Serum drops for ocular surface disease: national survey of Canadian cornea specialists

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ABSTRACT ●

Objective: To review the use and preparation of serum drops for the treatment of ocular surface disease in Canada and to assess the need for an improved access to this therapy.

Design: Cross-sectional study.

Participants: Cornea specialist members of the Canadian Ophthalmological Society and Canadian laboratories preparing serum tears.

Methods: A confidential survey was emailed to participants in April 2016 and continued through September 2016. Descriptive statistics on serum drops accessibility, production, and use are reported.

Results: Thirty-four cornea specialists (out of 93) and 8 laboratories completed the survey. Half of respondents (47%) described serum drops as inaccessible in their practice setting, mainly because of financial (75%) and logistic (66%) barriers. The use of allogeneic serum was perceived as a potential solution to poor accessibility by 62% of ophthalmologists. A private laboratory or pharmacy produced serum drops for 52% of respondents, whereas 32% coordinated serum drop procurement through a hospital laboratory. No serological tests were routinely performed, and sterility checks were done by one laboratory. Over the last year, each laboratory prepared serum tears for 49 ± 32 patients, representing a median of 15 patients per ophthalmologist.

Conclusions: Although most cornea specialists agree that serum drops are indicated in several refractory ocular surface disorders, there is significant discrepancy in accessibility to this treatment across Canada. This study confirms the need for an improved access to serum drops. Use of autologous serum is limited by logistic and financial barriers, which could be reduced by the introduction of an allogeneic serum drop.

Serum eye drops are indicated for the treatment of ocular surface disorders, including dry eye, neurotrophic keratitis, exposure keratitis, graft-versus-host disease, Sjögren syndrome, and mucous membrane pemphigoid.[1–13] Controlled clinical trials have shown the superiority of autologous serum eye drops compared with artificial tears when used to treat some of these conditions.[7,14,15] Serum contains important substances for corneal and conjunctival integrity, such as vitamin A, epidermal growth factor, transforming growth factor-β, and fibronectin.[16–18] These nutritive elements promote the viability, proliferation, migration, and differentiation of corneal epithelial cells.[19,20] Serum drops also contain a variety of proneuronal factors, such as nerve growth factor and insulin-like growth factor, and have been shown to be helpful in nerve regeneration and restoration of nerve topography.[21] Concentrations from 20% to 100% have been shown by in vivo confocal microscopy to increase nerve density and decrease nerve tortuosity, and this correlated with improvement in patient-reported photoallodynia and corneal neuralgia after LASIK surgery.[22,23]

Serum drops can be formulated using autologous or allogeneic serum in specialized laboratories. Autologous serum drops are produced from the patient's own peripheral blood, on a case-by-case basis.[24] Although autologous serum is more commonly used, it may be unavailable or contraindicated in several patients, including those with systemic infections, anemia or acute autoimmune diseases, the elderly or obese, and those with a phobia of blood sampling.[25] Allogeneic serum drops made from voluntary donors have been used in Denmark,[26] Norway,[27] and the Netherlands[28,29] as a means of minimizing the hazards and costs associated with the preparation of an autologous product. Allogeneic serum may be an appropriate alternative for selected patients who would benefit from serum treatment but whose autologous serum is unavailable or unsuitable.[25,30–32] The clinical efficacy of allogeneic serum eye drops has only been evaluated in open, uncontrolled studies[25,26]; however, there is no reason to believe that this treatment should be inferior compared with autologous eye drops.

The characteristics of serum drops use in Canada have not been previously reported. The purpose of this study was to review the use and preparation of serum eye drops for the treatment of ocular surface disease in Canada and to assess accessibility to this therapy.

Materials and Methods

This cross-sectional study was approved by the CHUM Research Ethics Committee. The study was conducted in compliance with the Declaration of Helsinki.

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First, a 2-part survey assessing serum drops accessibility, production, and use was developed. The first part of the survey was designed for ophthalmologists providing subspecialty care in cornea, and the second part of the survey was aimed toward the laboratories preparing serum drops in Canada.

Permission was obtained from the Canadian Ophthalmological Society (COS) to use its cornea subspecialty listserv as a means to disseminate the survey. An email invitation to participate in the survey was sent to ophthalmologists in April 2016, with a single reminder 2 months later. Laboratories were contacted by email once identified by responding ophthalmologists.

