ISRCTN52187987 https://doi.org/10.1186/ISRCTN52187987

A randomized, bilateral, controlled, prospective study to investigate the efficacy of corneal shape customised versus standard whole central cornea riboflavin/ultraviolet A corneal collagen cross-linking

Submission date
14/01/2018

Recruitment status
Stopped

Registration date
03/02/2018

Overall study status
Stopped

Last Edited
25/07/2022

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims

Keratoconus is an eye disease in which the cornea (the transparent dome at the front of the eye) thins and begins to bulge into a cone-like shape (known as ectasia), resulting in reduced and distorted vision. The condition affects both eyes (bilateral), often differently (asymmetrical), and usually starts around puberty and gets worse until the third or fourth decade of life. It affects about 1 in 500-1250 people, occurring in all ethnic groups and equally affects males and females. Riboflavin (vitamin B2)/ultraviolet A (UVA) (370nm) corneal collagen cross-linkage (CXL) is the first treatment which appears to halt the progression of keratoconus and other ectasias of the cornea. It involves removing the central corneal skin (epithelium), which grows back after a few days, applying vitamin B2 drops (Riboflavin), which soak into the substance of the cornea (stroma), and then shining ultraviolet light at 370nm onto the cornea. This has been shown to increase the strength of the cornea by cross-linking the protein molecules within it. In the standard technique ultraviolet (UV) light is shone at the central 9.0 mm of the corneal stroma, regardless of the position on the cornea of the bulging (known as the cone) and therefore the location of the weakened corneal tissue. In most cases this area is in the middle of the lower part of the cornea towards the side of the ear. This means that during the standard procedure both normal and abnormal tissue are irradiated. Interestingly, it has been found that better results tend to occur with more centrally located cones. This is perhaps because with centrally located cones, the conventional central (or axial) treatment is directed towards the site of the disease rather than the entire cornea. The aim of this study is to compare the effectiveness of tomography/topography orientated CXL, where the treatment is directed to the location of the main area of ectasia on the cornea (the cone), with the standard technique where the central 9.0 mm area of the cornea is treated regardless of the cone location. The location of the cone is determined by three-dimensional corneal imaging known as tomography using a simple, quick, painless no-touch device called the Pentacam (Oculus Inc, Arlington, Washington, USA). These measurements are entered into a programmable cross-linking UVA light emission system called

the Mosaic™ (Avedro Inc, Waltham, USA). This allows patterned, precise, tomography-guided CXL with the delivery of more UV energy precisely at the location of maximal corneal bulging (ectasia) where the cornea is weakest. It is hoped that this targeted treatment will improve the outcomes of CXL by stopping progression of the condition and flattening the cone, resulting in improved corneal shape and better visual outcomes compared to the standard procedure.

Who can participate?
Patients aged over 18 with mild to moderate bilateral keratoconus

What does the study involve?
Participants undergo a routine eye examination to determine the precise degree of keratoconus and then undergo cross-linking treatment to both eyes, with one eye randomly allocated to the standard central treatment and the other eye undergoing tomography-guided treatment. The second eye is treated within 3-4 months of the first eye. Participants are examined at 1 week and 1, 3, 6, and 12 months after the procedures.

What are the possible benefits and risks of participating?
Corneal collagen cross linking has been shown to stop the progression of keratoconus in up to 95% of cases with up to 6-10 years follow-up as well as improve the overall corneal shape in most eyes. Complications are few, with sight-threatening complications, such as infection and scarring and the need for a corneal transplant, occurring in less than 1% and often eyes gaining in vision, although such improvements may take months/years to become apparent. It is hoped, although not proven, that tomography-guided treatment will result in improved outcomes of CXL not only in terms of stopping progression of the condition but also with improved flattening of the cone, which will result in improved corneal shape and better visual outcomes compared to the standard procedure.

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 2018 to March 2021

Who is funding the study?
Eyehope charity (UK)

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

Contact information

Type(s)
Scientific

Contact name
Prof David O'Brart

Contact details

Guy's and St Thomas' NHS Foundation Trust
London
United Kingdom
SE1 7EH

Additional identifiers

Protocol serial number
Version 1

Study information

Scientific Title
A randomized, bilateral, controlled, prospective study to investigate the efficacy of tomography-orientated versus standard axial riboflavin/ultraviolet A corneal collagen cross-linking

Study objectives
The hypothesis is that the visual refractive and tomographic outcomes of tomography-orientated collagen cross-linking (CXL), where treatment is directed to the location of the cone, are superior to the standard technique where the central 8.0-9.0 mm is treated irrespective of the cone location.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled bilateral study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Keratoconus, corneal ectasia

Interventions
Patients will undergo a routine eye examination to determine the precise degree of keratoconus and then after full consent as to the risks and benefits of the procedure undergo cross-linking treatment to both eyes with one eye randomized to the standard central treatment and one undergoing tomography-guided treatment (randomisation by shuffled envelope system by nurse not involved in the study kept under lock and key in theatre). Patients will be examined at 1 week and 1, 3, 6, and 12 months after the procedures.

Intervention Type

Procedure/Surgery

Primary outcome(s)
Change in:
1. Refractive error (diopters)
2. Topographic simulated keratometry (diopters) (corneal curvature)
3. Maximum keratometry (Kmax)
4. Posterior corneal curvature
5. Pentacam-derived keratoconus indices
6. Belin-Ambrosio enhanced ectasia scores
7. Corneal pachymetry (micrometers)
8. Visual acuity (logMar)
Measured at baseline 6, 12 and 18 months

Key secondary outcome(s))
Stability in:
1. Refractive error (diopters)
2. Topographic simulated keratometry (diopters) (corneal curvature)
3. Maximum keratometry (Kmax)
4. Posterior corneal curvature
5. Pentacam-derived keratoconus indices
6. Belin-Ambrosio enhanced ectasia scores
7. Corneal pachymetry (micrometers)
8. Visual acuity (logMar)
9. Endothelial cell counts
10. Sight-threatening complications
Measured at baseline 6, 12 and 18 months

Completion date
31/03/2021

Reason abandoned (if study stopped)
The study was terminated early without full recruitment because of restrictions following public health guidance ,the inability to recruit patients, and the limited time the topography guided cross-linking equipment was available to the study team.

Eligibility

Key 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 to 18 months
2. Grade I-III keratoconus (3mm keratometry less than 55 diopters, cone apex power less than 70 diopters, central pachymetry greater than 400um)
3. Age over 18

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
34

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

Date of first enrolment
01/03/2018

Date of final enrolment
31/03/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
United Kingdom
SE1 7EH

Sponsor information

Organisation
Guy's and St Thomas' NHS Foundation Trust

ROR

https://ror.org/00j161312

Funder(s)

Funder type
Charity

Funder Name
Eyehope charity

Results and Publications

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 O'Brart. Data will be anonymized and only refractive, keratometric, visual, pachymetry data and endothelial counts will be available. Individual patient data, scans etc will not be available for data protection reasons. Data will only be released to those conducting research with full ethical approval and in agreement with the ethics committee and department of research and development.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		25/07/2022	25/07/2022	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes