ISRCTN14189908 https://doi.org/10.1186/ISRCTN14189908

Can DiaGO reliably and sensitively detect Graves' orbitopathy?

Submission date
25/09/2017

Recruitment status
No longer recruiting

Registration date
13/12/2017

Overall study status
Completed

Last Edited
13/12/2017

Condition category
Nutritional, Metabolic, Endocrine

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Thyroid eye disease (TED) is an inflammatory condition of the eyes associated with Graves' disease (the commonest cause of an overactive thyroid). TED is also known as Graves' orbitopathy (GO). In its most severe forms, TED can cause blindness. The earlier TED is treated the better the results. However, recognising TED can be challenging for doctors and delays in diagnosis are unfortunately common. Through patient support groups, such as the British Thyroid Foundation and the Thyroid Eye Disease Charitable Trust, it was discovered that patients place a high importance on receiving a diagnosis and appropriate treatment early, and therefore this is a priority. Researchers have developed DiaGO, a clinical assessment tool, to guide doctors in making a possible diagnosis of TED in patients with Graves' disease. DiaGO is a set of questions and a simple examination of the eyes that can be done quickly by health professionals. The DiaGO assessment tool has already been tested in a pilot study where we found that it can be used to accurately identify TED in patients with Graves' disease whose eye condition was previously undiagnosed. Making a diagnosis means that these people can be referred to specialist ophthalmologists (eye experts) who can make an early diagnosis and offer specialist treatment when it is required. The aim of this study is to test the DiaGO clinical assessment tool on a larger scale, across multiple UK hospitals, so that we can determine whether it can be used widely in outpatient endocrinology clinics (where Graves' disease patients are commonly seen regularly) to help detect TED in patients at an early stage.

Who can participate?
Adults who have Grave's disease.

What does the study involve?
The DiaGO assessment tool is made up of two sections. Participants in this study are asked 13 simple (yes/no answer) questions from section one (which takes approximately 3 minutes), and then a doctor will look at the participant's eyes and complete section two of the tool (which is made up of 7 further yes/no questions based on the appearance of the eyes). The doctor completing the examination then uses the tool to generate a score. The score can then be used to decide who should be referred to the eye specialists. In the first phase of this study, patients scoring on DiaGO will be referred to ophthalmology for further review. These individuals have signs and/or symptoms of TED and therefore this is part of their routine care. In the second

phase of this study, all patients completing the DiaGO questionnaire are referred to ophthalmology, regardless of their score. This is to see whether some people with TED are being missed by the DiaGO tool. Those patients who are invited to attend ophthalmology receive a separate appointment for this. This therefore involves a separate visit to the hospital outpatient clinic and the examination will take approximately 30 minutes. This appointment involves the ophthalmologist looking at the eyes in detail. This examination is not painful. If there is any evidence of TED, treatment may be offered if it is required.

What are the possible benefits and risks of participating?
There are no direct benefits or risks with participating.

Where is the study run from?
Royal Victoria Infirmary (UK)

When is the study starting and how long is it expected to run for?
August 2015 to June 2018

Who is funding the study?
Fight for Sight (British Eye Research Foundation) (UK)

Who is the main contact?
Dr Anna Mitchell

Contact information

Type(s)
Scientific

Contact name
Dr Anna Mitchell

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Contact details
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
31333

Study information

Scientific Title
Can the DiaGO (Diagnosis of Graves' orbitopathy) clinical assessment tool reliably and sensitively detect people with and without Graves' orbitopathy? A multicentre study

Study objectives
Hypothesis:
A previous pilot study led to the formulation of a simple clinical tool for early diagnosis of Graves' orbitopathy (DiaGO). The hypothesis is that further refinement and validation of DiaGO can result in a tool with high sensitivity and specificity for early diagnosis of GO in patients with Graves' disease and therefore prevent diagnostic delay and reduce the morbidity that is associated with this.

