A pilot study to investigate the functionality of intra-vaginal glucose sensor in vagina.

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

Summary

ID

NL-OMON47792

Source
ToetsingOnline

Brief title
Pilot Study intra-vaginal LiGalli ring * glucose sensor device

Condition

- Diabetic complications
- Diabetic complications

Synonym
Diabetes, intravaginal ring

Research involving
Human

Sponsors and support

Primary sponsor: Ligalli BV
Source(s) of monetary or material Support: Sponsor

Intervention

Keyword: diabetes, glucose sensor, intra-vaginal, LiGalli ring

Outcome measures

Primary outcome

The primary endpoint of this pilot study is to determine the efficacy of intravaginal device to measure glucose in vagina for up to 5 hours.

Efficacy is measured by:

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

* The correlation of glucose values measured with the glucose sensor at the vaginal wall with those found in blood both from finger stick glucose analysis and external CGM sensor will be made.

Secondary outcome

The secondary endpoint of this pilot study is to determine the compatibility of the intra vaginal device with surrounding tissues in the course of continuous glucose measurement.

Compatibility is measured by:

* Qualitative assessment gynecologist;

* Answers to questionnaires filled out by the subjects (information about comfort).

Study description

Background summary

Continuous Glucose Monitoring (CGM) has been shown to improve glucose regulation in patients with type 1 diabetes (Special issue on CGM in clinical

practice, Diabetes Technology& Therapeutics, volume 9, 2017). Current CGM systems are devices that measure glucose in the subcutaneous fluid and are applied to the skin. The disadvantages of the present systems are that they give skin irritations in about 9% of patients and are visible on the outside. A lot of patients (especially, but not only young women) don*t like the visibility of the device. Also, because glucose is measured in the subcutaneous fluid there is a *lagtime* between capillary glucose and subcutaneous glucose, especially when glucose values are rapidly changing. LiGalli BV is developing an intelligent intra-vaginal ring for drug delivery and diagnostics. The incorporation of a glucose sensor and insulin reservoir would provide flexibility in dosage, schedule and timing. To the best of our knowledge there is only one study in the open literature measuring glucose from vaginal wall transudation. In this study the change of glucose was measured in vaginal secretions during glucose tolerance testing (Ehrström et al., Obstetrics & gynecology, 2006, 108, 1432*1437). According to Ehrström et al. the median level of glucose in vagina secretions of healthy women was 5.2 mM before and 3.7 mM after oral glucose tolerance test, while plasma glucose was 5 mM before and 5.8 mM after oral glucose tolerance test. Also, one women with insulin-dependent diabetes was analyzed in this research. Although the plasma glucose of this women was equal to 14.3 mM, the level of glucose in vaginal secretion was only 6.2 mM. The results of this small study suggest that there is no correlation between blood glucose and vaginal fluid glucose concentrations. Yet, it should be noted that glucose concentration was measured from the pool of vaginal fluid in the deepest part of the vagina (fornix posterior) which is composed of past secretion of cervical mucus and transudate. Moreover, the measurement was done by use of a sterile, weighted strip of filter paper, thus glucose was not measured directly from the vaginal mucosa.

To the best of our knowledge there are no data on the correlation between the concentration of glucose in blood and vaginal wall transsudate. The current embodiment is in direct contact with the mucosal wall only a few millimeters away from the very richly vascularized area of the vagina. Glucose can pass these anatomical borders easily. It is plausible that vaginal wall transsudate glucose might reflect the actual changes in blood glucose concentrations. The ring and measuring sensor are placed directly against the vaginal wall in a flexible manner and do not penetrate the tissue itself.

NovioSense and LiGalli have combined technologies to develop an intravaginal glucose sensor to determine glucose levels in vaginal wall transudate. A vaginal ring developed by LiGalli, housing components developed by NovioSense BV and Philips Medimetrics is placed into vagina and by its design offers a stable contact positioning of the glucose sensor to the vaginal wall. The device uses the NovioSense glucose sensing platform to determine the glucose concentration of vaginal wall transsudate.

This pilot study will evaluate the ability of the intravaginal device to measure vaginal wall glucose and correlate that value to blood glucose and subcutaneous measured glucose by currently used CGM systems.

