ISRCTN95901685 https://doi.org/10.1186/ISRCTN95901685

Aniracetam for prevention of hypoglycemia in type 1 diabetes

Submission date	Recruitment status	[X] Prospectively registered
07/02/2025	Recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
22/04/2025	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
22/04/2025	Nutritional, Metabolic, Endocrine	[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Type 1 diabetes (T1D) requires lifelong insulin therapy. Hypoglycaemia (low blood sugar) is a common and potentially life-threatening complication of insulin treatment. Despite advances in insulin types and delivery methods, hypoglycaemia remains a significant side effect, contributing to impaired quality of life for patients and their loved ones, and increased healthcare costs.

Hypoglycaemia poses significant risks including confusion, seizures, and coma. Recurrent hypoglycaemia can lead to hypoglycaemia unawareness; usually people who are treated with insulin are aware that their blood sugar is low and can take action to treat this (by consuming fast acting sugar). People who have hypoglycaemia unawareness do not have symptoms or signs, therefore their diabetes management is more complicated and they are at a much higher risk of severe hypoglycaemic events, including seizures and coma.

By investigating a supplement that counteracts the underlying mechanisms of hypoglycaemia, we have the potential to improve hypoglycaemia management and the quality of life for individuals with type 1 diabetes. There is no current preventative treatment for insulin induced hypoglycaemia. Current treatment strategies for hypoglycemia in type 1 diabetes primarily involve glucose monitoring and administration of glucose or glucagon. However, these approaches may not always be effective in preventing or resolving hypoglycemic episodes, especially if there is hypoglycaemia unawareness.

There is a need for treatments that can complement existing treatments to provide more targeted management of hypoglycemia in individuals with type 1 diabetes, and a need for treatments that can prevent the disabling and dangerous side effect of hypoglycaemia.

This study is investigating the effects of the supplement aniracetam during hypoglycaemia in individuals with T1D. Scientific studies so far lead us to think that supplementation with aniracetam will lead to improved control, a reduction in hypoglycaemic episodes, and, in the future, enhanced overall well-being in participants with type 1 diabetes.

Who can participate?

People aged 21-70 who have had Type 1 diabetes for 5 years or more.

What does the study involve?
This study involves three visits to Edinburgh Royal clinical research facility for one screening visit, including blood tests, then two hypoglycaemic clamp studies, separated over one to two months. This clamp study is safe and well recognised in the field of diabetes research. It involves a 6 hour visit where blood glucose is carefully and slowly lowered into low blood glucose levels (hypo) to measure, using blood tests, the body's response to this. One clamp will test the body's response alone and one will test the body's response using aniracetam.

What are the possible benefits and risks of participating?
Benefits. If the results are positive this will change diabetes management. This has the potential to reduce the disabling and dangerous side effect of insulin therapy: Hypoglycaemia.
Risks. There are no risks. The clamp study is considered safe and is the gold standard procedure used in research.

Where is the study run from?
The Edinburgh Clinical Research Facility, Scotland (UK)

When is the study starting and how long is it expected to run for?
October 2024 to December 2027

Who is funding the study?
The Helmsley Charitable Trust (USA)

Who is the main contact?
Professor Shareen Forbes, Shareen.Forbes@ed.ac.uk

Contact information

Type(s)
Public, Scientific, Principal Investigator

Contact name
Prof Shareen Forbes

ORCID ID
http://orcid.org/0000-0002-9127-0641

Contact details
University of Edinburgh, BHF Centre for Research Excellence, Queen's Medical Research Institute, 47 Little France Crescent
Edinburgh
United Kingdom
EH16 4TJ
+44 1312426736
Shareen.Forbes@ed.ac.uk

Type(s)
Scientific

Contact name
Dr Nicola Baillie

Contact details
University of Edinburgh, BHF Centre for Research Excellence, Queens Medical Research Institute, 47 Little France Crescent
Edinburgh
United Kingdom
EH16 4TJ
+44 1312426736
Nicola.Baillie@ed.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
349276

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Repurposing positive allosteric modulators of glutamate receptors to prevent hypoglycemia in type 1 diabetes: a pilot clinical study

Acronym
APHiD

Study objectives
We hypothesise that aniracetam, a positive allosteric modulator of the α-cell AMPA/kainate receptors, can increase the counterregulatory response of glucagon in response to hypoglycaemia in people with T1D.

