patients, the ophthalmologist sees a "white" eye with no clinical inflammation. Of course, changes can be seen in the precorneal tear film, with instability indicated by a short break-up time, and in some cases moderate superficial punctate keratitis is detectable, suggesting chronic inflammation of the corneconjunctival surface caused by long term topical treatment, particularly when the staining is predominantly located both on the nasal conjunctiva and on the inferior part of the cornea.⁷ However, these clinical findings are present when the deleterious effect of preservatives has already taken hold, or in other words, when the risk factors for surgical failure are high. To achieve maximum efficacy and increase considerably the rate of success in filtering surgery, a preclinical test to detect local changes in the ocular surface early would be useful and could also serve in determining the best time for surgery. Impression cytology, which studies the main cellular populations of the conjunctival epithelium—the epithelial cells, the goblet cells and the antigen-presenting cells—has advanced in this direction. Several markers on these cells help improve the understanding of the cellular mechanism of toxicity and of other chronic ocular surface diseases such as dry eye or rosacea.⁸ Human leucocyte antigen (HLA) DR was systematically overexpressed in all of these conditions and is now currently used as the main inflammatory marker of the conjunctiva. Moreover, Baudouin *et al* have also shown a high level of HLA-DR expression by epithelial cells taken from the conjunctiva of patients treated for only 6 months with topical eye drops, but with no clinical signs

of toxicity.⁹ Furthermore, mucin detection, indirectly evaluated by goblet cell density evaluation, was also shown to be associated with these processes, with an earlier decrease in these cells. These results were tested in pathologies such as dry eye and ocular rosacea, but also in cases of ocular surface aggression with topical eye drops for glaucoma and in contact lens wearers; MUC5AC expression was routinely used for detection of both secreted mucin and cells. Finally, we obtained a conjunctival profile of subclinical inflammation with a high level of expression of HLA-DR antigens and a considerable decrease in goblet cells, suggesting conjunctival epithelial metaplasia caused by inflammatory processes. This profile evaluation could be a useful tool for clinicians seeking to evaluate the success rate of filtering surgery and to predict a switch from preserved to unpreserved drugs when possible, or the use of topical anti-inflammatory agents before surgery. However, this technique requires a high level of laboratory technology, and the scientific knowledge necessary for interpretation is time-consuming, thus may not be used routinely by all. However, these studies open the door to ocular surface evaluation for subclinical detection of the earliest epithelial changes. In the near future, this approach could greatly benefit from new imaging technology exploring the anterior segment, such as confocal microscopy or very-high-frequency ultrasound imaging.^{10 11} Fundamental research could finally join clinical practice, with direct benefits for our patients.

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Intraocular pressure

Intraocular pressure-lowering efficacy of bimatoprost 0.03% and travoprost 0.004% in patients with glaucoma or ocular hypertension

R Noecker

The efficacy of bimatoprost and travoprost in patients with glaucoma and ocular hypertension

Dr Cantor's article¹ (see page 1370) on the efficacy of bimatoprost and travoprost in patients with glaucoma and ocular hypertension shows again that both these drugs are efficacious

in lowering intraocular pressure (IOP). The study is a prospective, randomised investigator-blinded trial, which has results similar to those found in studies carried out with the drugs in this class.

Dr Cantor found that bimatoprost lowered IOP slightly more than travoprost in this study population. This is the first relatively large two-arm study to show this in a head-to-head design. The current study supports others who have shown that bimatoprost is somewhat more efficacious than travoprost.

