Keratocytes and Mitomycin C

We read with great interest the article about corneal wound healing after excimer laser surface ablation recently published by Marino et al.1 We agree with the authors that understanding the corneal wound healing response and the factors associated with the development of haze after surface ablation are of great interest for refractive surgeons. It is well known that a short intraoperative application of mitomycin C (MMC) helps prevent haze after these procedures and that its use has been one of the main factors responsible for the renewal of interest in surface ablation techniques.2

Nevertheless, we have to disagree with the authors when they state that “the consequent diminished cellular repopulation of the anterior stroma after MMC treatment, leading to an early decrease in keratocyte density and decreased collagen production, has raised concerns about its long-term effects,” quoting studies by Safianik et al.3 and Kim et al.4 Safianik et al.,3 did not study the effect of MMC on the cornea after laser surgery, but just described the serious corneoscleral complications that may occur when MMC is applied as a coadjuvant after pterygium excision. The MMC may cause vascular endothelial injury2 and ischemic damage in richly vascularized tissues such as the conjunctiva or the sclera. Because the cornea is already avascular, it does not suffer from this ischemic mechanism from the MMC. No serious corneal complication has been reported after a single application of this drug during corneal surface ablation.2

On the other hand, Kim et al.,4 analyzed the effect of MMC in rabbit corneas, not in human corneas, with only a 3-month follow-up.

We found that although there was a transient decrease in the keratocyte population in human corneas after surface ablation with MMC, the keratocyte density recovered normal values after a 3-year follow-up.5 Other human studies support this lack of long-term keratocyte depletion.

We believe that this evidence and the lack of long-term complications reported so far support the use of MMC in surface ablations and that new publications should not encourage fears about long-term keratocyte depletion after MMC if they are not supported by new scientific evidence.

Naturally, we believe that efforts to find other drugs to further prevent haze after surface ablation are welcome, but there is no need to demonize a drug that is already working safely and effectively.

REFERENCES


Miguel A. Teus, MD, PhD
Laura de Benito-Llopis, MRCOphth, MD, PhD
Madrid, Spain

The authors have no financial or proprietary interest in the materials presented herein.

Reply

I thank Professor Teus and Ms. Benito-Llopis for their comments on our work.1 Our article did not “demonize a drug.” In fact, as we pointed out, I have used mitomycin C (MMC) after photorefractive keratectomy in most of my patients over the past decade. However, there are many things we don’t know about corneal biology. For example, recent work has shown that there are differing phenotypes for keratocytes in a single cornea and that some of them are keratocyte stem cells.2 Nothing is known about the long-term effects of MMC on these cells. Keratocyte density measured either histologically or with in vivo confocal microscopy is a crude measurement that tells us only the density of all cells in the stromal tissue. These methods tell us nothing about the phenotype or physiology of these cells.

It is my belief that we will not know that MMC is truly safe until many decades have passed with corneas being treated without untoward effects because the long-term effects of treatment on these stromal stem cells and to the biology and health of the cornea are unknown. I could cite dozens of examples of clinical interventions that resulted in long-term unexpected outcomes because of a lack of knowledge about tissue biology. Probably the best example for the cornea is the effect of cataract surgery and poorly designed intraocular lenses triggering the bullous keratopathy epidemic a couple of decades ago, prior to our better understanding of the biology of the corneal endothelium.

We must remain vigilant and not be lulled into a false sense of security because we have not seen any is-
sues related to MMC in only a decade of use. We have no idea what the effects might be after 60 years in a particular patient’s eye.

REFERENCE


Steven E. Wilson, MD
Cleveland, Ohio

The author has no financial or proprietary interest in the materials presented herein.

doi:10.3928/1081597X-20160609-01