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Study: Epithelium-on cross-linking not yet hitting goal

Modified riboflavin solution leads to better efficacy in animal models but not in humans, study shows.

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Removal of the epithelium is still a crucial step in the cross-linking procedure, according to a study recently published in the *Journal of Refractive Surgery*.

“The modified riboflavin solution containing benzalkonium chloride (BAC-EDTA), which raised hope for the epithelium-on procedure in preclinical studies, has had disappointing results in human,” **Farhad Hafezi, MD, PhD**, principal investigator, told *Ocular Surgery News*.

In a prospective, multicenter study involving the university hospitals of Geneva and Dresden and St. Thomas’ Hospital in London, 26 eyes of 26 patients with progressive keratoconus were treated with transepithelial cross-linking using the modified BAC-EDTA riboflavin solution instilled every minute for 30 minutes. The cornea was then irradiated at 9 mW/cm² for 10 minutes.

“The treatment failed in 12 of the 26 patients, who at 1 year showed a Kmax increase of more than 1 D. If we look at the overall results, no significant change in mean Kmax or visual acuity was observed,” Hafezi, an OSN Europe Edition Board Member, said.

The high 46% failure rate is far from the 3% to 5% failure rate of epithelium-off studies and shows that the barrier effect of epithelium in human corneas is still a limitation to riboflavin absorption and oxygen diffusion even with a modified high-concentration riboflavin solution.

“In humans, epi-on CXL with the reinforced riboflavin is no better than with the basic formulation. It simply does not work,” Hafezi said.

Two lessons learned

The first lesson learned from this study is that laboratory and clinical results sometimes do not go in the same direction.

“People like us, who do basic research as well as clinical practice, know well that experimental studies are very necessary, but we always have to verify if the results reflect clinical reality,” Hafezi said.

A study by Torricelli and colleagues found that transepithelial cross-linking with BAC-EDTA riboflavin had an even greater biomechanical stiffening effect than the standard epi-off procedure in rabbit corneas.

“The opposite happened with moderately accelerated CXL (9 mW/cm²), which was shown in the lab to have a lower efficacy but is clinically still enough to stop keratoconus progression. We always have to be careful in interpreting lab results,” Hafezi said.



Farhad Hafezi

The second key message of the study is that transepithelial cross-linking does not work reliably with the techniques and tools currently available, and clinicians should be aware of such limitations.

“Our conclusion for 2016 is that as much as we want to use epi-on in every case, it works, but the success rate is much lower and we should only use it in very special cases,” Hafezi said. “My personal advice is to consider it in cases with increased risk of postoperative infection, such as children and Down syndrome patients, because they rub their eyes and are not cooperative with medications. If infection after surgery is more of a concern than reduced success, transepithelial CXL may be a reasonable compromise.”

However, the goal of performing cross-linking without removing the epithelium is still something to pursue, in his opinion, “We are trying something, and I am quite sure we will succeed eventually. Epi-on is not a dead technique — it just needs more modifications,” he said. – *by Michela Cimberle*

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