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REVIEW

Autologous blood in the management of ocular surface disorders

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Abstract

Autologous blood therapy has emerged as a promising modality in managing ocular surface disorders. This review provides a comprehensive overview of the current literature regarding the use of autologous blood in ocular surface disorders, encompassing its physiological basis, clinical applications, techniques, challenges, and future perspectives. The ocular surface, comprising the cornea, conjunctiva, and tear film, plays a critical role in maintaining visual function, and its disruption can lead to various pathological conditions. With its rich composition of growth factors, cytokines, and other bioactive molecules, autologous blood offers therapeutic potential in promoting corneal wound healing, reducing inflammation, and improving tear film stability. Clinical studies have demonstrated the efficacy and safety of autologous blood therapy in diverse ocular surface disorders, including persistent epithelial defects, neurotrophic keratopathy, and dry eye disease. However, challenges such as variability in treatment response, adverse effects, and optimal patient selection remain areas of concern. Further

research is needed to elucidate the underlying mechanisms of action, refine treatment protocols, and explore synergistic approaches with other therapeutic modalities. Despite these challenges, autologous blood therapy holds promise as a valuable adjunctive treatment option for ocular surface disorders, offering new avenues for improving patient outcomes and quality of life. This review examines the mechanisms underlying ocular surface disorders while discussing existing autologous blood-based therapies for managing these disorders. Current clinical trials are also summarized, and a comparison between autologous blood therapy and conventional eyedrops is attempted. Finally, safe techniques and protocols for autologous blood medicine are elucidated, and adverse effects and future perspectives of this novel therapy are reviewed.

Key Words: Autologous blood; Ocular surface disorder; Cytokines; Tear film; Dry eye

Core Tip: There are several reviews in the literature about autologous tissue therapy and its usefulness in eye care including stem cells and tissue transplants. Blood derivatives are playing a progressively significant role in management of ocular surface disorders. This paper reviews studies on autologous blood use in ocular surface disorders, its preparation and administration, patient selection and potential side effects. Recent clinical trials are also reviewed and future considerations are discussed.

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INTRODUCTION

Ocular surface diseases (OSD) are disorders plaguing the surface structures of the eyes; namely the conjunctiva, cornea, and tear glands[1]. The most common manifestations of OSDs are dry eyes and blepharoconjunctivitis. OSDs usually present with gritty sensations, redness, mucous or stringy discharge, occasional blurry vision, and excessive tearing. OSDs often lead to visual impairment and consequently reduced quality of living[2]. Although autologous blood medicine has been known for centuries, its use in the care of OSD is relatively novel and has not been extensively reviewed. The authors sought to review all publications on autologous blood used in ocular surface disorders.

Anatomy and physiology of the ocular surface

The ocular surface constitutes the boundary between the most anterior ocular tissues and the external surroundings. It is most anteriorly lined by squamous epithelial cells and protected from foreign objects and desiccation by the reflex shutting of the lids. The eyelids are a door-like structure whose action dictates what enters the eye. The lids cover the anterior eye and divide into the superior and inferior lids, which are continuous with each other and with the skin and muscles of the face at the nasal and lateral canthi. The eyelids are like a hinged double door entrance regulator with hair follicles for eyelashes arranged in two to three rows at the point on the eyelid margin just anterior to the mucocutaneous junction. The mucocutaneous junction can be described as the transition point where the stratified squamous epithelial of the skin is replaced by the cuboidal epithelial cells of the conjunctival[3]. The opening and shutting of the eyelids are enabled by the levator palpebral superioris, and the orbicularis oculi respectively. The orbicularis oculi inserts posterior to the subcutaneous tissue of the eyelid and anterior to the tarsal plate. The meibomian gland has its origin in the tarsal plate. It has its excretory ducts running through the tarsal plate in an imperfect straight line-like manner and end up as orifices at the lid margin *via* which its secretions (meibum) are discharged. The meibomian gland secretes the outermost layer of the tear film, and there are approximately 40 to 50 meibomian glands in the upper lid and 20 to 30 meibomian glands in the lower lid[4]. The glands of Moll and Zeis are both exocrine glands that maintain the health of the lids and lashes. The Zeis gland is a unilobar sebaceous gland, located at the anterior aspect of the eyelash base in the lid margin, while the Moll gland is a modified apocrine sweat gland located at the posterior aspect of the base of the cilia[5].

The conjunctiva is a translucent, well-vascularised mucous membrane that extends from the mucocutaneous junction at the lid margins and is continuous throughout the ocular surface until its epithelium becomes continuous with the cornea epithelium at the corneoscleral junction. As it extends from the mucocutaneous junction, it is named according to the part of the ocular surface it covers namely; the palpebral, fornix, and bulbar conjunctiva. The palpebral conjunctiva is firmly attached to the underlying tarsal plate while the bulbar conjunctival is loosely connected to the tenons capsule which links the conjunctival to the underlying sclera[5]. At the nasal canthus, the bulbar conjunctival makes a small crescent fold known as the plica semilunaris, and just nasal to it, is a small, mildly elevated, pink-yellowish nodule that consists of a mixture of tissues called the caruncle or caruncular lacrimalis. Histologically, the conjunctival epithelium is three to five cells thick and its basal cells are made up of cuboidal cells which subsequently become polyhedral flattened

cells as they ascend more superficially[5]. The conjunctival epithelium consists of non-keratinized stratified squamous epithelia and stratified columnar cells. Goblet cells are scattered throughout the epithelium, having their greatest density in the inferonasal aspect of the conjunctival epithelium[6]. The conjunctival stromal or subtantia propria which is the deeper part of the conjunctiva consists of a more superficial adenoid layer and a deep fibrous layer, and the accessory lacrimal glands of Krause and Wolfring are located in the deeper fibrous layer. Numerous immune cells such as monocytes, neutrophils, plasma cells, and T and B lymphocytes are present within the conjunctival. However, blood vessels and lymph channels that empty into the pre-auricular and submandibular lymph nodes are found in the epithelium. While the deeper layer of the conjunctival stromal contains nerve supply and deeper blood vessels.

The conjunctival epithelium becomes continuous with cornea epithelial cells at the limbus. Stellate symmetric ridges found at the limbus form the palisades of Vogt, which is considered a reservoir for cornea stem cells[7]. The cornea is a transparent, absolute avascular, curved refractive tissue. The avascularity of the cornea is maintained by several factors including the absence of blood vessels, the manner of stromal fibrillar arrangement, and the cornea endothelium pump action. This 'no-blood' vessel status is necessary to maintain its transparency and refractive status. The cornea can further be described as the refractive powerhouse of the eye. It possesses an average refractive power of 43.00 DS, constituting about 75% of the total refractive power of the eye[8]. The cornea is divided into five layers namely; the epithelium, bowman's membrane, stromal, descemet membrane, and endothelium.

The cornea epithelium is about 50 μm thick and consists of five to seven layers of cells. The outermost layer of the cornea epithelium is made up of non-keratinized squamous epithelial cells. The cells of the cornea epithelial surface regulate the movement of substances into the cornea through the tears. These cells are attached at their lateral walls, close to the surface of the cell facing the lumen by tight junctions also known as zonular occludens[9]. This barrier complex forms an effective semi-permeable membrane that allows certain substrates through into the cornea. Furthermore, the surface epithelial cells produce a thick glue-like transcellular barrier known as glycocalyx; which helps to adjoin the mucin layer of the tears to the cornea epithelial surface[10]. Moreover, the surface epithelial cells possess finger-like (microvilli) and ridge-like (microplicae) projections which aid in fastening the precorneal tear film to the cornea epithelial surface. The middle layer of the cornea epithelium consists of polyhedral-shaped wing cells which are attached each to other by gap junctions and desmosomes, and to the underlying germinal basal layer by desmosomes. The basal layer of the corneal epithelium consists of a single layer of columnar cells. The basal layer is where mitosis occurs, thus, older basal cells move up to the middle layer to become rhombic-like wing cells and subsequently to the epithelial surface where they are finally sloughed off due to aging or epithelial erosion.

The pre-cornea tear film is three-layered namely; the lipid layer, the aqueous layer, and the mucin layer. The tear film is coated anteriorly by the secretion from the meibomian gland. This layer of the tear film ensures that the integrity of the precorneal tear film remains intact. The aqueous aspect of the tear film is produced chiefly by the lacrimal gland with additions from the accessory lacrimal glands. The innermost layer which adjoins the precorneal tear film to the cornea surface epithelium is produced by the goblet cells scattered throughout the conjunctival epithelium.

The anatomical orientation of the ocular surface structures is designed in such a way that confers on the globe the ability to protect, regulate entrance, lubricate, and refract light rays. The eyelids shut against invading foreign objects consequently, fortifying the eye from foreign entities which could pose significant injury and health risks to the globe. The precorneal tear film is a mixture consisting of epitheliotrophic factors[11]. In patients with ocular surface disorders, the keratinocyte morphology and function are affected, making the use of tear substitutes inadequate in addressing the problem of OSDs[12,13].

Composition of blood components

Blood is a multifaceted fluid composed of several elements that collaborate to maintain homeostasis and support various physiological functions. The main components of blood are red blood cells, white blood cells, platelets, and plasma. Red blood cells, or erythrocytes, are the most prevalent cellular element, responsible for carrying oxygen from the lungs to body tissues and aiding in the removal of carbon dioxide. White blood cells, or leukocytes, are essential for the immune response, protecting the body against pathogens and foreign invaders. Platelets, or thrombocytes, are small cell fragments that facilitate blood clotting and wound healing. Plasma, the liquid part of blood, acts as a medium for transporting nutrients, hormones, and waste products, and helps maintain electrolyte balance and pH levels[14]. Each component of blood is essential for overall health and well-being, contributing to the body's ability to function properly and respond to various challenges. Numerous studies have extensively explored the functions and characteristics of these blood components, highlighting their importance in health and disease[15-17].

Mechanisms underlying ocular surface disorders

The various pathways through which the diseases of the ocular surface structures exert their pathological changes on the ocular surface are dependent on the type and nature of ocular morbidity, severity, and the ocular surface structure involved. However, these pathogenic processes are often initiated secondary to the breakdown of the ocular surface defense system offered by the tear film. The breakdown of the precorneal tear film integrity can result from cellular infiltration of the serous glands[18], fibrosis of the serous glands[19], prolonged and subsequently auto-sustained inflammatory reaction of the ocular surface from activated acquired immunity as well as conjunctival epithelia metaplasia[20,21]. Other etiologic factors include iatrogenic factors[22], graft *versus* host disease, chronic meibomian dysfunction, trauma, hormonal and nutritional deficiencies, and drugs.

This review investigates the mechanisms that cause ocular surface abnormalities and explores the current autologous blood-based therapies used to treat these problems. The present study provides a concise overview of ongoing clinical trials, aiming to compare the effectiveness of autologous blood therapy with traditional eyedrops. The text provides a comprehensive explanation of the safe processes and protocols used in autologous blood medicine. It also examines the

potential adverse effects and future prospects of this innovative therapy.

