INTRODUCTION

Dry eye disease syndrome (DES) or disease (DED) is a multifactorial condition affecting the ocular surface and tears influenced by internal and external (i.e., physical, chemical and biological) causes.1-3 The prevalence of dry eye disease may range from 5% to 30% in adults over 50 and the incidence increases with aging, with women being more likely affected than males.3-5 Meanwhile, the prevalence based on merely clinical signs is generally higher and varies, reaching more than 70% of the population.6 The number is also calculated as 1.5–2.2 times higher in Asians.2 Some factors such as diabetes, contact lens usage, environmental factor, extended use of visual display terminal, being alcoholic, smoking, some medicines and systemic condition increase the number of DED.6,7 It has been more than 20 years since the most recent population-based epidemiology on the prevalence of DED in Indonesia was published. It is challenging to ascertain its prevalence due to the range of clinical manifestations and diagnostic standards, as well as the poor association between clinical indicators and symptoms.5

Until now, there is no known causative treatment for dry eye. Symptom management is the focus of typical therapy.4 Even though the symptoms usually improve with treatment, the disease is incurable, which can be frustrating for both patients and doctors.7 Untreated or inadequate response to the therapy may lead to interstitial keratitis, neurotropic keratitis, filamentous keratitis, trichiasis, keratopathy, symblepharon and corneal ulcer. In severe cases, the corneal ulcer can cause decreased visual acuity, perforation and endophthalmitis.8 At last, these processes will decrease work productivity and patient quality of life.8

Artificial tears are one of the traditional treatments widely used for dry eye disease.3 However, chemical preservatives in artificial tears can harm the eye’s inherent biological components by inducing inflammation, irritation and allergic reactions.3 This led to the finding of serum as dry eye therapy by Fox et al. in 1984.1 Epithelial growth factor, vitamin A, lysozyme, fibronectin and immunoglobulin (Ig)-A found in serum are identical to those found in the lacrimal gland’s tears and may help explain why serum tears have a positive impact on the corneal epithelium.3,9 The use of serum tears for ocular surface disease gained popularity after several kinds of research revealed patient improvement and described the stability of certain biochemical substances inside the serum, later termed autologous serum eye drops (ASEDs).9 Management of dry eye disease is still state of the art, more complex than rigid evidence-based algorithms that accommodate all patients with signs and symptoms of dry eye.6 Therefore, this knowledge on applying ASEDs will bring another perspective for doctors in treating DED.

METHOD

The method used was a literature review. A comprehensive search was performed on Pubmed and Google Scholar databases in December 2022 using each of the following keywords “ASEDs”, “serum”, “eyedrop”, “DED” and “DES”.

Conclusion: Dry eye disease is incurable and symptom management is the focus of therapy. Studies have shown that ASEDs reduced dry eye symptoms in over 60% of patients by inhibiting the release of inflammatory cytokines and increasing the number of goblet cells and mucin expression in the conjunctiva. The serum eye drop is typically well tolerated and can be one of the best treatment options for severe DED due to its close resemblance to tears, preservatives free and minimum side effects.

ABSTRACT

Background: Nowadays, there are a lot of treatment options available for dry eye syndrome (DES) or disease (DED). Autologous Serum Eye Drops (ASEDs) is one of the options that offer a potential advantage over conventional therapy. Biochemical elements in ASEDs resemble real tears and act as a lacrimal substitute to provide lubrication. As a severe dry eye treatment, using ASEDs has grown in favor.

Aim: This review aims to deliver knowledge from the current literature on applying ASEDs for dry eye disease in the medical worker.

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Keywords: Autologous serum; Dry eye; Severe; Tears; Treatment.

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Anak Agung Ayu Putri Oktiadewi1*, I Putu Rustama Putra2

Autologous Serum Eye Drops (ASEDs) as dry eye disease treatment option

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December 2022 using each of the following keywords “ASEDs”, “serum”, “eyedrop”, “DED” and “DES”, which are combined using the Boolean operators “OR” and “AND”. Of all the articles obtained from the search results, the authors reviewed 24 selected articles, studies and guidelines about the current applications of the ASEDs in dry eye patients.

