RESEARCH LETTER

Autologous artificial tears used for treatment of dry eye syndrome in patients with chronic graft versus host disease

Jolanta Antoniewicz-Papis, Elżbieta Lachert, Karolina Janik, Magdalena Łętowska

Department of Transfusion Medicine, Institute of Hematology and Transfusion Medicine, Warsaw, Poland

Introduction Dry eye syndrome (DES) is a multifactorial ocular disorder induced by insufficient tear secretion, enhanced evaporation, or abnormal composition.[1] Insufficient lubrication may cause ocular damage and epithelial exfoliation, resulting in visual disturbances, tear film instability, and ocular surface discomfort. Corneal and conjunctival epithelial defects enhance penetration of bacteria, viruses, and fungi and increase the risk of infection. Severe cases of DES involve ulcers, corneal and conjunctival perforations, and even loss of vision.

DES, currently observed in a growing number of patients, is associated with numerous diseases.[2] DES-related functional defects of the lacrimal gland have been reported, among others, in patients with chronic graft versus host disease (GVHD) following hematopoietic stem cell transplantation. Ocular lesions are among the most common complications of chronic GVHD, reported in up to 60% to 80% of patients.[3] Commercially available tear substitutes are not always effective, and sometimes contraindicated, owing to allergic reactions to the components used in these drops. In such cases, autologous serum can be considered as an alternative.

The aim of our study was to evaluate the efficacy of autologous artificial tears prepared from the serum of patients with DES and chronic GVHD who were allergic to commercially available tear drops.

Patients and methods The study was conducted over 4 years in 6 patients (3 women and 3 men; age, 19–56 years) after hematopoietic stem cell transplantation and with active chronic GVHD. During a single procedure, whole blood samples were collected at the volume of 150 ml, 300 ml, or 450 ml into a disposable quadruple set of bags routinely used in blood donation. Prior to collection, the anticoagulant was removed under sterile conditions. The volume of collected blood depended on the patient's general condition. Patients were subjected to several blood collection procedures, from 1 to 11, depending on the severity of DES and the decision of the responsible ophthalmologist. Serum obtained from whole blood was divided into 0.5-ml capsules, which were then separately frozen and stored at a temperature of –20°C.

Results A total of 22 procedures were performed; during 17 procedures, 300 ml of blood was collected; during 4 procedures, 150 ml; and during 1 procedure, 450 ml. Two patients were subjected to 1 procedure each, and the other 4 patients had either 2, 3, 4, or 11 procedures. The number of procedures depended mainly on the patients' subjective evaluation of symptoms and the frequency of application of eye drops. We observed no relation between the number of procedures and the effectiveness of treatment. During each procedure, a mean (SD) of 962 (178) single capsules were obtained. The frequency of eye drop application depended on the condition of the eye; it was usually applied several times a day with at least 3-hour intervals. Treatment efficacy was evaluated using a self-completed questionnaire. The results are presented in TABLE 1. No adverse reactions were reported.

Discussion The results of our study suggest the therapeutic potential of autologous artificial tears for the management of patients with DES and chronic GVHD after hematopoietic stem cell transplantation. According to the patients' self-assessment, a regular application of artificial tears resulted in a marked improvement of visual comfort and acuity. Patients no longer complained of eye pain and itching, and reported relief of eye redness. Similar results were presented by Pezzotta et al.[3] After the 3-year application of

Correspondence to:
Jolanta Antoniewicz-Papis, PhD,
Zakład Transfuzjologii, Instytut Hematologii i Transfuzjologii,
ul. Indiry Gandhi 14,
02-776 Warszawa, Poland,
email: jpapis@ihit.waw.pl
Received: August 21, 2017.
Revision accepted: October 6, 2017.
Published online: October 30, 2017.
Conflict of interests: none declared.
Pol Arch Intern Med. 2017;
127 (10): 705-707
doi:10.20452/pamw.4127

TABLE 1 Patients' self-assessment of the efficacy of artificial tears prepared from autologous serum

Eye symptoms	Relief of symptoms
Aching sensation	5 (83.3)
Itching	6 (100)
Burning sensation	6 (100)
Redness	5 (83.3)
Better visual acuity	5 (83.3)

Data are presented as number (percentage) of patients.

artificial tears, patients with DES after stem cell transplantation reported a reduction of symptoms on the Glaucoma Symptom Scale, which indicated improved visual comfort. However, sometimes it is impossible to collect autologous blood to prepare artificial tears, as in patients with infectious disease, those using medicines, or those with a difficult venous access. Therefore, some countries have allowed the use of allogenic artificial tears.[4,5]

In the recent years, DES has become an increasingly common problem for many patients, especially those hypersensitive to substances present in commercial tear substitutes.[6] One such special group are patients with DES who develop GVHD after hematopoietic stem cell transplantation. For such patients, artificial tears prepared from the patient's own blood seem to be the treatment of choice.

