Reducing glycemic variability and inflammation in type 1 diabetes with hybrid closed-loop therapy

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To elucidate whether reducing glycemic variability with hybrid closed-loop therapy inhibits the inflammatory response (e.g. leukocyte phenotype, cytokine production, inflammatory proteins) in people with T1DM. Our secondary objectives are to...

Ethical review	Approved WMO
Status	Pending
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON57374

Source
ToetsingOnline

Brief title
VARILOOP

Condition

- Diabetic complications

Synonym
insulin-dependent diabetes, Type 1 diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Diabetes Fonds

Intervention

Keyword: Glycemic variability, Hybrid closed-loop therapy, Inflammation, Type 1 diabetes

Outcome measures

Primary outcome

The main endpoint is the difference in monocyte count between intervention and control at the end of the study.

Secondary outcome

• Immunophenotyping of leukocytes and other blood cells

• Plasma levels of the following parameters:

o Cytokines (e.g. TNF-α, IL-6, IL-1β)

o Chemokines (e.g. MCP-1, IL-8)

o Atherogenic markers (e.g. VCAM-1, ICAM-1, E-selectin)

o Coagulation markers (e.g. Von Willebrand factor, factor VIII)

o hsCRP

• Proteomics on inflammatory markers measured by the Olink inflammation panel

• Production of pro- and anti-inflammatory cytokines following ex vivo stimulation of leukocytes

• Functional changes in monocytes (e.g. endothelial migration and adhesion, differentiation)

• Lipid profile (e.g. LDL, HDL, cholesterol, non-HDL, triglycerides)

• Gene expression changes in leukocytes

• Epigenetic changes in leukocytes

• Leukocyte metabolism

• ROS production in neutrophils

• Intracellular cytokine production of leukocytes

• Glycemic variability as determined by CV, glycemic variability percentage

(GVP) and other commonly used measures

• Urinary albumin/creatine ratio

• Markers of retinopathy as assessed with optical coherence tomography

angiography and optical coherence tomography

• Effect of reducing GV on patient reported outcomes

Study description

Background summary

People with type 1 diabetes mellitus (T1DM) are at high risk for cardiovascular complications. Chronic low-grade inflammation of the arterial wall is an important risk factor for atherosclerosis. We showed previously that hyperglycemia in T1DM increases inflammation of the arterial wall, but observed no differences based on average glucose values. Glycemic variability (GV) reflects the difference between high and low glucose values and the frequency of these changes. Interestingly, GV has independently been associated with cardiovascular events. We think that this can partly be explained by the effect of GV on systemic inflammation. Recent studies elucidated that variable glucose values have a greater impact on inflammation in vitro than high but stable glucose values. We hypothesize that reducing GV, through hybrid closed-loop therapy, leads to a decrease in systemic inflammation in people with T1DM.

Study objective

To elucidate whether reducing glycemic variability with hybrid closed-loop therapy inhibits the inflammatory response (e.g. leukocyte phenotype, cytokine production, inflammatory proteins) in people with T1DM. Our secondary objectives are to evaluate the effect of reducing GV on arterial wall inflammation as reflected by circulating surrogate markers, and the effect of improvements in GV on patient reported outcomes. We will also investigate whether reducing GV decreases the progression of retinopathy and nephropathy.

Study design

Randomized controlled trial with a waitlist control design

Intervention

The intervention is a hybrid closed-loop system that consists of the CamAPS FX algorithm, a mylife YpsoPump insulin pump and a Freestyle Libre 3 continuous glucose monitoring sensor.

Study burden and risks

The hybrid closed-loop system that will be used in this trial is CE-certified and brings minimal additional risks compared to conventional treatment for T1DM. Participants in the intervention arm will have five visits in the hospital. During these visits, a total of 160 mL blood, two ophthalmological assessments, two urine collections, and two questionnaire sessions will commence. The waitlist controls will have two additional visits, where 75 mL blood, one ophthalmological assessment, and one urine collection are required in addition to those during the intervention period.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

Diagnosis with T1DM >= 1 year prior to screening
High glucose variability (CV >= 36%) >= 4 weeks prior to screening
Age between 16 and 65 years
BMI between 18-30 kg/m^2
Average glucose between 4.4-11.1 mmol/L

Exclusion criteria

Current use of hybrid closed-loop therapy
Any event of cardiovascular disease in the past 5 years (e.g. myocardial infarction, stroke, symptomatic peripheral arterial disease)
Pregnancy or planned pregancy
Diagnosis with auto-inflammatory or auto-immune disease
Occupations that include highly irregular working schedules (e.g. shift work)

Study design

Design

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

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	03-02-2025
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO Date:	01-04-2025
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL87963.091.24