MacularNEWS

Autumn 2022 : Edition 24

The LADAMO study for diabetic macular oedema

An estimated 1.7 million Australians have diabetes, with rates on the rise worldwide. Diabetes is a common cause of visual impairment and blindness in working aged Australians, most often due to diabetic macular oedema (DMO). DMO occurs when fluid leaks from retinal blood vessels and pools in the central retina, or "macula". This can cause the loss of central vision (your reading vision) and legal blindness.

People with DMO have increased amounts of a molecule called vascular endothelial derived growth factor (VEGF) in their eyes. Blocking VEGF with VEGF inhibitors usually improves vision in eyes with DMO and is the current gold standard treatment. The problem is that the treatment needs to be given regularly by injections into the eye itself. An average of 15 injections over two years are needed to manage DMO, which is a burden for patients and our healthcare system. We need to find out if there are ways to reduce the number of injections needed while still managing the condition.

The **LADAMO study** was a randomised controlled trial based at the Save Sight Institute in collaboration with investigators from the Centre for Eye Research Australia in Melbourne. The study aimed to see whether using a type of retinal laser treatment in the retina would reduce the number of injections needed to manage DMO over a two-year period. The laser was applied to areas of the retina which had low oxygen levels due to poor blood flow, this is known as "ischaemia". Low oxygen levels stimulate the secretion of VEGF which causes the DMO.

Director's Message

This issue of MacularNEWS, focuses on our clinical research unit. We share the outcomes of a clinical trial for diabetic macular oedema, and were lucky to speak to one of our clinical research orthoptists, who shared his experience of working in clinical research during the pandemic.

Professor Mark Gillies
Macula Research Group

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We hoped that killing off these ischaemic areas would reduce VEGF levels so fewer injections of VEGF inhibitors would be required.

All patients had their eyes examined via a fundus fluorescein angiogram. This is a technique that uses a fluorescent dye and special camera to help clinicians examine the retina. In the study, it helped show ischaemic areas.

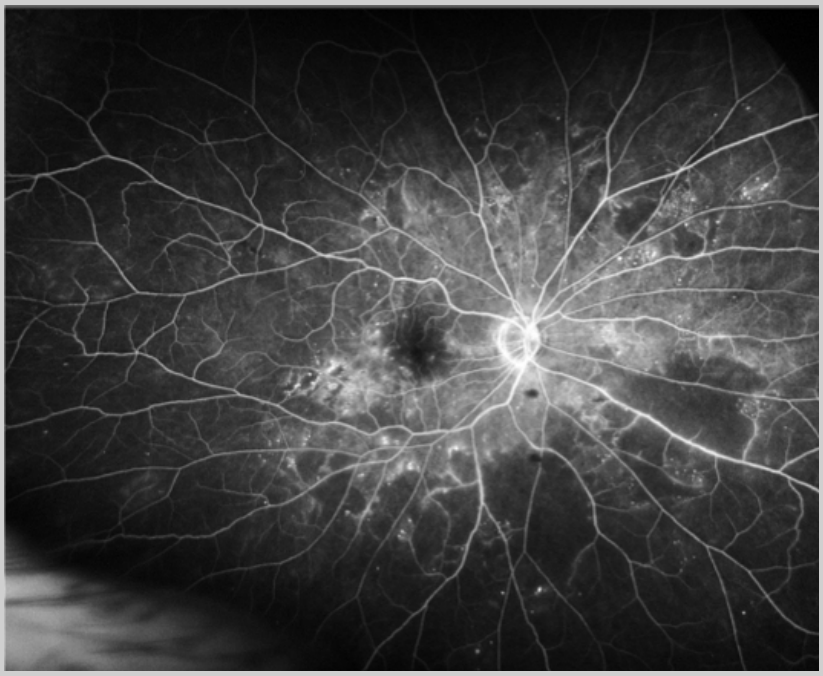

Figure 1: A retinal angiogram showing widespread retinal ischaemia towards the bottom of the retina. 'Normal' areas of the retina appear grey because the dye is present in the tiny blood vessel (capillaries) of the eye. The ischaemic areas are black with only the large blood vessels running through them and no capillaries.

