One size does not fit all:

Tailoring treatment for eye diseases

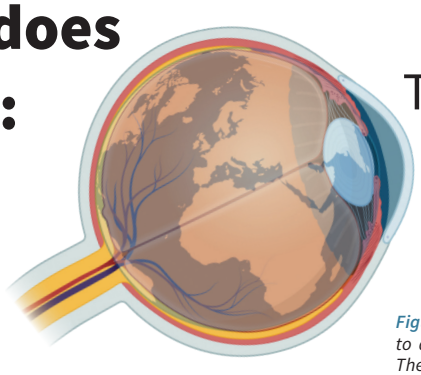

Figure 1. The global need for eye care is estimated to dramatically increase in the coming decades. The figure was created with BioRender.com

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On February 1, 2023, Heidrun Elisabeth Lode defended her thesis, "Strategies to improve treatment of retinal eye diseases" at the Faculty of Medicine at the University of Oslo (UiO) and Oslo University Hospital (OUH) in Norway. The PhD was conducted at the Department of Ophthalmology, Department of Pharmacology, and Department of Immunology at OUH Ullevål and Rikshospitalet in Oslo. The supervisors of the project were Professor Morten Carstens Moe, MD, PhD, Department of Ophthalmology, OUH Ullevål, and Professor Jan Terje Andersen, PhD, Institute of Clinical Medicine and Department of Pharmacology, UiO, Department of Immunology, OUH Rikshospitalet.

Key points:

- The new compounding procedure resulted in increased patient focus and cost savings.
- Collaboration with a medical device company led to the design of a tailored syringe.
- More albumin than antibodies exist in the eye.
- Albumin may be a good alternative carrier of VEGF inhibitors.

Introduction

One of the leading causes of vision loss in the industrialized world is age-related macular degeneration (AMD). In its most aggressive form, neovascular AMD (nAMD) leads to a rapid and permanent loss of central vision, resulting in difficulties recognizing faces, reading, and watching television, if left untreated. The development of nAMD is driven by an overproduction of growth factors, particularly vascular endothelial growth factor (VEGF), which promotes the growth of disease-causing blood vessels. Importantly, antibody-based biologics targeting and neutralizing VEGF have revolutionized the treatment of nAMD and other retinal diseases.

A burden for the patient and healthcare system

Retinal diseases, including nAMD, are often chronic and require long-term monitoring and treatment, burdening both patients and healthcare systems. Additionally, current clinical practice at many eye clinics can lead to loss of costly biologics, and withdrawal occurs under sub-optimal conditions, increasing the risk of complications. Moreover, most syringes used for IVIs are coated with silicone oil (SiO), which can lead to the deposition of SiO in the eye, causing symptomatic floaters and potential inflammatory reactions.

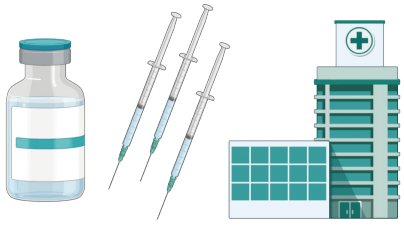

Figure 2. Multiple syringes are withdrawn from the same vial under aseptic conditions at the hospital pharmacy to improve patient care and achieve considerable cost savings. Figure created with BioRender.com

Focusing on the patient

By establishing and ensuring the quality of a method for compounding VEGF inhibitors in a syringe without SiO, we have improved the workflow by allowing health care personnel to focus on the patient rather than the preparation of the syringe. The syringes are now prepared under sterile conditions in the hospital pharmacy, potentially reducing the risk of infections following the injection while significant cost savings are achieved. This method has now been implemented in many eye departments across the Nordic countries.

During this work, an unmet need became evident for a syringe tailored for IVIs with high accuracy, with no dead volume, and without SiO. This challenge was addressed by initiating a collaboration with the Dutch medical device company, SSJ Solutions, through the technology transfer company, Inven2, resulting in a syringe specifically designed for ocular injections. As part of this PhD project, these syringes underwent extensive testing to ensure the same efficacy of the medications after withdrawal and storage. The syringes have recently been approved for the European market.

Improved efficacy and fewer injections

Most of the biologics used to treat nAMD are antibody-based, but little is still known about how these drugs are handled by the eye. We know from the literature and our studies that naturally very low levels of antibodies exist in the eye, and they are rapidly transported out after injection, causing the need for repeated treatment. Several studies have shown the presence of a receptor in the eye called the neonatal Fc receptor (FcRn), which acts as a regulator of antibodies. Additionally, FcRn is important for regulating a transport molecule in the body called albumin, which is naturally present in high levels in the eye. Therefore, we have investigated albumin as an alternative fusion partner for VEGF inhibitors. This may provide new information on how the bioavailability of biologics can be enhanced, and this work should motivate further research and development of antibody-albumin fusion formats for the improved treatment of retinal eye diseases.

Future directions:

- Further knowledge on how albumin and antibodies are transported will pave the way for more intelligent design of new treatments.
- Antibody-albumin fusion formats should be explored and developed for the improved treatment of retinal diseases.

References

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