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Heat application to the eyelids to enhance ocular drug delivery

Submission date	Recruitment status	[X] Prospectively registered
19/07/2023	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
27/09/2023	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
14/01/2025	Eye Diseases	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Glaucoma is an eye disease which can lead to irreversible loss of vision caused by damage to the optic nerve at the back of the eye. It is often associated with raised fluid pressure in the eye and is treated mainly by drops that lower this pressure. However, only a small amount of the eye drop enters the eye because of overspill onto the eyelids and excess tear formation. This can mean that the eye drops may not have the maximum effect on lowering the eye pressure and result in the need to use additional eye drops or progress to surgery. In the glaucoma clinic we try to keep to the simplest form of treatment to maintain eye health as this improves compliance, reduces the side effects of the drops and the risks associated with surgery.
As a result of this study, we hope that eye doctors will be able to determine whether the use of goggles that provide a gentle heat to the eyelids when the eyes are open will improve the effectiveness of the glaucoma eye drops. The warming goggles have been used for many years as a treatment to unblock the oil glands that are present on the upper and lower eyelids and have an excellent safety record.
Because we do not know whether the addition of heat will enhance the effectiveness of the eye drops, participants will be asked to attend the clinic for three visits where we will measure the eye pressures with and without the addition of eyelid warming.

Who can participate?
Patients diagnosed with Primary Open Angle Glaucoma (POAG) or Ocular Hypertension (OHT) that has treated with a prostaglandin analogue instilled in the morning for at least 6 months. Potential participants must be a minimum of 18 years old and have the following IOPs – POAG ≤24 mmHg in at least one eye and OHT ≤30 mmHg in at least one eye.

What does the study involve?
If patients agree to take part, they will be asked to attend their chosen hospital for the following visits:
Screening visit: to make sure that you are suitable to take part in the study.
This visit will include completing a consent form, starting a diary about how you use your eye drops, a visual field test (if this has not been completed within the last three months) and gathering some information about your health and eye history. This visit will take about 90 minutes.

Visit one: measuring the eye pressures without eyelid warming.
This visit will include completing two questionnaires one about your general health and one about how your eyes feel, we will examine your eyes using some bright lights and measure your vision. We will then ask you to put in your glaucoma eye drops and start measuring your eye pressures. We need to check the eye pressures at five different time points during the day (8:30, 10:30, 12:30, 14:30 and 16:30). You do not need to stay in the eye clinic in between these time points and you will be given an allowance for refreshments to use throughout the day. This visit will last about 8 hours.
Visit two: measuring the eye pressures with eyelid warming.
This visit will include completing two questionnaires one about your general health and one about how your eyes feel. We will examine your eyes using some bright lights and measure your vision. We will then ask you to wear the warming goggles for 10 minutes (we will ask you to keep your eyes closed during this time) before putting in your Glaucoma eye drops and start measuring your eye pressures. We need to check the eye pressures at five different time points during the day (8:30, 10:30, 12:30, 14:30 and 16:30). You do not need to stay in the eye clinic in between these time points and you will be given an allowance for refreshments to use throughout the day. This visit will last about 8 hours.
Visit three: measuring the eye pressures with goggles but no warming.
This visit will include completing two questionnaires one about your general health and one about how your eyes feel. We will examine your eyes using some bright lights and measure your vision. We will then ask you to wear the goggles for 10 minutes (with no heat – we will ask you to keep your eyes closed during this time) before putting in your Glaucoma eye drops and measuring your eye pressures. We need to check the eye pressures at five different time points during the day (8:30, 10:30, 12:30, 14:30 and 16:30). You do not need to stay in the eye clinic in between these time points and you will be given an allowance for refreshments to use throughout the day. This visit will last about 8 hours.
Visit four: safety check.
This visit will include a visual field test and vision measurements and will last about 1 hour.
We anticipate that you will complete the study within 3 to 4 months. You will be able to drive to these appointments if you are able, as no dilating eye drops will be used during these visits. Appointments can be made in advance to suit your schedule and a courtesy reminder phone call or email can be arranged before each visit.

