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A Study to Evaluate the Efficacy and Tolerability of STOPAIN in the Treatment of a Single Migraine Attack

Introduction:

Migraine is a neurologic disorder characterized by episodic attacks of headache and associated symptoms such as nausea, vomiting, photophobia and phonophobia. Migraine is a headache disorder often with unilateral location, pulsating quality, moderate to severe intensity and aggravation by routine physical activity (1). Notably, migraine headache is a common disorder, affecting 12% of the general population in the United States, with prevalence by gender of 18% female and 6% male (2). In the U.S. alone, an estimated 36 million people suffer from migraine.

Migraine headache incurs estimated annual costs totaling as much as 17 billion dollars in the United States. Most of the direct costs are for outpatient services: medications, office or clinic visits, emergency department visits, laboratory and diagnostic services, and management of treatment side effects. Indirect costs from lost productivity in the workplace add substantially to the total (3). In fact, the World Health Organization (WHO) states: "Not only is headache painful, but headache disorders are also disabling. Worldwide, according to the World Health Organization , migraine alone is 19th among all causes of years lived with disability (YLDs). Headache disorders impose recognizable burden on sufferers including sometimes substantial personal suffering, impaired quality of life and financial cost. Repeated headache attacks, and often the constant fear of the next one, damage family life, social life and employment. For example, social activity and work capacity are reduced in almost all migraine sufferers and in 60% of TTH sufferers."(4)

There are many options available for the treatment of acute migraine attacks. These include oral preparations, nasal sprays, rectal suppositories and a few injectables. Topical treatments are an attractive alternative for migraine due to accessibility, rapid onset of action, direct application to the area of discomfort and lack of systemic side effects. This becomes increasingly important for patients who typically have nausea and/or vomiting associated with their migraine attacks. It allows direct application of the product to painful areas of the head and neck without causing further gastrointestinal upset.

There have been some smaller topical treatment trials such as application of 10% menthol solution for migraine in which the menthol solution was statistically superior to the placebo with regards to 2 hour pain free and pain relief endpoints as well as for alleviation of associated symptoms of nausea and/or vomiting and phonophobia and/or photophobia (5). However, there have been no larger trials and very few in the migraine population found in the literature. It is evident that more trials of topical treatments in migraine are needed (6). "We therefore determined that STOPAIN gel is safe and effective in the treatment of an acute migraine attack."

Methods:

We conducted an open label, 2 visit, pilot study of 25 subjects with a diagnosis of episodic migraine with or without aura according to the International Classification of Headache Disorders (2nd Edition-2004).

Participants:

Patients attending a specialty care headache clinic at a university hospital between June and August of 2012, with a diagnosis (made by a specialist at the center) of episodic migraine, with or without aura, in the electronic medical record, were eligible. Upon screening or interview, patients were excluded if the diagnosis was inaccurate or included history of basilar or hemiplegic migraine, if medical or psychiatric conditions increased risk of adverse events or interfered with study assessments, if the subject participated in an investigational drug trial in the 30 days prior to the screening visit, or if they were pregnant or lactating. All participants provided written informed consent prior to any screening procedures being conducted. This study was approved by Thomas Jefferson University Institutional Review Board.

Study Procedures:

Subjects were screened at Visit 1 after being properly consented for participation in the study. Screening procedures included assessment of the medical history, headache history, current medications, vital signs, height and weight measurements and a urine pregnancy test for women of childbearing potential. Investigators determined the eligibility of study subjects. Subjects were instructed on how and when to apply the topical gel to treat a migraine attack as well as how to complete a take home diary. The study medication and take home diary were given to the subject to treat a single migraine attack at home and record headache assessments. Subjects were asked to treat a single migraine attack within 8 weeks of Visit 1. After treating the attack and completing the diary, they were asked to return to Jefferson Headache Center for a final visit (Visit 2) or to return the diary and other study supplies by mail. Shipping materials were offered to each participant. During the final visit, the study drug and diary were collected and reviewed, any changes in concomitant medications and/or medical conditions since screening visit were recorded, and any adverse events experienced since screening visit were recorded.