METHODOLOGY

Only full-length papers published in English language were used for this review. The PubMed (https://pubmed.ncbi.nlm.nih.gov) database was queried using the keywords "autologous blood ocular surface disease", generating the following search algorithm; ("autolog"[All Fields] OR "autologeous"[All Fields] OR "autologic"[All Fields] OR "autological"[All Fields] OR "autologous"[All Fields] OR "autologously"[All Fields]) AND ("blood"[MeSH Subheading] OR "blood"[All Fields] OR "blood"[MeSH Terms] OR "bloods"[All Fields] OR "haematology"[All Fields] OR "hematology"[MeSH Terms] OR "hematology"[All Fields] OR "haematoma"[All Fields] OR "hematoma"[MeSH Terms] OR "hematoma"[All Fields] OR "haemorrhage"[All Fields] OR "hemorrhage"[MeSH Terms] OR "hemorrhage"[All Fields] OR "haemorrhages"[All Fields] OR "hemorrhages"[All Fields] OR "haemorrhagic"[All Fields] OR "haemorrhaging"[All Fields] OR "hematologies"[All Fields] OR "haematomas"[All Fields] OR "hematomas"[All Fields] OR "hematoma s"[All Fields] OR "hematomae"[All Fields] OR "hemorrhaged"[All Fields] OR "hemorrhagic"[All Fields] OR "hemorrhagical"[All Fields] OR "hemorrhaging"[All Fields]) AND ("ocul surf"[Journal] OR ("ocular"[All Fields] AND "surface"[All Fields]) OR "ocular surface"[All Fields]) AND ("disease"[MeSH Terms] OR "disease"[All Fields] OR "diseases"[All Fields] OR "disease s"[All Fields] OR "diseased"[All Fields]). All publications retrieved were screened for relevance and eligibility by three authors (Suleman A, Aluyi-Osa G, and Musa M). A total of 169 publications were retrieved. 2 records were excluded for not having abstracts while 11 were out of scope.

Study selection

Three authors examined the extracted results for uniqueness, relevance to the topic, language, and content. Where one of the authors flagged a study as out of scope, the other reviewer was allowed to re-scrutinize before discarding the publication. There was no duration restriction on papers, but only papers in English language were included.

Results

Hence 153 manuscripts were included in this paper as shown in the PRISMA[23] diagram below. The guidelines of the PRISMA 2020 statement have been followed in this study (Figure 1).

MECHANISM OF ACTION

The mechanism of action of autologous blood is the promotion of cellular differentiation, proliferation, and migration of these cells due to the presence of very metabolically active substances such as growth factors, immunoglobulins, fibronectin, vitamins A, and anti-proteases[24-27]. Autologous blood therapy also supplies cytokines and growth factors that are found lacking in natural[28]. Autologous serum has been used in the development of cornea and oral epithelial cells making the case for its role in the proliferation of epithelial cells[29,30].

Autologous blood is usually used to treat persistent cornea defects and dry eyes. Still, it has also been shown to be effective in the management of superior limbic keratoconjunctivitis, recurrent erosion syndrome, aniridic keratopathy neurotrophic keratopathy, graft *versus* host disease, ocular cicatricial pemphigoid, Mooren's ulcer, filtering bleb post trabeculotomy and post-keratorefractive surgery[31,32]. In dry eyes the epitheliotrophic factors (fibronectin, growth factors, and vitamins) are reduced hence leaving the ocular surface at risk of infections, reduced optical properties, and persistent epithelial defect.

Shtein *et al*[33] in their review of 10 studies of the effect of autologous serum-based eyedrops on dry eyes and 4 studies of the effect on persistent epithelial defect showed that the majority of the studies reported a great improvement in symptoms, signs, or both. Unpreserved blood serum has shown similar properties to the tears hence the use of autologous blood serum in treating OSD[34,35]. The tears in basic terms is properly filtered blood[36]. In challenging and recalcitrant cases autologous blood has been used to reduce symptoms[37]. Thermally treated immunosafe autologous blood containing plasma rich in growth factors (PRGF) and eyedrops enriched in autologous growth factors have been shown to have promising results in treating cicatrizing conjunctivitis, and Sjogren syndrome[38-41].

Higuchi[42] showed a new serum protein selenoprotein which proved to be more efficacious in the treatment of dry eye by showing a better cornea fluorescein score and reduced cornea oxidative stress in eyes when it was applied compared to phosphate-buffered saline. Studies showed that when autologous blood is used as a therapy for dry eyes, there is a resulting improvement in tear stability, as seen by better staining scores under the slip lamp corneal examination[43,44]. Some reports showed that 20% autologous serum is effective in the management of epitheliopathy caused by antiglaucoma eyedrops[45,46]. Anitua *et al*[47] in their study, proved that PRGF improved the ocular surface wound healing and reduced scar formation better compared to autologous serum or insulin therapy. Autologous blood therapy has been shown to reduce the expression of mucin5AC (tumor-associated mucin) in the cornea amongst patients with limbal stem-cell deficiency and improve patient symptomatic perception, especially in those whose cornea was mildly affected before treatment initiation[48].

