



Topical Application of Vitreous Body as a New Alternative for the Treatment of Persistent Epithelial Defect and Dry Eye

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Abstract

Many growth factors and chemical agents were previously used to accelerate corneal epithelial wound healing and dry eye. One of the enriched substances is autologous blood introduced with multiple randomized controlled studies for those who are not responsive to conventional treatments. Vitreous body as a natural substance has some properties which seem to make it superior to autologous blood for the management of severe dry eye syndrome and even persistent epithelial defect. This theory is based on some clues listed as below:

Vitreous contains a high amount of water and little macromolecules, the character suitable for a substance to be used for relieving symptoms of dry eye as a wetting effect. Moreover, it contains some growth factors such as insulin like growth factors and pigment epithelium-derived factor and high amount of viscous materials such as Chondroitin Sulfates and Hyaluronic acids, all are compounds seems to be effective in the management of dry eye and acceleration of epithelialization. It has also anti-inflammatory features. The most important unique feature of vitreous in comparison with blood is its immune privilege property documented by previous studies. Vitreous can be obtained from brain dead patients and also from eye banks easily. As with all transplanted material of human origin, it carries risks of prion transmission; however, for intractable severe dry eye, benefits may greatly exceed the risk.

Keywords

Vitreous, Topical application, Dry eye, Treatment



Introduction

Autologous serum (AS) topical eye drops have been reported to be beneficial in the management of ocular surface disorders which are not responsive to the routine treatments (1).

Many patients with dry eyes show acceptable response to the conventional therapeutic options such as intensive tear supplements, punctal occlusion, contact lenses, and appropriate management of adnexal disease. As it is known enough, the ecosystem of the ocular surface is highly variable according to four parameters: The dynamic interactions of adnexae, adequate blink reflex, tear production, and ocular surface tissue, consisting of cornea and conjunctiva.

In spite of acceptable response in majority of patients, some patients with some underlying disorder such as Sjögren syndrome, severe filamentary keratopathy, persistent epithelial defect may not respond to these medications. This may result in significant visual impairment and disability.

Some uncontrolled studies were in favor of effectiveness of autologous blood in these patients. Further multiple controlled trials were designed to compare the use of this method instead of simple dry eye (2, 3). Several tear factors which have been identified to be of particular importance in the maintenance of normal corneal and conjunctival epithelium including epidermal growth factor (EGF), vitamin A, transforming growth factor β (TGF- β), fibronectin, and other cytokines. TGF- β is thought to control epithelial proliferation and maintain cells in an undifferentiated state (1, 2). However, the main problems with autologous serum are practical difficulties (3). Vitreous body is a jelly structure in the posterior segment of the eye enriched in some growth factors and also in Chondroitin Sulfate and Hyaluronic acid. As a natural substance, it seems to be containing of some properties, which make it superior to the autologous blood for the management of severe dry eye syndrome and even persistent epithelial defect.

The Hypotheses

Vitreous body or its derivatives may be used instead of current use of autologous serum for the management of persistent epithelial defect and dry eye syndrome.

This theory is based on some facts listed below:

1-vitreous contains about 98% water and only 0.15% macromolecules, character suitable for a substance to be used for relieving symptoms of dry eye as a wetting effect (4).

2-While the healing effect of autologous blood may pertain to some extent to multiple growth factors and also anti-inflammatory agents all are essential for acceleration of surface reparation and

also improvement of dry eye symptoms by resurfacing of epithelium, some growth factors such as insulin like growth factors and pigment epithelium-derived factor are found in the vitreous (3-5).

3-According to previous studies, Chondroitin Sulfates and Hyaluronic acids are all compounds seem to be effective in the management of dry eye and acceleration of epithelialization (6). Vitreous has a large amount of Hyaluronan, Chondroitin Sulfate and soluble proteins. Hyaluronan and Chondroitin Sulfate were found to occupy all of the space in the vitreous except for the collagen fibrils. This property is specified for the vitreous and is not achieved with usage of autologous blood. Autologous blood has not such a property.

4-vitreous was found to have some amount of anti-inflammatory substances such as neutrophil elastase inhibitor and tissue plasminogen activator inhibitors. This fact will be outstands more the benefit of vitreous in relieving dry eye discomfort in which inflammation confirmed to have an additive role (4-6).

5-The most important unique feature of vitreous in comparison with blood is immune privilege property documented by previous studies such as long term survival of grafts in this ocular compartment. This especial property of vitreous removed the limitation encountered with blood to be obtained widely from different individualized rather than just in autologous form (7, 8).