DRY EYE DISEASE (DED)

Definition, Risk Factor and Pathophysiology
Tear Film and Ocular Surface Society Dry Eye Workshop (TFOS DEWS) II 2017 define DED as “A multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film and accompanied by oculary symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles”.

Tear film is essential for lubricating and protecting the ocular surface, as well as maintaining a smooth refractive surface for the best visual acuity. Systemic inflammatory disorders such as Sjögren’s syndrome, rheumatoid arthritis, diabetes, systemic lupus erythematosus, acne rosacea, and Graves’ disease are linked to DED through lacrimal gland imbalance. Dry eye disease may also be influenced by hormonal changes, medications (such as systemic antihistamines, diuretics, and topical beta blockers for glaucoma therapy), operations (such as photorefractive keratectomy and laser in situ keratomileusis), frequent contact lens wear, and other factors.

The two main types of DED are Aqueous Deficient Dry Eye (ADDE) and Evaporative Dry Eye (EDE). A sub-classification tree was used to list a range of intrinsic and extrinsic potential etiological factors, as presented in Figure 1.

The normal osmolarity of the tear film is expected to be less than 300 mOsm/L, while DED patients have been observed to have as high as 360 mOsm/L. This hyperosmolarity condition induces a cascade of events in the epithelial cells of the ocular surface, implicating Mitogen-Activated Protein Kinases (MAPK) and Nuclear Factor κB (NFκB) signaling pathways and producing inflammatory cytokines (IL-1 [IL-1α; IL-1β]) and tumor necrosis factor-α [TNF-α] and proteases, such as matrix metalloproteinase-9 (MMP-9). These cause inflammatory cells to become activated and attracted to the ocular surface, producing further inflammatory mediators. Working in conjunction with tear hyperosmolarity, such mediators result in decreased glycocalyx mucin expression, apoptotic death of surface epithelial cells, and a reduction in goblet cell number. This altered glycocalyx mucin expression is the basis of ocular surface staining in DED and compromises ocular surface wetting and causes earlier tear film breakage. Each type of DED exhibits goblet cell loss, presented...
by low MUCIN 5AC (MUC5AC) levels in tears. Through non-apoptotic mechanisms, hyperosmolarity also causes the death of corneal epithelial cells. As a result, ocular surface hyperosmolarity is amplified or started, consequently completing the “Vicious Circle” (Figure 2). Regardless of the entry point, once a person enters the “Vicious Circle” the accompanying tear film instability, hyperosmolarity, and inflammation conspire to drive further negative change, frequently obfuscating the line between underlying aqueous deficiency and evaporative etiologies. 

**Clinical Sign and Diagnosis**

The most commonly reported symptoms that significantly influence patient quality of life include light sensitivity, foreign body sensation, red eyes, poor vision, and daily life constraints. Ocular dryness or irritation may also worsen these symptoms. There is no “gold standard” symptom or sign for the diagnosis of DED. It is advised to evaluate both the symptoms and the signs of DED because symptoms might exist without signs, and vice versa. Severity of subjective symptoms evaluation is measured by validated scored questionnaires such as Dry Eye Questionnaire, Dry Eye Questionnaire 5, OXFORD score, Ocular Surface Disease Index (OSDI), National Eye Institute Visual Functioning Questionnaire 25, Impact of Dry Eye on Everyday Life, McMonnies questionnaire, Symptom Assessment in Dry Eye, Standard Patient Evaluation of Eye Dryness questionnaire, Vision-Targeted Health-Related Quality of Life questionnaire (NIH Toolbox), dan Visual-analogue scale. Examinations for DED vary in terms of invasiveness. The enhanced tear osmolarity is the most outstanding clinical diagnostic for DED and the severity assessment, although it is generally limited to specialized practice. Additionally, Schirmer’s tests, fluorescein clearance, and fluorescein tear break-up time (TBUT) are currently used to assess tear production. Fluorescein and lissamine green dye staining are used to quantify ocular surface damage. Other advanced techniques for DED include tear-film interferometry, inflammaDry immunoassay and infrared meibography.