López-García *et al*[49] in a prospective study, showed improvement in ocular symptoms in patients with keratopathy associated with aniridia when autologous serum eyedrops were used. Autologous blood serum has also been found effective in treating neurotrophic keratopathy, resulting in epithelial healing. This led to the belief that autologous blood

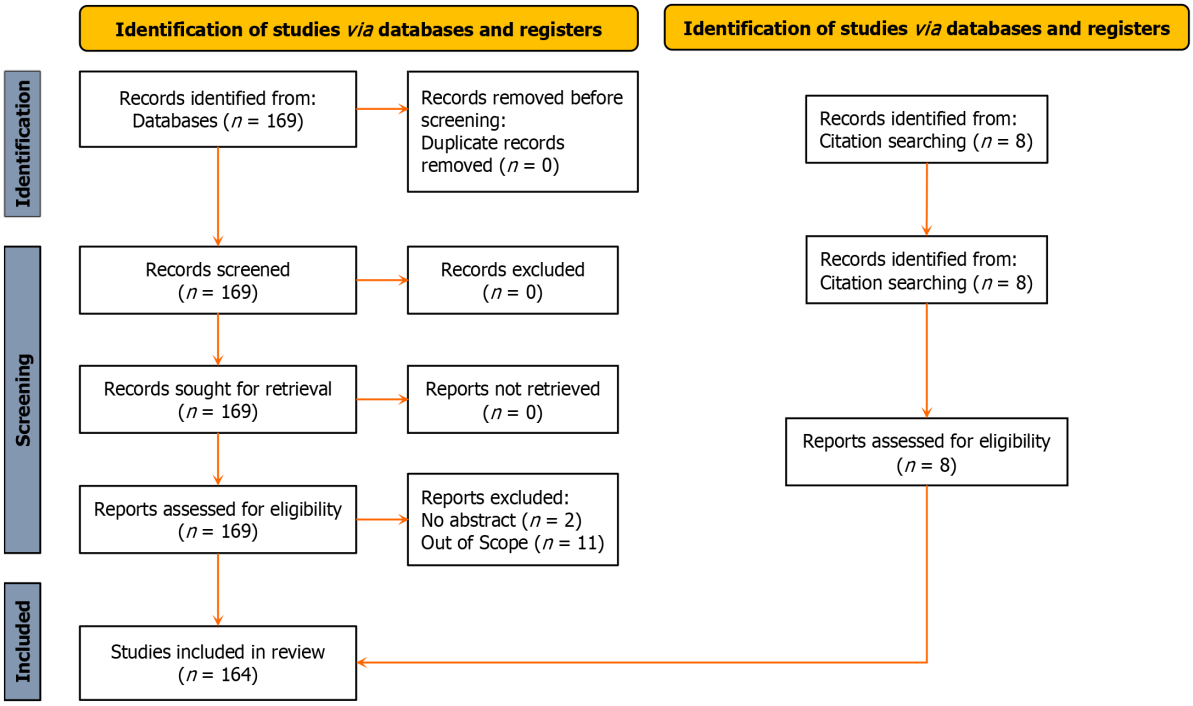

Figure 1 Selection of publications used for the review.

contains neurotrophic properties[50]. *In vivo* confocal microscopy has revealed early evidence that autologous plasma therapy can improve cornea nerve regeneration, this is beneficial in patients with neurotrophic keratopathy[51]. Mucin serum and retinoic acid are important components in the maintenance of healthy ocular surface[52]. In their work, Alio *et al*[22] found out that autologous serum eyedrops are effective management plan for post-lasik associated keratopathy. Patients who have undergone a corneal transplant are at risk of significant ocular morbidity in the healing phase[53-55]. They reported an amelioration of symptoms with this novel therapy. In patients with systemic autoimmune diseases that present with dry eye diseases, autologous serum therapy has been shown to improve both subjective and objective findings[56-59]. In patients with recurrent epithelial defects, autologous blood serum has been found to be useful when combined with contact lenses[60].