Ethics approval required
Ethics approval required

Ethics approval(s)
Not yet submitted 20/02/2025, South East Scotland Research Ethics Committee 1 (NHS Lothian, Waverley Gate, 2 - 4 Waterloo Place, Edinburgh, EH1 3EG, United Kingdom; +44 131465 5473; Sandra.Wyllie@nhslothian.scot.nhs.uk)

Study design
Randomised controlled exploratory physiological clinical trial

Primary study design

Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
Not available in web format. Please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Type 1 Diabetes

Interventions
This is a double blind, crossover, placebo controlled, exploratory physiological study. It is a single site study on 18 participants with T1D, who will be recruited over a 12 month period. The aim is to recruit 9 male and 9 female participants. Each participant will undergo two hypoglycaemic clamp studies, one study will analyse the body's response to Aniracetam 1500mg, the standard dose used in Europe, given during the clamp. The second study, 4-6 weeks later, will analyse the same parameters using the identical placebo. An NHS clinical trials pharmacist will be unblinded and therefore keep a record of which intervention each participant has had.

Intervention Type
Other

Primary outcome measure
Glucagon, measured during insulin clamp procedures

Secondary outcome measures
Cortisol, Adrenaline, Noradrenaline, Insulin and Glucose concentrations, measured during insulin clamp procedures

Overall study start date
01/10/2024

Completion date
01/12/2027

Eligibility

Key inclusion criteria
1. Participants with T1D with C-peptide levels less than 100pmol/L
2. Age 21-65 years
3. T1D for 5 years or more

Participant type(s)
Patient

Age group
Adult

Lower age limit
21 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
18

Key exclusion criteria
1. Proliferative retinopathy
2. History of Diabetic ketoacidosis in the preceding 6 months
3. Severe hypoglycaemic episode requiring external assistance in the preceding 6 months
4. History of Haemophilia, Cystic Fibrosis, pancreatic disease or complete pancreatectomy, ischaemic heart disease, cardiac arrhythmia, epilepsy or hypoglycaemia induced seizure
5. History of severe reaction or allergy to adhesive necessary to this study
6. Unable to adhere to study timetable
7. Unable to give informed consent
8. Pregnancy or planning pregnancy. We will perform a pregnancy test on all eligible participants at baseline
9. Concurrent use of any non-insulin glucose-lowering agent (including GLP-1 agonists, Symlin, DPP-4 inhibitors, SGLT-2 inhibitors, sulfonylureas). These may lower insulin requirements and predispose to diabetic ketoacidosis
10. Hypothyroidism
11. Concurrent use of medication that may affect blood glucose such as SSRIs
12. Inability to understand or speak English. Time is of the essence during the clamp procedure, there is no time for translation
13. A condition, which in the opinion of the investigator, would put the patient or study at risk

Date of first enrolment
01/07/2025

Date of final enrolment
01/07/2027

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Edinburgh Royal Infirmary Clinical Research Facility
51 Little France Crescent
Edinburgh
United Kingdom
EH16 4SA

Sponsor information

Organisation
Leona M. and Harry B. Helmsley Charitable Trust

Sponsor details
230 Park Avenue,
New York
United States of America
NY 1016
+1(212) 679-3600
grants@helmsleytrust.org

Sponsor type
Charity

Website
http://helmsleytrust.org/

ROR
https://ror.org/011x6n313

Funder(s)

Funder type
Charity

Funder Name
Leona M. and Harry B. Helmsley Charitable Trust

Alternative Name(s)
Helmsley Charitable Trust, The Leona M. and Harry B. Helmsley Charitable Trust, Leona M. & Harry B. Helmsley Charitable Trust, The Helmsley Charitable Trust

Funding Body Type

Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Publication and dissemination plan
Results will be published in a peer reviewed journals. Results will be disseminated at external and internal conferences and meetings.

Intention to publish date
01/06/2027

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Stored in non-publicly available repository