The tolerability of the ring shaped silicone device has been assessed as a

dummy device in 6 patients who could easily insert and remove the ring themselves. Two of them wore the ring for 4 weeks. The pilot was carried out at Maxima Medisch Centrum Veldhoven, the Netherlands in August 2015. The ring was found to be comfortable and did not illicit irritation from the surrounding tissue.
The functionality of the device was assessed in a second small pilot study performed in 1 healthy volunteer, carried out at Maxima Medisch Centrum Veldhoven, the Netherlands on the 20th of October 2016 (see summary of the report NS 12-2016 and NS 13- 2016). A Boston
Scientific explorer 360 electrocardiology catheter was retrofitted into the Ligalli ring and coated with NovioSense coating to form the intravaginal glucose sensor. The device was placed into the vagina in contact with the vaginal wall by a gynecologist and was examined for approximately 1 hour 20 min period. The in vivo pilot work demonstrated that the intravaginal device can function and give a stable and clear response in the vagina. Also, it was shown that the device can measure a shift in a glucose concentration following flushing near the sensor with different concentrations of glucose.
This pilot study will evaluate the ability and efficacy of the intravaginal device to measure glucose proximal to the vaginal wall. Moreover, it will give an answer if glucose sampled from the upper vaginal tract close to the cervix reflects levels of glucose found in blood as was seen in the previous study. The results will also be compared by those of currently used CGM devices.

Study objective

The objective of this pilot study is to investigate if glucose measurement on the vaginal wall can be an alternative for capillary and subcutaneous glucose measurement. The present study will look at the efficacy of an intravaginal device to measure glucose in the vagina up to 4.5 hours and to investigate if glucose sampled from vaginal wall transsudate reflects levels of glucose found in capillary blood and interstitial fluid measured with a currently used subcutaneous device.

Study design

This is a, nonrandomized, single-center, sponsor initiated pilot study.
The selected subjects will report on the day of the trial fasted on normal basal insulin and will be asked to wear the vaginal device throughout the trial for up to 4.5 hours in which the glucose measurements with the sensor from the vaginal wall will be taken. The capillary blood samples will be collected from finger stick glucose tests during the experiment time points for quantitative analysis of glucose levels and serve as a reference. Additionally, the glucose values from interstitial fluid will be measured by a CGM (continues glucose monitoring) sensor as a supporting control to the acquired data and given to a subject at least one day prior the trial. After insertion of the device by a gynecologist, the basal evaluation of glucose measurements will be performed

for 30 minutes. Next, the patients will take their own usual breakfast prior to which half the dose of their normal short-acting insulin will be administered.Half the dose of the short-acting insulin is chosen to increase the glucose value after the meal up to a level of about 15 mmol/L, a value that is not uncommon in everyday practice for patients with type 1 diabetes. Blood samples to measure glucose values during the experiment time points will be taken with Point-Of-Care system and serve as a reference. Additionally, patients should wear a commercially available CGM (continuous glucose monitor) sensor to serve as a supporting control to the acquired data. Data collection will proceed for a maximum of 4 hours and following the trial the patient will undergo follow up by the gynecologist.

Study burden and risks

The intravaginal ring device (dummy device) has been tested in women for up to 28 days and the functional device tested for 1 hour 20 min in vagina without any signs of irritation or an acute response. In both studies subjects did not report any discomfort or pain caused by a presence of the device in vagina.
The functional intravaginal device contains external connection to a potentiostat enabling electrochemical measurement of glucose concentration in vagina. Despite positive results obtained from previously conducted pilot trails, the tolerability was assessed on a small number of subjects recruited, thus there is still a possibility to sense a reduced comfort during wearing the device within time of the trial. Therefore a physician will be present throughout the trial and will remove the device immediately if any discomfort is experienced by the subject.
Moreover, as part of the initiated pilot study, the glucose levels in vagina will be determined by applying a small potential to the device (0.5 V). The produced current, in a range from 0 to 15 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 by physical separation of the electrodes, 100% inspection and testing of devices. The risk assessment exercise and precautions have been undertaken to mitigate any potential short circuit of the device. The patient can ask to terminate the measurement if they feel a sensation which is uncomfortable or unpleasant at any point. Additionally, in course of the trial (up to 4.5 hours), the subject will experience reduced mobility caused by external connection between device and the potentiostat.
In course of any failure of the device, as stated above, or any other unforeseen adverse event, the physician will remove the device immediately and will conduct necessary examination.
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 intravaginal glucose sensor device that could answer fundamental questions if there is a correlation between vagina wall glucose and blood glucose.

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 she signed the informed consent;
* Subject is taking oral contraceptive birth control (excluding vaginal contraceptive devices) and not menstruating;
* Diagnosed diabetes type 1;
* Wearing a CGM sensor;
* Signed informed consent.

Exclusion criteria

* Subjects having any historic vaginal disease;
* Pregnant subjects;

* Subjects having their menstrual cycles;
* 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):	15-12-2017
Enrollment:	5
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	15-09-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	20-11-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	03-04-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	27-03-2019
Application type:	Amendment
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	NL61811.098.17