**Current Treatment**

Treatment of DED is based on its subtype and severity. Mild DED is categorized by TBUT >10 seconds, moderate DED with TBUT 6-10 seconds and severe DED with TBUT ≤5 seconds and Schirmer score ≤5 mm/5 minutes. Initial treatment includes education, environment modification, elimination of offending topical and systemic agents, lid hygiene, warm compress, increased water intake, reduced alcohol consumption and preservative-free ocular lubricants. Several artificial tear formulations vary in electrolyte composition, osmolarity, viscosity, presence of preservatives, and suitable solutes. Over-the-counter (OTC) products are referred to as “artificial tears” because they lack of biological nutrients that support ocular surface renewal and immune defense. This is because tear film’s intricate structure and chemical composition are difficult to replicate synthetically. Other lubricants, such as carboxymethylcellulose and sodium hyaluronate, play an essential role in wound healing, inflammation and lubrication. Comprehensive step of treatment is available in Table 1. A study in 2016 revealed that the most frequently prescribed topical agents are 0.05% cyclosporine A (68%), 0.1% fluorometholone (60%), 0.5% loteprednol etabonate (51%) and autologous serum eye drops (49%), while for non-topical agent included essential fatty acid supplements (69%), low-dose doxycycline (61%), flaxseed supplements (33%) and punctal plugs (75%).

**ASEDs FOR DED TREATMENT**

**Composition and Applicability for DED treatment**

The term autologous means the serum donor comes from one’s own body and is used only for oneself. The use of autologous serum is justified by its close resemblance to tears in terms of pH (7.4) and osmolarity (298 mmol for tears and 296 mmol for serum). A detailed composition of tears and serum is described in Table 2. The total tear protein content is 7.51 mg/mL, around 10% of serum. The main proteins in tears are lysozyme, lactoferrin, and albumin, whereas the main proteins in serum are albumin and IgG. Both lysozyme and lactoferrin are believed to be released in high concentrations in tears because they guard against infection on the ocular surface and transport iron to the cornea, respectively. TGF-β is in the known to have antiproliferative properties, but large quantities of it may prevent the ocular surface epithelium’s ability to heal wounds. This discovery led to using a diluted serum solution to maintain TGF-β levels similar to those of tears.
TREATMENT

If step 1 options are inadequate, consider:

- Non-preserved ocular lubricants to minimize preservative-induced toxicity
- Tea-tree oil for Demodex, if present
- Tear conservations (punctal occlusion devices, moisture chamber spectaclesgoogles)
- Overnight treatment with ointments or moisture (such as ointments and moisture chamber devices)
- Physician administered, physical heating and expression of the Meibomian glands (including device-assisted therapies, such as Lipiflow), and intense pulsed light for Meibomian gland disease
- Prescription drugs to manage dry eye disease
  - Topical antibiotic or antibiotic/steroid combination applied to the lid margins for anterior blepharitis (if present)
  - Topical corticosteroid
  - Topical secretagogues (if available)
  - Topical non-glucocorticoid immunomodulatory drugs (such as cyclosporin)
  - Topical lymphocyte function-associated antigen-1 (LFA-1) antagonist drugs
  - Oral macrolide or tetracycline antibiotics

If step 2 options are inadequate, consider:

- Oral secretagogues
- Autologous and allogenic serum eye drops
- Therapeutic contact lens options (soft bandage contact lenses, rigid scleral contact lenses)

If step 3 options are inadequate, consider:

- Topical corticosteroid for longer duration (Tip: retinal nerve fiber layer [RNFL] of the optic disc and visual fields)
- Amniotic membrane grafts
- Ocular lubricants of various types (if Meibomian gland dysfunction present, consider lipid-containing supplements)
- Lid hygiene and warm compress of various types
- Identification and potential modification/elimination of offending systemic modifications and topical medications
- Education regarding potential dietary modifications (including oral essential fatty acid supplementation)
- Modification of local environment
- Over-the-counter drugs (such as antihistamines and decongestants)
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  - Topical non-glucocorticoid immunomodulatory drugs (such as cyclosporin)
  - Topical lymphocyte function-associated antigen-1 (LFA-1) antagonist drugs
  - Oral macrolide or tetracycline antibiotics

Patients with DED have lower Epithelial Growth Factors (EGF) levels in their eyes due to fewer tears. EGF plays a role in sustaining the repair of corneal and ocular wounds and encourages cell migration and proliferation, which results in tissue granulation during the healing of corneal lesions. According to Agung et al. study, exogenous EGF added at a 25 ng/mL concentration can boost and speed up corneal wound healing by increasing cell proliferation activity. Therefore, EGF availability in autologous serum should be maintained.

Production and Storage

Currently, no commercial form of ASEDs is available. The serum is often acquired through normal blood sampling using serum-separating tubes. After allowing the blood to coagulate at room temperature, centrifugation separates the supernatant (serum from the blood's solid constituents) for 10 minutes at 4,000 g. The serum can then be withdrawn and diluted with a balanced salt solution, sterile, preservative-free normal saline, or another eye-compatible solution at the proper concentration (the literature range for serum concentration is 20%-100%). These drops must be chilled while being used and frozen after being created. Generally, the manufacturing process is divided into clotting, centrifugation, dilution, and storage phases. Through the proper process, serum content can be adequately maintained.

As the serum does not contain preservatives, the danger of preservative-induced toxicity linked with other dry eye therapies decreases. However, theoretically, the absence of preservatives increases the danger of ocular infection. While in use, autologous serum can be kept at 4°C for less than a month (mostly two weeks) and up to 3 months at -20°C. Keeping vials containing autologous serum away from light is critical to avoid the breakdown of vitamin A. Storage at low temperatures is also necessary to maintain the stability of the active ingredient of autologous serum. The autologous serum has a constrained shelf life. Patients with dry eye syndrome who require long-term therapy benefit from ASEDs because they are easier to store and use. Patients can store it in a home-setting refrigerator with calibrated temperature parameters. As long as the patients can maintain the temperature, ASEDs can be carried everywhere in a special chamber.

Patients Selection

Despite the donor comes from one's own body and is utilized only for oneself, there are still safety requirements. The American Association of Blood Banks (AABB) and the Food and Drug Administration (FDA) in the US have established requirements for autologous blood donors, which include deferral for conditions posing a risk of bacteremia and a minimum hemoglobin level of 11 g/dL (hematocrit of 33%). Additional requirements may be imposed by specific blood collection facilities and medical professionals; these frequently state that the patient must be healthy enough to endure...
Table 2. Tears and serum composition.¹

