ISRCTN41530928 https://doi.org/10.1186/ISRCTN41530928

Comparing three early treatments for sudden-onset pancreatitis (inflammation of the pancreas) caused by high levels of fat in the blood

Submission date 14/10/2019	**Recruitment status** Suspended	[X] Prospectively registered [ ] Protocol
Registration date 10/12/2019	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 04/05/2020	**Condition category** Digestive System	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Acute pancreatitis is a serious condition in which the pancreas becomes inflamed over a short period of time. A high level of fats in the blood (hypertriglyceridemia) is one of the main causes of this inflammation. High blood fat levels might occur due to genetic or hereditary reasons, drinking alcohol or eating habits.
To treat acute pancreatitis, the excess fats could be removed. There are three different ways of doing this. The aim of this study is to compare the effectiveness of these three treatments and to find out whether early removal of these fatty acids from the blood helps patients with inflammation of the pancreas.

Who can participate?
Adults with pancreatitis (inflammation of the pancreas) caused by high levels of blood fat

What does the study involve?
The three methods of fat removal are listed below.
1. Plasmapheresis, which is a painless blood purification procedure. During plasmapheresis, patients will have a needle attached to a thin tube, called a catheter, inserted into a vein in each arm. The blood comes out through one of the tubes and goes into a machine that separates the fat-containing plasma from the blood cells. Then blood cells then get mixed with fresh donor plasma, and the new blood mixture goes back into the body through the other tube. Most treatments last 2 to 4 hours. The process isn't painful, and pain relief is not needed.
2. Insulin/heparin infusion. These drugs can break down the fats in the blood.
3. Intravenous fluid replacement, which also helps the degradation of blood fats.
The participants will be allocated at random to receive one of these treatments.

What are the possible benefits and risks of participating?
All treatments usually involve admission to hospital. The participation is free of charge and completely voluntary. The researchers expect that all the treatments will be equally effective. Participating in the study has very low risk. Patients will be monitored closely.

Where is the study run from?
University of Pécs Medical School (Hungary)

When is the study starting and how long is it expected to run for?
February 2019 to December 2024

Who is funding the study?
University of Pécs Faculty of Medicine (Hungary)

Who is the main contact?
Prof. Dr. Peter Hegyi, p.hegyi@tm-centre.org

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
V1

Study information

Scientific Title

Early elimination of fatty acids in hypertriglyceridemia-induced acute pancreatitis

Acronym
ELEFANT

Study objectives
Hypertriglyceridemia can cause the most severe type of pancreatitis with a high level of mortality. Recently available scientific data suggest that early elimination of triglycerides and their metabolites may be beneficial. This study intends to provide the first evidence concerning the necessity of early intervention.

Ethics approval required
Old ethics approval format

Ethics approval(s)
An application has been sent to the National Center for Public Health, Department of Health Administration, and the researchers expect a decision at the end of October 2019.

Study design
Interventional multicenter three-armed randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Hypertriglyceridemia-induced acute pancreatitis

Interventions
The randomization list will be generated by a computer programme. Information of randomization will be placed in sealed envelopes. The sequence of distribution will be prepared with variable block lenghts with an allocation ratio of 1:1:1 by the Independent Data Management Board (IDMB). Patients will be randomized into three different groups:

In Group A, patients will undergo plasmapheresis and additionally aggressive fluid replacement therapy will be performed.
Plasmapheresis (by plasma exchange) will be carried out within 12 h of randomization, until the triglyceride level is <5.6 mmol/l. A high flow central venous catheter will be inserted. Typically, 30-60 ml/kg of plasma are removed at each cycle, and will be replaced with 5% of human albumin solution. Intravenous calcium will be administered in order to avoid hypocalcemia. We will use citrate for anticoagulant. Aggressive fluid replacement will also be administered (Ringer-Lactate at 5-10 ml/kg/h) for the next 24 h.

