# **Research Submission**

## The Prevalence of Neck Pain in Migraine

Anne H. Calhoun, MD; Sutapa Ford, PhD; Cori Millen, DO; Alan G. Finkel, MD; Young Truong, PhD; Yonghong Nie, MS

Objective.—To determine the prevalence of neck pain at the time of migraine treatment relative to the prevalence of nausea, a defining associated symptom of migraine.

Methods.—This is a prospective, observational cross-sectional study of 113 migraineurs, ranging in attack frequency from episodic to chronic migraine. Subjects were examined by headache medicine specialists to confirm the diagnosis of migraine and exclude both cervicogenic headache and fibromyalgia. Details of all migraines were recorded over the course of at least 1 month and until 6 qualifying migraines had been treated. For each attack, subjects recorded the presence or absence of nausea as well as the intensity of headache and neck pain (graded as none, mild, moderate, or severe).

Results.—Subjects recorded 2411 headache days, 786 of which were migraines. The majority of migraines were treated in the moderate pain stage. Regardless of the intensity of headache pain at time of treatment, neck pain was a more frequent accompaniment of migraine than was nausea (P < .0001). Prevalence of neck pain correlated with chronicity of headache as attacks moved from episodic to chronic daily headache.

Conclusions.—In this representative cross-section of migraineurs, neck pain was more commonly associated with migraine than was nausea, a defining characteristic of the disorder. Awareness of neck pain as a common associated feature of migraine may improve diagnostic accuracy and have a beneficial impact on time to treatment.

Keywords: migraine, neck pain, nausea, cervicalgia, headache, prevalence

(Headache 2010;50:1273-1277)

#### BACKGROUND

Although the pain of migraine is most commonly perceived in the ophthalmic distribution of the

From the Carolina Headache Institute, Chapel Hill, NC, USA (A.H. Calhoun, S. Ford, and A.G. Finkel); University of North Carolina, Department of Psychiatry, Chapel Hill, NC, USA (A.H. Calhoun, S. Ford, and A.G. Finkel); University of North Carolina, Department of Physical Medicine and Rehabilitation, Chapel Hill, NC, USA (S. Ford); Blue Sky Neurology, Denver, CO, USA (C. Millen); University of North Carolina, Department of Biostatistics, Chapel Hill, NC, USA (Y. Truong and Y. Nie).

Financial support: This investigator-initiated study was funded by GlaxoSmithKline.

Address all correspondence to A.H. Calhoun, Carolina Headache Institute, 103 Market Street, Chapel Hill, NC 27516, USA.

Accepted for publication December 3, 2009.

trigeminal nerve, a substantial percentage of migraineurs are reported to experience pain in the neck (39.7%) and occiput (39.8%) with their attacks.<sup>1</sup> A prospective cohort study found that muscle tension in the neck increased the risk of subsequent occurrence of both headache and migraine, and was second only to menstruation in its predictive value for onset of migraine.<sup>2</sup>

When discussing neck pain in the context of migraine, it is important to distinguish migraine from cervicogenic headache, a disorder characterized by head or facial pain referred from a source in the neck. Supporting evidence for cervicogenic headache

*Conflict of Interest:* Dr. Calhoun is a consultant for Merck. Dr. Finkel is on Merck speaker bureau; Dr. Calhoun receives research support and is a consultant for Teva Pharmaceuticals; Drs. Ford, Millen-Schnurr, Truong, and Ms. Nie have no conflicts to report.

includes mechanical precipitation of an attack and a reduction in cervical range of motion.<sup>3,4</sup>

Neck pain in migraineurs can be reported either (1) as the initial site of pain that later radiates forward and reaches criteria for migraine; (2) as a concomitant site of pain with the acute migraine; or (3) as a site following the acute migraine phase. When neck pain is chronic, migraineurs often report that it is not only present interictally, but waxes in intensity with the acute migraine.