<table>
<thead>
<tr>
<th>Parameter/Constituent</th>
<th>Tears</th>
<th>Serum*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Proteins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Protein</td>
<td>7.51 mg/mL</td>
<td>66-81 mg/mL</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>2.36 mg/mL</td>
<td>5.0-10.2 µg/mL</td>
</tr>
<tr>
<td>Lactoferrin</td>
<td>1.84 mg/mL</td>
<td>0.17-0.28 mg/mL</td>
</tr>
<tr>
<td>Albumin</td>
<td>1.3 mg/mL</td>
<td>41-51 mg/mL</td>
</tr>
<tr>
<td>IgA</td>
<td>0.30 mg/mL</td>
<td>0.93-3.93 mg/mL</td>
</tr>
<tr>
<td>IgD</td>
<td>ND</td>
<td>0.03 mg/mL</td>
</tr>
<tr>
<td>IgE</td>
<td>0.1 µg/mL</td>
<td>0.4 µg/mL</td>
</tr>
<tr>
<td>IgG</td>
<td>0.126 mg/mL</td>
<td>8.61-17.47 mg/mL</td>
</tr>
<tr>
<td>IgM</td>
<td>8.86 µg/mL</td>
<td>0.33-1.83 mg/mL</td>
</tr>
<tr>
<td><strong>Antioxidants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CuZn-SOD</td>
<td>103 ng/mg protein</td>
<td>ND</td>
</tr>
<tr>
<td><strong>Growth Factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGF-α (males)</td>
<td>247 pg/mL</td>
<td>147 pg/mL</td>
</tr>
<tr>
<td>TGF-α (females)</td>
<td>180 pg/mL</td>
<td>147 pg/mL</td>
</tr>
<tr>
<td>TGF-β</td>
<td>ND</td>
<td>140.3 ng/mL</td>
</tr>
<tr>
<td>TGF-β1*</td>
<td>2.32 ng/mL</td>
<td>-</td>
</tr>
<tr>
<td>TGF-β2</td>
<td>55 pg/mL</td>
<td>-</td>
</tr>
<tr>
<td><strong>Vitamins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin A</td>
<td>16 ng/mL</td>
<td>200-500 ng/mL</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>117 µg/mL</td>
<td>5-9 µg/mL</td>
</tr>
<tr>
<td><strong>Carbohydrate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>26 mg/L</td>
<td>0.6-1.2 g/L</td>
</tr>
<tr>
<td><strong>Electrolytes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na⁺</td>
<td>148.5 mM</td>
<td>138-145 mM</td>
</tr>
<tr>
<td>K⁺</td>
<td>18.7 mM</td>
<td>3.6-4.8 mM</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>1.73 mM</td>
<td>8.8-10.1 mM</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>112 mM</td>
<td>101-108 mM</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>26 mM</td>
<td>21-29 mM</td>
</tr>
<tr>
<td>NO₃⁻</td>
<td>0.14 mM</td>
<td>0.19 mM</td>
</tr>
<tr>
<td>PO₄³⁻</td>
<td>0.22 mM</td>
<td>1.42 mM</td>
</tr>
<tr>
<td>SO₄²⁻</td>
<td>0.39 mM</td>
<td>0.53 mM</td>
</tr>
</tbody>
</table>

CuZn-SOD = Cu, Zn super-oxide dismutase; EGF = epidermal growth factor; TGF = transforming growth factor; ND = not detected.

¹Each value is the normal concentration in serum.
²Acid-activated tear.

These components are present in red blood cells at high concentration.

venepuncture multiple times per year and to resist blood loss. People with unstable angina, a recent myocardial infarction or cerebrovascular accident, a significant cardiac or pulmonary disease with chronic symptoms who have not been evaluated by the treating physician, untreated aortic aneurysms, and others are occasionally excluded explicitly from blood donation by blood collection facilities.⁴

It is strongly advised to perform donor’s blood-transmitted diseases (e.g., human immunodeficiency virus [HIV], hepatitis B virus [HBV], hepatitis C virus [HCV], and syphilis), that hospital staff is cautious of serum production, and that the identity of the recipient is confirmed in order to reduce the risk of viral transmission to others (e.g., production or nursing staff, children at home who may unintentionally use serum eye). There is no consensus regarding whether people with blood-transmissible diseases should be prohibited from donating serum when medically necessary, even though there are significant legal repercussions associated with the potential transmission of serum-based diseases to recipients of the serum as well as the medical staff.⁴,²¹

