deep sclerectomy. In two eyes, percolation through the trabeculodescemetic membrane was weak, so the procedure was supplemented by a trabeculotomy. In another four eyes, identification of Schlemm's canal was not made, so no deep sclerectomy alone nor added trabeculotomy could be done, and the procedure was converted into a guarded filtering procedure. Finally, in two eyes an inadvertent visible perforation of the trabeculodescemetic membrane occurred. The report of a high percentage of conversion to perforating filtering surgery and potential associated postoperative complications differs from our own experience in refractory congenital glaucoma. After both pure deep sclerectomies, hyphemas were reported as complications, although trivial. These may further result from possible microperforations, with a resultant high and abrupt change in IOP. We agree that deep sclerectomy alone is not applicable in most cases with complicated refractory congenital glaucomas. We make small visible perforations of the trabeculodescemetic membrane with the tip of a 30-gauge needle. Our incidence of nonidentified Sclemm's canal in congenital refractory glaucomas, however, is low.

Considering that only pure nonpenetrating filtering surgery is reported in this article, the IOP control after 19 months of follow-up was 50%, which, considering the high-risk failure rate for refractory congenital glaucoma, is not so bad.

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Author reply

Dear Editor:
Drs. Ravinet and Mermoud detailed their deep sclerectomy techniques for treatment of refractory congenital glaucomas in their comment on our retrospective case series.

Between our observation and the experience of Drs. Ravinet and Mermoud there is complete consensus that nonpenetrating deep sclerectomy alone is not applicable in most cases with refractory congenital glaucoma.

To enhance aqueous outflow after deep sclerectomy they needle the trabeculodescemetic membrane, which causes macroperforations. Additionally, to allow subconjunctival filtration, only loose readaptation of the superficial scleral flap is performed. In our opinion this technique is a variant of filtering surgery or, as we would term it, a "penetrating deep sclerectomy."

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Sildenafil-Associated NAION

Dear Editor:
Pomeranz and colleagues' case series describing the occurrence of nonarteritic anterior ischemic optic neuropathy (NAION) after ingestion of sildenafil in five subjects invites speculation about the causative mechanism.[1] Their thesis primarily emphasized the notions of disrupted autoregulation in the optic nerve head (ONH) or a toxic optic neuropathy from potentiation of nitric oxide by sildenafil. Importantly, although their five patients had crowded discs, mention of systemic arterial hypotension as a possibile etiology was omitted. Systemic hypotension is particularly relevant in the context of a structurally congested ONH that has vulnerable watershed zones in its microcirculation.[2]

In this regard, the manufacturer (Pfizer Pharmaceuticals, New York, NY) has reported that sildenafil reduces blood pressure (independent of the amount of drug) in healthy supine subjects, especially 1 to 2 hours after administration. Subsequent studies have confirmed that sildenafil can produce a small decrease in systolic and diastolic blood pressure, with some groups finding a fall as large as 20 mmHg (systolic) in certain individuals, suggesting perhaps a difference in interindividual sensitivity to the drug.[3,4] Some workers examining the hemodynamic effects of sildenafil have used conventional sphygmomanometry at the brachial artery to assess effects on blood pressure. It is rather thought provoking that sphygmomanometry may significantly underestimate hemodynamic disturbances (e.g., the fall in aortic systolic and pulse pressures) induced by vasodilator agents when compared with relatively sophisticated techniques.[5] Therefore, hypotension and other hemodynamic changes in the central circulation that affect ONH perfusion after vasodilator therapy may be overlooked when attention is focused on detecting changes in brachial arterial pressure with sphygmomanometry.[6] These transient fluxes in the central circulation (though not florid enough to produce acute symptomatic hypotension) may be sufficient to elicit the final insult of critical ischemia in the anatomically susceptible ONH.