There is support for neck pain being not simply a co-occurring condition in migraine, but rather related to the disorder itself. Studies show adolescent migraineurs demonstrate increased girth of neck muscles compared with nonheadache controls<sup>5</sup> as well as differences in neuromuscular function in the neck.<sup>6</sup> In this age group, frequent neck pain has been found to be associated with intractable headaches that are unresponsive to analgesics.<sup>7</sup> Similarly, a study showed that adults with transformed migraine were differentiated from those with episodic migraine by striking differences in pain threshold in the neck.<sup>8</sup> And importantly, the presence of neck pain accompanying migraine has been found to predict disability independent of headache characteristics.<sup>9</sup>

It is our intent to compare the prevalence of neck pain in migraine to that of nausea, one of the International Classification of Headache Disorders, 2nd edition (ICHD-2) diagnostic criteria<sup>10</sup> for the disorder. As nausea increases in prevalence with increasing pain of the attack, we chose to look at both of these symptoms at the time of migraine treatment to reduce bias.

#### **METHODS**

The institutional review board of the University of North Carolina approved the use of human subjects in this prospective, observational, cross-sectional study. To obtain a representative sample of migraineurs, participants were recruited both from within an academic headache clinic and from the general community. Exclusion criteria included fibromyalgia or known or suspected cervicogenic headache or history of significant cervical trauma or surgery. Over the course of 8 months in 2008, 323 individuals responded to a posting of the study, 234 were confirmed eligible, and 113 returned completed study diaries. After obtaining informed consent, subjects were interviewed and examined by headache medicine specialists to confirm diagnosis of migraine in accordance with ICHD-2 criteria.<sup>10</sup> To exclude both cervicogenic headache and fibromyalgia, the examination included physical attempts to mechanically precipitate pain, inclinometry measurements of cervical range of motion, and examination of fibromyalgia trigger points.

Details of all migraines were captured in a daily diary over the course of at least 1 month and until 6 qualifying migraines had been treated. Evidence shows that migraineurs can accurately identify migraine even in the mild pain stage.<sup>11</sup> Therefore, to obtain a balanced distribution of attack stages, subjects were permitted to treat at any stage with their customary acute agents. For each migraine attack, subjects recorded the presence or absence of nausea as well as the intensity of headache and neck pain, graded as none, mild, moderate, or severe (on a 0-3 scale).

All statistical analyses were conducted using SAS. McNemar's test was employed to compare the frequency of neck pain and nausea. Descriptive analyses were employed on demographic information. *P* values of less than .05 were considered statistically significant. Thirteen headaches were dropped from the sample because of missing data on 1 or more variable. Once missing data were deleted, the analyses were performed on 773 headaches.

#### RESULTS

The mean age of subjects was 37.4. Females accounted for 94.7% of the cohort, which was 84% non-Hispanic white. Mean body mass index was 25.7. Attack frequency ranged from episodic to chronic migraine, with almost half of the subjects (47.8%) recording headaches on 15 or more days each month.

Subjects recorded a total of 2411 headache days, 786 of which they identified as migraine days. Neck pain was more prevalent than nausea regardless of treatment stage; however, the majority of migraine attacks were first treated in the moderate pain stage.

Regardless of the intensity of headache pain at time of treatment, neck pain was a more prevalent accompaniment of migraine than was nausea (P < .0001) (Table 1, Fig.).

| Stage Treated | Number of migraines treated |           | Prevalence | Standard error<br>of prevalence | McNemar's test <i>P</i> -value |
|---------------|-----------------------------|-----------|------------|---------------------------------|--------------------------------|
| Mild          | 212                         | Neck Pain | 0.428      | 0.034                           | N = 210                        |
|               |                             | Nausea    | 0.175      | 0.026                           | P < .0001                      |
| Moderate      | 395                         | Neck Pain | 0.611      | 0.025                           | N = 391                        |
|               |                             | Nausea    | 0.357      | 0.024                           | P < .0001                      |
| Severe        | 166                         | Neck Pain | 0.726      | 0.035                           | N = 165                        |
|               |                             | Nausea    | 0.484      | 0.039                           | P < .0001                      |

Table 1.—Regardless of the Intensity of Headache Pain at Time of Treatment, Neck Pain Was More Prevalent Than Nausea at Time of Migraine Treatment

The prevalence of neck pain directly correlated with headache frequency (r = 0.32). Prevalence of nausea also correlated with headache frequency (r = 0.29); however, that correlation was dependent on the subjects with the greatest headache frequency (Table 2). When those experiencing headache on 23 or more days a month were excluded from analysis, the correlation was substantially weakened (r = 0.17).

