INFORMED CONSENT FORM

Preventive pancreatic stents in acute biliary pancreatitis

PREPAST

PERSONAL DETAILS:

First name:.....

Last name:.....

Date of Birth:.....

Insurance number:.....

NPR PATIENT NUMBER
COUNTRY, CITY
INSTITUTION
DOCTOR

SUMMARY:

Dear Patient!

Your doctor is involved in a research project at the First Department of Medicine, University of Szeged. **Please read thoroughly through the following information** and, if you agree, we ask you to undergo the below detailed intervention to support our research efforts. In case you do not want to participate in the research, we respect your decision of course and your decision will not result in any penalty, loss of benefits or change of treatment.

Referring to the experimental nature of the research, the aim and duration of the research, the number of people included, the course of the research, the nature and frequency of the planned intervention:

Twenty percent of acute biliary pancreatitis (ABP) is severe, carrying a risk for severe, even potentially lethal complications. Pathomechanisms of ABP are not clearly understood. Mortality of this disease has not been changed in the past decades even with the new research data and refinement of therapy. Its endoscopic therapy includes early endoscopic retrograde cholangiography (ERCP), endoscopic sphincterotomy (EST) and stone extraction from the common bile duct within a specific timeframe (eg. therapeutic window). Endoscopic therapy has been debated since the first meta-analysis in 2008 and this debate is still ongoing even after the new guidelines. The contradictory results could be caused by a few facts: firstly that ERCP can cause further pancreatic damage similarly to post-ERCP pancreatitis and secondly that early endoscopic intervention does not always relieve the pancreatic duct obstruction. We demonstrated in our previous study that using small caliber (ie. preventive) pancreatic stents (PPS) at the early course of ABP significantly improves the outcome. We hypothesize that PPS insertion not just prevents the injury caused by ERCP but may be beneficial for every ABP patient by maintaining the outflow of pancreatic juices.

The aim of the trial: The main question of this trial is whether using PPS at the early course of ABP can cause significantly less compliations and therefore better overall outcome compared to the standard ERCP tehcniques irrespective of the degree of cannulation difficulty, co-existing acute cholangitis and the proposed severity of ABP at admission. Furthermore we would like to investigate the success rate of PPS insertion and its technical details (eg. influence of endoscopist' experience on final outcome) and the consequences of attempted but failed PPS insertion.
Approximately 230 patients, above the age of 18 years having acute biliary pancreatitis (male-female 50-50%), will be enrolled from centers participating in the research. Inclusion criteria are the written informed consent and the possibility of performing ERCP within 48 hours from the onset of pain.

Inclusion criteria: Diagnosis of acute pancreatitis is based on the latest international guideline (IAP/APA evidence-based guideline for the management of acute pancreatitis. Pancreatology, 2013) „2 out of 3" of the following criteria present: upper abdominal pain; serum amylase or lipase >3x upper limit of normal range (ULN); characteristic findings on imaging studies (abdominal ultrasound (US)/CT/MRI); however those patients without abdominal pain will be excluded because the onset of AP cannot be assessed. Informed consent will be obtained from each participating patient prior to randomization in oral and written form. A detailed briefing and explanation will be given to every participating patient on the nature, aim, scope and consequences of the study by a participating physician before consenting. The participation of the patient is voluntary and anonymous, the consent may be withdrawn at any time either verbally or in writing. The withdrawal of consent will not result in any penalty or loss of benefits and data will not be used. The patient may contact the coordinator of the research and ask questions at any time.

HUNGARIAN PANCREATIC STUDY GROUP
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Exclusion criteria: age under 18 years, pregnancy; AP due to alcohol, malignancy or post-ERCP pancreatitis; pain onset >48 hours; abscence of abdominal pain (the onset cannot be assessed); liver cirrhosis Child score C; pancreatic fluid collections or necrosis on initial imaging at presentation; INR>1.6 and uncorrectable by the time of ERCP, previous endoscopic sphincterotomy, or if the voluntary consent is withdrawn.

Patients participating will be allocated into 3 groups and the groups will be divided into further sub-groups. Patients with ABP and co-existing acute cholangitis will recieve early endoscopic intervention (**group A**). Patients in group A will be randomized either into group A1 (ERCP, ES treatment) or into group A2 (ERCP, ES + PPS treatment). Randomization lists will be prepared with a block size of 4 and with an allocation ratio of 1:1. In case of withdrawn of a volunteer, he/she will be substituted by a new one. For this purpose, an additional sample size will be randomized for each centrum, which can be applied if needed.
Patients with ABP but without evidence of acute cholangitis will be assessed for evidence of cholestasis. Patients without co-existing acute cholangitis but evidence of cholestasis will be randomized (**group B**). Patients in group B will be randomized either into group B0 (conservative treatment), into group B1 (ERCP, ES treatment) or into group B2 (ERCP, ES + PPS treatment).
Patients receiving conservative treatment will be assessed at 24 hours after randomization (not later than 72 hours from the onset of pain) for clinical and laboratory signs of persistent cholestasis. If this is present, patients will receive ERCP, ES and bile duct clearance and their data will be collected separately. Randomization lists will be prepared with a block size of 6 and with an allocation ratio of 1:1:1. In case of withdrawn of a volunteer, he/she will be substituted by a new one. For this purpose, an additional sample size will be randomized for each centrum, which can be applied if needed.
Patients without signs of cholestasis (and acute cholangitis) will recieve conservative treatment (**group C**), and will not be randomized.

