ISRCTN31223901 https://doi.org/10.1186/ISRCTN31223901

Application of HYLO CARE® eye drops in dry eyes after cataract surgery

Submission date
14/04/2023

Recruitment status
No longer recruiting

Registration date
17/04/2023

Overall study status
Completed

Last Edited
03/07/2024

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
Eye surgery for cataracts, photorefractive correction or glaucoma may influence the ocular (eye) surface (OS). Cataract surgery is one of the most common potential risk factors for iatrogenic dry eye disease (DED). Disturbances of the tear film were observed after cataract surgery using the phacoemulsification technique or femtosecond laser-assisted cataract surgery (FLACS) and even after manual small incision cataract surgery (SICS).
The cornea (the transparent front part of the eye) is innervated by parts of the trigeminus and sympathetic nerves. After surgery, there is a variable degree of regeneration, which usually depends on the location and extent of the injury. Eye surgery may result in damage to the OS and deteriorate the tear film layer and/or production of the tear film, causing moistening disturbances.
The prevalence of OS dysfunction in patients undergoing cataract surgery is high, with a risk of exacerbation after cataract surgery. In eyes with a healthy tear film, dry eye syndrome may occur after surgery. Clear corneal incision in cataract surgery inevitably damages sensible nerves. However, a healthy OS depends on intact neuronal feedback between the lacrimal gland and the eye surface. If this feedback is disturbed, dry eye symptoms may exacerbate.
Additional risk factors are associated with cataract surgery that may cause dry eye: during surgery, the eye may dry out due to air and intense light of the microscope; use of topical anaesthesia and postoperative eye drops containing antibiotics, steroids or nonsteroidal anti-inflammatory drugs (NSAIDs) and preservatives such as benzalkonium chloride.
The most common DED therapy is substitution of the tear film. Tear replacement with ocular lubricants is traditionally considered a mainstay of DED therapy. Ophthalmic lubricants have no specific pharmacological effects, e.g. stimulation or inhibition of receptors. Various types of ophthalmic drops, gels, and ointments were developed to substitute different phases of the tear film. Eye drops are usually water-based and contain viscosity-enhancing polymers, e.g. hyaluronic acid, hydroxypropylmethylcellulose (HPMC) or polyvidone. These chemically inert molecules substitute the aqueous/mucinous phase of the tear film. They bind physically to the OS and increase the retention time of water molecules. Preparations containing hyaluronic acid have been reported to be used successfully in various disorders of the eye. Studies have shown that the subjective well-being of the patient improves dramatically with the use of eye drops containing sodium hyaluronate.
HYLO CARE® eye drops contain sodium hyaluronate, dexpanthenol, citrate buffer, and water.

HYLO CARE® is free of phosphates and preservatives, does not contain any emulsifiers and is certified for postoperative application. Dexpanthenol is a substance belonging to the group of B vitamins and shows a high water-binding capacity. As clinical studies have shown, the topical application of products containing dexpanthenol increases the water content of the epithelia of the skin. Due to these properties, dexpanthenol supports the moistening of the surface of the eye with sodium hyaluronate. It assists the eye during the phase of intensive regeneration while the lubricating properties of sodium hyaluronate further support this process. Dexpanthenol also supports wound healing and thus superficial erosions on the OS caused by an insufficient tear film as well as wounds, which are sometimes the result of surgical procedures, can both heal faster.

Who can participate?
Patients older than 18 years with dry eye undergoing standard cataract surgery

What does the study involve?
The effectiveness, tolerability, and physicians' and patients' assessment of HYLO CARE® are documented with a wide range of eye tests and methods from the first measurement before surgery to 35 days after surgery. The main goal is to demonstrate that tear film breakup time does not deteriorate when patients are treated after surgery with HYLO CARE® 3-4 times per day.

What are the possible benefits and risks of participating?
The use of lubricating eye drops is one of the main pillars in the treatment of dry eye symptoms as patients usually have a high level of suffering and impaired life quality. The application of lubricating eye drops may lead to a significant improvement in symptom severity. In addition, dexpanthenol supports wound healing and thus superficial erosions on the OS caused by an insufficient tear film as well as wounds, which are sometimes the result of surgical procedures, can both heal faster. Participants in this study profit from the close support of the doctor during the study period. Treatment with HYLO CARE® eye drops can lead to side effects or unwanted symptoms. With the application of HYLO CARE® eye drops, mild irritation of the eyes is possible. The side effects and symptoms observed so far include local irritation of the eye such as a burning sensation or itching in the eye. These symptoms have so far only been observed very rarely (<0.01% = in 1 or less of 10,000 people treated). As with any new preparation, new, previously unknown side effects can also occur when using HYLO CARE®. In addition, the measures taken as part of this clinical trial can lead to symptoms (e.g. irritation of the eye) or might involve risks (e.g. allergy to a preparation required for diagnostics). HYLO CARE® eye drops are a certified medical device for the treatment of dry eye symptoms containing well known substances to treat the given symptom. Based on the existing clinical experience with this product, no serious unwanted events or unwanted long-term effects are expected for the treatment with HYLO CARE® eye drops. In contrast, HYLO CARE® opens up a treatment option for post-operative irritation associated with dry eyes.