There was a consistent linear correlation with neck pain throughout the full range of headache frequency (Table 2). In contrast, the prevalence of nausea remained relatively constant – affecting roughly half of all attacks at the time of migraine treatment – until headache frequency was 23 or more days a month. At that point, nausea was present in roughly two-thirds of attacks. One factor that might help explain this association is that subjects with chronic headaches treated at a higher mean level of headache pain (2.16 vs 1.72) than did those with episodic migraine.

#### DISCUSSION

Two specific measures were taken to enhance this study's generalizability to the larger population, specifically (1) including a balanced cross-section of patients recruited both from within a specialty headache clinic and from the general population; and (2) allowing treatment of migraine at varied stages, providing information on mild, moderate, and severe attacks. These factors may help explain the lower

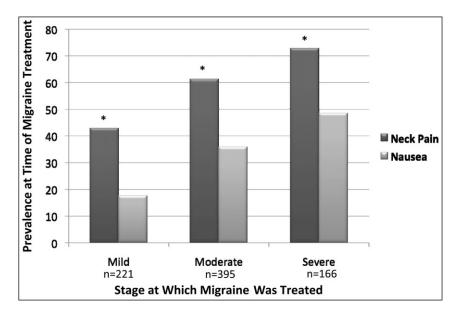


Figure.—Prevalence at time of migraine. \*P < .0001.

| HA<br>days/month | No. of<br>subjects | No. of<br>migraines<br>treated | Subject's average<br>HA days/month | Subject's average<br>NP days/month | By subject              |                             | By group                |                             |
|------------------|--------------------|--------------------------------|------------------------------------|------------------------------------|-------------------------|-----------------------------|-------------------------|-----------------------------|
|                  |                    |                                |                                    |                                    | % of<br>attacks<br>w/NP | % of<br>attacks<br>w/nausea | % of<br>attacks<br>w/NP | % of<br>attacks<br>w/nausea |
| 1-8              | 28                 | 166                            | 6.7                                | 4.2                                | 41.2                    | 24.4                        | 41.6                    | 55.1                        |
| 9-14             | 28                 | 208                            | 11.0                               | 9.2                                | 54.9                    | 25.3                        | 54.3                    | 53.1                        |
| 15-22            | 30                 | 211                            | 18.2                               | 14.1                               | 65.7                    | 37.9                        | 66.4                    | 53.6                        |
| 23-30            | 26                 | 162                            | 27.0                               | 21.0                               | 73.4                    | 48.7                        | 72.2                    | 66.7                        |

Table 2.—Descriptors for the Population, Divided into Quartiles Based on Recorded Headache Frequency

HA = headache; NP = neck pain.

prevalence of nausea in our study, compared with its reported prevalence in migraine treatment trials<sup>12</sup> in which subjects are instructed to wait until an attack is moderate to severe before treating. Similarly, higher rates are reported in retrospective interviews<sup>13</sup> of patients presenting at tertiary headache centers. In our series, 65.5% of subjects had nausea with at least 1 migraine in the preceding month.

Although all attempts were made to exclude cervicogenic headache and fibromyalgia, it is possible that if subjects who concomitantly had those diagnoses were included, there might be an increased prevalence of neck pain related to those chronic conditions, independent of migraine.

Prevalence of neck pain in our series was higher than that reported in a retrospective database analysis,<sup>1</sup> a difference possibly related to recall bias, or to the patient's attribution of the pain to other causes, with consequent failure to mention it to the examiner.

