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Issues related to artificial tears were discussed at the 33rd Regional Congress of the International Society of Blood Transfusion (ISBT) in Gothenburg, June 17–21, 2023

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Serum-based artificial tears are becoming increasingly popular worldwide. During the ISBT (International Society of Blood Transfusion) congress held in Gothenburg, Sweden, in 2023, research centers from various countries shared their experiences on the topic. Artificial tears are primarily used in the treatment of dry eye syndrome (DES), a condition associated with abnormal secretion of the tear film. Visual disturbances and headaches associated with DES have a negative impact on every day activity. In his 2021 study, Papas states that the prevalence of DES is growing and currently affects nearly 10% of the global population [1]. Because the procedure of collecting blood from older individuals or persons undergoing cancer treatment may often prove problematic, more attention is focused on allogeneic tears which are becoming increasingly popular.

During the first day of the ISBT congress, which was dedicated to Scandinavia (Nordic Day), Sofia Frändberg from Sahlgrenska Universitetssjukhuset in Sweden presented the activities of her centre as regards the preparation of serum-based eye drops. The centre has been involved in the preparation of autologous serum-based tears since 2016. Three types of eye drops are produced: 100% and 20% serum-based eye drops and eye drops with platelet-rich plasma (PRP). The eye drops are prepared following orders from ophthalmic clinics. The COL 10/20 system from Biomed Device is used for capsule portioning, and then the eye drops are frozen and stored at –20°C until release, which occurs when microbiological tests prove negative. The amount of capsules issued is sufficient for a 2-month treatment of DES. Between 2019 and 2020, the number of referrals for artificial tears at Sahlgrenska Universitetssjukhuset increased by 45%, which only confirms the growing interest in serum-based artificial tears [2].

During the poster session, as many as 7 posters were dedicated to artificial tears. Specialists from various countries presented their own experiences on the topic. The Rambam Health Care Campus in Israel described their experience from the preparation of autologous artificial tears. The procedure was implemented in 2022, when the Israeli Ministry of Health entrusted the supervision and production of artificial tears to blood banks. Patients received a 20% or 50% concentration of serum eye drops to be administered 4 to 8 times daily for 2 to 3 months. During 12 months of their activity, 135 patients benefited from autologous serum tears. The main indications for treatment were: dry eye syndrome (DES) associated with Graft-versus-Host Disease (GvHD) and corneal neuralgia. The procedure was implemented in blood banks and this move resulted in a widespread adoption of the method and an easier access for Israel patients to artificial tear drops [3].

The scientists from Uniklinik Köln in Germany presented their 11-year experience related to the preparation of autologous eye drops. As it

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was sometimes difficult to obtain samples of whole blood from patients, the research team also concentrated on the production of allogeneic tears and presented their 6-year experience in the field. In total, the Uniklinik Köln produced 2466 preparations of autologous and allogeneic tears. Between 2017 and 2022, 556 allogeneic tear products were prepared for 140 patients, children included. For allogeneic tear production, it was necessary to find a suitable donor eligible for whole blood donation. The donor was selected for a specific recipient based on ABO blood group and Rh antigen (D antigen) compatibility. The tear drops were issued once a negative microbiological test result became available The entire procedure however, (starting with suitable donor search) is time-consuming and that may be a problem for patients who require urgent intervention [4].

Storage and issue of serum eye drops may pose a challenge for many centres. Because of the excellent treatment outcomes with both autologous and allogeneic tears, centres worldwide are striving to find the most convenient method for capsule storage. No preservatives are added to serum and the shelf life of thawed serum is short, therefore the system used for portioning and application must be adapted to serve only several applications. The volume of serum in the capsule should not be too large so as to avoid wastage and, most importantly, to prevent bacterial contamination of artificial tears. One of the topics discussed at the poster session of the ISBT congress was the use of the Meise Medizintechnik GmbH system by the Australian Red Cross Lifeblood in Australia for the preparation of serum tears. In May 2020, the Australian Red Cross Lifeblood introduced the packaging process for artificial tears using Meise technology. A specific group of patients received tears packaged in the new vials and were asked to complete questionnaires to assess improvement or deterioration of their health condition as well as their experience using the Meise system. The patients used the eye drops approximately five times daily. The centre also shared the results obtained from patients treated with autologous and allogeneic serum. Surveys were collected from 24 patients who had previously received autologous tears, as well as from 40 new patients. Additionally, feedback was obtained from 10 regular patients and 8 new patients who used allogeneic tears. The average age was 57 years (± 13) for patients using autologous tears and 70–74 years (± 11) for those applying allogeneic tears. The results obtained for Australian patients indicate better efficacy of autologous tears. The Meise system was positively evaluated; however, some patients reported difficulties with opening and closing the vials [5].

The Institute of Hematology and Transfusion Medicine (IHTM) presented three posters devoted to autologous and allogeneic artificial tears. The statistical data from IHTM included 1493 autologous donations for the production of artificial tears. Both adults and paediatric patients benefited from the use of the artificial tears. Over the course of 3 years since 2019 when allogeneic tears were first introduced, 114 patients had benefited. An analysis of the medical conditions for which patients sought treatment with artificial tears was also presented. The most common indication for the use of artificial tears was dry eye syndrome (DES), including DES of various aetiologies: Sjögren's syndrome, Graft-versus-Host Disease (GvHD), cataracts, glaucoma, and corneal damage resulting from mechanical trauma or surgical procedures. The analysis also included the assessment of the Ocular Surface Disease Index (OSDI) in patients participating in the study devoted to the use of allogeneic tears. Between 2019 and 2022, 51 patients returned completed OSDI questionnaires. The average OSDI score before the use of allogeneic serum tears was 67.94. After the use of allogeneic serum tears without any additional processing, the OSDI score was reduced to 51.60. The OSDI score after the use of inactivated allogeneic serum tears was 44.75. In all three cases, the eye drops were used for one month. The effect of using the eye drops was reported to be very good, with the questionnaires indicating a significant improvement in the patients' health condition [6].

