VIA MEDICA

REVIEW ARTICLE

Journal of Transfusion Medicine
2023, vol. 16, no. 1, 23–26
DOI: 10.5603/JTM.2023.0002

ISSN 1689-6017
e-ISSN 2080-1505

What's new in the field of serum-based eye drops

Joanna Janus, Katarzyna Chmielewska, Agata Mikołowska, Jolanta Antoniewicz-Papis

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

Summary

Worldwide serum-based eye drops are successfully used in the treatment of the Dry Eye Syndrome (DES). Autologous serum eye drops (ASEDs) are most common but allogenic eye drops were introduced in many countries mostly because of the COVID-19 pandemic. Not all aspects of the product formula have however been worked out so far. Each medical entity involved in the preparation, packaging and distribution of the product performs according to its own procedures.

Various actions have therefore been undertaken to standardize, harmonize and exchange the experience in this field. In 2022 the 5th edition of EDQM's Guide to the quality and safety of tissues and cells for human application was issued. Within the EU4Health Programme a new group for Recommendations and Guidance Documents for the Management of Substances of Human Origin (SoHO) in Hospitals is being formed. International cooperation of serum-based product users lead to the establishment of working group events — Workshops on the Eye Drops of Human Origin (EDHO) and Serum eye drop manufacturer's group.

Despite the widespread use of serum-based eye drops all over the world, in almost none of the countries, EU included, are there strict legal regulations for handling the product. It is therefore necessary to come up with a universal definition of artificial tears therapy and to determine specific procedures for the product preparation.

Key words: serum-based eye drops, autologous eye drops, allogenic eye drops, dry eye syndrome

J. Transf. Med. 2023; 16: 23–26

Introduction

Serum-based eye drops are successfully used in the treatment of Dry Eye Syndrome (DES) around the world. Artificial tears made from serum were first used in the 1970s and since then they gradually became more common. Most common are autologous serum eye drops (ASEDs) but in many countries allogenic eye drops were introduced due to COVID-19 pandemic. Frequently allogeneic drops were the only therapeutic option when autologous donations were limited to a minimum or even stopped altoghether.

European standards

Not all aspects of product formula have however been worked out. Each medical entity involved in the preparation, packaging and distribution of the product performs according to in-house

Correspondence address: mgr Joanna Janus, Department of Transfusion Medicine, Institute of Hematology and Transfusion Medicine, ul. Indiry Gandhi 14, 02–776 Warsaw, Poland, phone: +48 22 34 96 388, e-mail: jjanus@ihit.waw.pl

Translation: mgr Krystyna Dudziak

procedures. This applies to both autologous and allogeneic preparations [1, 2]. In December 2022 the 5th edition of *Guide to the quality and safety of tissues and cells for human application* was issued [3]. One of the chapters is dedicated to good practices for preparation of autologous and allogenic artificial tears. The edition of the Guide that first mentioned serum eye drops did not come forward with any strict rules to be applied by European countries but merely with guidelines.

Currently a group for Recommendations and Guidance Documents for the Management of Substances of Human Origin (SoHO) in Hospitals is being formed as part of EU4Health Programme for the period 2021–2027. The main aim is to strengthen the quality, safety and efficacy of SoHO in health care entities. The recommendations would refer to blood products, serum eye drops included [4].

International experience and cooperation

Working groups of ISBT are also involved in the development of consensus guidelines and expertise on regulations, methodology and clinical use of serum eye drops. On May 2022, Vienna hosted Workshops on the Eye Drops of Human Origin (EDHO) which had been planned for March 2020 but were postponed due to COVID-19 pandemic. The workshops were conducted both on-line and on-site and included over 80 participants. One of the topics were the results of ISBT survey provided by Australian Lifeblood showing how the methods/procedures of eye drop preparation vary between countries as does the source of serum/ /plasma (whole blood, cord blood, platelet lysate). The sessions also focused on the comparison of the human tears and serum tears, tissue engineering of lacrimal glands, different eye diseases that require EDHO as well as issues related to manufacture, labelling and processing. Several presentations referred to the advantages of introducing EDHO at early stages of the diseases for better results. The subject of allogeneic eye drops and their advantage over autologous drops was also addressed. One of the approaches to allogenic eye drops preparation is pooling and pathogen inactivation. Participants from many countries raised the crucial problem of the lack of regulations and classification of the EDHO — blood product, drug, pharmaceutical product [5].

