

Migraine Spray Aims to Reduce Headache Pain with Capsaicin

A new take on an old botanical remedy could yield rapid pain relief for some.

A Q&A WITH ANJAN CHATTERJEE, MD

If it wasn't presented at the AAN's annual meeting it might sound like a fraternity house hazing stunt: chili pepper extract, delivered intranasally. Indeed, hot pepper extract is not being not delivered as a prank but ideally for migraineurs to achieve pain relief. Delivery of intranasal capsaicin via a new spray formulation was the subject of Dr. Anjan Chatterjee's poster in Philadelphia. Ahead, he talks about his company's formulation, Ausanil.

YOU MADE A POSTER PRESENTATION AT THE ANNUAL MEETING IN PHILADELPHIA ABOUT INTRANASAL CAPSAICIN (IC) FOR MIGRAINES, CLUSTER HEADACHE, AND OTHER SEVERE FREQUENT HEADACHES. WHAT CAN YOU TELL US ABOUT IC AND HOW YOU BECAME INTERESTED IN IT?

As background, I should note that capsaicin is a constituent of oleoresin capsicum, which is an extract of the chili pepper plant, *capsicum annuum*.

Extracts of the plant, including *capsicum annuum* and its constituent capsaicin, have for centuries been used as an analgesic and more recently, they have been studied in the treatment of severe nerve pain in conditions such as post shingles pain and diabetic neuropathy.¹ In the last two decades, clinical data has demonstrated that intranasal administration of *capsicum annuum* or its components like capsaicin can successfully treat pain associated with cluster headaches and migraine.^{2,3}

What is less well understood is whether intranasal capsaicin can treat other types of headaches and what is the natural history of its treatment effect. In other words, how fast does IC work? How tolerable is it? What is the extent of the stinging associated with IC? What is the therapeutic tradeoff for

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the patient with severe headaches who is currently less than optimally managed by her current regimen? Specifically, we wanted to take a closer look at what the potential nasal administration of extracts of chili pepper such as capsaicin may offer in terms of response time to pain relief and tolerability, as it is thought to deplete the proximate cause of headache pain: calcitonin gene-related peptide or CGRP.

I became interested in IC for personal reasons. After several years in pharmaceutical drug development where I worked on different iterations of the CGRP antagonism idea for migraines, I came upon this novel line of research. As a lifelong migraineur myself, and one who had limited options for treatment because of side effects and my medical history, what began as curiosity to learn more became a research challenge. Then, I wanted to better understand if this could ever be a commercially viable treatment option for patients.

WHAT IS THE MECHANISM OF ACTION?

Intranasal administration of extracts of *capsicum annuum*, are thought to work locally in the nose by desensitizing the trigeminal nerve, resulting in the reduction

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(depletion) of CGRP. CGRP is thought to be the proximate cause of pain in migraines and other trigemino-vascular headaches by causing vasodilation and inflammation in the cranial blood vessels. Since both these blood vessels and the sensory supply of the nose are from CN5 (the trigeminal nerve), the desensitization of the trigeminal nerve is thought to result in the treatment of the pain in these headaches.

When administered locally in the nose, extracts of capsi-cum annuum will cause a stinging sensation (related to the local release of substance P) that indicates the action on the sensory nerve has taken place and that the treatment will begin to work to treat the headache.^{4,5}

WHAT WERE THE DESIGN AND RESULTS OF YOUR STUDY?

In terms of design, 18 patients, ages 28-65, with varying severe headache diagnoses (cluster headache, post-traumatic headache, tension type headache and medication overuse/rebound headache) and migraine were treated with intranasal capsaicin. All 18 patients suffered moderate to severe functional disability as a result of their headaches and expressed dissatisfaction with their treatment regimen, which included several commonly used prescription and non-prescription treatments such as naproxen, piroxicam, butalbital, sumatriptan, eletriptan, rizatriptan, verapamil, oxygen and prednisone (for cluster headache).

Patients were asked to use intranasal capsaicin (50µL, ipsilateral nose) to treat their headaches without the use of any additional medication and report on the effectiveness and tolerability of the medication and whether they would continue to use it for future headache episodes.

Results showed that over 72 percent of patients (N=13) experienced complete pain relief, as reported on a five-point scale from no relief to complete pain relief. Most remaining patients also reported experiencing some pain relief (4 patients) and one patient reported no pain relief.

- Eight patients (44.4 percent) reported immediate pain relief in less than one minute after use, seven (38.9 per-

cent) had intermediate onset of pain relief (between one to three minutes after use), two (11.1 percent) had “delayed” relief after more than three minutes after use and one had no response to the medicine.

- Reported relief duration ranged from 30 minutes (for the patient with cluster headaches) up to several hours.
- All 18 patients reported experiencing the local adverse event of the nasal sting, lasting between two to 10 minutes, and some reported sneezing and lacrimation (tearing of the eyes).
- All 17 patients who achieved pain relief continued to use intranasal capsaicin for subsequent episodes and reported that the sting would not dissuade them from using the medication.

In this study, a nasal sting, lacrimation and sneezing were the localized side effects reported and no body wide (i.e. systemic) side effects occurred.

WHAT IS THE APPROPRIATE PATIENT PROFILE TO RECOMMEND THIS THERAPY?

Intranasal administration of extracts of capsi-cum annuum, such as capsaicin, may be an appropriate treatment option for severe headache and migraine patients who are looking for rapid pain relief without systemic side effects or adverse drug interactions.

As background, patients often note that many treatments for severe headaches and migraine have limitations due to a variety of factors, including: onset of effect (some medications require up to an hour or more to achieve significant effect), systemic side effects (such as gastrointestinal ulcers, liver damage and risk of dependence), and potential adverse interactions with other medications, including antidepressants and blood thinners. Certain treatments may also be contraindicated for those with heart disease or a family history of heart disease or diabetes.

WHAT'S NEXT FOR IC USE IN MIGRAINES?

The purpose of this case series was to create a foundation to further examine the use of intranasal administration of extracts of capsi-cum annuum such as capsaicin for the pain relief associated with various severe headaches and migraine.

VR1 Corporation has developed and recently launched a homeopathic nasal spray in the US, which uses capsi-cum annuum to treat the pain of headaches and migraines. It is available without a prescription at www.ausanil.com. ■

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