The IHTM also highlighted the stability of vitamin A in artificial tears, which is essential for the proliferation and proper functioning of corneal epithelial cells. For healthy individuals, the reference range for serum vitamin A concentration is typically 0.2–0.43 mg/L. On average, the initial concentration of vitamin A in the samples was 0.33 mg/L. After a 6-month storage period, the average concentration of vitamin A was 0.36 mg/L. According to the presented findings, vitamin A in serum remains stable for up to 6 months if stored under standard conditions for this preparation, which is typically at –18°C [7].

The IHTM conducted another study in which the concentrations of interleukins IL-1β, IL-6, IL-2, IL-10, and vascular endothelial growth factor (VEGF) were examined. The analysis included 38 serum samples collected from autologous donors and 10 serum samples collected from 7 do-

Table 1. Information on artificial tears. Data from the ISBT congress held in Goteborg (Sweden) in 2023

Medium	Serum dilution (%)	The system used for instillation	Dosage	Application
Sahlgrenska Universitetssjukhuset (Gothenburg, Sweden)	100% 20%	COL system (Biomed)	Not specified	DES and DES of various etiologies: GvHD, Sjögren's syndrome, mechanical corneal injury
Rambam Health Care Campus (Haifa, Israel)	50% 20%	COL system (Biomed)	4–8 times daily	DES, DES associated with GvHD, corneal neuralgia
Uklinik Köln (Cologne, Germany)	Not specified	Meise system (Meise Medizintechnik GmbH)	Not specified	DES, DES associated with GvHD
Australian Red Cross Lifeblood (Australia)	Not specified	Meise system (Meise Medizintechnik GmbH)	5 times daily	Not specified
Institute of Hematology and Transfusion Medicine (Warsaw, Poland)	100%	Long Drains (Technochemistry)	2–6 times daily	DES of various etiologies: Sjögren's syndrome, GvHD, cataracts, glaucoma, mechanical damage to the cornea, or damage resulting from surgical procedures

GvHD — graft-versus-host disease; DES — dry eye syndrome

nors. The cytokine concentrations in the 6 samples from allogeneic donors were significantly lower than in the autologous samples, with the exception of IL-2. During the study, very high levels of cytokines IL-1β (47.26 pg/mL), IL-2 (0.49 pg/ /mL), IL-6 (55.60 pg/mL), IL-10 (34.83 pg/mL), and VEGF (63.86 pg/mL) were observed in one of the donors, with negative impact on the efficacy of their serum for patients. The patients reported improvement in eye condition, although not as satisfactory as in the case of eye drops prepared from the serum of other donors. The high cytokine levels in the "outlier" donor may indicate the onset of an infection, recent surgical procedure, or the early stages of an autoimmune disease. During the screening of blood donors for the preparation of allogeneic artificial tears, it may be beneficial to expand the medical interview and include cytokine profiling as part of the examination [8].

The Blood Services and Apheresis Institute in Israel presented the protocol of preparing eye drops from fresh frozen plasma dedicated to individuals with DES associated with GvHD. The patients were treated for three months only with FFP eye drops. The eye drops were prepared from apheresis plasma. The plasma was aliquoted using the COL system by Biomed. Patients were asked to complete the OSDI questionnaire, they had the fluorescein eye stain test, and were provided with a questionnaire to assess the quality of life after using the eye drops. The eye drops were compatible with the patients' blood groups and only one AB blood type patient received group A eye drops. 25 individuals were enrolled in the study. One of them reported ocular irritation after using the tear drops for 2 months but the irritation resolved when a different batch of eye drops was used. No other adverse reactions were reported. This prospective phase II study demonstrated that the treatment of chronic GVHD with drops prepared from allogeneic fresh frozen plasma is safe and effective. This therapy is beneficial in the case of GVHD, because allogeneic FFP contains no pro-inflammatory cytokines and immunological factors that may be present in autologous serum or plasma [29].

The growing interest in the use of artificial tears, has led to increasingly high numbers of products prepared in centres which implement new formulas and procedures for autologous and allogeneic artificial tears. Indeed, the current situation calls for development of standardized procedures to ensure that the treatment with artificial tears meets the specific needs of patients.

Treatment with both autologous and allogeneic artificial tears gives very good results in the therapy of the dry eye syndrome (DES) as well as in the treatment of patients with DES associated with graft-versus-host disease (GVHD). One of the challenges that the centres face is the lack of standardized procedures for producing highest

possible quality tears. Preparation stages such as clotting, centrifugation, or dilution, may have impact on the biochemical properties of artificial tears. According to a study conducted by Jaksche A. in 2005, undiluted serum provided slightly better results than diluted serum [10]. It seems necessary to establish a working group that would be responsible for developing guidelines for the preparation of both autologous and allogeneic artificial tears. Table 1 shows the collected data from the ISBT congress in Sweden and presents the differences in the methodology of preparing artificial tears in different countries.

Development of a standardized patient eligibility protocol and selection of the appropriate source material (serum/PRP, autologous/allogeneic) would facilitate the implementation of the procedure in a greater number of centres, thus improving access to treatment. The above mentioned centres report an increase in the number of patients, which further confirms the need to establish uniform standards and to continue research on artificial tears.

Conflict of interest: none declared

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