CLINICAL AND RESEARCH APPLICATIONS

Merayo-Lloves *et al*[61] and Anitua *et al*[62] in their retrospective cohort study, showed that PRGFs could be a safe and effective treatment of refractory OSD. The safety profile of autologous blood therapy in a hospital setting was proven true under strict protocol of storage and preparation[63]. In cases of ocular burn, autologous serum tears derived from the umbilical cord are more effective than artificial tears, as seen in the double-blind prospective randomized clinical control research by Kumar *et al*[64] and similar studies[65,66]. Edelmann *et al*[67] in a clinical trial carried out amongst dogs with spontaneous chronic cornea epithelial defects post epithelial debridement with diamond-burr showed no significant statistical difference in epithelization when using platelet-rich plasma or artificial tears. Mircheff *et al*[68] and Fea *et al*[69] in their clinical studies using *in vivo* confocal microscopy, confirmed that autologous platelet lysate eyedrops improved the ocular surface disease indices in patients with primary Sjogren syndrome. Other researchers have gone as far as recommending the autologous blood is adopted as a standard of care therapy for ocular surface wound healing[70]. Studies have been carried out to ascertain the effectiveness of platelet-rich fibrin derivative as compared to the human amniotic membrane, they found out that platelet-rich fibrin had more efficacy, probably due to its anatomical and chemical makeup[71-74]. Noble *et al*[75] in their randomized controlled trial, showed that autologous blood therapy (ABT) proved beneficial to patients with severe ocular surface disorders, as most patients reported improvement in symptoms.

Urzua *et al*[76] in a randomized double-blind clinical trial, proved that autologous serum in the short term provided better symptomatic relief in comparison to conventional artificial tears. Comparison of the autologous serum and plasma-rich protein in terms of epitheliotrophic properties showed negligible difference in baseline conditions. Platelet rich plasma is usually easier to prepare hence it is a viable substitute for autologous serum[77,78]. Rawat *et al*[79] showed that autologous platelet rich plasma was more effective in the management of moderate to severe OSDs. Platelet rich plasma lysate have also been indicated in the management of OSDs[80,81] In comparison with artificial tear substitutes, there is low evidence of their efficacy in managing dry eye diseases[82]. Randomized controlled trials have shown that there is a better improvement in OSDI scores when autologous blood therapy is used compared to artificial tears[83,84]. The effect of amniotic membrane suspension and autologous serum varies from individual to individual, depending on individual

growth factor concentration[85-88]. Semeraro *et al*[89] in their clinical trial, showed that 50% blood serum improved the signs and symptoms of patients formally treated by conventional therapy. Zheng and Zhu[90] also suggested autologous serum eyedrops to be more effective than artificial tears in treating complaints associated with moderate to very severe dry eyes, and might therefore be a better option.

Factors influencing patient selection include: (1) The severity of the ocular surface disorder: Patients with moderate to severe OSDs who didn't respond well to conventional therapy could benefit from autologous blood therapy; (2) Certain types of dry eye disease that other treatments may not have helped such as dry eyes secondary to meibomian gland dysfunction or aqueous deficiency; (3) Cornea epithelial damage, recurrent erosion of the cornea, or persistent defect of the epithelial despite the use of standard therapy; (4) Patients with an inflammatory component to OSD could benefit from ABT due to the anti-inflammatory properties present in autologous blood; (5) Patients with blood diseases who have contraindications to blood collection are not recommended for ABT; (6) The patient's willingness to undergo the procedure involved in ABT[91]; (7) Techniques and protocols for autologous blood preparation and administration; (8) Blood component differentiation and separation was pioneered in 1960[92]. While there are several ways blood can be collected for ocular therapy, two major routes are; (9) Fingerprick method; here blood is collected by pricking the fingers and the blood collected is applied on the lower fornix[93]. This method has been advocated by several authors to be efficacious especially in the absence of serum[94-96]; and (10) Blood collection *via* the arm; here the blood is collected directly from the arm of the patient usually consisting of plasma and platelet concentrates after preparation from the initial peripheral blood[97].

