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# Two topical analgesics being studied for use after PRK

## Topical morphine and topical sumatriptan target specific receptors on corneal nerve cells to relieve pain after surgery.

By Matt Hasson
OSN STAFF WRITER

Topical morphine 0.5% significantly reduced pain, caused no complications and did not impede corneal healing after PRK, according to a team of researchers in California.

Now, the investigators are conducting a phase 2 clinical trial comparing 1% topical morphine, a topical form of the migraine medication Imitrex (sumatriptan, GlaxoSmithKline) and a vehicle control.

Ella G. Faktorovich, MD, said the off-label use of sumatriptan as an eye drop to control pain after PRK received investigational new drug approval from the U.S. Food and Drug Administration. A sumatriptan nasal spray is being formulated as an eye drop.

"We hypothesize that just as with morphine, this could also be a targeted analgesia that would have no side effects on the cornea," Dr. Faktorovich said in a telephone interview with Ocular Surgery News. "Sumatriptan selectively inhibits neurons by targeting a subset of serotonin receptors, including the 1D subtype (5HT1D). One of the co-investigators of the study, Andrew H. Ahn, MD, PhD, at the University of California, San Francisco, Department of Neurology and Anatomy, found the 5HT1D receptor expressed on unmyelinated (ie, pain-responsive) nerve fibers in the cornea. This finding offers a clear scientific rationale for the use of sumatriptan as a topical analgesic in the cornea."

Topical nonsteroidal anti-inflammatory drugs and topical anesthetics have been associated with keratitis, delayed epithelial healing, increased corneal permeability, swelling and diminished corneal transparency, she said.


Ella G. Faktorovich

Topical morphine and topical sumatriptan target specific receptors on corneal nerve cells, relieving pain without inhibiting epithelial cell growth.

Dr. Faktorovich and colleagues presented their findings of the 0.5% topical morphine study at the 2007 American Society of Cataract and Refractive Surgery meeting and plan to publish their data in an ophthalmic journal.

She cited a study published in the British Journal of Ophthalmology in 1994 showing that 0.5% topical morphine reduced response to corneal aesthesiometry in patients with corneal abrasions.

### 0.5% topical morphine study

The 0.5% topical morphine study included 40 patients randomly assigned to two groups. One group received 0.5% morphine drops, and the other group received a vehicle control (Tears Naturale II, Alcon). Patients in both groups averaged 35 years in age. They used the drops every 2 hours on the day of the procedure and

then four times a day on postoperative days 1, 2 and 3. Bandage contact lens was removed on postoperative day 4.

Patients took pain assessment questionnaires involving a visual descriptor scale, a numerical rating scale and a visual analog scale. They recorded oral analgesic use and underwent slit lamp examinations daily for 4 days, weekly for 4 weeks and monthly for 3 months. Researchers evaluated epithelial healing, corneal infiltrates, epithelial haze and stromal haze.

On the visual analog scale, patients in the topical morphine group had 50% less pain than patients in the control group after surgery, she said.

Patients in the topical morphine group also took fewer oral analgesics than those in the control group.

"Another salient feature about the results is that we did not see any difference in corneal healing or epithelialization with topical morphine compared to the artificial tears control," she said. "This is really key because there is possibly a pain reliever unlike traditional anesthetic, unlike topical nonsteroidal, that does not interfere with other functions of the cornea. This gets to the heart of why this is a targeted analgesic."

## Current study

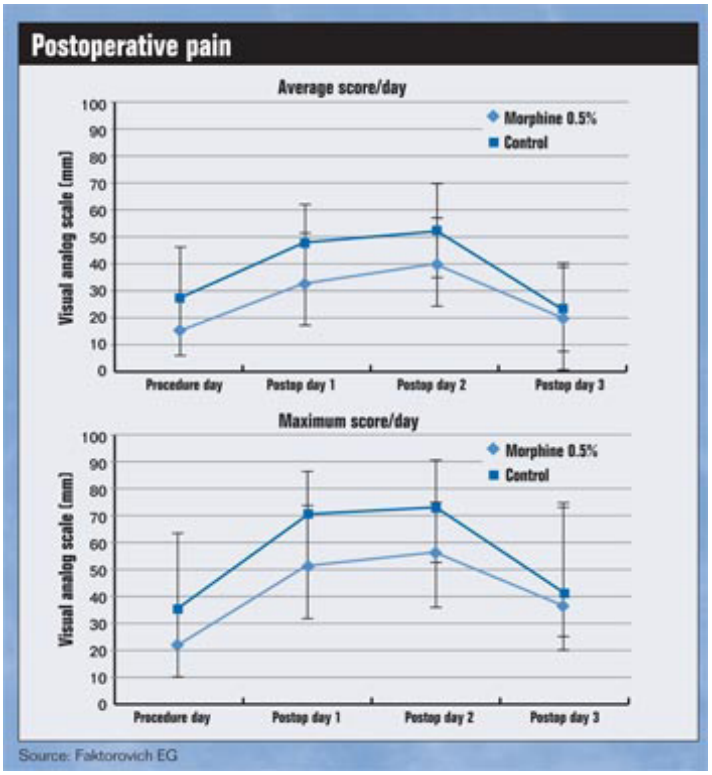
In the current trial, 24 patients were randomly assigned to three groups: 1% topical morphine, 1.2% topical sumatriptan succinate and control, Dr. Faktorovich said. The study began in April and is scheduled to end later this year. By the end of study, 20 patients in each of the three groups are expected to be enrolled.

"It is the first study of its kind for pain control after PRK, so we don't really know what concentration of Imitrex will provide the analgesic effect," she said. "We're using the concentration that we're using because it could be easily and cost-effectively re-formulated from the nasal spray."

Dr. Faktorovich predicted that 1% topical morphine will likely offer more pain relief than a 0.5% concentration, with no adverse effects.

To date, the researchers have observed no differences in epithelialization among the three groups, she said.

"I'm excited about sumatriptan and the novel use of that medication as a topical agent," Dr. Faktorovich said. "It is encouraging to see that there is no difference in corneal healing between the three groups. We'll see what the efficacy is of this particular concentration, and we'll go from there."




## For more information:

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