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Closed-loop in pregnancy day and night home feasibility study (CLIP 24/7)

Submission date
07/01/2016

Recruitment status
No longer recruiting

Registration date
08/01/2016

Overall study status
Completed

Last Edited
29/08/2018

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Controlling blood sugar levels during pregnancy is very important for the health of the mother and the baby. However, many women with type 1 diabetes find it hard to avoid high blood sugar levels without experiencing low blood sugar levels (hypoglycaemia). Closed-loop systems consist of a continuous glucose monitor (CGM), a computer algorithm (mathematical instructions which calculate the insulin dose) and an insulin pump. During closed-loop, the CGM measures the glucose levels and relays them to the computer. The computer calculates an appropriate insulin dose according to the algorithm. It communicates with the insulin pump to give out the particular dose of insulin every 12 minutes. The closed-loop system has already been tested in women with type 1 diabetes during early, mid and late pregnancy. How it adapts insulin for the changing needs of pregnancy both in hospital and at home overnight has already been studied. In addition, a
study similar in design to this one has tested the use of overnight closed-loop insulin delivery compared with using an insulin pump and continuous glucose monitor alone and demonstrated that the technology was safe and worked well. This study will test how day and night closed-loop compares to the overnight glucose control achieved by an insulin pump and CGM without closed-loop.

Who can participate?
Pregnant women with type 1 diabetes.

What does the study involve?
Participants are randomly allocated to one of two groups. All of them wear an insulin pump and a CGM sensor continuously during their time in the study. Those in group 1 also use the closed-loop technology for insulin delivery overnight for 4 weeks. Participants in group 2 use the insulin pump and GSM without the closed-loop for 4 weeks. After this time, all participants resume their normal treatment for 1-2 weeks. They are then allocated to the other group and treated accordingly for a further 4 weeks (i.e. those participants that were using the closed-loop now don't, and vice versa).
Once the participants have completed both treatments, they are asked to complete questionnaires and interviews about their experience of the closed-loop system. They have blood tests to find out the effect of the closed-loop system on their glucose control. They also

wear a wrist band to measure their sleep both before and during their time in the study. After the end of the study, the participants have the opportunity to continue on either of the study treatments until the end of their pregnancy and up until 6 weeks after they deliver their baby.

What are the possible benefits and risks of participating?
Participating in this study may help people to better understand what happens to their blood sugar levels during pregnancy. It will also help research into the development of closed-loop systems. Participants may also benefit from wearing a CGM and insulin pump. Studies suggest that using CGM helps women to improve blood sugar control and reduces the risk of delivering a large baby. Outside pregnancy, insulin pump use is associated with better glucose control and improved quality of life. The University of Cambridge insurance policy will include cover both for negligent and for non-negligent harm. The cover for non-negligent harm is not usually offered for clinical studies and may be considered as an additional benefit. The insulin pump and CGM sensor may produce mild pain when inserted into the skin. There is a low risk for developing a local skin infection at the site of the insulin pump or CGM insertion. Itchiness, redness, bleeding, and bruising at the pump and CGM insertion sites may occur as well as local tape allergies. Participants will be alerted by a systems alarm if the closed-loop system stops working or malfunctions in any way, for example loss of connection between the closed-loop computer and the insulin pump. If the participant does not respond to the alarm, their usual basal insulin delivery will be automatically started. During the study, participants may experience a hypo (low blood sugar levels) as may happen in everyday life. There will always be either a health professional from the study team contactable by phone to help adjust to insulin doses, and advise regarding treatment.

Where is the study run from?
NHS hospitals belonging to one of the following four NHS trusts: Cambridge University Hospital NHS Foundation Trust, Norfolk and Norwich University Hospitals NHS Foundation Trust, Ipswich Hospital NHS Trust and King's College Hospital NHS Foundation Trust.

When is the study starting and how long is it expected to run for?
January 2016 to December 2016.

Who is funding the study?
The National Institute of Health Research (UK)

Who is the main contact?
Dr Zoe Stewart
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Contact information

Type(s)
Public

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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Evaluation of the feasibility, utility, safety and efficacy of day and night closed-loop insulin delivery at home in women with type 1 diabetes during pregnancy

Acronym
CLIP 24/7

Study objectives

An automated closed-loop insulin delivery system can be used reliably, safely and effectively by pregnant women with type 1 diabetes in the home setting, to improve day and night glucose control.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee East of England - Cambridge Central, 11/09/2015, ref: 15/EE/0278

Study design
Interventional study - a multi-centre, open-label, randomised crossover design.