Neck muscle tenderness during migraine has been shown not to be reflective of generalized pericranial tenderness, but rather, specifically related to muscle hyperesthesia, including sternocleidomastoid, suboccipital, and temporalis.<sup>14</sup> This suggests spread and referral of pain via trigemino-cervical interaction, resulting in hyperalgesia and allodynia. Potential mechanisms include convergence of trigeminocervical afferents or central sensitization.

The high prevalence of neck pain in migraine – and its reported association with treatment resistance and disability – support the hypothesis that this neck pain may represent hyperalgesia or allodynia.

#### CONCLUSIONS

Neck pain is a common and integral feature of migraine. In this sample of migraineurs, neck pain was more commonly associated with migraine than was nausea, one of the defining characteristics of the disorder. Greater awareness of neck pain as an associated symptom of migraine may improve diagnostic accuracy and have a beneficial impact on time to treatment.

#### STATEMENT OF AUTHORSHIP

#### **Category 1**

(a) Conception and Design

Anne H. Calhoun; Sutapa Ford; Cori Millen; Alan G. Finkel

- (b) Acquisition of Data Anne H. Calhoun; Sutapa Ford
- (c) Analysis and Interpretation of Data Anne H. Calhoun; Sutapa Ford; Young Truong; Yonghong Nie

#### **Category 2**

(a) Drafting the Article

Anne H. Calhoun; Sutapa Ford; Yonghong Nie

(b) Revising It for Intellectual Content Anne H. Calhoun; Sutapa Ford; Cori Millen; Alan G. Finkel; Young Truong; Yonghong Nie

#### **Category 3**

(a) Final Approval of the Completed Article Anne H. Calhoun; Sutapa Ford; Cori Millen; Alan G. Finkel; Young Truong; Yonghong Nie

### REFERENCES

- Kelman L. Migraine pain location: A tertiary care study of 1283 migraineurs. *Headache*. 2005;45:1038-1047.
- 2. Wober C, Brannath W, Schmidt K, et al. Prospective analysis of factors related to migraine attacks: The PAMINA study. *Cephalalgia*. 2007;27:304-314.
- Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders. *Cephalalgia*. 2004; 24:1-160.
- Sjaastad O, Bovim G. Cervicogenic headache. The differentiation from common migraine. An overview. *Funct Neurol.* 1991;6:93-100.
- Airi O, Erkintalo M, Metsahonkala L, et al. Neck muscles cross-sectional area in adolescents with and without headache – MRI study. *Eur J Pain*. 2008; 12:952-959.
- Oksanen A, Poyhonen T, Ylinen JJ, et al. Force production and EMG activity of neck muscles in adolescent headache. *Disabil Rehabil*. 2008;30:231-239.
- Laimi K, Salminen JJ, Metsahonkala L, et al. Characteristics of neck pain associated with adolescent headache. *Cephalalgia*. 2007;27:1244-1254.

- Kitaj MB, Klink M. Pain thresholds in daily transformed migraine versus episodic migraine headache patients. *Headache*. 2005;45:992-998.
- Ford S, Calhoun A, Kahn K, Mann J, Finkel A. Predictors of disability in migraineurs referred to a tertiary clinic: Neck pain, headache characteristics, and coping behaviors. *Headache*. 2008;48:523-528.
- The International Classification of Headache Disorders, 2nd edn. *Cephalalgia*. 2004;24(Suppl. 1):9-160.
- Ng-Mak DS, Cady R, Chen YT, Ma L, Bell CF, Hu XH. Can migraineurs accurately identify their headaches as "migraine" at attack onset? *Headache*. 2007;47:645-653.
- 12. Lipton RB, Pascual J, Goadsby PJ, et al. Effect of rizatriptan and other triptans on the nausea symptom of migraine: A post hoc analysis. *Headache*. 2001;41:754-763.
- 13. Kelman L, Tanis D. The relationship between migraine pain and other associated symptoms. *Cephalalgia*. 2006;26:548-553.
- Fernandez-de-Las-Penas C, Cuadrado ML, Arendt-Nielsen L, Pareja JA. Side-to-side differences in pressure pain thresholds and pericranial muscle tenderness in strictly unilateral migraine. *Eur J Neurol.* 2008;15:162-168.