The field of novel blood-derived products, including serum-based eye drops, still requires development and improvement. Recently, DES affects more and more patients, and so the serum eye drops therapy is gradually becoming more popular worldwide. The last several years have come up with numerous publications on artificial tears. Articles have also appeared on the International Society of Blood Transfusion (ISBT) Virtual Meeting 2022.

The center from Malaysia presented a poster referring to the use of autologous serum in the treatment of patients with chemical eye injury. Chemical injury to the eye may lead to permanent vision loss unless promptly recognized and treated. The paper presented the management outcome of a 29-year-old patient who suffered from explosion of high-pressure acetylene gas with damage to his eyes. The patient was treated with autologous eye serum. Saline hydration was administered immediately (pH dropped from 9.0 to 7.0 after administration of a total of 7 L of saline per eye [6]. Slit-lamp examination revealed bilateral eyelid edema, conjunctival damage, limbal ischemia, visualization inability while pupil and iris lesions were classified as grade IV chemical injury. Following saline hydration, the next stage of management was the use of topical antibiotics, steroids and commercial eye drops. Conventional therapy was ineffective so autologous serum eye drops (ASEDs) were introduced on the seventh day of injury. Drops were applied to each eye every 2 hours. After 4 months of treatment, the patient's visual acuity improved in both eyes.

The Institute of Hematology and Transfusion Medicine (IHTM), Warsaw, Poland presented the research on inactivation used in processing of allogenic "artificial" tears [7]. The aim was to analyze the opinions of patients regarding allogeneic "artificial tears", pathogen inactivated with the Mirasol system as well as their impact on vision-related quality of life.

Autologous "artificial tears" (from patient's serum) have been prepared at the Institute since 1991. Over the period of 30 years, 662 patients with eye disorders such as Sjögren's syndrome or graft-versus-host disease (GvHD) following allogeneic haematopoietic stem cell transplantation have benefited from this form of therapy. However, to prepare an autologous product is not always possible. Since 2021, the PRT system with Mirasol has been implemented for pathogen inactivation during preparation of allogeneic "artificial tears". This was caused by the threat brought about by the ever-present infectious agents and the necessity to strengthen microbiological safety of the product.

In 2021, 40 patients (9 men and 31 women) with Sjögren's syndrome (44%), dry eye syndrome (33%, GvHD (11%) and other diseases such as glaucoma or eye damage in (12%) were found eligible for the study. Whole blood was collected from healthy AB men (RhD irrelavant) with no transfusion history. The blood units were incubated for clotting, then centrifuged to obtain cell-free serum. Serum was inactivated in the MIRASOL system and then transferred into tubes (under sterile conditions) and divided into 0.5 ml capsules to be stored frozen at < –18°C for up to 12 months. Before therapy and one month after its termination, each patient was requested to complete the OSDI questionnaire (Ocular Surface Disease Index), which is a reliable tool for assessment of the severity of dry eye syndrome.

The average OSDI score prior to therapy was 69 (22.5–100) and after a month of using MIRASOL inactivated "artificial tears", the value decreased to 44, which only confirms the positive attitude of patients to the therapy. Patients experienced better eye lubrication/hydration (intensified tear production), less pain and sensitivity to light as well as much clearer vision. Only two patients reported adverse reactions after using inactivated "artificial tears". The adverse reactions included the feeling of sand under the eye lid and eye irritation. Effective treatment was reported in 12/14 patients (93%). In conclusion, allogeneic eye drops, subjected to inactivation in the Mirasol system, are effective for the management of the dry eye syndrome, Sjögren's syndrome and GvHD. The inactivation procedure has no adverse effect on the eye drops.

