A follow-up study to investigate the functionality of a glucose sensor device in the human eye.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Observational invasive

Summary

ID

NL-OMON46205

Source
ToetsingOnline

Brief title
NSGSIIb

Condition

- Diabetic complications
- Diabetic complications

Synonym
Diabetes type 1, Insulin-dependent diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Noviosense BV
Source(s) of monetary or material Support: Funded by the sponsor

Intervention

Keyword: diabetes, eye, Glucose, sensor

Outcome measures

Primary outcome

The primary endpoint of this pilot study is to determine the efficiency of a glucose monitor device to measure in the tear fluid of human eye for up to 6 hours.

Efficiency is measured by:

* The ability to measure a repeatable stable signal in the eye;

* The correlation of glucose values in the eye with those found in blood both from blood analysis and CGM sensor.

Secondary outcome

The secondary endpoint of this pilot study is to ensure that the functional prototype device has equally good tolerability with surrounded tissues in course of continues glucose measurement as it has been confirmed when dummy devices were trailed. Therefore, basic information about ease of positioning, removal, on the measurement or data quality and compatibility of the prototype device with surrounded tissues in course of continues glucose measurement will be evaluated.

Additional tolerability of the glucose sensor. This is measured as follows:

* Qualitative assessment of irritation by an ophthalmologist;

* Comparison of the diameters of the capillary veins on conventional photographs taken before installation and after removal of the device (possible irritation would lead to dilatation of the veins);

Answers to questionnaires filled out by the subjects (information about red

eyes, itching, burning feeling etc.);

Study description

Background summary

NovioSense is developing a new minimally-invasive glucose monitoring device. This device will be positioned in the eye (inferior conjunctival fornix) and will monitor the glucose levels in tear fluid. In a functional device, the information will be transmitted to a cell phone receiver that will translate the tear glucose into equivalent blood glucose levels. In this way, diabetict subjects can better control their blood glucose levels and keep it within acceptable bounds as much as possible. This pilot study will evaluate ability of the sensor to measure glucose in the tear fluid of a human eye, thus the functional wired prototype of the device will be used. It*s configuration is identical in dimension, materials and shape to the final functional device with the exception that the electronics portion is connected to an industry standard measurement system to avoid any effects of the electronics on sensor performance. The device underwent a positive animal test where 5 sheep in total were examined. The maximum exposure time of the dummy device in the eye was 5 hours and no irritation or damage to the eye was observed (see IMDD for summary of animal experiments). The tolerability of the device has been also assessed in a pilot study performed on 4 healthy volunteers, carried out in Sf. Spiridon Hospital, Iasi, Romania on 7th of August 2015 (see summary of the report NS 01-2015). Dummy devices were placed into the inferior conjunctival fornix of the human eye and the subjects were examined for 5 hours by an ophthalmologist. No signs of reddening of the conjunctiva or conjunctival fornix were observed and the devices worn by the subjects, did not induce any discomfort or pain. The rational for the relatively short duration of the device placement in the eye was to maintain the evaluation time comparable to the input from previous animal tests.
On 24h November 2017, the study protocol NSGS201702 received approval from Medisch Ethische Toetsingscommissie Zuidwest Holland with given identification number NL61532.098.17. Six clinical subjects successfully completed the pilot clinical trial conducted between 22nd of December 2017 and 13th of April 2018. The tear glucose sensor was able to measure stable and repeatable signals for up to 5 hours with high tolerance. The analysed data gave evidence for the correlation between glucose in tears and blood and interstitial fluid. However, the population of enrolled subjects (six subjects) was not enough to provide a more comprehensive analysis of the capability of the sensor and to assess the lag time between blood and tear glucose. On completion of this pilot study without major adverse events, such as significant irritation or damage to the

eye and good tolerability, a new study will investigate the accuracy of the device by continual measurement of glucose concentrations in a tear fluid of human eye involving a larger group of subjects. Therefore a folllow-up study is initiated where additional 24 clinical subjects will be recruited.
In this study, the evaluation time will also be limited to 6 hours. The rational with a short time scale trials and not to include a longer duration pilot is to collect additional feedback about tolerability and measurement ability before continuing with longer- term experiments. These longer-term studies do require a different logistic, for example, to have an ophthalmologist stand-by during the night-time periods. So, before proceeding to this set-up the initial feedback will be collected in this follow-up case and analysed.

Study objective

The objective of this pilot study is to investigate the efficiency of a glucose monitor device placed in a tear fluid of human eye to measure glucose for up to 6 hours and its correlation to blood glucose values. Additionally, more information will be collected to confirm the tolerance of the device in a human eye.

