Glucose control through a bihormonal artificial pancreas in patients after total pancreatectomy for cancer (PANORAMA): multicenter randomized controlled cross-over trial - Dutch Pancreatic Cancer Group (DPCG)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON53782

Source
ToetsingOnline

Brief title
PANORAMA

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes

Research involving

Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: KWF

Intervention

Keyword: artificial pancreas, bihormonal closed loop, diabetes, total pancreatectomy

Outcome measures

Primary outcome

The main study endpoint is the percentage of time spent in the normal glucose range, defined as sensor glucose values within 70 to 180 mg/dl (3.9 to 10 mmol/l).

Secondary outcome

- Mean sensor glucose concentrations;

- Glycemic variability; coefficient of variation and standard deviation

- Day and night time spent in hypo-, hyper- and euglycemia;

- Day and night median glucose concentration;

- Daily insulin and glucagon use;

- Mean HbA1c and percentage of patients achieving HbA1c <= 53 mmol/mol at baseline and after each treatment period;

- Quality of life / patient reported outcomes

Study description

Background summary

The feasibility of the BIHAP was tested in the clinical research center (CRC)

and at home (APPEL 1-3 study). Although the prototypes were bulky, these studies showed that closed loop glucose control was similar to standard open loop control. To make the closed loop system suitable for daily use at home, all components were integrated into one wearable device. This miniaturized prototype was tested for three days at home in eleven patients with type 1 diabetes (APPEL 4 study).The median glucose level for closed loop and open loop therapy was comparable, while the time spent in range
(3.9-10 mmol/l) was higher for closed loop.
The results of the APPEL 4 study15 were used as input for risk management, after which the system was further developed. The performance and safety of this updated BIHAP was assessed in the APPEL 5 study.5 In this study, 23 patients were included in the data analysis. The participants used the DHFCL system for 2 weeks at home, preceded by a 4-day training period. The patients also completed a 2-week control period, which was open
loop control with their own insulin pump, with or without a glucose sensor. The APPEL 4 and the APPEL 5 study have shown that the device is capable of a solid improvement in glycemic control.

Most recently the APPEL 5+ study was carried out. In this blind-randomized monocenter trial, 10 patients with TPD were randomized into BIHAP or standard diabetes treatment for 7 days. Patients received blinded CGMs. Time spent in euglycemia was significantly higher with BIHAP treatment (71-82% versus 52-81%). Also, hypoglycemia occurred less often (0% [IQR 0.0-0.0] vs 1.6% [IQR 0.8-3.8], p=0.004).

Study objective

To assess the efficacy of the BIHAP (AP® 5, Inreda Diabetic BV) using glucagon and insulin during a three-months period. It is hypothesized that treatment with BIHAP provides better glucose control than current diabetes treatment. Main parameter to evaluate glucose control is time spent in euglycemia (glucose value 3.9-10.0 mmol/l or 70-180mg/dL).

Study design

This study is a randomized, multicenter cross-over trial in an outpatient setting. The design is chosen because of the reduced influence of confounding covariates and the requirement of less patients compared to other designs. The duration of the study per patient is three months with current diabetes care and five training days followed by three months BIHAP treatment (or in reversed order). Between both arms there is a wash-out period of three months. The total duration of the study will therefore be approximately ten months.

Intervention

Prior to the start of the intervention period, the patients must attend an

instruction day at a central location. This training will be given by trained personnel from Inreda Diabetic BV, simultaneously the BIHAP will be attached. Afterwards, patients will be sent home and the five-day training period starts. During this period, the settings and algorithm of the BIHAP will be individually adjusted and patients will be monitored closely. After successful completion of the five-day training period, the main study can start.
The investigational device is a dual-hormonal fully closed loop system (BIHAP; industrial name AP® 5, Inreda Diabetic B.V.) which aims at optimally controlling plasma glucose levels. This BIHAP contains of two pumps for subcutaneous infusion of either insulin or glucagon via an infusion set, two subcutaneously placed glucose-sensors and an algorithm driving pump infusion rates based on the sensor input. In this way, the algorithm can maintain blood glucose level within the target limits, i.e., between 3.9 and 10.0 mmol/l.
Daily self-measurements of blood glucose
(SMBGs; Accu-Chek Instant, Roche) are needed for calibration of the glucose sensors. The BIHAP-system has to be worn continuously, except while showering.

During the control period of the trial, patients will continue their usual diabetes therapy (CSII therapy or subcutaneous insulin injections). All patients will wear an open glucose sensor (Freestyle Libre Pro IQ, Abbott) for data collection. Patients are asked to scan their glucose level with FSL at least three times a day during the study period, so that we have 24 hours of glucose levels. More frequent scans will be performed according to the patients* own judgement. The measured glucose levels will be automatically transferred to an online database of Abbott. No calibrations are required for the glucose sensor Furthermore, the patients may perform SMBG according to their own insight.

Study burden and risks

All patients undergoing total pancreatectomy will develop insulin dependent diabetes. Glucose control in TPD-patients is highly challenging due to the complete loss of pancreatic endocrine parenchyma, which predisposes to severe postoperative hypo- and hyperglycemia. TPD-patients have no endogenous production of either insulin or glucagon. TPD patients are therefore the target population to benefit from the BIHAP.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients who underwent total pancreatectomy
Age >= 18 years

Exclusion criteria

Impaired awareness of hypogycemia;
Total pancreatectomy performed within less than 3 months before start of trial;
BMI >35kg/m2;
HbA1c > 97 mmol/mol;
Presence of a medical or psychiatric condition, longstanding serious adherence problems, anticipated problems in handling over diabetes control to a device or use of a medication that could comprise the results of the study or the safety of the participant

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-04-2023
Enrollment:	40
Type:	Actual

Medical products/devices used

Generic name:	Bihormonal artificial pancreas (BIHAP)
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	14-03-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-05-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL82557.018.22