A centre from the Netherlands presented a poster on which micro sized and conventional sized eye drop systems used for the preparation of allogenic serum were compared [8]. Research was performed on the use of capsules in micro size and the capsules that are normally dispensed to patients. Effectiveness of therapy was based on the OSDI index. For one month patients applied micro capsules and then conventional capsules. Fifty-three patients took part in the study and 48 completed the trial. For both types of capsules the improvement was significant as reflected by the OSDI index (from 0 to 100) which was used to compare patients' satisfaction before and after the use of both types of capsule sizes. After using the micro capsules the OSDI dropped from 52 to 41 and after standard size capsules — from 53 to 45. The smaller size capsules showed similar efficacy to the standard size 'artificial tears'. The smaller capsules are a good alternative because of the lower serum content, but they are less convenient.

In November 2020, the serum eye drop manufacturer's group was initiated by the representatives of Meise Medizintechnik GmbH. The participants are centres from European countries, as well as Australia, South Africa and Asia, which produce autologous and allogeneic artificial tears. The topics discussed during the last meeting included: management under COVID-19 pandemic conditions of serum eye drops preparation in NHS Blood and Transplant, Liverpool, UK as well as strengthening the safety of allogenic eye drops by inactivation in the Institute of Hematology and Transfusion Medicine (IHTM), Warsaw, Poland. The discussion focused mainly on allogeneic eye drops, which are currently gaining popularity because they strengthen patient's safety, are easily accessible and perform better than ASEDs in patients suffering from numerous disorders (autoimmune disorders included).

Summary

Despite the widespread and worldwide use of serum-based eye drops, there are no strict legal regulations for handling the product. There is also the problem of qualifying serum eye drops to the appropriate group of medicinal/blood products. It therefore seems necessary to implement appropriate regulations for placement of artificial tears therapy and to define specific rules of performance which would be the same across Europe.

All attempts at unification and determination of regulations among expert groups, such as the EU4Health Program or workshops on EDHO will certainly contribute to safer and wider use of artificial tears.

Conflict of interest: none declared

Financial support: none

References

1. Antoniewicz-Papis J. Artificial tears to treat dry eye syndrome. Acta Haematol Pol. 2021; 4: 412–415.
2. Seghatchian J, van der Meer PF. 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. Transfus Apher Sci. 2015; 53(1): 85–87, doi: 10.1016/j.transci.2015.05.013, indexed in Pubmed: 26143344.
3. Guide to the quality and safety of tissues and cells for human application, 5th edition, European Directorate for the Quality

of Medicines & HealthCare of the Council of Europe (EDQM), 2022.
4. https://ted.europa.eu/udl?uri=TED:NOTICE:712271--2022:TEXT:EN:HTML
5. Gabriel Ch, Marks D, Schallmoser K, et al. Workshop on Eye Drops of Human Origin, Transfusion Today. 2023; 134: 12–13.
6. Ashamuddin N, Mohd Noor S, Mahamud M, et al. Thicker than tears: Autologous Serum Eyedrop (ASED) for chemical eye injury patient. Perks and barriers in Malaysia, Vox Sanguinis 2022; 117, S1, P098.
7. Chmielewska K, Janus J, Mikołowska A., et al. Inactivation used in processing of allogenic 'artificial tears. Vox Sanguinis 2022; 117, S1, P103.
8. Vermeulen C, van der Burg L, van Geloven N, et al. Allogeneic micro sized serum eye drops compared to conventional sized serum eye drops: A prospective, randomized, non-inferiority, investigator-masked, cross-over, multicenter clinical. Vox Sanguinis 2022; 117, S1, P107.