In Group B, patients will undergo aggressive fluid replacement therapy with intravenous infusion of regular insulin and subcutaneous injection of low molecular weight heparin.
Aggressive fluid replacement therapy will be performed in exactly the same way as in Group A. The rate of insulin infusion is 0.1 U/kg/h, and heparin 4000 IU will be administered every 12 h. If

the blood sugar level is between 8.3 mmol/l and 11.1 mmol/l, in order to prevent hypoglycemia 5% dextrose infusion will be administered. We will monitor the serum triglyceride level in every 12 h and when it is <5.6 mmol/l the insulin-heparin treatment will be stopped.

In Group C patients will receive aggressive intravenous fluid replacement, performed in exactly the same way as in Group A and Group B.

Furthermore patients in Group A, B and C will receive the standard treatment for acute pancreatitis based on the IAP/APA guideline.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Frequency of severe AP according to the revised Atlanta Classification measured by clinical assessment at discharge or mortality from admission to discharge
1. Frequency of severe AP according to the revised Atlanta Classification, measured by clinical assessment at discharge
2. Mortality, measured from admission to discharge, assessed daily during the study
These outcomes will be evaluated using yes/no questions as part of a questionnaire filled out by the doctor who examines the patients (who is not the doctor who made the randomisation).

Key secondary outcome(s))
1. Serum triglyceride level measured by standard laboratory test daily during the study
2. Serum albumin level measured by standard laboratory test daily during the study
3. Serum calcium level measured by standard laboratory test daily during the study
4. Pain assessed using a visual analog scale at 1, 2 and 3 days after randomization
5. C-reactive protein (CRP) serum levels measured by standard laboratory test daily during the study
6. Leukocyte count measured by standard laboratory test daily during the study
7. Length of hospital stay in days assessed daily during clinical visits
8. Need for ICU admission measured at admission and daily during the study, based on the state of the patients at physical examination, mental state, vital parameters (blood pressure, pulse, O2 saturation) and laboratory parameters (e.g. blood urea nitrogen [BUN], creatinine)
9. Length of ICU stay in days assessed daily during clinical visits
10. Organ failure (divided into transient and persistent organ failure) measured at admission and daily during the study according to the revised Atlanta Classification
11. Complications of plasmapheresis measured at admission and daily during the study, by clinical assessment
12. Healthcare cost spent on each patient will be calculated by a healthcare economist after the trial is completed

Completion date
01/12/2024

Eligibility

Key inclusion criteria
1. Aged 18-80 years
2. Diagnosed with AP on the basis of the '2 out of 3' criteria in the IAP/APA guidelines:
2.1. Upper abdominal pain

2.2. Serum amylase or lipase >3x upper limit of normal range
2.3. Characteristic findings on pancreatic imaging
3. HTG is diagnosed: if the blood TG level is at least 1000 mg/dl (11.3 mmol/l)
4. Signed informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Pregnancy or breast feeding
2. Any of the interventions is not available within 48 h calculated from the start of abdominal pain
3. Any of the interventions can not be started within 12 h calculated from the venepuncture which provided the blood sample for HTG analysis
4. Coma
5. Malignancy
6. Early ARDS
7. Renal failure
8. Allergy to insulin or heparin
9. Chronic pancreatitis
10. Hospitalisation before admission
11. Any reasons contraindicating plasmapheresis: severe active bleeding or disseminated intravascular coagulation (hematocrit level <20%), other forms of coagulopathy; hemodynamic instability; potassium plasma levels <3.5 mEq/l, sepsis, allergy to albumin, chronic heart failure (NYHA Grade II or more or ejection fraction lower than 50%) or symptoms of fluid overload at recruitment or long QT syndrome

Date of first enrolment
03/02/2020

Date of final enrolment
01/12/2023

Locations

Countries of recruitment
Germany

Hungary

Spain

Study participating centre
University of Pécs, Medical School, Institute for Translational Medicine
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Sponsor information

Organisation
University of Pécs Medical School

ROR
https://ror.org/037b5pv06

Funder(s)

Funder type
University/education

Funder Name
Általános Orvostudományi Kar, Pécsi Tudományegyetem [University of Pécs Faculty of Medicine]

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Péter Hegyi MD (p.hegyi@tm-pte.org).

IPD sharing plan summary

Available on request