Early and Late Treatment of Migraine with DHE NS (Migranal®)

Meryl Latsko, MD, MPH; Stephen D. Silberstein, MD

Jefferson Headache Center, Thomas Jefferson University, Philadelphia, PA

OBJECTIVE:

To examine the use of DHE NS (Migranal®) in the early and late treatment of migraine in subjects with a history of cutaneous allodynia.

BACKGROUND:

Early migraine treatment with triptans, before the onset of central sensitization, is more effective than late treatment. In contrast, pre-clinical studies and a pilot study with injectable DHE have not shown a difference in outcome with respect to time of treatment.

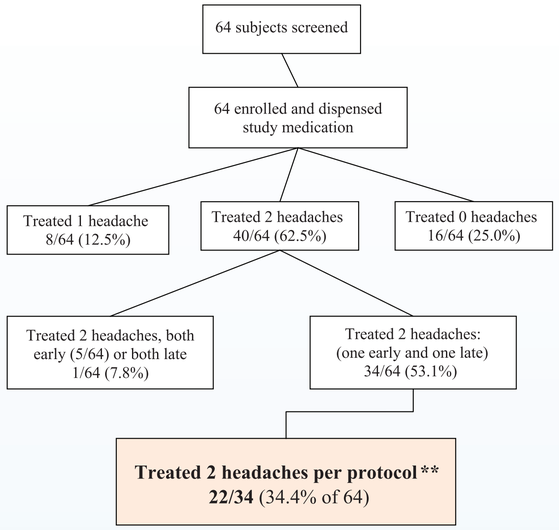
METHODS:

- Included patients with episodic migraine and a history of cutaneous allodynia.
- Subjects treated two qualifying migraines at home with open label DHE NS (Migranal®): one attack at 1 hour after the onset of throbbing pain and one attack at 4 hours after the onset of throbbing pain.
- Head pain, the presence of allodynia, migraine associated symptoms, and the use of rescue medication were assessed at defined time intervals from baseline through 24 hours after taking study medication.

RESULTS:

- No statistically significant differences in demographic and baseline headache characteristics of subjects who were randomized but did not treat 2 headaches (N=24) and those who treated 2 headaches (N=40).
- No statistically significant difference in proportion of subjects who were pain free at 2 hours post treatment:
  - Subjects who treated one early and one late headache, irrespective of compliance with time of treatment (N=34): 8/34 (23.5%) and 11/34 (32.4%) were pain free at 2 hours post study drug when treating early and late, respectively. (McNemar Test; Exact; p=0.508).
  - Subjects who treated 2 headaches per protocol (N=22): 4/22 (18.2%) and 8/22 (36.4%) were pain free at 2 hours post study drug when treating early and late, respectively. (McNemar Test; p=0.289).
- No statistically significant difference in pain reduction utilizing 4 point pain scale in subjects who treated per protocol (N=22):
  - Pain reduction defined as 2 or more point decrease: 8/22 (36.4%) and 9/22 (40.9%) had pain reduction with early and late treatment, respectively (McNemar Test; p=1.000).
  - Pain reduction defined as a 1 or more point decrease: 14/22 (63.6%) and 15/22 (68.2%) had pain reduction with early and late treatment, respectively (McNemar Test; p=1.000).

Subject Participation*



* Of subjects who treated 1or no headaches, 5 subjects were lost to follow-up, 6 subjects withdrew consent, 1 subject was discontinued due to poor compliance, and the remainder did not treat an eligible headache(s) within the time designated in the study protocol.

** Early: treatment occurred at ≤ 1.25 hr. after onset of throbbing; Late: treatment occurred at ≥ 3.5 hr after throbbing.