Evaluation of Hypotheses and Experimental data

One of the methods of preparing blood for the treatment of ocular surface disease is the use of bovine umbilical cord serum because it contains high levels of growth factors; however, this method is associated with high rate of allergic reaction (9). As was mentioned this adverse effect is not expected with the use of homologous vitreous or its derivatives for the management of dry eye (7, 8).

To begin with, the hypotheses can be evaluated experimentally on animals with injured lacrimal gland and severe dry eye. Then it can be investigated on humans by preparing vitreous from eye bank or brain deaths individuals who will undergo full examination for absence of any infection transmission. After obtaining vitreous the protocol for making eye drops and preservation will be the same as preparing eye drops with autologous blood i.e. vitreous will be left to clot at 4°C for 10 to 12 hours before centrifuging at 4500 rpm for 15 minutes and diluted with sterile saline (0.9%) to a 20% concentration. The vials will be kept in a frozen condition at -20°C. A fresh bottle of eye drop is used for treatment every 24 hours (10). All patients will be on topical chloramphenicol drops.

Discussion

Early coverage of injured cornea by epithelium is essential in signal inhibition of any cascade responsible for corneal inflammation. Therefore, many growth factors and chemical agents were previously used in order to accelerate wound healing and to minimize scarring and haze formation (1, 2). One of the enriched substances suitable to reach this goal is autologous blood has been introduced with multiple randomized controlled studies for severe ocular surface disease not responsive to other commercial artificial tears. In most of these patients, autologous serum was more effective than conventional treatment for improving ocular surface health and subjective comfort (1-3). Although, the true mechanisms of action of autologous serum are not yet identified, some knowledge about them is available in literature (3). It is mentioned that the main effect of autologous serum will be via some components changed cell proliferation, migration and differentiation of the eye surface epithelial cells (4, 5).

It is known that some serum components have some trophic effect on the eye surface epithelial cells because of their action on the epithelial cell dynamics, and proliferation of epithelial cells in the limbus and cornea (9). The main limitation of autologous blood is the preparation of them which is patient dependent and this will be increase the chance of contamination (10). If it is proved that vitreous body is effective in dry eye, it is possible to be commercially and not individually available. As was mentioned some growth factors are found in the vitreous, and researches will be ongoing to find more details in this relation (3 -5). Hirai et al. evaluated the effects of various lubricants on the

corneal surface regularity in rabbits. They concluded that topical instillation of 0.1% Hyaluronic acid or 1.0% Chondroitin Sulfate increase tear stability and will be potentially effective in patients with dry eye (6). Other studies were conducted to support this result (11, 12). While autologous blood is devoid of these substances, vitreous body is enriched of both of them (4). Moreover, the immunologic properties of vitreous body are recognized to some extent. Preliminary experimental evidence suggests an immunologically inert characteristic for vitreous. This idea is originated from the surveillance of transplanted pancreatic tissue and tumor cells in the vitreous space and absence of inflammatory reaction following injection of LPS antigens in to this space (7, 8). Usage of vitreous derivatives can be clinically applicable in forms of commercially available ophthalmic drops as a multipurpose drug to treat intractable severe dry eye or persistent epithelial defect. Nevertheless, risk of prion transmission still a concern even with tissues obtain from eye bank where donors are checked for all other infections (13).

Conclusion

Vitreous body seems to have properties fulfilled the criteria for a substance used for the treatment of ocular surface disease such as dry eye. Indeed, the promising immunologically inert feature of vitreous and the presence of high viscous materials make it superior to autologous blood. Vitreous derivatives obtained easily from brain death individuals. As with all transplanted material of human origin, it carries risks of prion transmission; however, for intractable severe dry eye, benefits may greatly exceed the risk.

Overview Box

First Question: What do we already know about the subject?

We already tried to explain some interesting properties of vitreous body which are seem to make it as a proper substance for management of severe intractable dry eye and persistent epithelial defect. It is clinically applicable by using vitreous derivatives in a form of commercially available multipurpose eye drop.

Second Question: What does your proposed theory add to the current knowledge available, and what benefits does it have?

Since management of severe dry eye and persistent epithelial defect is a subject of current studies and attempts are toward ways to find suitable substances to treat these sophisticated conditions, giving information about vitreous body as a natural substance with promising properties to be used in these conditions will be of particular benefits.

Third question: Among numerous available studies, what special further study is proposed for testing the idea?

To begin with, it's better to evaluate the hypothesis on animals with injured lachrymal gland and severe dry eye and then it can be tested on humans by preparing vitreous body from brain death individuals or eye banks. As with all transplanted material of human origin, chance of prom transmission is still an obstacle to use this method widely; however, for intractable severe dry eye, benefits may greatly exceed the risk.

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