The email was sent in French and English. It contained a PDF of the survey in both languages, as well as a direct link to a secure off-site server (Qualtrics Labs Inc, Provo, Utah), allowing the survey to be answered online. A statement describing the study purpose and privacy measures and reassuring confidentiality within the study was also included in the email. The respondents had the choice of submitting the survey online or returning a printed version by mail. The survey remained available for completion for a 6-month period between April 2016 and September 2016.

The survey aimed toward ophthalmologists contained 15 questions addressing demographics, current use of serum drops, and opinions on serum drop safety and accessibility in clinical practice. The survey for laboratories contained questions on serum drop preparation, production costs, and number of patients served annually. Questions that were answered were included in the calculations. If a respondent left one of the questions blank, only the blank response was excluded from the analysis. Descriptive statistics, including medians and ranges for continuous data and proportions for categorical data, are presented. Data were analysed using the Fisher exact test. Statistical significance was determined at a threshold alpha level of 0.05. Correlation between variables was assessed by the coefficient of determination R^2 in a linear regression model.

Results

Thirty-four Canadian cornea specialists and 8 laboratories completed the survey. Considering that 93 members of the COS specialize in medical or surgical cornea, the participation rate was 37%. The majority of participants were practicing at a university hospital centre (59%) or private clinic (38%). Of all respondents, 47% were based in Ontario, 29% in Quebec, 9% in Manitoba, and 6% in Saskatchewan and British Columbia, respectively. The mean duration of practice as a cornea specialist was 18 ± 14 years (range 1–44 years).

Forty-seven percent of respondents described serum drops as very or somewhat inaccessible in their practice setting, principally because of financial (75%) and logistic (66%) barriers. Specifically, the inadequate reimbursement to maintain the service was perceived as the main financial barrier, whereas the lack of qualified personnel for the preparation of drops was perceived as the main logistic barrier to autologous serum treatment. Most (62%) agreed that drops made of allogeneic serum would allow this treatment to be provided more readily.

Sixty-eight percent of respondents agreed or strongly agreed that they would increasingly use serum tears in their practice if they were more easily accessible. In a scenario in which access to serum drops was not a limiting factor, each ophthalmologist would prescribe this treatment to a mean of 26 ± 16 new patients every year (range 0–50 patients). This represents a 2.3 times increase in the median annual number of patients per ophthalmologist who would be offered or maintained on serum drops for the treatment of ocular surface disease. Furthermore, among the 12 ophthalmologists not currently using serum drops for their patients, 75% stated that they would be very interested in integrating them into their practice.

Most ophthalmologists agreed or strongly agreed that serum drops are a safe (85%) and minimally invasive (85%) treatment that should be more available in daily practice (85%) and are a good option for patients with various ocular surface disorders that are refractory to other available treatments (85%). The most common indications for serum tear treatment (Fig. 1) included neurotrophic keratitis (91%), persistent epithelial defect (88%), Sjögren syndrome (85%), graft-versus-host disease (76%), and mucous membrane pemphigoid (65%). The median duration of treatment was 2–5 years, depending on underlying pathology, but 32% of specialists had been treating their patients with serum drops for more than 5 years.

Serum drops were produced by a private laboratory or compounding pharmacy in 52% of cases and by a hospital laboratory in 32% of cases. Among ophthalmologists having their eye drops prepared by a hospital laboratory, 60% had an agreement with another hospital. Three ophthalmologists had serum drops prepared directly at their ophthalmology department. Only 2 ophthalmologists had a formal cooperation agreement with their local blood bank for the preparation and supply of serum drops. Ophthalmologists who had an agreement with a private laboratory were generally more satisfied with drop accessibility compared with those having their drops prepared by a hospital, with 63% versus 17% characterizing serum drops as very or somewhat accessible ($p = 0.02$). Accessibility also varied among Canadian provinces (Table 1).

For all reporting ophthalmologists and laboratories (100%), serum drops were exclusively made of autologous serum. No serological tests on the patient or quality control tests were routinely performed. Sterility of the drops was verified by only one laboratory. Serum concentration varied across a wide range of 20% (5 labs), 25%