Clinical Uses of Autologous Serum Eye Drops as Tears in Ophthalmology

A stable tear film is a prerequisite to maintain the ocular surface health. The ocular surface stability depends of neuroanatomical interaction of the compositional factors and hydrodynamics factor. [for reviews see [1;2]] Among compositional factors, healthy ocular surface epithelia with normal proliferation and differentiation are an important component. There are several proteinaceous and non-proteinaceous factors in the tears that are essential to maintain the normal epithelial health. For example, the tears contain essential components such as epidermal growth factor (EGF)[3], vitamin A[4], TGF-β{782}, fibronectin[5], and others cytokines[6]. These factors regulate the proliferation, differentiation and maturation of the ocular surface epithelia. In patients with very severe aqueous tear deficiency secondary to lacrimal gland dysfunction, these factors are severely depleted, and thus may explain in part the difficulty of the ocular surface to be kept in a healthy state. Because these factors are also present in the serum [7], many studies shown below have formulated artificial tears by diluting patient's autologous serum with saline solution to treat a number of ocular surface diseases.

For Treating Keratoconjunctivitis Sicca Caused by Dry Eye:

In 1984, Fox et al[8] first reported a successful use of autologous serum diluted with sterile saline (preservative free) to 50% as an alternative treatment in a total of 15 patients with the diagnosis of keratoconjunctivitis sicca in 7 patients and Sjögren's Syndrome in 8 patients. They used scores of rose bengal staining and patient's symptoms to judge the efficacy. For a mean follow-up of 10 months, they found that the mean score of subjective symptoms and rose bengal staining significantly improved following the use of autologous serum eye drops. In addition, they also performed bacteriologic cultures of manufactured serum drops and did not note any growth when they were stored at –20 °C for up to 3 months and at 5 °C for 25 hours.

In 1999, Tsubota et al[9] evaluated the efficacy of 20% autologous serum drops diluted with saline for the treatment of dry eye in 12 patients with Sjögren's Syndrome, and used such clinical parameters as fluorescein and rose bengal staining, TBUT, and

subjective symptomatic score. All parameters improved when measured at the second and fourth weeks after application of autologous serum eye drops. They further used the expression of MUC-1 in cultured conjunctival epithelium under the influence of serum and speculated that the increase of MUC-1 expression by serum stimulation explained why the rose bengal staining was improved following the treatment. They used a conjunctival epithelial cell line, CCL.20.2 (American Type Culture Collection [ATTC], Rockville, MD, USA) and cultured them in a medium 199 (Gibco, Grand Island, NY, USA) supplemented with 10% fetal calf serum (FCS) (Gibco) and antibiotics solution, then the medium was changed to a FCS-free medium 1 day before the experiments and latter treated with 15% or 30% human serum for 24 hours before subjecting them to flow cytometry for the expression of MUC-1. They also measured the content of vitamin A and TGF-β in prepared autologous serum stored at different temperature (4 ˚C and -20 ˚C) for different times (1 month and 3 months). They found that such storage of autologous serum in refrigerator at 4 ˚C was stable for 1 month and in the freezer at -20 ˚C was stable for 3 months.

Poon et al[10] recently also reported their experiences using 20% autologous serum drops to treat 11 dry eyes of 9 patients with KCS, and noted 60% improvement based on fluorescein, rose bengal staining and subjective symptoms score. In this study the authors did not mention if these patients had punctal occlusion and whether the inclusion criteria were stringent enough so that other confounding factors have been excluded.

For Treating Ocular Surface Dryness Caused by Other Diseases:

Clinically autologous serum eye drops have also been used to treat patients with adry eyes caused by diseases other than Sjogren's syndrome, especially when these patients undergo ocular surface reconstruction. Tsubota et al[11] in 1986 used autologous serum eye drops to treat patients with severe dry eyes following reconstruction of the ocular. Surface. Fourteen eyes of 11 patients including seven patients with ocular cicatricial pemphigoid and four with Stevens-Johnson syndrome were treated with a combination of allograft limbal transplantation, amniotic membrane transplantation, and tarsorrhaphy, followed by autologous serum drops every 15 min. For a mean follow-up of 143 days the

success of ocular surface reconstruction was noted in 12 eyes, with minimal recurrence of symblepharon. Failure occurred in only two eyes of to younger patients who had severe surface keratinization..

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For Treating Ocular Surface Squamous Metaplasia Caused by Superior Limbic Keratoconjunctivitis (SLK):

Goto et al[12] treated 11 patients with superior limbic keratoconjunctivitis with 20% autologous serum drops for 4 weeks, and noted partial efficacy in 82% of them. They used fluorescein and rose bengal staining as well as subjective symptom score. They recommended that autologous serum should only be considered as a second choice only if punctal occlusion is not effective. They also pointed out in the study that autologous serum drops might also provide lipids, a very important component of the tear, but did not perform any evaluation of the meibum gland or any other measure of lipid components.

For Promoting Epithelial Healing:

Tsubota et al[13] in 1989 used 20% autologous serum eye drops in 16 such patients following keratolimbal allograft transplantation when they manifested postoperative persistent epithelial defects. They were inflicted with ocular cicatricial pemphigoid or Stevens Johnson syndrome (n= 6), post-corneal transplantation (PK) (n=4), herpes keratitis (n=3), GVHD (n=2), and post radiation (n=1). Their results showed that autologous serum eye drops were effective in healing these defects in one month in 62.5% of the cases, and in two weeks in 43.8 % of the cases with persistent corneal epithelial defects. In this study, the flourescein staining was used to detect epithelial defects. They also measured the corneal sensation, and noted that patients with worst sensitivity had a tendency to be less responsive to the treatment, but this relation was not statistically significant. It is important to mention that diversities of patient's diagnosis made it difficult to know the exact effect of autologous serum drops in healing these

persistent epithelial defect (PED). For example, they did not mention whether all patients had punctal occlusion.

As mention above, Poon et al [10] recently reported their experiences in using autologous serum drops to treat 15 eyes of 13 patients with persistent corneal epithelial defect. PED, They noted 60 % of such eyes improved in 29 days. In addition, they also treated 2 patients after penetrating keratoplasty, which was performed for perforations secondary to PED. Although both patients (100%) improved in one week, they deteriorated when autologous serum drops discontinued. Again no mentioning if punctal occlusion had been performed during or before the study. They also examined the in vitro toxicity exposing cultured human corneal epithelial cells with 20% serum or unpreserved hypromellose 0.3%, and performed viability studies using flourescent viability staining (Calcein AM ethidium homodimer) and ATP assay**.** Their results showed that morphology and ATP levels of cultured epithelial cells exposed to 20% serum were better maintained than those exposed with hypromellose 0.3%.

Stangogianis et al[14]recently (in a poster presented at ARVO 2002) compared undiluted autologous serum and 2% Hydroxypropylmethylcellulose in promoting reepitheliazation in 18 rabbit's corneas created by mechanical debridement of the corneal epithelium. It is not clear if they used each rabbit's own serum or serum from only one rabbit. They showed that autologous serum was the least effective in promoting corneal reepitheliazation, measured by light and transmission electron microscopy, and fluorescein staining. Because it has been known that wound healing in rabbits in vivo is rapid, it is technically difficult to resolve such a difference.

Reference List

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