Allogeneic serum micro eye drops compared to conventional sized eye drops: a prospective randomized non-inferiority, investigator-masked, cross-over multicenter clinical study.

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The main objective is to determine whether the administration of allogeneic serum micro eye drops using the mu-Drop device is non-inferior to the conventional sized drops in terms of effectiveness and safety.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Ocular infections, irritations and inflammations
Study type	Interventional

Summary

ID

NL-OMON44587

Source
ToetsingOnline

Brief title
Assessment of the mu-Sized Serum Eye Drops (AmuSED)

Condition

- Ocular infections, irritations and inflammations

Synonym
corneal lesions, Dry eye syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Sanquin Bloedbank
Source(s) of monetary or material Support: Sanquin Bloedbank

Intervention

Keyword: Allogeneic serum eye drops, Cross-over multicenter trial, Micro eye drops, Ocular Surface Disease Index (OSDI)

Outcome measures

Primary outcome

The improvement in OSDI score will be determined both for conventional sized and micro drops of allogeneic SEDs adjusted for randomization arm. An alpha of 0.05 will be considered to be statistically significant. In a second, non-inferiority, analysis the difference between conventional sized and micro drops will be determined, also adjusted for randomization.

Secondary outcome

Using the same statistical model, the secondary study parameters will be analyzed.

Other parameters will be included in the evaluation when part of the standard treatment and examination of the patient as part of their regular care. This might include, but is not limited to: visual acuity, refraction, eye pressure, corneal thickness, other eye medication.
The ease of use of the systems will be included in the evaluation. For evaluation, the patients diary will be used, including experiences like how easy the system is to handle or specific problems for using as judged by the

patients.

Study description

Background summary

Serum eye drops (SEDs) are used to treat patients with severe signs and symptoms of dry eyes and other diseases, like corneal defects. SEDs are used in ophthalmic cases where conventional eye drops have insufficient effect. The use of SEDs in dry eye patients usually has a rapid effect. Most patients claim the effect to be instantaneous and most symptoms improve by 48 hours.
There is evidence suggesting that serum may enhance corneal epithelial healing. Some biologically active substances are thought to contribute to the positive effects, like epidermal growth factor, fibroblast growth factor, fibronectin, and vitamin A.
Autologous SEDs are used internationally on a regular basis, while allogeneic SEDs are becoming standard care. In the Netherlands, only autologous SEDs are used. A prospective double-blinded randomized cross-over trial, comparing the effectiveness of allogeneic SEDs and autologous SEDs, is currently being performed at the RadboudUMC in Nijmegen, the Netherlands.
For administration of eye drops, commonly administration systems with a drop size of 40 to 50 µl are used (further on referred to as conventional sized).
From previous studies done with medicinal eye drops we learned that smaller eye drops, so called micro drops, can be just as effective and sometimes even superior to conventional drops in eye disease. This can be explained by the underlying physiology. The surface of the eye is protected and nourished by the tear film which has a delicate structure. The first mucous layer serves to prevent dry spots, the second aqueous layer is an extract from the blood and the third outer layer is made from lipids to prevent evaporation. By blinking, the structure of the tear film is continuously maintained. The tear film has a volume of approximately 10 µL and an additional temporary storage capacity of approximately 20 µL. There is constant renewal by a flow of about 1-2 µL per minute. Consequently, a conventional sized eye drop of 40 to 50 µL washes away most of the tear film which creates irritation and reflex tearing. Only 1 to 7% of a conventional sized eye drop is taken up by the cornea, 15% is washed away over the cheeks and 80% flushed through the nasolacrimal tube from where it is absorbed into the circulation. Alternatively, a micro drop of 5 to 10 µL fits the eye, leads to less damage of the tear film and creates less irritation and reflex tears.
If micro drops are just as effective or maybe even superior to conventional sized eye drops is currently unknown for the use of SEDs. With the proposed study we would like to compare the feasibility and effectiveness of allogeneic serum micro eye drops to the conventional sized allogeneic serum eye drops. For the administration of the serum micro drops the mu-Drop applicator will be used

