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Trans-epithelial corneal cross-linking to halt the progression of keratoconus

Submission date
29/09/2013

Recruitment status
No longer recruiting

Registration date
12/11/2013

Overall study status
Completed

Last Edited
20/08/2020

Condition category
Eye Diseases

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

Plain English Summary
Background and study aims
Keratoconus is an eye condition that involves thinning of the cornea and bulging. This irregular corneal shape results in reduced vision. This condition affects both eyes although often affects one eye more than the other. It usually occurs around puberty continuing until middle age. It affects about 1 in 1750 individuals, occurring in all ethnic groups and equally affects men and women. Riboflavin/ultraviolet corneal collagen cross-linkage (CXL) appears to be the first treatment that stabilizes the cornea and stops the progression of keratoconus. The standard treatment involves removing the central corneal skin, applying vitamin B2 drops, which soak into the substance of the cornea, and then shining ultraviolet light onto the cornea. This treatment has been shown to increase the strength of the cornea by cross-linking the molecules within it. Iontophoresis has been used routinely for many decades to allow certain drugs to penetrate the skin and eye without the need for injections and has been shown to be effective in allowing riboflavin to enter the cornea without the need to remove the corneal skin. This may speed up recovery after the operation, and reduce pain and the risk of infection and scarring. The aim of this study is to compare the effectiveness of an epithelium-on (trans-epithelial) technique with the standard epithelium-off procedure.

Who can participate?
Adults with mild to moderate bilateral keratoconus with no corneal scarring, evidence of disease progression in both eyes within the past 1-2 years, and with no other eye disease or previous eye surgery.

What does the study involve?
Patients will undergo a routine eye examination to find out the extent of keratoconus and then after full consent undergo cross-linking treatment to both eyes, with one eye randomly allocated to the standard epithelium-off treatment and the other eye undergoing trans-epithelial (epithelium-on) treatment. After the surgery patients will be asked to fill out a questionnaire regarding the amount of pain they experienced during the first 5 days after surgery. Patients will be examined at 1 week after the treatment and four more times in the year after the procedures. The second eye will be treated within 3-4 months of the first eye.

What are the possible benefits and risks of participating?
The benefits are that it may halt the progression of keratoconus in up to 90% of cases as well as improve the overall corneal shape in the majority of eyes. Risks are few but removal of the corneal epithelium in the standard epithelium-off technique results in significant post-operative pain and increases the rare risks of post-operative infection and scarring. The epithelium-on technique should reduce pain after the operation and speed up recovery as well as possibly reduce the small risks of infection and scarring. However, it is unknown whether the epithelium-on technique will be as effective in halting keratoconus progression as the epithelium-off technique.

Where is the study run from?
St Thomas Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2014 to December 2017

Who is funding the study?
The Eye Hope Charity (UK)

Who is the main contact?
Prof. David P.S. O'Brart
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Contact information

Type(s)
Scientific

Contact name
Prof David O'Brart

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Additional identifiers

EudraCT/CTIS number

IRAS number
133912

ClinicalTrials.gov number

Secondary identifying numbers

IRAS Project ID: 133912

Study information

Scientific Title
A randomized, bilateral, controlled, prospective study to investigate the efficacy of trans-epithelial riboflavin/ultraviolet A corneal collagen cross-linking using iontophoresis to halt the progression of keratoconus

Study hypothesis
Trans-epithelial riboflavin/ultraviolet A corneal collagen cross-linking using iontophoresis is as efficaceous as the standard epithelium off technique to halt the progression of keratoconus.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London - City Road & Hampstead, 26/02/2014, ref: 13/LO/1895

Study design
Randomized bilateral prospective study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Condition
Keratoconus, post-refractive surgery ectasia

Interventions
Patients will be recruited from the corneal clinics at Guy's and St Thomas' NHS Trust. All patients will have bilateral keratoconus or post-laser refractive surgery iatrogenic keratoconus. Patients will have a history of progression or documented progression of keratoconus over the preceding 2 years. Patients will be fully counselled as to the rationale and experimental nature of the study. Patients will undergo a full pre-operative examination including refraction, corneal topography and tomography (scans of corneal shape), pachymetry (measurements of corneal thickness) and endothelial (cells on the inner layer of the cornea that help maintain its transparency) cell counts. All of these tests are part of the routine work-up for this procedure.

Patients will be randomized to receive trans-epithelial cross-linking to one eye or epithelium-off cross-linking treatments to the other. Patients will be offered treatment of both eyes within 3-4 months. The optometrist performing pre- and post-operative measurements will be observer masked as to which eye received which treatment. Patients will be asked to grade their experiences of pain using a visual analogue score of 0 to 10 every 6 hours for 5 days following surgery. Patients will be examined at 1 day, 1 week, 1, 3, 6 and 12 months.

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Stability of refractive error (diopters)
2. Topographic simulated keratometry (diopters) (corneal curvature)
3. Corneal pachymetry (micrometers)
4. Visual acuity (logMar) at 12 months compared to pre-operative values

These parameters will be measured pre-operatively and at 3, 6 and 12 months.

Secondary outcome measures
1. Visual analogue pain scores documented for 5 days after surgery. Patients will be asked to grade the pain they are experiencing every 6 hours after surgery from 0 (no pain) to 10 (worse pain they have ever had) for 5 days following surgery
2. Complications if present will be documented at 1 week and 1, 3, 6 and 12 months after surgery

Overall study start date
01/01/2014

Overall study end date
31/12/2017

Eligibility

Participant inclusion criteria
1. Progressive keratoconus defined by an increase in refractive astigmatism, maximum keratometry, apex power of the cone by more than 1 diopter and/or a decrease in central corneal pachymetry by 10% in the preceding 2 years
2. Grade I-III keratoconus (3 mm keratometry less than 55 diopters, cone apex power less than 70 diopters, central pachymetry greater than 400 um)
3. Age over 18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex

Both

Target number of participants
46

Total final enrolment
46

Participant exclusion criteria
1. Advanced keratoconus (3 mm keratometry greater than 55 diopters, cone apex power greater than 70 diopters, central pachymetry less than 400 um)
2. Pregnancy
3. Corneal scarring
4. Co-existant ocular pathology other than keratoconus
5. Age less than 18 years

Recruitment start date
01/07/2014

Recruitment end date
01/02/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St Thomas Hospital
London
United Kingdom
SE1 7EH

Sponsor information

Organisation
Guy's & St Thomas' Foundation NHS Trust (UK)

Sponsor details
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Charity

Funder Name
Eye Hope Charity (UK)

Results and Publications

Publication and dissemination plan
The aim is to submit for publication by the end of 2017 to peer-reviewed ophthalmic journals.

Intention to publish date
31/12/2017

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. David P.S. O'Brart (davidobrart@aol.com).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		19/08/2020	20/08/2020	No	No
HRA research summary			28/06/2023	No	No