for recurrences. In addition, constant VEGF suppression may contribute to an increased risk of toxicities in normal tissues.

For treating our patients with off-label bevacizumab, despite favourable short-term safety, it seems advisable to limit the number of treatments to as few as necessary.

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Retrobulbar haemodynamics

Retrobulbar haemodynamics in non-arteritic anterior ischaemic optic neuropathy

G T Feke

Clinical evaluation of the optic nerve circulation in NAION remains an elusive goal yet to be fully achieved

In this issue of the journal, Kaup *et al*¹ (see p 1350) report results relating to blood flow dynamics in the ophthalmic artery, the nasal and temporal short posterior ciliary arteries and the central retinal artery in patients in the acute stage of non-arteritic anterior ischaemic optic neuropathy (NAION). Although they are not the first group to conduct such a study, they are the first to compare their findings in patients with NAION with those measured in a group of age-matched controls.

Before commenting on specific results, it is instructive to consider the problem of blood flow and NAION from first principles. As initially described by Henkind *et al*,² and recently by Arnold³ in his excellent review, histopathological examination shows that there is occlusive vasculopathy in the optic nerve microcirculation located primarily in the retrolaminar region of the nerve head in patients with NAION. The first question,

then, is “What is the blood supply to this region?”

The answer to this question is beautifully shown in the photomicrograph published by Olver *et al*,⁴ which is reproduced in fig 1. It is the paraoptic branches of the nasal and temporal short posterior ciliary arteries that supply the so-called “Circle of Zinn–Haller”, which in turn supplies the retrolaminar, laminar and prelaminar regions of the optic nerve microcirculation. The second question becomes “Can the blood flow dynamics in these paraoptic branches be measured using any existing technique?”

In short, the answer is “No”. In another excellent and instructive review, Hayreh⁵ also describes the anatomical details of the blood supply to the optic nerve head and, in addition, proceeds to critique the various experimental methods that have been used to evaluate the optic nerve head circulation. The specific question posed is

“Do colour Doppler imaging findings in posterior ciliary arteries provide information relevant to the optic nerve head microcirculation?” Hayreh points out what is quite clear from examination of fig 1—that is, it is simply impossible for colour Doppler to differentiate the individual paraoptic branches of the short posterior ciliary arteries. As Hayreh describes, “... all of them are lying jumbled and intertwined as a vascular bundle”. Therefore, when users of colour Doppler imaging claim to obtain haemodynamic results from short posterior ciliary arteries, they are likely to be obtaining an averaged result from several arteries in a bundle. Furthermore, as these arteries are the primary supply to

Figure 1 Scanning electron photomicrograph of the “Circle of Zinn–Haller” (centre) formed by the paraoptic branches of the temporal (upper right) and nasal (lower left) short posterior ciliary arteries. It is believed that a diminished blood supply in the Circle of Zinn–Haller is associated with non-arteritic anterior ischaemic optic neuropathy. Reproduced with permission from Olver *et al*.⁴

the choroid, the blood speed data obtained do not reflect blood flow or vascular resistance changes in the optic nerve head, but only in the choroid. The blood flow through the paraoptic branches is only a fraction of the flow through the much larger posterior ciliary arteries.

Colour Doppler findings in the short posterior ciliary arteries are thus, in practice, not relevant to the optic nerve head circulation, and, by extension, to a study of patients with NAION. Hayreh⁵ points out that researchers have been misled to believe that blood flow evaluation in these arteries provides information about the optic nerve circulation. Also, measurements of the ophthalmic artery circulation are not at all relevant to the optic nerve head nor to studies of NAION. Optic nerve head blood flow is only a minuscule fraction of ophthalmic artery flow.

The question arises as to the relevance of central retinal artery blood flow characteristics to the optic nerve head circulation and to NAION. Kaup *et al*¹ report reduced blood speed in the central retinal artery in their patients with NAION. A similar finding was reported by Flaharty *et al*⁶ who also used colour Doppler imaging. Hayreh⁵ points out that the central retinal artery supplies only the surface nerve fibre layer of the optic nerve head and thus has no

real role in the blood supply to the regions of the nerve head associated with NAION. Arnold,³ reviewing fluorescein angiographic findings in NAION, does note, however, that in some cases impaired filling patterns in the surface vasculature have been observed. Kaup *et al*¹ suggest that involvement of the central retinal artery in NAION may be secondary to the oedema of the optic nerve surrounding the artery.

How, then, can the optic nerve head microcirculation relevant to NAION be reliably evaluated? With fluorescein angiography, the filling of the laminar and retrolaminar regions of the nerve head is obscured by fluorescence from the surface. Several laser Doppler techniques have been used to study NAION, most recently by Collignon-Robe *et al*.⁷ The issue becomes one of penetration depth of the probing laser beam and the relative contributions of the various depths sampled to the analysed signal. Collignon-Robe *et al* did report circulatory decreases of up to 20% in NAION, but what remains unclear is the relative contribution to the signal from the more anterior layers of the nerve head not directly associated with the occlusive vasculopathy. A Doppler signal derived solely from a deeper region would probably have shown more of a decrease in circulation.

In summary, clinical evaluation of the optic nerve circulation in NAION remains an elusive goal yet to be fully achieved.

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Preoperative glaucoma assessment

Conjunctival markers as predictable markers for preoperative glaucoma assessment

P-J Pisella

Glaucoma and the conjunctiva

Filtering surgery throughout its development has mainly focused on the ocular surface, most particularly the conjunctiva. Similarly, all doctors treating patients with glaucoma should also concentrate on the status of the patient's ocular surface, not only at the time of surgery but especially before. The glaucomatous patient is the primary category of patients who may have side effects from long term topical treatment.

Currently, it is well known that the chronic use of eye drops has a cumulative toxic effect on the conjunctival epithelium. Broadway *et al*^{1,2} have shown the role of medical treatment as a risk factor for filtering surgery failure. They

clearly showed that the success rate was considerably lower (55%) in patients treated with one or more drugs for glaucoma for at least 3 years than in other patients (94%, $p < 0.001$). Later, Baudouin *et al*³ showed the major component of conjunctival toxicity inside a bottle of eyedrops for glaucoma—preservatives, with few differences between the various types, but particularly well studied in benzalkonium chloride (BAK), still the most frequently found preservative in eye drops.³ The toxic effect of BAK on the epithelium has long been known,⁴ but the relationship between the presence of BAK in eye drops and changes in the conjunctival epithelial profile has been

described only more recently. Briefly, BAK toxicity is twofold: (1) an indirect toxicity on the lipid layer of the lacrimal tear film is found because of the soap effect of quaternary ammonium and, as a consequence, an increase in functional and clinical signs of dry eye; (2) a direct cytotoxic effect on conjunctival epithelial cells is clearly shown experimentally, in vivo and in vitro.^{5,6} In this way, subclinical inflammation takes place inside the conjunctiva and plays a major part in fibrosis development after filtering surgery. These results were confirmed throughout the world and prompted manufacturers of ophthalmic solutions to produce, when chemically possible, eye drops for glaucoma without preservatives in single-dose or filtering multi-dose bottle forms. In fact, the main family of anti-glaucoma drugs available without preservative remains the β blockers.

What are the clinical manifestations of this toxicity, and how can the doctor easily detect a conjunctival profile with major risk for surgical failure?

The answer is simple, as all clinicians know that in most cases this is difficult to detect. A clinical examination of the ocular surface does not provide sufficient information to diagnose an inflammatory profile of the conjunctiva, because, in many