disproportionately in erythrocytes in blood.[3] Therefore, we suspect that the fluctuation in dosing could be responsible for abrupt changes in plasma levels and thus, disproportionate carbonic anhydrase activity in susceptible individuals. Similarly, it implies that any insult to the red cells could result in an unexpected change of topiramate plasma levels.

In our opinion, the sudden changes in the plasma levels of topiramate should be avoided if possible and its mode of titration be reviewed in conjunction with both neurologists and pharmacologists.

Conflict of interest

The authors declare no conflict of interest.

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Sir,
Response to 'Comment on Topiramate maculopathy secondary to dose titration: first reported case'

We agree with Kozner *et al* that the maculopathy reported in our case[1] likely represents a mild form of the idiosyncratic reaction causing choroidal effusion, induced myopia, and angle-closure glaucoma that has been reported with topiramate and other sulfur-containing medications. In these cases, it is a consistently reported feature that the reaction generally occurs within days following commencement of the drug or an increase in dose.[2] In Kosner's case,[3] the reaction occurred 3 days after discontinuing topiramate and a sulfur-containing antibiotic, but the patient had commenced the medication 10 days prior to presentation. It is therefore difficult to be sure of the precise trigger in this case.

The important clinical point is that discontinuation of the drug leads to resolution of the symptoms. In some reports, resolution has possibly been hastened following the administration of IV methylprednisolone.[2,3]

Conflict of interest

The authors declare no conflict of interest.

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Sir,
TLP: a premature concept

Siaudvytyte *et al*[1] present a literature review and meta-analysis regarding translaminar pressure difference (TLPD) in open-angle glaucoma. Five studies that demonstrated a higher TLPD in open-angle glaucoma have been analyzed in detail.

TLP defined as intraocular pressure (IOP) minus cerebrospinal fluid pressure (IOP – CSF-p)[2] is an interesting mechanical concept. However, there are some critical considerations concerning the interpretation and implementation of TLP we would like to mention.

First, as discussed by Siaudvytyte *et al*[1] both IOP and CSF-p used in the equation for TLPD are dynamic and fluctuate independently over time with numerous variables affecting both intracranial pressure and intraocular pressure measurements. Therefore, the estimation of TLPD would be best done by a simultaneous measurement of both IOP and CSF-p. None of the presented studies did it and thus all TLPD studies are dealing with two non-dependent and ever-changing variables to a definite time leaving us without a correlation that would fulfill the requirements of the simple physical equation of pressure, which is force over area at a definite time.

Second, in four out of the five analyzed studies, CSF-p has been measured by lumbar puncture and the lumbar CSF-p was extrapolated to the retrolaminar CSF-p. The assumption the lumbar CSF-p might equal the retrolaminar CSF-p only holds if the CSF-p is homogenous distributed in all CSF spaces, inclusively the subarachnoid space of the

optic nerve. However, at least in NTG[3] CSF does not communicate freely between the intracranial subarachnoid space and that of the optic nerve. The optic canal is extremely narrow and due to the mechanosensitivity of meningothelial cells[4] that line the canal, the anatomy of the canal can change the anatomical pathway for CSF.

Third, as pressure is defined as force over area, the area involved in TLP needs to be known. The area in question is a complex and irregular arrangement of ovaloid circles that are arranged within an annulus[5] and is not known in any of the patients presented. Thus, the forces in the equation for TLPD cannot be calculated.

Given these missing information and uncertainties, the concept of TLP seems still premature.

Conflict of interest

The authors declare no conflict of interest.

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Sir,
Reply to: 'TLP: a premature concept'

We would like to thank authors Killer and Pircher[1] for their thoughtful comments. Foremost we agree that although the importance of translaminar pressure (TLP) in glaucomatous pathophysiology is beginning to emerge, there are many unanswered questions. Therefore, our article was created to investigate the current state of knowledge of translaminar pressure difference (TLPD) in open-angle glaucoma, provide the first comprehensive meta-analysis on available data, and to identify gaps in knowledge that should be addressed.

The idea of simultaneous measurement of both intraocular pressure (IOP) and cerebrospinal fluid pressure (CSF-p) provided by Killer HE and Pircher A technically leads to the idea of monitoring. Several reports have demonstrated a good safety and tolerability of the contact lens sensor (CLS) for 24-h use[2,3] as well as good reproducibility of measurements.[4] However, in clinical practice the use of CLS is still under investigation as variations in IOP lead to changes in ocular volume and dimensions, measurements are provided in relative units and direct comparisons between routine tonometry measurements in mmHg cannot be performed.

Continuous monitoring of intracranial pressure (ICP) using currently available invasive techniques is not preferable in routine glaucoma practice. Besides, to date no studies have conclusively been able to demonstrate whether bilateral ICP monitoring should be undertaken routinely.[5]

We agree that TLPD is a relatively simplistic term. Still optic nerve subarachnoid space and cerebrospinal fluid lie within 1 mm of the optic disc surface and CSF-p has significant impact on axonal transport across the optic disc. Compression and displacement of the lamina cribrosa leads to blockade of axoplasmic flow.[6] Authors note that the area involved in TLP needs to be known. At this point we need to separate two definitions—TLP gradient depending on the pressure difference and the distance between the intraocular compartment and the retrobulbar fluid filled compartment. Although the TLPD depends on the IOP and retrobulbar CSF-p, leaving the area aside the definition.

In summary, only with advancement in non-invasive methodologies will the breadth of data be available to provide new evidence on importance of TLPD in glaucoma.

Conflict of interest

The authors declare no conflict of interest.

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