ISRCTN96827601 https://doi.org/10.1186/ISRCTN96827601

# Ketoacidosis in type 2 diabetics on SGLT-2 inhibitors

| Submission date | Recruitment status | [X] Prospectively registered |
|---|---|---|
| 08/09/2016 | No longer recruiting | [ ] Protocol |
| **Registration date** | **Overall study status** | [ ] Statistical analysis plan |
| 12/09/2016 | Completed | [ ] Results |
| **Last Edited** | **Condition category** | [ ] Individual participant data |
| 12/09/2016 | Nutritional, Metabolic, Endocrine | [ ] Record updated in last year |

## Plain English summary of protocol

Background and study aims

Diabetes is a condition that causes a person's blood sugar level to become too high. Insulin is the hormone made by beta-cells in the pancreas and controls the amount of glucose in the blood. There are two main types of diabetes: Type 1 where the pancreas does not produce any insulin and type 2. In type 2 diabetes, the body does not produce enough insulin for it to work properly or the body cells do not react properly to insulin (insulin resistance). A person is more likely to develop diabetes if they are overweight, do not do a lot of exercise, eat an unhealthy diet or are an older person. Type 2 diabetes is an increasing problem worldwide. There is now a new type of treatment that has been shown to work well at preventing serious complications of type 2 diabetes. The treatment is a medication that works by allowing the kidneys to pass sugar from the blood into the urine, thereby reducing the amount of sugar in the blood. These drugs have been shown to be very good at controlling the blood sugar, helping to lose weight and may in fact help protect against heart disease. More and more people will probably be started on this treatment because of these benefits. There have been some reports of a complication called ketoacidosis in people with type 2 diabetes on this treatment. Ketoacidosis commonly occurs in people with type 1 diabetes where there is no insulin available. The cells in the body cannot use sugar as energy and start breaking down fats, making a chemical called ketones as a by-product. High levels of ketones can cause a condition called acidosis when the blood becomes very acidic and this can be life-threatening. It does not normally occur in type 2 diabetes but may occur more frequently if people with type 2 diabetes are on this treatment. In this study, investigators will check the levels of ketones in people with type 2 diabetes who are on the new treatment. This will be done firstly when the patients are well, as they join the study, and also when they become unwell. The results of the study will then be looked at to see if ketoacidosis is a common complications or a rare complication of the new treatment.

Who can participate?

Adults (aged at least 18) with type 2 diabetes and being treated with SGLT2i

What does the study involve?

Potential participants for this study have already been on the new SGLT2i treatment for a time before joining the study. During the study period, each participant is asked to provide blood samples when they first join (and they feel well) and again when they feel unwell. The

researchers then look t the results of the study to find out whether ketoacidosis is common in people on the treatment who feel unwell.

What are the possible benefits and risks of participating?
The benefit is that if the test for ketoacidosis is confirmed, a patients treatment can be looked at again to see whether it's a good idea to continue with the treatment. There are no risks apart from the inconvenience of the extra blood test

Where is the study run from?
Southend University Hospital (UK)

When is the study starting and how long is it expected to run for?
May 2016 to November 2017

Who is funding the study?
Southend University Hospital NHS Foundation Trust

Who is the main contact?
Dr Gowrie Balasubramaniam

# Contact information

### Type(s)
Scientific

### Contact name
Dr Gowrie Balasubramaniam

### ORCID ID
http://orcid.org/0000-0002-4935-7233

### Contact details
Department of Acute Medicine and Nephrology
Southend University Hospital
Southend
United Kingdom
SS0 0RY

# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
P0922

# Study information

## Scientific Title
Ketoacidosis in type 2 diabetics on SGLT-2 inhibitors: a prospective observational cohort study

## Study objectives
One complication of SGLT2i treatment that is unusual in type 2 diabetics is ketoacidosis. This occurs when the amount of sugar available for cells is low and so fats are used as fuel, this releases ketones as a waste product. Ketones are an acid and it is normal to have low levels sometimes, during periods of starvation or alcohol excess. When the levels get too high, they can case a condition called acidosis which can be life-threatening.

This complication is common in type one diabetics who have no insulin production in their body and no way of getting sugar into cells. The diagnosis of ketoacidosis comprises of having a high sugar reading, along with high levels of ketones and acid in the blood. However, there have been reports of ketoacidosis in type 2 diabetics on SGLT2i4,5,6. Even though the number of cases reported from the studies is low, this may be due to the confusion with the diagnostic criteria as the sugar levels may not become very high. This type of ketoacidosis is called euglycaemic ketoacidosis, and it is unclear how prevalent this is in patients taking SGLT2i.

We want to undertake a prospective observation cohort study of patient on SGLT2i to see what the levels of ketones in their blood is when they are recruited to the study, and also when they become unwell during the period of the study.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Pending

## Study design
Prospective observational cohort study

## Primary study design
Observational

## Secondary study design
Cohort study

## Study setting(s)
Hospital

## Study type(s)
Diagnostic

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

## Health condition(s) or problem(s) studied
Type 2 diabetes mellitus

### Interventions
Potential participants for this study have already been on SGLT2i treatment for a time prior to enrollment and are identified when they attend their usual primary care or secondary care appointment as per their usual diabetes care.

During the study period, ketone levels are measured for each participant via analysis of blood samples . Measurements will be taken as at the start of the study (when they are feeling well) and again if they become unwell (i.e. if ketoacidosis develops).

Ketone levels are measured by blood analysis, either using a pin prick test or blood test. Urine results are recorded if obtained.

The researchers then use this information to see whether ketoacidosis is a common complication or a rare complication of this treatment.

There is no follow up of participants after the study is complete.

### Intervention Type

### Primary outcome measure
Number of episodes of ketoacidosis, from blood analyses using samples taken via a pin prick test or blood test. Measured at baseline and when the participant is feeling unwell during the study period.

### Secondary outcome measures
N/A

### Overall study start date
01/05/2016

### Completion date
01/11/2017

## Eligibility

### Key inclusion criteria
1. Patients with type 2 diabetes taking SGLT2i
2. Age > 18
3. Able to give consent

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex

Both

**Target number of participants**
60 (estimated)

**Key exclusion criteria**
Participants that do not meet inclusion criteria

**Date of first enrolment**
01/11/2016

**Date of final enrolment**
01/11/2017

# Locations

**Countries of recruitment**
England

United Kingdom

**Study participating centre**
**Southend University Hospital**
Prittlewell Chase
Westcliff-on-Sea
Southend
United Kingdom
SS0 0RY

# Sponsor information

**Organisation**
Southend University Hospital NHS Foundation Trust

**Sponsor details**
Prittlewell Chase
Westcliff-on-Sea
Southend
England
United Kingdom
SS0 0RY

**Sponsor type**
Hospital/treatment centre

**ROR**
https://ror.org/05fa42p74

# Funder(s)

**Funder type**
Hospital/treatment centre

**Funder Name**
Southend University Hospital NHS Foundation Trust

# Results and Publications

**Publication and dissemination plan**
To be published in peer reviewed journals

**Intention to publish date**
01/11/2018

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**
Not expected to be made available