



# Attention Pharma & Headache Researchers! Nasal Spray Timolol May Be the Next Great Thing for Acute Migraine

by John C. Hagan, III, MD

**There is potential for a major new method of treating acute migraines using a nasal spray beta blocker. It is way past time for larger studies.**

Migraine is the third most prevalent disease in the world and foremost among common neurological illnesses. One out of every four households in the United States has someone with migraine; there are over forty-two million Americans and more than a billion migraine headache sufferers world-wide.<sup>1,2</sup> Most people with migraine are not satisfied with their current headache treatment. Many are looking for something better to add to

or replace their present acute migraine medications. These migraineurs and their physicians should be heartened by the article “Nasally Delivered 0.5% Timolol Beta Blocker Successfully Treats Acute Migraines in a Referral Headache Clinic: A Case Series” in this issue. It is a first world literature report; hopefully larger studies will follow and confirm our positive results and lead to an FDA approved migraine medication.



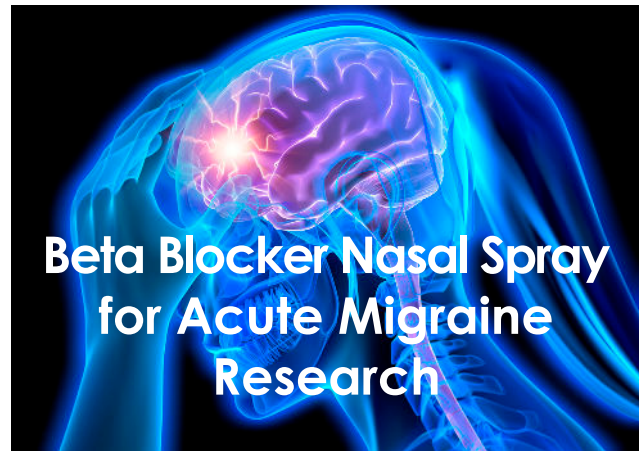
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There is the potential for a major new method of treating migraines using nasal spray beta blockers (BB), in this study timolol 0.5%. That is there is potential if a pharmaceutical company or a group of migraine researchers develop an interest, fund, then conduct a desperately-needed large, multi-center, placebo-controlled study. That quest has been the central focus of my research efforts for the past 11 years. The glacial pace of research development is inexcusable.

In 2014, Carl V. Migliazzo, MD, and I reported the world's first case-controlled series of acute migraine responsive to timolol 0.5% eye drops applied topical to normal eyes. The mechanism is simple and forthright; the timolol travels from the external eye through the lacrimal duct into the nose where it is very rapidly absorbed by nasal mucosa. Therapeutic migraine attenuating blood levels are reached in minutes. Taken as a pill orally at first onset of acute migraine, BBs have not worked because they have slow absorption and never reach therapeutic levels. Our good results were subsequently vindicated in a small, placebo control study done at University of Missouri - School of Medicine<sup>4</sup> and a large, placebo-controlled study reported in *JAMA Ophthalmology* (50 patients with over 600 acute migraines).<sup>5</sup> In the same issue published comment about the latter article, the concept, and need for further research were endorsed by an internationally known migraine authority.<sup>6</sup>

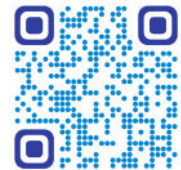
Why put BB in the eye when you want BB on the nasal mucosa? Good question and one Dr. Migliazzo and I proposed in our 2014 article. We suggested direct nasal application by BB spray. For the past 10 years I have been trying to interest academia and big-small-medium size pharma in just such a study of nasal spray BB. Like most things in life, it boils down to money. For academia, at present, not enough money to fund a large study. For pharma, not enough perceived potential for over-the-top profits. As one company told me, "Why would we want to develop an effective BB nasal spray that would compete with our more expensive and profitable migraine medications?"

My disgust and rage bubbled to the surface in the *Missouri Medicine* editorial of January/February 2022, "It Should Not Be This Difficult to Engage Pharma in an Effective, Safe, Inexpensive Product for Acute Migraine, the Third Most Prevalent Disease in the World."<sup>3</sup> Ever optimistic, some would say naïve, I expected to hear from pharma companies anxious to fund development and/or headache researchers intent on writing a large grant proposal to NIH. The lone response I got was from Steven C. Kosa, MD, a highly regarded headache specialist at our North Kansas



### SCAN CODE TO TRACK RESEARCH

- 2022 Beta Blocker Acute Migraine and Pharma Funding
- 2018 Research Update: Beta Blocker Eye Drops for Acute Migraine
- 2014 Beta Blocker Eye Drops for Acute Migraine



City Hospital. Working with O'Brien Compounding Pharmacy a 0.5% timolol nasal spray was developed, and tested in Dr. Kosa's referral headache clinic. The encouraging results are reported herein.

Our hope is that based on multiple positive published studies that either pharma or a group of neurology departments will fund and conduct larger studies that are needed. I fervently believe eventually an FDA approved BB nasal spray will be available to migraine patients who live in a world of hurt.

Let's make it happen!

### References

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