The study was a "randomised clinical trial", so patients were randomly assigned either treatment with an VEGF inhibitor, called aflibercept, or a combination of laser therapy and aflibercept. Patients that were treated with aflibercept only also received placebo (pretend) laser treatment so that neither the patients nor the researchers knew who had received what treatment. The placebo laser was performed in the same way, but with the power set to zero.

Both groups had experienced an improvement in vision and a reduction in the amount of DMO by the end of the two-year study. Unfortunately we found no significant difference in the number of injections needed by the two study groups. Patients receiving aflibercept only were given an average of 12 injections, while patients receiving laser therapy and aflibercept were given an average of 11 injections. We are unable to say whether eyes that received laser treatment might have done better if the study had gone longer.

At least we can say that this treatment should now be avoided because there is no evidence to support it, which is a useful contribution because some doctors were using it. We are looking for other ways to get the best results for our patients with DMO while trying to reduce the number of injections needed.

Working in clinical research during a global pandemic

We've all had to change the way we do things due to COVID-19. However, it's more difficult to change certain things, such as seeing patients face-to-face, than others. Thomas Groeneveld, a Clinical Research Orthoptist from the Macula Research Group, shared his experiences of working in clinical research during the pandemic.

Figure 2 (L-R): Clinical Research Orthoptists Hong Vu, Damian Stephens and Thomas Groeneveld in their PPE. The team wear coloured stickers to show that they have passed a COVID-19 screening.

With a number of different complex ocular conditions seen in a fast-paced hospital outpatient setting, our clinical trials unit can face new challenges on a daily basis. We found ourselves facing unprecedented challenges as we suddenly had to recontextualise patient safety, as well as the safety of our team when the pandemic hit.

Face-to-face appointments are quite literal in ophthalmology. Our hands and faces need to be quite close to those of our patients to move lenses and other equipment towards patient eyes in tests and examinations. This close proximity work highlighted obvious risks. Urgent safety measures, in accordance with the international clinical trials rules we are required to comply with, were immediately put in place to reduce the risk of exposure to the virus for both patients and our team members. Contingency plans included reducing the number of clinics we conducted and splitting into two teams, staff wearing PPE to all clinics, prioritising the assessments for the study eye for each patient, pausing recruitment for some studies and prioritising certain treatment studies in which treatment was crucial.

Securing PPE was particularly difficult in the early weeks of the pandemic due to the sudden surge in demand, and masks were not even mandatory for both staff and patients.

Changes in COVID-19 policies at both the state government level and within our local hospital kept our daily work lives in a constant state of flux. The conditions of entry would frequently change at the COVID-19 screening station, with mandatory testing and vaccination status being recent additions to the conditions. PCR testing was briefly made mandatory for certain staff living in hotspot areas which put considerable strain on our team during flare-ups in case numbers. Visitors were also not allowed on site during these same time points and so monitors for our trials were not able to conduct site monitoring visits at their intended intervals. During work hours, we sometimes found ourselves needing to weave through the people in the expansive queues for both the hospital PCR testing and COVID-19 screening lines. Working from home was encouraged but not always possible, and even travelling to and from work became difficult with compulsory travel permits and public transport operating at a reduced capacity.

As the pandemic stubbornly persists, we know there will be ongoing challenges that will need to be overcome well into the foreseeable future. These pale in comparison to those faced by other front-line health workers and those who have unfortunately lost work, and we do not take this for granted. In the midst of the pandemic, I appreciate being able to continue to provide the service our clinical trials unit offers and I'm sure this sentiment is shared by my colleagues.

If you would like to make a tax-deductible donation or discuss leaving a bequest to support macular research please visit our website **sydney.edu.au/medicine/eye**, call us on **(02) 9382 7309** or post a cheque to: Save Sight Institute, South Block, Sydney Eye Hospital, 8 Macquarie Street Sydney NSW 2000 made out to 'The University of Sydney'

Save Sight Institute is a centre of The University of Sydney.

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