Where is the study run from?
Universitätsklinikum Heidelberg - Augenklinik (Prof. Dr. med. Gerd U. Auffarth) (Germany)

When is the study starting and how long is it expected to run for?
January 2019 to June 2021

Who is funding the study?
URSAPHARM Arzneimittel GmbH (Germany)

Who is the main contact?
Dorothea Gross, d.gross@ursapharm.de

Contact information

Type(s)
Scientific

Contact name
Mrs Dorothea Gross

ORCID ID
https://orcid.org/0000-0002-0726-9868

Contact details
Industriestrasse 35
Saarbrücken
Germany
66129
+49 (0)6805 9292 132
d.gross@ursapharm.de

Type(s)
Public

Contact name
Dr Stefan Schorr

Contact details
Industriestrasse 35
Saarbrücken
Germany
66129
+49 (0)6805 9292 139
stefan.schorr@ursapharm.de

Additional identifiers

Study information

Scientific Title
Observation of the changes in Fluorescein Tear Film Breakup Time and tolerability of HYLO CARE® eye drops in postoperative lubricating disorders in patients after cataract surgery:lipids: a monocentric, prospective, randomized open clinical trial

Acronym
HYLOKAT

Study objectives
The aim of this clinical test is to confirm the qualification with regard to the effectiveness and tolerability of HYLO CARE® as a wetting agent for postoperative aftercare after cataract surgery. The main target parameter is the Tear Film Breakup Time (TBUT) 5 weeks postoperatively compared to preoperatively.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Confirmed 25/02/2019 (this study does not require approval (§23b German MPG) by an ethics committee but professional advice of the Ethics Committee of the Medical Faculty, Heidelberg University), Medical Association of Baden-Württemberg (Alte Glockengießerei 11/1, D-69115 Heidelberg; +49 (0)6221 562646 0; ethikkommission-I@med.uni-heidelberg.de), ref: S-773/2018

Study design
Monocentric prospective open clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Postoperative lubricating disorders after cataract surgery

Interventions
This trial includes four visits: one initial examination before cataract surgery (D0); two follow-up examinations (D1 and D7) and one final examination (D35). The preoperative examination is before cataract surgery (D0). The follow-up examinations are defined in the trial protocol as day 1 (D1) and day 7 (D7) ± 3 days (=1 week) after cataract surgery. The final examination is scheduled for day 35 (D35) ± 5 days (=5 weeks) after cataract surgery.

During participation in the trial, no other preparations or medications should be used or previous habits should not be changed. Eye drops for dry eyes, which are already used, must be discontinued for the period of this clinical trial on the operated eye.

Patients included in this trial will receive HYLO CARE® eye drops. Patients are instructed to use their eye drops in accordance with the package information leaflet (PIL). Dosing of HYLO CARE® is 3-4 times daily one drop in the conjunctival sac of the eye that underwent surgery. Approximately 2 hours before an examination, no application of eye drops is allowed. Patients are instructed to apply HYLO CARE® at least 15 minutes after eye drops prescribed for postoperative treatment. HYLO CARE® had to be applied as the last medication.

1. Change in Tear Break-up Time (TBUT) from first measurement preoperatively (D0) compared to measurement on day 35 (D35) ± 5 days (= 5 weeks) postoperatively.
2. Baseline (preoperative) values of ocular surface disease index (OSDI)
3. Subjective discomfort feeling according to Symptom Assessment in Dry Eye (SANDE) questionnaire using a visual analogue scale (VAS)
4. Corrected visual acuity (VA)

5. Slit lamp examination of eyelids, conjunctiva, and cornea
5.1. Assessment of lid margins
5.2. Assessment of conjunctiva (conjunctival hyperemia, chemosis)
5.3. Corneal findings (corneal staining with fluorescein, corneal infiltrates, central corneal edema, descemet folds, corneal erosion)
5.4. Assessment of the anterior chamber (flare and cells)
6. Schirmer's test (aqueous tear secretion)
7. Intraocular pressure (IOP)
8. Subjective assessment of tolerability by patient
9. Evaluation of efficacy and tolerability by the investigator