What is reassuring about this study is that there are no surprises, and the results appear to be consistent with what has been seen in the collection of other studies comparing drugs in this class. The relative degrees of IOP reduction, rates of hyperaemia and clinical success parameters are within the range reported in smaller studies and larger multiple comparison studies.^{2–6}

What has differed from study to study is the cohort of patients examined, and the treatment of the data both from the standpoints of study design and statistical treatment. These factors can influence the results to some extent, but taken in the context of the body of

information we have at hand, the results fall into a range with certain trends evident. For example, in the Cantor study, bimatoprost was found to be more efficacious in lowering IOP than travoprost and the degree of difference is somewhat different from that reported in other studies, but similar. Also, the hyperaemia rate was higher with bimatoprost than travoprost. In this study, the difference was not significant, although it has been in others.²

The clinical question at hand is, "are the differences found in studies like the current one clinically relevant?" The first issue is which agent should be chosen to primarily treat a new patient with glaucoma or ocular hypertension. The second clinical issue is, "are the differences in efficacy enough to switch between agents in this group if the first one is not as efficacious as necessary for an individual patient?" Neither of these issues exist in a vacuum and in the real world; there are issues such as formulary status, hyperaemia and bottle differences. It is reassuring that both the drugs work well in lowering IOP. It gives practitioners confidence if choices are restricted by formulary issues.

Although studies such as Dr Cantor's may show differences between populations, individual differences are more difficult to tease out of the data. When treating glaucoma and ocular hypertension, there is an increasing body of evidence showing that it may be important to decrease IOP consistently, so as to minimise the occurrence of higher IOPs at which the damage to the optic nerve may occur.

The authors in this study chose to emphasise mean IOP reduction. Mean

IOP is a commonly used parameter that gives an overall impression of efficacy, but it can be influenced by outlier data points and it assumes that all patients follow a similar IOP curve throughout the day and over time. This may or may not be true. We are increasingly aware that an individual patient's IOP stability may be a more important factor in controlling the progression of glaucoma.

Both bimatoprost and travoprost have fairly flat diurnal curves when group means are evaluated. It would be interesting and helpful to analyse these data and other similar data looking at the profiles of individual patients. This would be useful in confirming our impression that these drugs are indeed superior to those in other classes when used as monotherapy. Likewise, if we do see a difference between the drugs, we might be more likely to use them preferentially over another that does not have this feature.

On the basis of this, there is probably no need to conduct a study similar to Dr Cantor's again. What is needed, however, is a look at data in terms of fluctuation. Looking for statistical significance in regard to the differences among the drugs in terms of lowering IOP at a given time point is probably no longer a worthwhile endeavour, given the body of evidence that is presently available in literature. Further information about this group of drugs compared with others and more information about combination treatment is the next step.

Bimatoprost and travoprost along with latanoprost have changed the way the glaucoma has been treated over the past 5 years. These drugs have become the de facto preferred treatments for glaucoma. Furthermore, with the recent Food and

Drug Administration recommendation for bimatoprost to be used as a first-line agent, the choice really becomes one of choosing the agent that offers the best chance of clinical success. The current study adds to the body of information about the relative efficacy of these drugs and will help clinicians make decisions via evidence-based medicine.

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Smoking and the ophthalmologist

Smoking and the ophthalmologist

M Belkin

Emphasising the adverse effects of smoking on eye diseases

Both my daughters smoke. This fact annoys me greatly, not only because of the damage they are knowingly doing to themselves but also because it underscores the apparently insurmountable difficulties all of us have in trying to minimise the enormous health effect of this chronic self-poisoning. Why do intelligent,

well-informed people like my daughters not give up this habit? Is it because of the chemical addiction originated by the first puff and enhanced by subsequent ones,¹ emotional dependence, provision of stress relief, the power of routine practices, social pressures and coziness, lack of information, the infinite capability that people have for denying

threatening realities, the unwillingness of governments to reduce important revenue source or all of the above? I do not know the answer to this question, nor can I explain the failure of humankind to eliminate smoking, by far the most important modifiable risk factor for diseases of all body systems of users, and, in the form of second-hand smoke, of people in their environment. Smoking rates increase steeply the world over, mainly as a result of higher consumption in developing countries. Furthermore, the decline in smoking rates in Western countries stalled recently and, according to the Center for Disease Control and Prevention, teenage smoking in America is on the increase again. This occurs despite the clear evidence given by the World Health Organization that smoking is