What are the possible benefits and risks of participating?
There are no direct benefits of taking part in this study. Any pre-existing problems with the oil glands may be improved because of using the lid-warming goggles. The additional eye pressure measurements will be made available to the treating consultant to help with the future management of the participants' condition. The information generated in this study could improve our understanding of treating glaucoma with eye drops and help doctors treat patients more effectively in the future and help to reduce costs to the NHS.
Most of the tests that are included in this study are straightforward, take seconds to perform, and most are part of your regular eye examination in the clinic. Therefore, there is minimal added risk by involvement in this study as compared to a regular eye examination.

Where is the study run from?
North West Anglia NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
August 2022 to February 2026

Who is funding the study?
1. Sight Research UK
2. North West Anglia NHS Foundation Trust (UK)

Who is the main contact?
Ophthalmology Research team at North West Anglia NHS Foundation Trust, nwangliaft.
ophthalmologyresearch@nhs.net

Contact information

Type(s)
Public, Scientific

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Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
271825

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 271825, CPMS 58752

Study information

Scientific Title
A feasibility study: The efficacy and safety of heat applied to closed eyelids in enhancing the delivery of ocular hypotensive eye drops in the treatment of primary open-angle glaucoma

Acronym
HALO

Study objectives
The primary objective of the study is to demonstrate that heat applied directly to closed eyelids in combination with the instillation of anti-glaucoma eye drops induces a further lowering of intraocular pressure (IOP) when compared to the use of anti-glaucoma eye drops alone.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 03/01/2024, East of England - Cambridge East Research Ethics Committee (2 Redman Place, London, EC20 1JQ, United Kingdom; +44 (0)207 104 8181; cambridgeeast.rec@hra.nhs.uk), ref: 23/EE/0261

Study design
Feasibility single-centred interventional study

Primary study design
Interventional

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
Glaucoma

Interventions
One week prior to the baseline visit and whilst participating in the study the patients will be asked to complete a ‘drop compliance diary’ documenting when and how frequently they are using their glaucoma medication. This is to ensure that they are adhering to their advised schedule of drop regime beforehand and that taking part in the study is not influencing their habitual drop routine. This approach is to help confirm that the reason for any reduction in IOP over the course of the study can be more confidently attributed to the intervention of heat rather than a possible phenomenon that being part of the study might naturally improve compliance with their eyedrops and hence IOP would be reduced in this manner.

The patient will attend the clinic for three separate visits each approximately one week apart, starting with phasing ‘without heat’, then phasing ‘with heat’ and lastly phasing wearing the Blephasteam mask but with no heat as a control. The Blephasteam mask will only be used on the days of the clinic visits, the participants will not be required to use the device at home. The heat masks will be designated to the same patient throughout the study for hygiene reasons. The inserts for the mask will be moistened and fitted according to the manufacturers' instructions. The participants will instil their habitual glaucoma eyedrops then wear the mask and be instructed to close their eyes, this occurs once at the start of each visit. The device warms the ocular surface for a set time of 10 minute, after which the mask will be removed and the IOP will be measured at the first time point. Although both eyes will be treated with the heat mask only the right eye results (to eliminate bias) will be used for the statistical analysis. During the visits the patients’ will have their BCVA reviewed before and after measurements are taken. IOPs are measured first using the ORA tonometer (Reichert Inc., Germany) followed by the Goldman tonometer (Haag-Streit AG,
Switzerland) five minutes later as per previous studies measuring IOP with the sequential use of tonometers (Tejwani et al., 2015). These IOP measures are taken at five set time points during the day called ‘phasing’: 08:30 +/- 30 mins, 10:30 +/- 30 mins, 12:30 +/- 30 mins, 14:30 +/- 30 mins and 16:30 +/- 30 mins. An average of three measures will be taken using the ORA machine, when using the Goldman tonometer three measures will only be taken if the first two are not within >2mmHg of each other. The procedure for the Goldman tonometer will be as follows: Two individuals (an operator and a reader) will perform the readings for the study visits. The operator will be responsible for operating the slit lamp, tonometer and the instrument dial, while the reader will read and record the results. A full anterior segment slit-lamp examination will be performed at the end of each phasing visit to ensure there are no adverse effects experienced following the treatment, including grading of the Meibomian glands (Efron scale). Additional assessments include adverse events and quality of life and ocular questionnaires.