Routes of administration

Generally, the route of administration of ABT is topical, applying the serum directly on the ocular surface is usually done frequently to improve discomfort experienced by the patient[98]. The amount of times it would be applied depends on the degree of discomfort and symptoms experienced by patients[99,100]. In some studies, they confirmed that the sub-conjunctival surface can also be a route of application of autologous blood concentrate in the treatment of ocular burn, and this might even be a more economical and practical technique[101-103].

Adverse effects and complications

Success has been reported in most of the cases in published literature, with a few rare complications[104]. The limitations of ABT are the cost and inconvenience of obtaining blood-derived products[105,106], and the paucity of data with strong evidence from randomized double-masked clinical studies supporting its use[107-110]. Transmission of blood-borne diseases is possible if autologous serum is not aseptically acquired[111]. The lack of standardized protocol for blood collection, centrifugation, and other things needed makes it difficult to attain clinical use of autologous blood serum[112, 113]. One major challenge faced during outpatient therapy, is usually based on good manufacturing and delivery medium from the point of production to centers these autologous blood serums are finally utilized[114-116]. In line with this challenge of storage of autologous serum, studies suggest that autologous serum can be stored for about 6 months in freezer conditions, without alteration in potency, and still be used to attain re-epithelization in cases of ocular surface anomaly[117-120]. More studies have to be done on the effect of different levels of immunosuppressives on ocular surface integrity and symptomatic relief[121].

Variability in treatment response

There seems to be no significant difference in tear osmolality in patients with dry eye disease and those without dry eye disease who underwent autologous serum therapy[122]. Mesenchymal stem cell and limbal stem cell-derived autologous serum have been shown to have similar potency in treating OSD, as seen in the work carried out by Campbell *et al*[123]. Amniotic assisted conjunctival epithelial redirection, proves to be viable in reducing complications associated with the sequential sector conjunctiva epitheliopathy[124]. In some retrospective comparative case series, epithelial cells obtained from oral mucosa, are capable of staying on the cornea following transplantation, and maintain good corneal surface integrity[125]. Autologous serum eyedrops and allogenic serum eyedrops are almost equally effective in ameliorating symptoms and improving quality of life[126-129].

Integration with other treatment modalities

Umbilical cord blood or serum has been shown to contain a lot of biologically active chemicals that can nourish the ocular surface thus treating OSDs[130]. Hassan *et al*[94] in their feasibility studies, showed that autologous blood obtained from pricking the finger can be used as an adjunct to conventional medical therapy to improve the OSDI score.

Allogeneic blood therapy has also been shown to improve epitheliotrophic properties of the ocular surface in patients with OSDs similar to autologous blood therapy[131]. Calf blood extract gel has been shown to relieve dry eye symptoms in patients with chronic graft *versus* host disease due to its ability to promote healing and regeneration of epithelial cells [131,132]. Autologous blood therapy when used with punctal plugs has been shown to improve symptoms and signs in patients with chronic graft *versus* host disease refractory to artificial tears[133]. Autologous serum eyedrops obtained post-plasmapheresis and IV immunoglobulin infusion have been said to help manage patients with ocular complications secondary to toxic epidermal necrolysis[134].

Studies have isolated tumor necrosis factor as an inflammatory marker for dry eyes[135]. Tumor necrosis factor-inhibiting protein (a component of autologous blood lysate) has been found to help suppress signs related to Sjogren syndrome, by affecting histopathology of the lacrimal gland but having no effect on the conjunctiva tissues[136-139]. De-proteinized calf blood extract has also been reported to reduce the recovery time of patients who underwent pterygium excision, even when compared to the use of non-steroidal anti-inflammatory drugs, or even ocular lubricant[140]. The use

of autologous serum in cases of severe reduction in limbal stem cells secondary to contact lens used has been found to substitute for the need for surgical intervention, especially if attended to on time and aggressively[141,142]. It is important to note that prompt ophthalmic evaluation and an interdisciplinary approach to care are very important, especially in cases where transplantation of tissue is involved, in other to prevent progressive and subsequent vision deterioration[19].

