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Investigating the limits of reversibility of type 2 diabetes

Submission date
08/08/2012

Recruitment status
No longer recruiting

Registration date
09/08/2012

Overall study status
Completed

Last Edited
04/08/2015

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and aims
Type 2 diabetes is regarded as an irreversible disease of the pancreas. It is now known that this is not true. A study performed in Newcastle has shown that people with short duration type 2 diabetes can regain normal blood sugar (glucose) control after a period of strict dieting. This study will examine whether the reversal of diabetes using a very low calorie diet is possible in individuals with long duration diabetes as well as short duration disease. It will establish the sustainability of the reversal of type 2 diabetes, and the best approach to maintaining the beneficial effects of this period of dieting using longer term lifestyle modification. Finally, the mechanisms behind the reversal of diabetes will be defined, looking in particular at the effect of fat on the pancreas. By using MRI scans of the pancreas and liver, along with tests using glucose and insulin, the effect of fat in the 'wrong' place will be defined. Together, this information would be of enormous importance to all people with type 2 diabetes, improving our understanding of the condition and exploring the potential of a medication-free treatment strategy.

Who can participate?
People aged between 25 and 80 years who have type 2 diabetes of less than 4 years or more than 8 years duration.

What does the study involve?
The research involves an 8-week period of very low calorie dieting to induce weight loss and improve blood glucose control. Participants will then be asked to follow a weight maintaining diet and physical activity plan for 6 months with education and support throughout. Detailed metabolic tests and magnetic resonance imaging (MRI) scans will be performed on three occasions with more regular, shorter visits throughout the 8-month study.

What are the possible benefits and risks from taking part in this study?
The weight loss achieved during the study is likely to bring substantial benefits to health. Participants will gain a better understanding of type 2 diabetes and its management. There are no major risks from taking part in this study. The very low calorie diet is safe under medical supervision. The intense dieting and longer term lifestyle change are challenging but full support will be given. Occasionally there may be some mild discomfort at the sites of the plastic

tubes for a few hours after removal. The MRI scans are non-invasive, safe and do not use X-rays or any other harmful radiation. It makes a high-pitched sound and you will be given ear-muffs to wear. There is a very small risk (less than one in a million) of an allergic reaction to a substance used in the study called Intralipid. This only occurs in people who are allergic to soy protein or eggs so if you have these allergies you will not be able to take part in the study.

Where is the study run from?
Newcastle University (UK).

When is the study starting and how long is it expected to run for?
The study started in August 2012 and will run for 2 years.

Who is funding the study?
Novo Nordisk UK Research Foundation and the Newcastle NIHR Biomedical Research Centre.

Who is the main contact?
Dr Sarah Steven
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Contact information

Type(s)
Scientific

Contact name
Dr Sarah Steven

Contact details
Newcastle University
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Additional identifiers

Protocol serial number
12627

Study information

Scientific Title
Characterisation of the principle determinants of long term reversal of type 2 diabetes

Study objectives
Restated hypothesis as of 31/07/2015:
Prevalence of Type 2 diabetes increases sharply with age. Our recent work has shown that the twin defects of insulin resistance and inadequate insulin secretion can be entirely reversed by short term calorie restriction resulting in long term withdrawal of oral hypoglycaemic agents

and insulin. Three distinct questions must now be answered:
1. What is the interaction of duration of type 2 diabetes with reversibility?
2. Does dietary modification over 6 months protect the return to normal blood glucose control and beta cell function in the group achieving restoration of normality?
3. Does increased daily physical activity or increased monounsaturated fat intake enhance this protection?

Previous hypothesis:
Prevalence of Type 2 diabetes increases sharply with age. Our recent work has shown that the twin defects of insulin resistance and inadequate insulin secretion can be entirely reversed by short term calorie restriction resulting in long term withdrawal of oral hypoglycaemic agents and insulin. Three distinct questions must now be answered:
1. What is the interaction of duration of type 2 diabetes with reversibility?
2. Does dietary modification protect the beta cells from longer term deterioration of function after restoration of normality, as seen in vitro?
3. Does increased daily physical activity enhance this protection?

On 31/07/2015 the overall trial end date was changed from 01/09/2013 to 30/06/2014.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Newcastle and North Tyneside 2 Research Ethics Committee, 22/06/2012, ref: 12/NE/0208

Primary study design
Interventional

Study design
Randomised interventional trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diabetic Control, Nutrition, Obesity

Interventions
Restated interventions as of 31/07/2015:
Dietary modification, Very low calorie diet; Physical activity, Increased physical activity levels. The weight maintenance interventions are of 6 months duration and primarily involve a level of calorie intake to maintain weight steady. The randomised sub-study tests involve either a high monounsaturated fat diet or usual diet, and increased physical activity or usual physical activity.

Previous interventions:
Dietary modification, Very low calorie diet; Physical activity, Increased physical activity levels. The weight maintenance interventions are of 6 months duration and involve either a high monounsaturated fat diet or usual diet, and increased physical activity or usual physical activity.

Intervention Type
Behavioural

Primary outcome(s)
Restated primary outcome measures as of 31/07/2015:
Fasting plasma glucose at 6 months in the group achieving non-diabetic levels at 10 weeks (following VLCD and return to normal eating)

Previous primary outcome measures:
Beta cell function measured at baseline, 8 weeks and 8 months

Key secondary outcome(s)
Added 31/07/2015:
Change in beta cell function from 10 weeks to 6 months

Completion date
30/06/2014

Eligibility

Key inclusion criteria
1. Type 2 diabetes of < 4 years or > 8 years duration
2. HbA1c < 80 mmol/l / 9.5%
3. BMI 28-40kg/m2
4. Age 25-80 years
5. Stable weight for previous 6 months (within 5kg)
6. Male and female participants

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Current treatment with thiazolidinediones, GLP-1 agonists or steroids
2. Renal or hepatic dysfunction
3. Contraindications to MRI
4. Alcohol consumption > 3 units per day for women and > 4 units per day for men
5. Allergy to soybean or eggs
6. Highly restrictive diet

Date of first enrolment
31/08/2012

Date of final enrolment
11/09/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Newcastle University
Newcastle upon Tyne
United Kingdom
NE4 5PL

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
National Institute of Health Research [NIHR] - Biomedical Research Centre (UK)

Funder Name
Novo Nordisk UK Research Foundation

Alternative Name(s)
Novo Nordisk UK Research Foundation (NNUKRF), The Novo Nordisk UK Research Foundation, ovo Nordisk Research Foundation UK, NNUKRF

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2015		Yes	No