One to two weeks after completion of the study the patients will undergo a further visual fields test (Humphrey sita fast 24-2) to ensure no significant progression of their disease has occurred as a result of the study regime. All data will be recorded and stored for analysis at the end of the trial. At the end of the trial the patients will continue their glaucoma visit schedule as requested by their treating Ophthalmologist.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Blephasteam

Primary outcome(s)
Ocular IOP measured in mmHg by Goldman and ORA at baseline, and then at five subsequent set time points during the day called ‘phasing’: 08:30 +/- 30 min, 10:30 +/- 30 min, 12:30 +/- 30 min, 14:30 +/- 30 min and 16:30 +/- 30 min. This same procedure will be repeated on visits one, two and three.

Key secondary outcome(s))
1. Adverse events that occur will be recorded at baseline and visits one, two and three
2. Quality of life measured using EQ-ED-5L and OSDI at baseline and visits one, two and three

Completion date
28/02/2025

Eligibility

Key inclusion criteria
1. Informed consent signed and dated
2. Patients diagnosed with bilateral primary open-angle glaucoma (POAG) or ocular hypertension (OHT)
3. Patient aged ≥18 years old
4. Both eyes with a central corneal thickness of between 500-600 µm
5. Both eyes with a diagnosis of POAG or OHT, initially treated and controlled for at least six months by a prostaglandin analogue monotherapy (mane instillation)
6. IOP ≤ 24 mmHg in at least one eye POAG
7. IOP ≤ 30 mmHg in at least one eye OHT

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Fundus examination not performed or not available within 12 months
2. Visual field not performed or not available within 12 months
3. Advanced stage of glaucoma, defined by at least one of the following criteria:
4. Absolute defect in the ten degrees central point of the visual fields
5. Severe visual field loss: MD < -18 dB
6. Risk of visual field worsening as a consequence of participation in the study according to the investigator’s best judgment
7. Far best corrected visual acuity ≥ +0.7 logMAR
8. History of trauma, infection, clinically significant inflammation within the previous three months
9. Ongoing or known history of ocular allergy and/or uveitis and/or viral infection
10. Clinically significant or progressive retinal disease (e.g. retinal degeneration, diabetic retinopathy, retinal detachment)
11. Conjunctival hyperaemia (Grade 5 - Efron scale)
12. Superficial punctate keratitis (Grade 4/5 – Oxford scale)
13. Blepharitis (Grade 3 – Efron scale)
14. Severe dry eye as assessed by the investigator
15. Corneal ulceration

16. Any palpebral abnormality incompatible with a good examination
17. Any other abnormality preventing accurate assessment e.g. reliable tonometry measurement, visual field examination, fundus examination.
18. A patient judged to have poor compliance with their glaucoma drops according to the investigator's best judgement

Date of first enrolment
01/07/2024

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
North West Anglia NHS Foundation Trust
Peterborough City Hospital
Bretton Gate
Bretton
Peterborough
United Kingdom
PE3 9GZ

Sponsor information

Organisation
North West Anglia NHS Foundation Trust

Funder(s)

Funder type
Charity

Funder Name
Sight Research UK

Alternative Name(s)

National Eye Research Centre, SightResearchUK, SRUK, NERC

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Funder Name
North West Anglia NHS Foundation Trust

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository (North West Anglia Foundation Trust). The participant's name, DOB, NHS and hospital numbers, will be linked in a password-protected screening log with their anonymised number. Paper CRFs will be completed by a member of the research team for each visit including a brief summary of their ocular medical history, any AEs, results of the questionnaires and the IOP measurements. This paperwork will be stored securely in a locked office with only members of the research team having the access code to the door. Results of the IOP measures will also be entered onto Medisoft which is an online medical records system used by the eye clinic at NWAFT, this can only be accessed by members of the patient's direct care team and will give further information to their standard of care treatment. Patients would be able to gain access to copies of their notes through the medical records service normally within 28 days, they would also be provided with a letter generated after each visit with details of their IOP results included.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	03/07/2023	04/08/2023	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file		13/06/2023	04/08/2023	No	No