Study Treatment Gel:

Stopain Migraine Headache Relief Formula (TM) **Troy Healthcare, LLC**
Drug Facts
Active Ingredients Belladonna3X HPUS .....*throbbing headache, vertigo* Nux Vomica6X HPUS.....*pounding pain, light and noise sensitivity* Iris Versicolor6X HPUS.....*sick headache, blurred vision, nausea* Sanguinaria Canadensis6X HPUS.....*headache over eyes* Mentholum (l-menthol)1X HPUS.....*frontal headache*
USES: Temporary relief of symptoms of migraine

Warnings: Ask a doctor before use if pregnant or nursing. Consult a physician if symptoms persist for more than 7 days or worsen. Keep this and all medications out of the reach of children. Do not get gel in eyes or on mucus membranes. If this happens flush with cool water.
Ask a doctor before use if you have: never had migraines diagnosed by a health care professional – have fever or stiff neck – headache caused by head injury – daily headaches – asthma – severe vomiting with your headache
Directions: Apply 1-2 pumps worth of gel to the back of neck area between and from back of each ear. If pain does not subside within 30 minutes reply the gel if desired.
Inactive Ingredients: Water (USP), ethanol (USP), cambopol polymer, propylenediglycol, triethanolamine

The gel was applied to the area below and abutting the back base of the skull to base of neck and span from behind and between both ears. The quantity used was two pumps from the metered dosing bottle. If there was no reduction in symptoms after 30 minutes, subjects were asked to repeat the application. If there was no relief after 2 hours, the subject was allowed to use other rescue medication.

Headache Diary:

Completed subject diaries were collected to provide data on headache severity and the presence or absence of nausea, vomiting, photophobia and phonophobia. Time of resolution of both the headache and accompanying symptoms was collected. The subject was asked to record migraine pain severity and the presence or absence of associated symptoms at 30, 60, 90 minutes and 2, 4, and 24 hours after the administration of study drug.

Results:

Participants consisted of 32 patients enrolled into the Troy STOPAIN gel study, and of those 32 patients, 25 patients completed. The primary endpoint measurement of effectiveness is the rate of responders for study gel treatment at 2 hours post gel-application compared to pre-treatment. The primary endpoint will define responders as: 1) patients with moderate to severe headaches pre-treatment that achieve pain relief (no pain) or pain reduction to mild severity two hours after gel application, and 2) patients with mild headache pre-treatment that achieve pain relief (no pain) or experience no pain progression (headache stays mild) two hours after gel application. A secondary endpoint was to compare headache severity between pre-treatment and 24 hours after gel application. For statistical analysis, ordinal conversion of pain levels were assigned as 0 = no pain, 1 = mild pain, 2 = moderate pain, and 3 = severe pain. Of the 25 completed patients, 7 patients had mild pain, 13 patients had moderate pain, and 5 patients had severe pain before treatment (pre-treatment) with study gel. Of the 25 completed patients, 7 patients had no pain/pain relief, 7 patients had mild pain, 6 patients had moderate pain, and 5 patients had severe pain 2 hours after gel application. Of the 25 completed patients, 22 patients had no pain/pain relief, 2 patients had mild pain, 1 patient had moderate pain, and no patients had severe pain 24 hours after gel application. Using ordinal conversion of headache severity, the mean headache severity at pre-treatment = 1.92 (close to moderate pain), at 2 hours = 1.36 (between mild and

moderate pain), and at 24 hours = 0.16 (very mild pain). The Wilcoxon Signed Ranks Test was used to compare pre-treatment pain severity with pain severity 2 hours after gel application. Of the 25 completed patients, 13 patients (52%) had improvement in headache pain by at least one severity level (i.e., from severe to moderate), 4 patients (16%) had worse pain, and 8 patients (32%) had no pain progression 2 hours after gel application. Asymp. Sig. (2-tailed) test statistics = .029 indicate that study gel treatment had statistically significant improvement of headache pain severity at 2 hours after study gel application compared to pre-treatment. The Wilcoxon Signed Ranks Test was also used to compare pre-treatment pain severity with pain severity 24 hours after gel application. Of the 25 completed patients, 24 patients (96%) had improvement in headache pain by at least one severity level, 1 patient had worse pain, and 0 patients had no pain progression 24 hours after gel application. Asymp. Sig. (2-tailed) test statistics = .000 indicate that study gel treatment had statistically significant improvement of headache pain severity at 24 hours after study gel application compared to pre-treatment.

Discussion:

Study results show a statistically significant improvement in headache pain by at least one severity level in 52% of patients; whereas 16% of patients had worse pain, and 32% of patients had no pain progression 2 hours after gel application. We therefore determined that STOPAIN gel is safe and may be effective in the treatment of an acute migraine attack.

References:

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