Current clinical practice in using ASEDs for DED

According to Shtein et al. (2020), ASEDs are viable for people with dry eyes or epithelial abnormalities that will not repair.⁹ Indonesian Ophthalmologist Association suggested the use of ASEDs for severe DED patients with TIBUT scores ≤5 seconds. Patients receiving 20% to 50% have observed subjective improvement in dry eye symptoms. Generally, doctors will decide the dosage according to the patient’s need. The number of dosages per day ranged from four to eight times, noted objective improvement based on fluorescein staining and the results of break-up time tests.²⁰ Fluorescein staining of the cornea, a decreased sense of foreign bodies, and a decreased sense of burning were the top 3 signs and symptoms indicative of treatment response.³ The improvement begins soon after the therapy (from 1 to 4 weeks).¹¹

Autologous serum eye drops are distinct from other ophthalmic treatments in that they are created especially for each patient from their blood. Different nations have different laws governing the donation of autologous blood. There is currently no federal protocol and no requirements in the United States for using or preparing ASEDs, though some states have regulations.⁹ Center for Biologics Evaluation and Research (CBER) of the FDA regulated in terms of blood intended for transfusion and blood derivatives.⁴ In the UK, National Health Service Blood and Transplant (NHSBT) has offered ASEDs service since 2014.¹⁶ Until now, the Indonesian government does not have specific regulations on the use of ASEDs as a dry eye treatment. However, the dry eye consensus by the Indonesian Ophthalmologist Association has included ASEDs as a DED treatment and some hospital in Indonesia has already made this an option of treatment.⁶

Issues in ASEDs

Autologous serum eye drops are typically well tolerated, with most recipients reporting less discomfort. Since serum-
based solutions are essentially growth media, the main safety concern for ASEDs is the risk of microbial growth during preparation, storage, and use. Patients may occasionally experience increased discomfort, mild epitheliopathy (dropout of corneal epithelial cells, similar to fluorescein staining of the eye's surface), bacterial conjunctivitis, or eyelid eczema. Thanathanee et al. reported that 6.1% of the cultures were positive for bacteria or fungi in 100% concentration of ASEDs used throughout the study, but none of the patients developed any symptoms of ocular infection. The antimicrobial effect of the serum, the patient's innate immune response, and an intact corneal epithelium might be the reasons behind this condition. When prepared and stored according to a stringent methodology, ASEDs can be utilized safely in both inpatient and outpatient settings. The addition of lyoprotectant, which is then lyophilized using the freeze-drying procedure to create a dry autologous serum, is a strategy to increase the shelf life of autologous serum. The stability of autologous serum can be improved by drying it for up to 3 months of storage.

In terms of blood collecting, it may not be possible to collect enough blood due to patient-specific factors such as inadequate venous access, low hemoglobin levels, needle phobia, advanced age, or limited mobility. Other issues related to its use are that studies have not looked at the ideal frequency and/or length of ASEDs for a particular therapeutic indication and an appropriate time to stop the treatment. A professional and well-trained lab technician is needed in the manufacturing process, although doctors supervise the product quality. By this highly maintained procedure and limited regulation, ASEDs are categorized as a high-cost treatment and generally not covered by medical insurance. This made ASEDs limited to severe cases only. To support the benefit of ASEDs, comprehensive guidelines and regulations should be made in Indonesia.

CONCLUSION
The prevalence of dry eye is expected to rise as the population ages, but the condition is frequently misdiagnosed and undertreated. Dry eye also impacts workplace productivity by making it more challenging to use a computer or read for extended periods, decreasing tolerance for certain environments, and reducing work time. Most patients of ASEDs indicate that their discomfort has improved, and ASEDs are typically well tolerated as no negative symptoms have been reported due to the treatment. The use of ASEDs is consequently restricted to more severe cases or those who have not improved with more widely accessible and less expensive treatments because of their limited accessibility and high cost. According to the findings of the studies published in the peer-reviewed literature, this therapy is a viable choice for people who have dry eyes or epithelial abnormalities that will not repair.

CONFLICT OF INTEREST
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REFERENCES

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