

TME COURSE OF SYMPTOM RELIEF WITH VARIOUS ANTI-MIGRAINE THERAPIES

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*On behalf of all Investigators who participated in these studies

BACKGROUND

- Aside from pain, associated symptoms of migraine occur in a large percentage of migraine patients. According to the database of POZEN clinical studies, 60% report nausea and approximately 80% report photophobia and phonophobia during a migraine attack.
- Little is known about the relationship of migraine pain to these associated symptoms over time, and how various anti-migraine therapies affect these symptoms. Studies evaluating migraine-associated nausea and its relationship to migraine pain have shown that nausea subsides as the pain of migraine abates, suggesting these two symptoms are related¹.
- The mechanism of migraine pain involves the activation and sensitization of the trigeminal vascular system. Two changes occur as a result of this activation: vasodilation of dural blood vessels and neurogenic inflammation. The 5-HT_{1B/1D} receptors are particularly important in migraine pain because they are located on intracranial blood vessels and in the central trigeminal system².
- Several anti-migraine therapies are available with differing mechanisms of action. Dihydroergotamine (DHE) and the triptans act on the trigeminal vascular system as 5-HT_{1B/1D} receptor agonists. This leads to constriction of dilated extracerebral intracranial blood vessels, reduction of the transmission of pain, and prevention of the cascade of migraine events.
- The therapeutic activity of NSAIDs in migraine treatment is attributed to a reduction in the degree of neurogenic inflammation that results from NSAID effects on prostaglandins. Antiemetic drugs offer additional relief due to increased gastric motility and a decrease in the associated symptom of nausea.
- The objectives of this presentation are 1) to compare the effects of five anti-migraine therapies on pain relief, and 2) to compare the effects of anti-migraine therapies on the secondary symptoms of nausea, photophobia, and phonophobia.

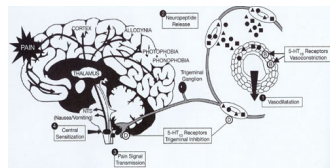


Figure from www.medscape.com - Mathew, NT. Clinical Cornerstone 2001; 4(3): 1 – 17.

METHODS

CLINICAL STUDIES OVERVIEW

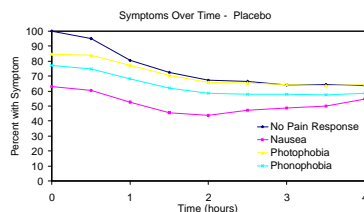
- Data was integrated from randomized, double-blind, placebo-controlled clinical studies in migraine patients given a single dose of study medication. The studies compared:
 - Study 1: Combination NSAID and sumatriptan vs. sumatriptan vs. NSAID vs. placebo
 - Study 2: Subcutaneous DHE vs. placebo
 - Study 3: Combination antiemetic and NSAID vs. NSAID vs. sumatriptan vs. placebo
- Moderate to severe baseline migraine pain in accordance with the International Headache Society (IHS) criteria was required before study drug administration³.
- Patients in study 2 returned to the clinic for subcutaneous study drug administration within 6 hours of migraine onset and were then discharged. Patients dosed themselves at home with oral study medication in the other studies.
- Measurements of pain, nausea, photophobia, and phonophobia from 0 – 4 hours were included in this analysis.
- Pain and nausea intensity were recorded from 0 (none) to 3 (severe).
- Only the presence or absence of photophobia and phonophobia was recorded.
- Rescue medication was allowed if moderate to severe pain remained at 2 hours (study 1 and 3) or 4 hours (study 2).

RETROSPECTIVE ANALYSIS OVERVIEW

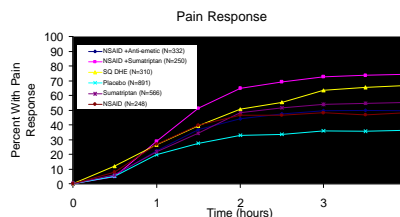
- Data from each time point from 0 to 4 hours (0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5 and 4 hours) were utilized measuring the percentage of patients at any time point that reported a particular symptom (pain, nausea, photophobia, or phonophobia).
- Data from all three studies were integrated into a meta-analysis.
- Treatments were compared at each time point using the chi-square test.

RESULTS

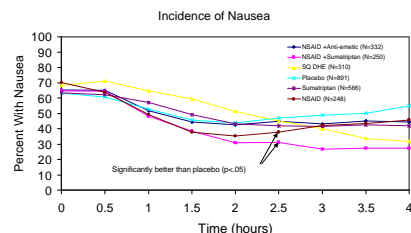
In the absence of treatment, the percentage of patients with symptoms decreased over the first 2 hours post-dose in the placebo group, and then either plateaued (pain, photophobia, phonophobia) or increased (nausea) from 2 to 4 hours.



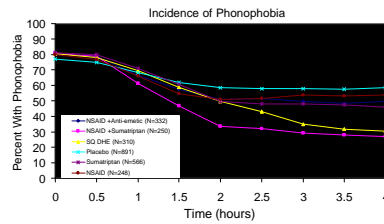
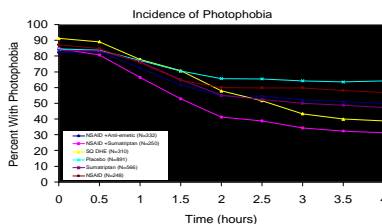
In pain response, a combination of an NSAID and sumatriptan was significantly better than other active treatments and placebo at only 1.5 hours after dosing. All active treatments were also significantly superior to placebo at 1.5 hours.



Only the combination NSAID and sumatriptan group and the NSAID group were significantly more effective than placebo at 2.5 hours after dosing in reducing the incidence of nausea.



In reducing the incidence of photophobia and phonophobia, only the NSAID and sumatriptan combination treatment was significantly superior to placebo at 1.5 hours after dosing.



CONCLUSIONS

- Pain response with any of the active treatments separated from placebo earlier than all other symptoms.
- Nausea subsided at a slower rate than migraine pain with active treatment.
- The NSAID and sumatriptan combination group demonstrated the fastest relief of photophobia and phonophobia.

REFERENCES

- Lipton RB, Pascual J, McCarroll KA, et al. Cephalgia 2001; 21 (Abstract P2-K39): 422.
- Mathew, NT. Clinical Cornerstone (www.medscape.com) 2001; 4(3): 1 – 17.
- Headache Classification Committee of the International Headache Society. Cephalgia 1988; 8 (Supp 7): 1 – 96.

- A combination of an NSAID and sumatriptan showed a consistent benefit with regard to the relief of pain and associated migraine symptoms compared to the other treatments. This suggests that targeting more than one mechanism of pain is crucial in treating moderate to severe migraine.