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Type 1 diabetes in pregnancy

Interventions
The investigational treatment is the FlorenceD or follow-up prototypes of the automated overnight closed-loop system manufactured by the Cambridge University Hospitals NHS Foundation Trust. Component versions will be identified during regulatory submission to the MHRA. Eligible participants, who provide informed consent, complete training for the study pump and the study CGM and are competent and compliant in the use of both devices, will be randomised using a 4-block randomisation based on computer-generated random code. The study reporting period is from the time of recruitment (obtaining informed consent) until 6 weeks post-partum. After completing the two active study arms (4 weeks of closed-loop insulin delivery and 4 weeks of sensor-augmented pump therapy), participants will have follow-up HbA1c measurements at 28, 32 and 36 weeks gestation, and 6 weeks post-partum. Obstetric and neonatal outcomes will be collected at the end of pregnancy. Adverse events that continue after the subjects discontinuation or after 6 weeks post-partum will be followed until their medical outcome is determined or until no further change in the condition is expected.

Intervention Type
Device

Primary outcome measure
Time spent in the target glucose range from 3.5-7.8 mmol/L, as recorded by continuous glucose monitoring (CGM) during the 28 day intervention periods.

Secondary outcome measures
1. Time with glucose levels in the hypoglycaemic range, based on continuous glucose monitoring (glucose levels < 2.8 mmol/L)
2. Time with glucose levels in the hyperglycaemic range, based on continuous glucose monitoring (glucose levels > 7.8 mmol/L)
3. Metabolic control assessed by change in HbA1c after the use of closed-loop system for 28 days, compared with that during continuous glucose monitoring without the closed-loop system for 28 days. HbA1c will be measured before and after each intervention arm
4. CGM data collected during intervention arms will be compared to baseline CGM readings
5. Trends in CGM data collected within intervention arms will also be evaluated on weekly basis (i.e. week 1 versus week 2 versus week 3 versus week 4)
6. CGM data collected after the intervention arms i.e. during pregnancy and up to 6 weeks post-partum will also be compared to baseline and intervention arm readings using CGM summary statistics and functional data analyses

Overall study start date
01/06/2015

Completion date
31/12/2016

Eligibility

Key inclusion criteria
1. Signed informed consent obtained before study-related activities. Study-related activities are any procedure that would not have been performed during standard medical care
2. The participant is between 18 and 45 years of age (inclusive)
3. A viable singleton pregnancy confirmed by ultrasound, at gestational age ≥ 8 and ≤ 24 weeks
4. The participant is on intensive insulin therapy (≥3 injections or CSII) and compliant with diabetes self-management i.e. doing ≥4 SMBG tests per day
5. The participant is able and willing to use the study devices and complete the CGM and study pump run-in assessments
6. The participant is able to speak and understand English

Participant type(s)
Patient

Age group
Other

Sex
Female

Target number of participants
16

Key exclusion criteria
1. Non-type 1 diabetes mellitus
2. Any other physical or psychological disease likely to interfere with the normal conduct of the study and interpretation of the study results such as coeliac disease or untreated hypothyroidism.
3. Current treatment with drugs known to interfere with glucose metabolism as judged by the investigator such as systemic corticosteroids, non-selective beta-blockers and MAO inhibitors.
4. Known or suspected allergy against insulin.
5. Women with nephropathy, neuropathy, gastroparesis or proliferative retinopathy as judged by the investigator that is likely to interfere with the normal conduct of the study and interpretation of study results.
6. Very good or very poor glycaemic control i.e. first antenatal HbA1c ≤ 47mmol/mol (<6.5%) and current (within 2 weeks of recruitment) HbA1c ≥10% (86mmol/mol)
7. Total daily insulin dose 1.5 IU/kg at booking
8. Severe visual or hearing impairment
9. Unable to speak and understand English

Date of first enrolment
12/01/2016

Date of final enrolment
30/06/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Cambridge University Hospital NHS Foundation Trust
Cambridge University Hospitals
NHS Foundation Trust
Box 277, Addenbrooke's Hospital
Hills Road
Cambridge
United Kingdom
CB20QQ

Study participating centre
Norfolk and Norwich University Hospitals NHS Foundation Trust
Norwich
United Kingdom
NR4 7UY

Study participating centre
Ipswich Hospital NHS Trust
Heath Rd
Ipswich, Suffolk
United Kingdom
IP4 5PD

Study participating centre
King's College Hospital NHS Foundation Trust
Denmark Hill
London
United Kingdom
SE5 9RS

Sponsor information

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Sponsor type
Hospital/treatment centre

Organisation
University of Cambridge

Sponsor details
Research Office
University of Cambridge
16 Mill Lane
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United Kingdom
CB2 1SB

Sponsor type
University/education

Organisation
Cambridge University Hospitals NHS Foundation Trust

Sponsor details

Sponsor type
Not defined

Website
http://www.cuh.org.uk/

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
We plan to publish the results of this study in a peer-reviewed journal within 2-3 months of the completion of the study. We will also forward the results of the study to all participants in the study and to the funders.

Intention to publish date
30/03/2017

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2018		Yes	No
HRA research summary			28/06/2023	No	No