Efficacy and safety of Autologous Serum Tears for the Management of Severe Dry Eye Disease. A prospective, double-blind, randomized, controlled, contralateral study.

Background & Significance

Dry eye disease (DED) or dry eye syndrome (DES) affects millions of people worldwide with varying degrees of severity and prevalence as high as 50%.[1] The economic impact of DED is significant as well due to the resultant productivity loss.[2] Most patients experience mild to moderate DED symptoms (e.g. irritation, burning, itching) that can be alleviated with conservative measures such as the regular use of artificial tears. However, for patients with DED due to underlying immunologic conditions such as Sjogren's syndrome, symptoms can be debilitating (e.g. ocular pain, constant light sensitivity) and significantly downgrade quality of life. At its extreme, untreated severe DED can progress to blindness.[3]

Severe DED management is challenging both for the treating physician and the patient. Immune-based DED arises from insufficient tear production due to immunologic destruction of the lacrimal gland and from an unhealthy tear film that lacks essential components.[3,4,5,6] A potential breakthrough in tear film replenishment was the discovery that blood serum shares an overall similar composition to natural tears. Over the last decades, the use of autologous serum (AS) tears for patients with DED has gained popularity among cornea and ocular surface disease specialists.[7] The evidence, however, that suggests a clear benefit of AS tears for patients with DED refractory to other treatments remains insufficient and controversial.[8] A few small and underpowered studies have established the safety of AS tears but efficacy has not been determined yet.[7,8] A recent report by the American Academy of Ophthalmology notes that although autologous-based tears may be effective in the treatment of severe dry eye, conclusions are limited due to the absence of controlled trials.[7] Thus, a well-designed, prospective, double-blinded randomized, controlled clinical study in this area is of utmost importance.

Purpose

To assess the efficacy of AS tears in severe DED patients with signs and symptoms refractory to their conventional treatments via a real-world double-blinded, randomized, controlled, contralateral study with sufficient follow up, as compared to traditional artificial tears.

Specific Aims

Primary Aims:

- To assess the degree of improvement between the two groups, at 1, 2 and 3 months by using objective assessment tests, such as corneal fluorescein and conjunctival rose bengal staining,
- To assess the degree of improvement between the two groups, at 1, 2 and 3 months by using objective assessment tests, such as tear break up time and Schirmer's test.

Secondary Aim:

- To assess the safety and potential adverse effects of AS tears.

Methods

Forty (40) eyes of twenty (20) adult patients with severe DED due to Sjogren's syndrome (either primary or secondary to rheumatoid arthritis), mucous membrane pemphigoid, graft-versus-host disease, and Stevens-Johnson syndrome will be contralaterally randomized to the use of AS tears or regular artificial tears.

Inclusion criteria:

- Age $\geq$ 18 years old.
- All participants should have had severe DED symptoms for at least 6 months prior to study enrolment.
- Clinical signs of DED should be detected via slit lamp examination and by Schirmer's test on two consecutive visits, the screening visit and the randomization visit *(please refer to study timeline below).*

- Symptoms of severe DED should be recorded both at the screening visit and at the randomization visit via the Ocular Surface Disease Index (OSDI) questionnaire.

N.B. The OSDI questionnaire is a validated questionnaire adopted by the National Eye Institute in the United States and the Tear Film and Ocular Surface Society (TFOS) in DED clinical studies due to the inconsistent correlation between reported symptoms and ocular signs.[9]

- Compliance (>90%) during the run-in period *(please refer to study timeline below).*

Exclusion criteria:

Any condition or treatment that can affect the signs of dry eye such as pregnancy, regular use of contact lenses, use of topical glaucoma medications, and prior corneal, refractive or glaucoma surgery.

Study timeline:

Severe dry eye disease subjects will be identified over the course of 16-18 months. Each eligible subject will be given a 14-day supply of the active control (artificial tears) in non-transparent vials. At the end of the run-in period, adherence will be assessed and only subjects with ≥ 90% compliance will be contralaterally randomized to AS tears or regular artificial tears. After randomization, study visits will be conducted at 1, 2 and 3 months.

N.B. The run-in period serves to minimize dropouts and missing data. This is a real-world trial, thus, all participants will be allowed to continue any dry eye regimens they had been using on a regular basis (i.e. standard of care), as long as they commit to continuing them throughout the duration of the study.

AS tears production protocol:

The AS tears production protocol is simple. The patient undergoes a regular venous blood draw, the blood is centrifuged and the supernatant serum is diluted to 30 % with artificial tears. The dosage of eye drops will be 4 times a day for both the control and the active groups.

Strengths of the study

In contrast to prior trials, this study is designed so that the results will be generalizable and directly applicable to real-world patients. In this study, subjects with severe dry eye symptoms recalcitrant to current treatments will be allowed to continue their current therapies, as performed in clinical practice. The control group will receive artificial tear drops, which is the most widely used treatment regimen for DED. The AS tears in the active group will be diluted in artificial tears to a concentration of 30%. Thus, any difference between the groups will be due to the additional AS components in the active group.

Anticipated results

We expect to show that in patients presenting with severe immune-based DES, the use of AS tears 30% improves the DED objective measures of ocular surface dryness compared to the use of artificial tears at 3 months.

References

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