Mix headache: A valid clinical entity?

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ABSTRACT

Background: Chronic daily headache (CDH) patients respond better with a combination of anti-migraine and anti-stress medications, irrespective of clinical diagnosis of chronic migraine (CM) or chronic tension-type headache (CTTH). Hypothesis: “CDH: Mix headache” type is a valid clinical entity.

Materials and Methods: A total of 70 participants fulfilling the diagnosis of “primary CDH,” aged between 15 and 55 years were taken up for the present study. All these patients were subdivided into either CM or CTTH, based on the predominance of symptom profiles in these patients, in confirmation with the International Headache Society guidelines (International Classification of Headache Disorders-2, 2004). Schedules for clinical assessment in neuropsychiatry (SCAN) were applied to these patients to collect information about any mental or behavioral symptoms present at the time of the study. Psychiatric comorbidity was confirmed according to the International Classification of Diseases (ICD)-10.

Results: Forty-eight (68.6%) patients could be differentiated into CM and rest 22 (31.4%) patients were given a diagnosis of CTTH. SCAN and ICD-10 diagnosis revealed the presence of comorbid anxiety and depressive illness in 47 (67.2%) patients. Thirty-four of them belonged to CM (MH) group and the rest 13 had CTTH.

Discussion: We propose that these 47 (67.2%) patients of CDH form our special category of “CDH - mix headache” subtype. Thus, 14 (20%) patients constitute “CDH - migraine” subtype and rest 9 (12.8%) patients have a diagnosis of “CDH - tension headache” subtype.

Conclusion: Findings of the present study validate the concept of “mix headache” and explains the clinical observation that chronic daily headache (CDH) patients responds better with a combination of anti-migraine and anti-stress medications.

Key words: Chronic daily headache, chronic migraine, chronic tension-type headache, “mix headache”

INTRODUCTION

Chronic daily headache (CDH) is defined as a headache without underlying lesions and without symptoms of a disease that might be causing this chronic headache, occurring on more than 15 days a month for more than 3 months and lasting for more than 4 h/day if untreated. The classification of CDH is controversial even although the criteria proposed by Silberstein and Lipton (criteria) in 1994 and 1996 have been widely used.¹²

The second edition of the international classification of headache disorders (ICHD-II) did not comprise any CDH...
category as such but provided criteria for all four types of CDH: chronic migraine (CM), chronic tension-type headache, (CTTH), new daily-persistent headache, and hemicrania continua (HC). CM is said to be the most common of the CDHs.\(^{[2-4]}\)

Numerous attempts to relate migraine and TTH have been made in the past.\(^{[4-7]}\) Clinically, it has been observed that many patients with migraine or TTH over time can “transform” from episodic headache into a daily or near-daily headache pattern wherein the two headache types appear intimately interrelated.

It is a common clinical observation that “CDH” patients clinically respond better with a combination of anti-migraine and anti-stress medications, rather than responding either to anti-migraine or anti-stress treatment alone, irrespective of clinical diagnosis of CM or chronic tension-type headache CTTH).

This clinical experience has led us to postulate a hypothesis that “CDH: Mixed type” is a valid clinical entity. The present study conceptualized to explore and validate this clinically and diagnostically less explored the region in CDH.

**MATERIALS AND METHODS**

The study was conducted at the headache clinic run by the Department of Psychiatry, Universal College of Medical Science, Teaching Hospital, Bhairahawa, Nepal. It is a descriptive study in nature with a cross-sectional design for which we did purposive sampling technique according to certain inclusion and exclusion criteria.

The sample was recruited from Headache clinic run by the Department of Psychiatry; in UCMS Teaching Hospital from August 2011 to January 2012 (approximately 6 months). Patients referred from other departments meeting the inclusion criteria were also taken. A total of 70 cases fulfilled the inclusion and exclusion criteria were taken for the present study.

Inclusion criteria were subjects fulfilling the diagnosis of “primary CDH,” age between 15 and 55 years and having given informed consent from them for the study. Exclusion criteria were all secondary causes of CDHs such as patients having the history of head injury (posttraumatic headache), chronic physical illness or chronic infection, error of refraction and other ophthalmic illness, substance abuse or dependence, analgesic or ergotamine use daily for the past 3 months, epilepsy (convulsive or nonconvulsive), and hypertensive headache.