The role of arterial hypotension deserves explicit consideration in these five patients, where crowded ONHs were exposed to a drug known to modify systemic hemodynamics. Moreover, an allusion to this established mechanism does not invalidate Pomeranz et al's proposition that sildenafil might interfere with regulation of ONH microvasculature, because both local and systemic circulatory effects could conspire in the pathogenesis. Their alternative theory of a toxic optic neuropathy from sildenafil is less compelling because all five patients have clinical and investigative evidence compatible with classic NAION.

It is difficult to be specific about the mechanisms responsible for NAION secondary to sildenafil because rigid statements cannot be supported by existing evidence. Certainly, we cannot be dogmatic or claim omniscience because the pathophysiology of NAION is still poorly characterized. Suffice it to say, there are many predisposing and precipitating factors for NAION, and various permutations of these risks can generate ischemia at the ONH.[7] Sildenafil (like other antihypertensives or, indeed, like other acquired risks) may serve as a trigger given a strong enough predisposition.

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Author reply

Dear Editor:

I am in complete agreement with Dr. Gandhi's comments. One of the reasons that systemic hypotension was not mentioned as a possible mechanism for ischemia to the optic nerve in association with sildenafil use in our article was the absence of microvascular risk factors in all of the five patients described. Two of the five patients had microvascular risk factors. Patient 4 had a history of nonarteritic anterior ischemic optic neuropathy (NAION) in the fellow eye. Patient 5 was a smoker and had coronary artery disease and diabetes. The other three patients did not have any identifiable microvascular risk factors. It is certainly possible that systemic or nocturnal hypotension could have been a risk factor for some or all of these patients.

Since this article was published, 10 additional cases of sildenafil-associated NAION have come to my attention. A summary of these cases is now being prepared for submission for publication. Interestingly, all of these additional 10 patients have microvascular risk factors, including hypertension, diabetes, or hyperlipidemia. Three of the patients had bilateral sequential NAION. One of them had final visual acuities of light perception (right eye) and hand motions (left eye).

I thank Dr. Gandhi for bringing the readers' attention to this important possible mechanism for sildenafil-associated NAION.

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Latanoprost versus Bimatoprost

Dear Editor:

Gandolfi and Cimino[1] report on a small series of patients who did not respond to latanoprost but did respond to bimatoprost. I congratulate them on their planned, prospective, balanced, crossover design. This design is very powerful for discerning small differences by diminishing the effects of biologic variability.

There are several items reported that need clarification. The characterization of bimatoprost as a prostamide is speculative and without literature support. The reference cited by the authors is a theoretical construct article without data.[2] Repetition of a theory does not produce a more valid statement. There is evidence that the bimatoprost free acid activates the human $F_{2\alpha}$ receptor, similar to latanoprost and travoprost.[3] There is also evidence that bimatoprost amide (Lumigan, Allergan, Inc., Irvine, CA) is hydrolyzed to the free acid by the human cornea.[4] Therefore it is more likely that bimatoprost is a prostaglandin analogue, the same as latanoprost and travoprost, but with poor corneal penetration. This would explain the need for the sixfold higher concentration of bimatoprost (0.03%) compared with latanoprost (0.005%). It is possible that some eyes are deficient in corneal esterase ability and may not be able to convert latanoprost into the free acid adequately. This is a more plausible explanation for the study findings than the prostamide theory.

The authors cite a prior work purporting to show "a greater percentage of eyes reaching target [intraocular pressures] in the low teens,"[5] yet have ignored published criticism regarding the incomplete and incorrect method of analysis to achieve this result.[6] The cited study showed no difference in intraocular pressure (IOP)–lowering ability between bimatoprost and latanoprost over the 3-month period. It is not valid to extract a subset of data for special analysis as was done for the target IOP results.

Lastly, it is difficult to generalize the findings of this study to clinical practice due to the highly selected study group. Everyone who practices medicine encounters patients who respond in unusual ways. Clinically there are patients who respond to latanoprost but do not respond to bimatoprost. What would a study of this group prove? The missing data from the present study are the denominator. How many patients were screened, in total, to find the group studied? Only by knowing the probability of finding such a patient can we make sense of the findings.

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