

## Simerdip Kaur takes a look at the latest ophthalmology-related news stories and asks which are based on facts and which are 'fake news'?

### Headline: Patients use their own blood to treat dry eye symptoms

**G**rossman first described the technique of using whole blood and plasma for the treatment of corneal ulcers in 1947 [1]. The use of blood and its products in ophthalmology is not uncommon, ranging from fibrin glue as a tissue adhesive for attaching conjunctival autografts following pterygium excisions, to intrableb autologous blood injection for chronic hypotony [2]. Human blood shares similarities with tears in the composition of vitamins and growth factors, which has prompted its use in ocular surface disease as a tear substitute, in particular the use of autologous serum (AS) eye drops.

Serum consists of blood plasma without clotting factors and is of comparable osmolality and near neutral pH as tears. It contains more vitamin A, transforming growth factor beta (TGF- $\beta$ ), lysozyme and fibronectin with less immunoglobulin A (IgA), epithelial growth factor (EGF) and vitamin C than tears [3]. In 1975, Ralph reported positive outcomes in patients with diseased corneas who received continuous infusion of AS and other fluids such as artificial tears via a mobile pump onto their ocular surface [4]. His research led to a cascade effect in the use of AS as eye drops.

In 1984, Fox et al. were the first to prepare and trial the use of 30% AS eye drops in 30 eyes of 15 patients suffering keratoconjunctivitis sicca (KCS) over three weeks. They found improved Rose Bengal staining on the ocular surface in keeping with patient reported symptomatic relief. Six patients were enrolled into a double-masked crossover placebo trial and reported exacerbation of their dry eye symptoms within 96 hours of switching from AS drops [5].

Then in 1999 Tsubota et al. described the use of 20% AS drops in persistent epithelial defects (PED) in 16 eyes. At two weeks approximately 44% of PEDs had healed and this result improved to 62.5% at one month [6]. In a separate study they also proved that the AS drops were stable after preservation in a refrigerator and freezer after one and three months respectively with no alteration in the concentration of EGF, vitamin A and TGF- $\beta$  [7].

A Cochrane review in July 2016 identified five randomised controlled trials (RCT) to assess the efficacy and safety of AS drops [3]. Each trial was single-centred and with small sample size using 20% concentration of AS drops against artificial tears or saline. The authors concluded that in the short-term, at two weeks most patients were less symptomatic from their ocular surface disease, but this effect was not seen over a longer period. Additionally, the evidence for objective measures of improvement were inconclusive.

AS drops, whilst therapeutic for the subgroup of patients who benefit from them, are not without their drawbacks in terms of production time and cost, storage, need for approval and strict eligibility criteria. It is these barriers that make fingerprick autologous blood (FAB) an appealing alternative option. Than et al. conducted a pilot interventional case series to assess the feasibility of FAB in patients with dry eye syndrome (DES) [8]. They included 29 eyes of 16 patients with DES who were trained to obtain whole fresh FAB using clean washed hands, alcohol wipes and a diabetic lancet. The patients applied one drop of blood to the lower fornix of their eye using a fresh finger for each eye four times a day for eight weeks. Patients then ceased treatment and were reviewed four weeks later. They found improvement in the ocular comfort index (OCI) scale, tear film break-up time (TFBUT), Oxford corneal staining scale and mean visual acuity at eight weeks and these results were statistically significant. Four weeks after stopping FAB there was worsening OCI score and corneal staining in over 50% patients. None of the patients experienced ocular or digital complications and reported decreased use of their artificial tears. Some patients have continued to use FAB for over two years with reduced frequency of application to once or twice a day [8]. As part of their feasibility study they also performed a qualitative assessment on the acceptability of the FAB technique,

which was rated 2.2 overall (with one being completely acceptable and five being completely unacceptable) and found that all of their patients would recommend the treatment to their family or friends should they need it [9].

Following on from the success of their trial, the researchers went on to assess the use of FAB in PED [10]. They recruited 10 patients, of which three were excluded from the final due to incomplete follow-up for reasons other than intolerance of the intervention. They applied the same dosing regimen as for the DES patients, but a shorter duration of treatment of four weeks. At day 28 they observed 60% efficacy of FAB at healing the epithelial defect and this result is comparable to Tsubota's use of AS drops for PED.

Whilst encouraging, both the FAB studies have been carried out on small sample sizes. The question remains, is FAB likely to translate into real world use outside of these trials? The low cost of the FAB technique with the purchase of wipes and lancets amounting to £12 vs. £320 per month for AS drops makes it a viable option, especially in patients who are unable to undergo regular venesection due to their comorbidities. Undoubtedly, further research is required to assess FAB against current conventional therapy, ideally in a large RCT crossover trial, and its long-term complications, risk of infection and cellular mechanism of action, to list a few. However, Dr S Balal is hopeful and states, "It must also be remembered that diabetics prick their fingers multiple times a day with no immediate benefit, unlike dry eye patients who obtain relief and healing."

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