preventive effect on post-endoscopic retrograde cholangiopancreatography pancreatitis in a multicenter prospective randomized study / Fujishiro H., Adachi K., Imaoka T. [et al.] // J Gastroenterol Hepatol.

— 2006. — Vol. 21. — P. 1065–1069.

57. Use of corticosteroids in the prevention of post-ERCP pancreatitis / G. R. Wiener, J. E. Geenen, W. J. Hogan [et al.] // Gastrointest. Endosc. — 1995. — Vol. 42. — P. 579–583.

58. Utility of bolus somatostatin administration in preventing pancreatitis after endoscopic retrograde cholangiopancreatography : a controlled, non-randomized study / Vila J.J., Jiménez F.J., Prieto C. [et al.] // Gastroenterol Hepatol. — 2006. — Vol. 29. — P. 231–236.

Table 1

Duration of hyperamylasemia in patients after ERCP, which was accompanied by difficulties in cannulation of BDP

Complexity of the cannulation: -		Number of observations	Duration of hyperamylasemia		P-level
			Average	SD	
Group	1	60	0,25	0,11	>0,1
	2	54	0,04	0,12	
Complexity of the cannulation: +		Number of observations	Duration of hyperamylasemia		P-level
			Average	SD	
Group	1	59	0,78	0,11	<0,05
	2	66	0,42	0,11	

Table 2

Duration of hyperamylasemia in patients after ERCP, which was accompanied by the preliminary dissection of the mouth of the BDP

Preliminary dissection of the mouth of BDP: -		Number of observations	Duration of hyperamylasemia		P-level
			Average	SD	
Group	1	95	0,27	0,07	>0,1
	2	90	0,24	0,40	
Preliminary dissection of the mouth of BDP: +		Number of observations	Duration of hyperamylasemia		P-level
			Average	SD	
Group	1	24	1,46	0,35	<0,05

Table 3

Duration of hyperamylasemia in patients after ERCP upon applying enhanced drug prevention

Contrast of Wirsung's duct: -		Number of observations	Duration of hyperamylasemia		P-level
			Average	SD	
Group	1	101	0,32	0,07	<0,05
	2	97	0,13	0,04	
Contrast of Wirsung's duct: +		Number of observations	Duration of hyperamylasemia		P-level
			Average	SD	
Group	1	17	1,59	0,44	<0,05
	2	23	0,74	0,25	

Comparative analysis of methods of prevention of drug- ERCP-induced pancreatitis

I. H. Aminov, M. V. Churkin, E. J. Plotnikova, V. I. Podoluzhny, K. A. Krasnov, O. A. Krasnov

Key words: acute pancreatitis, endoscopic retrograde cholangiopancreatography, Wirsung's duct, Oddi's sphincter, endoscopic papillosphincterotomy, proton pump inhibitors, premedication retrograde cholangiopancreatography

Endoscopic retrograde cholangiopancreatography (ERCP) is an invasive procedure that is performed for diagnosis and treatment of pancreatic and biliary diseases. Approximately in 5–40% of cases the procedure itself causes side effects. The most common complication of post-ERCP is acute pancreatitis. Identifying risk factors and groups is a necessary measure of prevention of pancreatitis after ERCP. This paper provides an overview of research on drug prevention of post- ERCP acute pancreatitis. Early detection of complications and early intervention can minimize the morbidity and mortality associated with this complication. The original scheme for the prevention of this complication is proposed. This set of expanded premedication allowed significantly reduce the incidence of ERCP -induced pancreatitis.