Study design

This is a non-randomized, single-center sponsor initiated follow-up study by enrolling volunteers with diagnosed diabetes type 1, insulin dependent, that signed an informed consent form.
This study is initiated to investigate the efficiency of a prototype glucose sensor device able to measure glucose levels in a tear fluid of human eye. 24 volunteers, a mix of gender will be recruited, all following the in- and exclusion criteria. It is expected to dedicate a day for each subject, separately. Before the follow-up study will take place, the subject is expected to report to the site fasted but on their normal basal insulin where the basic eye examination supported with pictures will take place by ophthalmologist. The commercial available CGM device (Abbott FreeStyle Libre device) must be attached into subject upper arm at least one day prior the trial and used as an additional reference through all pilot study. Blood samples to measure glucose values during the experiment time points will be taken with Point-Of-Care system and serve as a reference. The insertion of the investigated sensor coil into an inferior conjunctival fornix will be done using specially designed insert devices (see details in protocol). After insertion of the device into the inferior conjunctival fornix by a specialist. It will be given a period of 60 minutes to stabilize the sensor where no measurements will be taken. After that, the measurement with NovioSense device will be performed continuously for the next 30 minutes where usual meal prior to which half the dose of their normal short- acting insulin will be administered. In parallel to the NovioSense measurement, blood samples will be taken and the external GCM device

will be scanned to record glucose concentration values with 15 minutes interval and serve as a reference. The subject will be asked to wear a device for 6 hours (trial duration). The data collection will proceed for a maximum of 5 hours and following the trial the patient will undergo follow up by the ophthalmologist, where the pictures will be taken. At the end of the study, the subject will fill out a questionnaire.

Study burden and risks

The glucose monitor device (dummy device) has been tested in animals and humans for up to 5 hours in the eye without any signs of irritation, infection or damage. However, duration of the tolerability study involving the group of subjects was influenced by the results acquired from animal tests. Sheep model used within a study, possess a third eyelid which caused dislocation of the device during the experiments enabling to assess tolerability only up to 5 hours. It was demonstrated in a small group of volunteers that in the human setting dislocation did not occur. Moreover, the subjects did not report any discomfort or pain caused by a presence of a dummy device in inferior conjunctival fornix.
Despite positive results obtained from a dummy device in both "in vivo* and pilot clinical settings, there still is a possibility of dislocation with repeated rubbing or mechanical stimulation. The functional prototype device contains external connection Pt/Ir wires (3 electrodes, see description in section 3.1 of the protocol), firmly immobilised onto side of the face, connected to a mechanical interlock connected to a potentiostat enabling conducting measurement of glucose concentration in the eye. Consequently, there is a risk of reduced comfort of a subject during the experiment. Moreover, within the initiated study, the glucose levels in a tear fluid of human eye will be determined by applying a small voltage (0.5 V) to the device. The produced current, in a range from 0 to 25 micro amp will be measured. This measurement technique is identical to that employed in all current marketed CGM devices. The risk of short circuit occurrence has been mitigated for in the risk assessment exercise and precautions have been undertaken to mitigate any potential cohort circuit of the device by installing physical controls as well as a patient operated interlock which allows them to break the contact and terminate the measurement with minimal force if they feel a sensation which is uncomfortable or unpleasant.
The subjects will be under continuous supervision of an ophthalmologist during the duration of the study. In course of any failure of the device, as stated above, or discomfort of the subject, the physician will remove the device immediately and will conduct necessary eye examination, funds photography.
There are no direct clinical benefits for the subjects by participation in this pilot study other than a significant contribution towards a next step in developing a minimally invasive glucose sensor device that can help diabetic patients to better manage their glucose levels.

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

* Subject is > 18 years old on the date he/she signed the informed consent;
* Diagnosed diabetes type 1;
* Insulin dependent;
* Wearing FreeStyle Libre CGM device;
* Signed informed consent.

Exclusion criteria

* Subjects having any eye surgery in the past;
* Subjects having any historic disease of the eye (e.g. conjunctivitis, keratitis, dry eye, diabetic retinopthy with lasercoagulation);

* Subjects that wear contact lenses;
* Not able or willing to comply to the protocol;
* Subjects with signs/ symptoms of any additional disease except diabetes (medical judgement and/or medication history).

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-10-2018
Enrollment:	24
Type:	Actual

Medical products/devices used

Generic name:	Point of Care device
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	19-09-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL66681.098.18