Autologous artificial tears are mostly prepared from serum due to its composition and properties. Serum itself and serum-derived artificial tears contain numerous growth factors, interleukins, and vitamins that alone or in combination induce the healing of tear film damage.[7,8]

Autologous artificial tears are free of coagulation factors that are removed in the process of coagulation. After their application, patients report relief from eye itching and burn. Growth factors and healing substances in artificial tears prepared from the patient's own serum enhance the regeneration of the damaged epithelium. Commercially available eye drops have no such properties. Moreover, autologous artificial tears contain no preservatives and therefore cause no allergic reactions. Their biomechanical and biochemical properties, as well as osmolarity and serum pH, are comparable to those of natural tears. Patients with DES reported significant improvement and symptom relief. However, the inconvenience of drains for tear drop application was also reported, although there were no such complaints in our study.[6]

Adverse reactions related to application of artificial tears are rather difficult to assess, so no wonder patients rarely report such reactions. Any adverse reaction observed by the patient may be related to the underlying disease, other concomitant therapies, or inadequate application of eye drops by the patients themselves.[6]

Artificial tears can serve as an alternative to conventional DES treatment. Our own research and other studies have demonstrated a growing demand for the product.[6] This explains why in some countries artificial tears are prepared also from the allogenic serum of healthy blood donors.

So far, no universal method for the preparation of artificial tears has been developed, either from autologous or from allogenic blood.[4,6,9] On the one hand, allogenic components pose the risk of immunological incompatibilities that may affect not only the ABO system but also human leukocyte antigens (HLAs). A variety of solutions are therefore being discussed, one of which is to prepare serum exclusively from ABO-compatible donors, and only from men with no history of blood transfusions (HLAs are less likely).[5] On the other hand, allogenic artificial tears are said to have an advantage over autologous tears because the latter come from patients with autoimmune diseases and therefore may have traces of medicinal products.[10]

There have also been studies on the use of platelet-rich plasma. Zallio et al[11] investigated platelet lysate obtained after freezing and thawing of platelet-rich plasma and reported promising results with the application of such components. An additional benefit is the higher content of growth factors released from platelets during lysis.

However, it seems to be necessary to implement standardized methods for preparing artificial tears as well as to unify the quality standards.[9,12] Moreover, it would be advisable to routinely determine the cytokine content in patients' blood to improve the clinical effects.[7,10] It is our intention to perform such studies.

In conclusion, based on our own observations and with full awareness of the limitations of our study, we believe that autologous artificial tears can be considered a safe and effective supportive therapy for patients with chronic GVHD and coexisting DES. They effectively moisturize the eyeball and bring relief, with no adverse reactions having been reported.

REFERENCES

1 Ambroziak AM, Szaflik J, Szaflik JP, et al. Immunomodulation on the ocular surface: a review. Centr Eur J Immunol. 2016; 41: 195-208.

2 von Hofsten J, Egardt M, Zetterberg M. The use of autologous serum for the treatment of ocular surface disease at a Swedish tertiary referral center. Int Med Case Rep. J 2016; 9: 47-54.

3 Pezotta S, Del Fante C, Scudeller L, et al. Long-term safety and efficacy of autologous platelet lysate drops for treatment of ocular GVHD. Bone Marrow Transpl. 2017; 52: 101-106.

4 Espinoza A, Hjorth-Hansen H, Aasly K, et al. Implementation of a standardized method for the production of allogenic serum eye drops from regular blood donors in a Norwegian University Hospital: Some methodological aspects and clinical considerations. Transf Aph Sci. 2015; 53: 88-91.

5 Harristhøj LH, Nielsen C, Ullum H, et al. Ready-made allogenic ABO-specific serum eye drops: production from regular male blood donors, clinical routine, safety and efficacy. Acta Ophthalmol. 2014; 92: 783-786.

6 Marks DC, Fisher J, Mondy P, et al. Serum eye drop preparation in Australia: Current manufacturing practice. Transf Apher Sci. 2015; 53: 92-94.

7 Stenwall PA, Bergström M, Seiron P, et al. Improving the anti-inflammatory effect of serum eye drops using allogeneic serum permissive for regulatory T cell induction. Acta Ophthalmol. 2015; 93: 654-657.

8 Lopez-Garcia JS, Garcia-Lozano I, Rivas L, et al. Stability of growth factors in autologous serum eyedrops after long-term storage. Curr Eye Res. 2016; 41: 292-298.

9 van der Meer PF, Seghatchian J, Marks DC. Quality standards, safety and efficacy of blood-derived serum eye drops: a review. Transf Aph Sci. 2016; 54: 164-167.

10 Seghatchian J, Espinoza A, Burnouf T. Commentary on technical specifications and safety requirements of serum eye drops: Keeping a close eye on the content of cytokines. Transf Aph Sci. 2016; 54: 170-171.

11 Zallio F, Mazzucco L, Monaco F, et al. A single-center pilot prospective study of topical application of platelet-derived eye drops for patients with ocular chronic graft-versus-host disease. Biol Blood Marr Transpl. 2016; 22: 1664-1670.

12 Seghatchian J, van der Meer P. A concise overview of advances in therapeutic efficacy of serum eye drops and their alternatives to treat dry eye syndrome: verifying the narratives of clinical consistency beyond the periphery of international inconsistency on the methods of collection and application. Transf Aph Sci. 2015; 53: 85-87.