FUTURE PERSPECTIVES AND DIRECTIONS

The use of autologous blood in the management of OSDs is affected by financial and logistic barriers[143]. The lack of proper regulation on the use of autologous blood serum in the eye care world makes its widespread use in the management of ocular surface disorders controversial[144]. There is limited information on the side effects of serum-based eyedrops, and modalities for monitoring need to be put in place if used should be to a large extent generalized for the treatment of OSD[145-147]. It is important to ensure strict monitoring of patients using autologous serum eyedrops that are not preserved, in other to avoid infection in the long run[148]. A standard protocol for the formulation should be adopted[149].

Potential advancements in autologous blood therapy and emerging research trends

Autologous serum-impregnated soft bandage contact lens shows promising results in the treatment of dye eyes stemming from autoimmune conditions like Sjogren syndrome[150]. Ang *et al*[151] showed that autologous serum-derived oral epithelial cells can be used for treating severe OSDs. Studies have also confirmed a dose-dependent effect of autologous serum on outcomes in dry eye diseases[152,153]. The use of isolated stem cells, through clonal analysis, has been found to also be effective in the treatment of corneal defects due to its ability to regenerate corneal tissue[154]. Some evidence also points to the effectiveness of complete autologous submandibular gland replacement, as it has been shown to have a good outcome, relieve symptoms, and improve quality of life[155-157]. Autologous tear serum has been found to affect the corneal nerve plexus as seen using *in-vivo* confocal microscopy[158,159]. Chiang *et al*[160] reported on a case series of patients treated with allogenic tear serum after suffering graft *versus* host disease. The use of corneal sheets mounted on platelet-poor plasma is an emerging trend in cases of limbal stem cell deficiency, and it helps in the treatment of bilateral ocular surface disorders[161-163]. Recent research has also been directed toward hemoderivatives including the platelets; associated with the platelets are the growth factors that are involved in the wound-healing process of the cornea and the conjunctiva[164].

The use of Xeno-feeder-free limbal stem cells in the treatment of ocular surface disorders is on its way, as it might be a potential substitute imminently, so more studies are being carried out in this regard[165]. Multiple research publications have found that a novel treatment (platelet-rich plasma) could ameliorate persistent epithelial defects and attributed it to the fact that it contains a lot of epidermal growth factor[166,167]. By the process of inducing the presence of anti-inflammatory mediators, dry eyes stemming from autoimmune conditions can be alleviated and this is a possible area of interest in the near future[168,169].

Considerations of long-term use of autologous blood therapy for ocular conditions

Wiącek *et al*[170] examined the long-term effects of autologous blood therapy in the management of retinitis pigmentosa by monitoring key indices at one month and then every quarter leading up to a year. They reported the therapy to be safe and efficacious over the one-year period. Lee and Chen[171] also evaluated the safety profile of long-term autologous blood therapy in managing chronic dry eye. They reported no significant complications even up to 17 months of constant use among a section of the cohort. Platelet-lysate drops, an autologous blood derivative, have also been reported to have long-term usefulness in the management of ocular graft *versus* host disease[172].

Limitations and challenges

While some smaller-scale data exists, the authors could not find studies on large-scale or multicenter experimental studies comparing autologous blood therapy to conventional drugs.

CONCLUSION

Autologous blood therapy in ocular surface disorder management presents an interesting proposition to the eye care industry. Autologous blood serum has successfully been used to manage many ocular surface disorders arising primarily secondary to other conditions and surgeries. The results of this review underscore the potential of autologous blood therapy to enhance patient outcomes in ocular surface disorders. Implementing this therapy in clinical practice could enhance healing, reduce inflammation, and improve the overall management of these disorders. It combines well with conventional medications and compares favorably with them. While it's widespread use is still hampered by regulations and the absence of a unanimous guideline for preparation and prescription.

FOOTNOTES

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