**Assessment tools**

Following tools were used for the study:

1. Sociodemographic and clinical data sheet:
   A semi-structured pro forma especially drafted which contained all the sociodemographic and clinical details of the patient relevant to the study

2. International headache society guidelines for classification and diagnosis of headache (ICHD-2):\(^{[3]}\)
   Headache cases were diagnosed according to IHS criteria, 2004

3. Schedules for clinical Assessment in Neuropsychiatry (SCAN), version 2.1 glossary. World Health Organization, Geneva, 1999.\(^{[8]}\)

4. International Classification of Mental and Behaviour Disorder-10: Psychiatric co-morbidity was established according to international classification of diseases (ICD-10)\(^{[9]}\)

5. Twenty-item symptom check-list for headache especially developed for the present study.

**Assessment procedure**

All the new cases registered at the headache clinic were taken up for initial screening for the purpose of the present study. During the 6-month study, a total of 486 patients attended our headache clinic. Among them, 136 of them were registered for the first time. A detail assessment of all these new cases was done in the beginning. A total of 70 cases were finally taken up after applying the inclusion and exclusion criteria set for the present study.

All these 70 cases were worked-up in detail, and a diagnosis of chronic headache was made by the individual residents posted in the headache clinic. Cases thus assessed were discussed with the consultant-in-charge of the headache clinic. The final diagnosis of chronic headache was noted after detail discussion with the consultant-in-charge in confirmation with IHS criteria 2003 (ICHD-II).

Sociodemographic and clinical data received from these patients were filled in a pro forma specially designed for the present study. All these patients were subdivided into either CM or CTTH, based on the predominance of symptom profiles in these patients. Each of these cases were then administered SCAN (version 2.1) to collect information about any mental or behavioral symptoms present at the time of the study. Each SCAN interview took approximately 45–60 min. The data thus received was recorded on “SCAN CODING BOOKLETS” according to rating scales fixed in each section. SCAN glossary was used to settle any ambiguity regarding differential definitions, symptoms, and ratings. The data thus received were then verified according to ICD-10 to confirm the presence or absence of psychiatric diagnosis and the precise diagnosis, wherever present. Finally, twenty-item “symptom Check-list for headache,” especially developed for the present study, were used to note down common symptoms of headache in these patients.

Data thus available were analyzed through computer-assisted statistical package. Percentage profile of different clinical and sociodemographic variables among different groups and sub-groups were calculated and described. For continuous data “t-test” was applied and “Chi-square”
test with Yate’s correction, whenever appropriate, was applied to categorical data.

RESULTS

A total of 70 patients (54 females and 16 males) were taken up for the present study. The mean age of our patient population was 29.5 years with 80% (56) of them belonged to age group of 15–35 years and 77% (54) of them were represented by females. Mean duration of headache was 19.4 months (standard deviation = 24.4). Migraine was diagnosed in 48 (68.5%) cases and Tension-Type of Headache in 22 (31.4%) cases [Table 1].

Table 2 reveals that there was no significant difference between CM and CTTH on most demographic parameters. Females were shown to have significantly more migraine type of a headache whereas males suffer more from tension type of headache ($\chi^2 = 5.9, P = 0.01$). Patients from Hilly region had significantly more number of migraine headache than patients coming from Tarai region ($\chi^2 = 6.6, P = 0.01$).

Although there are few parameters to assess, diagnosis of migraine headache, and tension headache is usually based on the presence of throbbing headache in migraine (CM) (95.8% cases) and dull-aching character of headache (90.9% cases) in CTTH. If we consider only these two characteristics of headache, i.e., throbbing or dull-aching nature of headache, we can differentiate CM and CTTH with significant precision ($P < 0.001$) [Table 2].

Tables 3 and 4 enumerate prevalence of various symptoms, as assessed by ‘symptom check-list of headache’, in CM and CTTH respectively. It is evident that CM and CTTH overlaps on a number of symptoms, making it difficult to differentiate CM and CTTH, routinely, in a clinical setting [Table 5]. Most significant among these symptoms, which is possible to rate and quantify with some precision, is the presence or absence of comorbid anxiety and depression.

Mix headache group is formed by 34 patients from CM group and 13 patients added from CTTH group, who had significant comorbid anxiety and depressive symptoms. They form 67.2% (47) of a total number of CDH patients (70) initially enrolled for the present study.