Other accepted treatments available for the participant, information on the fact that the research may cause a pause in the started treatment, possible consequences of the pause of the treatment:
The treatments and therapic interventions applied througout the research are completely corresponding to the accepted professional protocols of gastroenterology. For patients with ABP and co-existing acute cholangitis, professional guidelines suggest ERCP and ES treatment to avoid further damage of the pancreas. This research applies this suggestion, with the supplementary intervention of inserting a small (3-5 cm) pancreatic stent into the pancreatic duct for a group of patients. The time of the endoscopic intervention will last for maximum 10 minutes longer. All stents will be removed at a second endoscopic procedure within a few days when ABP has resolved or significantly improved, therefore no long-term complications (e.g. obstruction) are involved. Patients may withdraw their consent either orally or in written form at any time. They may do so by only rejecting the stent insertion and permitting the other endoscopic interventions, or rejecting all endoscopic interventions too. For patients with ABP without co-existing acute cholangitis but evidence of cholestasis professional guidelines suggest either ERCP and ES treatment or conservative therapy (fluid resuscitation, pain relief, anti-inflammatory treatment). But in case of cholestasis not improving within 24-48 hours, endoscopic intervention is justified.
For patients without signs of acute cholangitis and cholestasis, conservative treatment is suggested. The data of this group of patients will be analysed separately.

Treatment of possible and expected consequences, risks and inconveniences: Participating centers are prepared to treat the possible complications of ERCP, endoscopic sphincterotomy and pancreas stent insertion. In case of serious complication the in-patient department or the intensive care unit can be contacted immediately.

Expectable benefits:
The utility of endotherapy has been debated over the last few years as certain meta-analyses did not find better outcome (in terms of morbidity and mortality) compared to conservative treatment in ABP patients. The contradictory results could be caused by the fact that early endoscopic intervention does not always relieve the pancreatic duct obstruction. We demonstrated in our previous study that using small caliber (ie. preventive) pancreatic stents (PPS) when cannulation of the papilla of Vater proved to be difficult at the early course of ABP, significantly improves the outcome compared to the standard EST. Based on these data we hypothesize that PPS insertion not just prevents the injury caused by ERCP but may be beneficial for every ABP patient by maintaining the outflow of pancreatic juices. The main question of this trial is whether using PPS at the early course of ABP can cause significantly less compliations and therefore better overall outcome compared to the standard ERCP tehcniques irrespective of the degree of cannulation difficulty, co-existing acute cholangitis and the proposed severity of ABP at admission.

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The probability of randomly being allocated to a certain treatment group, if any: The PREPAST trial is a prospective, randomized and multicenter study, the patient allocation to treatment groups are randomized.

Liability insurance covering the treatment and compensation of injury caused in connection with the research: The insurance of the Medical Faculty, University of Szeged covers the above detailed research only at the University of Szeged. All joined institution needs to have their own Insurance Liability.

Expense cover for participants if any: There is no expense cover or any allowance for participating in the research.

Rules of data collection and handling and access to collected data: All relevant clinical data will be collected during hospital admission using electronic case record form (eCRF), eg. patients' baseline characteristics, relevant laboratory and imaging results, endoscopy procedures, accessories used, outcomes. The data collected through the study will be entered in a validated electronic data management system, which can be assessed by the study doctors with unique usernames and secret passwords in order to treat data secretly and confidentially.

Ethical committee providing ethical opinion/approval necessary for the launch of the research: Scientific and Research Ethics Committee, Secretary of the Medical Research Council

Contact information of the Chair of the institutional research ethics committee: Prof. Dr. Tibor Wittmann, First Department of Medicine, University of Szeged, H-6720 Szeged, Koranyi fasor 8-10., Hungary Tel: +36 62 545-189

Contact information of the independant doctor required by the Decree 23/2002. (V. 9.) Paragraph 12. § (5): Dr. Ferenc Nagy, professor, Dr. Tamás Molnár, professor, First Department of Medicine, University of Szeged

Your participation in this research study is voluntary. You may withdraw your consent to participate at any time either verbally or in writing. The withdrawal of your consent will not result in any penalty or loss of benefits.

After reading the 3 page patient information and the above summary, and after listening the doctor providing information, I understand the purpose of this trial (ethical approval number: 034524/2014/OTIG, registration number: ISRCTN13517695). I do not have further questions for now. I give my consent to participate in this study. I give my consent to use my data for scientific purposes and to release them in publications without mentioning my name. Furthermore, I give my consent to store my data at the place of the research during the time of the research, until its withdrawal or at least 30 years after acquiring data.

At the time of signing I received a copy of the consent form and summary information.

……., ……day……month……20…..

……	……	…….
researcher/doctor providing information	signature of participant (patient)	signature of legal representative[1]

[1] Compulsory in case of incapacitated patient. In case of illiteracy of the participant or his/her legal representative, two witnesses and their signatures are needed for the valid consent.

We, the undersigned, have witnessed and confirm that accurate information was given to the participant/legal representative of the participant and we confirm that the individual has given consent freely and voluntarily.

……	……
signature of witness 1	signature of witness 2
Name: ……	Name: ……
Address: ……	Address: ……
ID number: ……	ID number: ……