and for administration of the conventional sized drops the Meise applicator. Both systems have a closed manufacturing system that allows the production under GMP conditions. Moreover, the mu-Drop system is designed for single use that guarantee the microbiological safety. Additionally, because the use of smaller drops, many more patients can be treated with a single blood donation. In that way donations are used more efficiently, e.g. serum from one blood donation can be used to prepare about 1500 mu-Drop applicators, compared to 130 Meise applicators and with an expected average use of 3 applications per day this is a factor 4 difference between both systems.

Study objective

The main objective is to determine whether the administration of allogeneic serum micro eye drops using the mu-Drop device is non-inferior to the conventional sized drops in terms of effectiveness and safety.

Study design

Prospective randomized non-inferiority, investigator-masked, cross-over multicenter clinical study. For patients the study will be non-blinded. For the observer the study will be blinded (OSDI score, Schirmer*s test, tear break up time and corneal punctates will be judged without knowing the study arm). A non-inferiority design is selected because of expected benefits using smaller drops, such as economical use of valuable donor serum, better fitting the physiology of the eye, ease of use of the applicator.

The duration of the entire study is 6 to 12 months and will be performed in an outpatient setting. Per patient, the on-study time is 3 months. During this period the patient is asked to keep a diary on the use of serum eye drops and experience with the applicators.

There are 3 sections in the treatment period:
In the first month, conventional sized or micro allogeneic SEDs administrated either with Meise or mu-Drop applicators will be provided.
In the second month, regular eye medication (the same as the one(s) used before onset of the study) will be applied (wash-out period).
In the third month, depending on the treatment the patient received in the first month, conventional sized or micro allogeneic SEDs administrated either with Meise or mu-Drop applicators will be provided.

In the month prior to start of the study, the patient has to remain on their current eye medication, which will be continued during the second month of the treatment period.
Prior to and at the end of each section of the treatment period, the OSDI questionnaire will be filled out by the patient. Schirmer*s test will be performed to determine tear production. The tear break up time will be

measured. Fluorescein will be used to stain the corneal punctates. After staining, the percentage of affected surface will be estimated in a standardized way. Only if possible, a photograph of the cornea will be taken to count the number of corneal punctates. At the end of the study the diary will be collected from the patient.

Intervention

N.v.t.

Study burden and risks

Potential risks of blood-borne diseases are present with donor products, but the risk is probably much lower as for regular transfusion products, as the quarantine period effectively eliminates the risk of disease transmission.
In a broader perspective, from previous studies done with medicinal eye drops we learned that smaller eye drops, so called micro drops, can be just as effective and sometimes even superior to conventional drops in eye disease. The current study will provide more data to ensure that evidence based medicine is used for the treatment of dry eyes with SEDs.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Subjects with severe signs and symptoms of dry eyes
Age 18 years or older
Punctate staining of the cornea
Expected to benefit from SEDs
Not previously treated with SEDs

Exclusion criteria

* Actively or previously treated for Herpes Simplex Virus (HSV) keratitis
* Corneal lesions, more than punctate
* Untreated Meibomian gland disease
* Pregnant or lactating or intending to become pregnant in the next 3 months
* Unable or unwilling to give informed consent
* Active (systemic) microbial infection
* The use of all types of contact lenses
* Discontinuous use of medication that affects the dry eye sensation is not allowed (e.g. discontinuous use of local corticosteroids). Continuous use of co-medication, like lubricants, anti-glaucoma eye drops or other drops, that have to be used on a daily basis are allowed, and are expected to be used throughout the study period in both eyes (continuous use of the same medication is allowed if used at least one month prior to start of the study).

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-12-2018
Enrollment:	54
Type:	Actual

Ethics review

Approved WMO Date:	09-04-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-12-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL63119.091.17