Demographic Characteristics of Study Participants

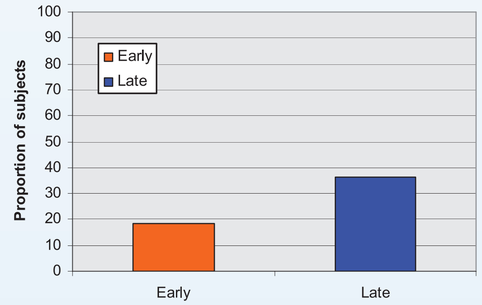
All study participants: N=64	
Age: Mean ± SD (Range)	40.86 ± 10.47 (19 – 65)
Gender	
Female	53/64 (82.8%)
Male	11/64 (17.2%)
Race	
African-American	19/64 (29.7%)
Caucasian	42/64 (65.6%)
Hispanic	2/64 (3.1%)
Other	1/64 (1.6%)

Baseline Headache Characteristics of Study Participants

All study participants: N=64	
Duration of history of migraine (yrs.) Mean ± SD (Range)	19.31 ± 12.13 (1 – 50)
Average frequency of migraine attacks per month* Mean ± SD (Range)	5.25 ± 2.13 (1 – 10)
Severity of migraine attacks Mean ± SD (Range)	7.43 ± 1.59 (5 – 10)
Type of Episodic Migraine	
Episodic Migraine with Aura	5/64 (7.8%)
Episodic Migraine without Aura	42/64 (65.6%)
Episodic Migraine with and without Aura	17/64 (26.6%)
History of triptan use	
Current	27/64 (42.2%)
Never	27/64 (42.2%)
Past	10/64 (15.6%)
History of DHE use (injectable or nasal spray)	
Current	7/64 (10.9%)
Never	48/64 (75.0%)
Past	8/64 (12.5%)
Migraine Preventive Use	
Present use	26/64 (40.6%)
Comorbid Conditions**	
Depression	12/64 (18.8%)
Bipolar	3/64 (4.7%)
Anxiety	3/64 (4.7%)
Epilepsy	1/64 (1.6%)
Fibromyalgia	2/64 (3.1%)

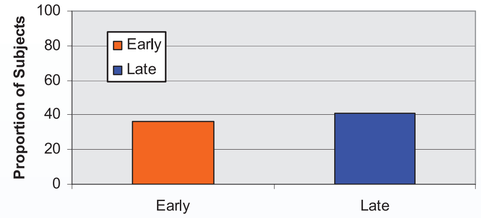
* 1/64 subjects had 1 migraine attack/month; 63/64 subjects had between 3 and 10 attacks/mo.
** Other comorbid conditions include asthma, attention deficit disorder, back pain, hyperlipidemia.

Pain Free at 2 Hours



Analysis based on subjects who treated "per protocol", N=22.
McNemar Test, p=0.289, NS

Headache Relief at 2 Hours



Analysis based on subjects who treated "per protocol", N=22.
McNemar Test, p=1.000

Adverse Events*

Nasal burning, stuffiness or discomfort	5/48 (10.4%)
Bad taste or throat discomfort	3/48 (6.2%)
Nausea	6/48 (12.5%)
Brief increased heart rate and palpitations	2/48 (4.2%)
Jaw Pain (transient)	1/48 (2.1%)
Lethargy	1/48 (2.1%)
Transient chest pain	1/48 (2.1%)

*Included all subjects who treated with any study medication (N=48).
19/48 subjects (39.6%) had at least 1 AE; 29/48 (60.4%) had no AEs

DISCUSSION:

This pilot study suggests that DHE, unlike triptans, may be as effective with late treatment as with early treatment in subjects with allodynia. However, it is possible that this study did not demonstrate a difference because of the small number of subjects and, therefore, limited power. These findings warrant larger placebo-controlled studies.

REFERENCES:

1. Goadsby PJ (2008) The 'Act when Mild' (AwM) study: a step forward in our understanding of early treatment in acute migraine. Cephalalgia 28 Suppl 2: 36-41
2. Oshinsky ML (2006) Insights from experimental studies into allodynia and its treatment. Curr Pain Headache Rep 10: 225-230
3. Saper JR, Silberstein S, Dodick D and Rapoport A (2006) DHE in the pharma-cotherapy of migraine: potential for a larger role. Headache 46 Suppl 4: S212-20
4. Silberstein SD, Young WB, Hopkins MM, Gebeline-Myers C and Bradley KC (2007) Dihydroergotamine for early and late treatment of migraine with cutaneous allodynia: an open-label pilot trial. Headache 47: 878-885

STUDY SUPPORT:

Valeant Pharmaceuticals supplied funding for the execution of this study.