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
HYLO CARE

Primary outcome(s)
Change in Tear Break-up Time (TBUT) measured in seconds rounded to 1 decimal place using a non-automated method as described by Jacobi and Cursifen 2010 from first measurement preoperatively (D0) compared to measurement on day 35 (D35) ± 5 days (= 5 weeks) postoperatively

Key secondary outcome(s))
1. Baseline (preoperative) values of ocular surface disease index using a standardized set of questions as defined in the Ocular Surface Disease Index (OSDI) questionnaire at D0
2. Subjective discomfort feeling according to the Symptom Assessment in Dry Eye (SANDE) patient questionnaire using a visual analogue scale (VAS) comparing baseline preoperatively (D0) to measurement on day 35 (D35) ± 5 days (= 5 weeks) postoperatively
3. Corrected visual acuity (VA) measured in decimal numbers with correction (cc) on D0, D1, D7 ± 3 and D35 ± 5
4. Slit lamp examination of eyelids, conjunctiva, and cornea by the investigator on D0, D1, D7 ± 3 and D35 ± 5:
4.1. Assessment of lid margins using a slit lamp
4.2. Assessment of conjunctiva (conjunctival hyperemia, chemosis) using a slit lamp
4.3. Corneal findings (corneal staining with fluorescein, corneal infiltrates, central corneal edema, descemet folds, corneal erosion) using a slit lamp
4.4. Assessment of the anterior chamber (flare and cells) using a slit lamp
5. Schirmer's test (aqueous tear secretion) on D0 and D35±5 using test strips to determine the lubrication of the strip in mm
6. Intraocular pressure (IOP) measured using an applanatoric tonometric approach at D0, D1, D7 ± 3 and D35 ± 5
7. Subjective tolerability by the patient, assessed by questioning on day D7±2 and day D28±3
8. Evaluation of efficacy and tolerability by the investigator, assessed by questioning on day D35 ± 5

Completion date
10/06/2021

Eligibility

Key inclusion criteria
1. Male and female patients >18 years
2. Age-appropriate cataract (uni- or bilateral)
3. Standard cataract surgery is possible, according to the surgeon
4. Preoperatively subjective complaints indicating a dry eye (foreign body sensation, dryness, burning, tearing, tired eyes) for at least 3 months:
4.1. VAS ≥2/10
4.2. OSDI ≥16
4.3. Fluorescein TBUT ≤10 s
5. Stable therapy (topical and systemic) ≥4 weeks
6. Patient is willing to participate in the trial
7. Patient is willing and able to fulfil the requirements of the trial protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
49

Key exclusion criteria
1. Dry eye due to systemic disease, concomitant medication, or malign conditions
2. Simultaneous preoperative use of other therapeutic ophthalmics
3. Ocular or systemic pathologies that could, according to the surgeon’s medical evaluation, have an influence on postoperative irritation (acute viral or bacterial inflammation of the conjunctiva/cornea, chronic inflammatory/infectious uveitis)
4. History of ocular surgery during the past 3 months
5. Malposition of the lids and/or lagophthalmos
6. Punctum plugs during the past 3 months
7. Contact lens wearers (no wearing of contact lenses 3 months before surgery)
8. Hypersensitivity against one of the ingredients of HYLO CARE®
9. Patient is a pregnant or breastfeeding woman
10. The patient is a woman with childbearing potential without the regular and correct use of contraception with error quote <1 % (e.g. sexual abstinence, estrogenic- and metagene-containing contraceptive, vasectomy, intrauterine pessary with hormones)
11. Concomitant participation in a clinical trial or another trial within the last 4 weeks and 4 weeks after the end of the trial

12. Earlier participation in this clinical trial or the patient being an investigator or a member of the personnel involved in this clinical trial.
13. Inability for linguistic or content comprehension of written patient information

Date of first enrolment
24/04/2019

Date of final enrolment
23/04/2021

Locations

Countries of recruitment
Germany

Study participating centre
Universitätsklinikum Heidelberg - Augenklinik (Prof. Dr. med. Gerd U. Auffarth)
Im Neuenheimer Feld 400
Heidelberg
Germany
69120

Sponsor information

Organisation
URSAPHARM (Germany)

ROR
https://ror.org/031t42b47

Funder(s)

Funder type
Industry

Funder Name
URSAPHARM Arzneimittel GmbH

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		25/05/2024	03/07/2024	Yes	No