Study Aims:
To refine and determine the sensitivity and specificity of DiaGO, to determine ease of use of DiaGO by endocrinologists and its acceptability and to determine whether use of DiaGO results in earlier employment of treatments to manage GO.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West of Scotland REC 3, 18/02/2016, ref: 16/WS/0046

Study design
Observational; Design type: Cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Specialty: Metabolic and endocrine disorders, Primary sub-specialty: Metabolic and endocrine disorders; UKCRC code/ Disease: Metabolic and Endocrine/ Disorders of thyroid gland

Interventions
This will be a multicentre study across 6 UK centres (Newcastle upon Tyne, Gateshead, Exeter, Cardiff, Oxford and Leeds).

Phase 1: Refinement of DiaGO and reproducibility:
This phase includes an initial study of DiaGO across multiple sites, aiming to collect 50 cases with signs or symptoms of GO as identified by DiaGO, those triggering a referral to ophthalmology are reviewed in ophthalmology as part of standard patient care. Collection of anonymised feedback from participating endocrinologists and ophthalmologists regarding acceptability /practicality of the tool by online email survey is conducted. The refinement of DiaGO tool is based on analysis of data from the above 50 cases and user feedback. The intra- and inter-observer reproducibility of refined DiaGO using 10 patients and 10 clinician observers is determined.

Phase 2: Validation of refined DiaGO:
This phase is a further study of refined GO tool. 150 patients with GD not previously diagnosed to have GO screened across all participating sites with “blinded” receive an ophthalmology review regardless of DiaGO trigger for referral including documentation of diagnosis (GO or not) and treatment plan. Tool specificity is determined from this data. Data analysis is done to validate the tool sensitivity in an independent data set (compared to the pilot study data), determine which signs and symptoms most strongly correlate to a diagnosis of GO.

Phase 3 - Final analysis of full data set: Jan 2017.

Intervention Type
Other

Primary outcome measure
Sensitivity and specificity of DiaGO using initial DiaGO data (at baseline, assessment in Endocrine clinic) and diagnosis of GO at six months (after assessment in ophthalmology clinic).

Secondary outcome measures
Ease of use of DiaGO by endocrinologists and its acceptability at baseline by a user questionnaire
Whether use of DiaGO results in earlier employment of treatments to manage GO by clinical records review at six months.

Overall study start date
01/08/2015

Completion date
01/06/2018

Eligibility

Key inclusion criteria
1. Diagnosis of GD
2. Hyperthyroidism/subclinical hyperthyroidism and smooth, symmetrical goitre or positive TSH receptor antibodies
3. Euthyroid/hypothyroid/hyperthyroid and positive TSH receptor antibodies

Participant type(s)

Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 400; UK Sample Size: 400

Key exclusion criteria
1. People with Graves' Disease already reviewed by ophthalmology
2. Remain under the care of ophthalmology with GO
3. Children under 18 years of age

Date of first enrolment
21/07/2016

Date of final enrolment
01/12/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Victoria Infirmary
Endocrinology offices
Leazes wing level 6
Queen Victoria Road
Newcastle
United Kingdom
NE1 4LP

Sponsor information

Organisation
The Newcastle Upon Tyne Hospitals NHS Foundation Trust

Sponsor details

Freeman Hospital
Freeman Road
High Heaton
Newcastle-Upon-Tyne
England
United Kingdom
NE7 7DN

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Charity

Funder Name
Fight for Sight UK

Alternative Name(s)
Fight for Sight

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Results and Publications

Publication and dissemination plan
In order to disseminate the findings of this project, a publication in an open access journal, peer-reviewed journal with high impact factor will be sought.

Intention to publish date
01/06/2019

Individual participant data (IPD) sharing plan

The datasets generated will be published as supplemental data in a peer reviewed open access journal

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V3	22/02/2016	13/12/2017	No	Yes
HRA research summary			28/06/2023	No	No