DISCUSSION

CDH is proposed more as a syndrome, not a diagnosis.[10] CDH is a widespread clinical syndrome, but still, not much data are available regarding actual incidence and prevalence of this disorder. Four to five percent of the general population is said to suffering from primary CDH. Many of the entities now included under CDH have been labeled differently in the past – “chronic tension headache” (CTH), “mixed headache syndrome,” “tension-vascular headache,” etc.[11,12] The concept of transformation of episodic migraine into a CDH (transformed migraine) was first introduced in 1982 by Mathew et al. Subsequently, based on the clinical history, various categories of CDH are recognized.[3,4,13,14]

We tried to differentiate our study group of 70 CDH patients into two simple groups, CM and chronic tension-type headache (CTTH). Based on the characteristic of headache and other symptom profiles, we diagnosed 68.6% (48) patients as having CM and rest 31.4% (22) patients had a diagnosis of CTTH [Table 1]. This finding is at par with that available in existing literature. Chronic transformed migraine is the most common and most easily recognizable and specifically treatable of the primary headache disorders. Mathew et al. reported 77% of their chronic headache patients had a diagnosis of transformed migraine.[4,15]

Analyzing headache symptoms in our CM and chronic tension-type headache (CTTH) patients, we found there is

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**Table 1: Distribution of demographic and clinical variables (n=70)**

| Variables                                | n (%)       |
|------------------------------------------|-------------|
| Age in years (SD)                        | 29.5 (8)    |
| Sex                                      |             |
| Male                                     | 16 (22.9)   |
| Female                                   | 54 (77.1)   |
| Education                                |             |
| Literate                                 | 50 (71.4)   |
| Illiterate                               | 20 (28.6)   |
| Marital status                           |             |
| Married                                  | 51 (72.9)   |
| Unmarried                                | 19 (27.1)   |
| Residence                                |             |
| Rural                                    | 55 (78.6)   |
| Urban                                    | 15 (21.4)   |
| Geographical distribution                |             |
| Terai region                             | 36 (51.4)   |
| Hilly region                             | 34 (48.6)   |
| Duration of headache in months (SD)      | 19.4 (24.4) |
| Intensity of headache                    |             |
| Mild/moderate                            | 23 (32.9)   |
| Severe/incapacitating                    | 47 (67.1)   |
| Location of headache                     |             |
| Frontal                                  | 23 (32.9)   |
| Central/occipital                        | 7 (10.0)    |
| Temporal                                 | 29 (41.4)   |
| Diffuse                                  | 11 (15.7)   |
| Lateralization of headache               |             |
| Lateralized                              | 47 (67.1)   |
| No lateralization                        | 23 (32.9)   |
| Quality of headache                      |             |
| Throbbing                                | 48 (68.6)   |
| Dull aching                              | 22 (31.4)   |
| Precipitating/aggravating factor         |             |
| Present                                  | 49 (70.0)   |
| Comorbidity of headache                  |             |
| Present                                  | 47 (67.1)   |
| Diagnosis of headache                    |             |
| Chronic migraine                         | 48 (68.6)   |
| Chronic tension type headache            | 22 (31.4)   |

SD – Standard deviation
significant overlap on various symptom domain [Table 5]. As reported earlier, in our study also, often it became difficult to distinguish between CM and CTTH due to such overlapping symptoms. The current opinion increasingly supports the view that there can be considerable overlap between the clinical features of migraine and tension-type headache and that these two conditions may coexist in the same patient and that migraine and tension-type headache are physiologically related entities.[11,16] Raskin (1988) proposed that migraine and TTH be considered opposite ends of a clinical spectrum of headache activity.[13] Cady et al., in a review on primary headache mentioned that the similarities between migraine and TTH often outweigh the differences and so they hypothesized that these headaches share a common pathophysiology.[17] Patients with symptoms of CDH could be categorized into one of the other major diagnoses such as migraine or tension headache, but very often these individuals did not fit into any clear-cut category.[17]

| Table 2: Few demographic and clinical variables compared with the diagnosis of headache |
|-----------------------------------------------|
| Variables | Chronic migraine (n=48) | CTTH (n=22) | χ²/df | P |
| Age (years) | 30.3 (7.7) | 27.8 (8.6) | 1.2 | 0.2 |
| Sex | Male | 7 | 9 | 5.9 | 0.01** |
| | Female | 41 | 13 |
| Marital status | Married | 37 | 14 | 1.3 | 0.2 |
| | Unmarried | 11 | 8 |
| Education | Literate | 35 | 16 | 0.00 | 0.9 |
| | Illiterate | 13 | 6 |
| Residence | Rural | 38 | 18 | 0.06 | 0.7 |
| | Urban | 10 | 4 |
| Region | Terai | 19 | 16 | 6.6 | 0.01** |
| | Hills | 29 | 6 |
| Family | Nuclear | 8 | 5 | 0.3 | 0.5 |
| | Joint | 40 | 17 |
| Employment status | Employed | 10 | 7 | 1.3 | 0.5 |
| | Unemployed | 12 | 6 |
| | Housewife | 26 | 9 |
| Duration of headache in months (SD) | 20.1 (24.5) | 18.0 (24.8) | 1.1 | 0.2 |
| Throbbing headache | 46 (95.8) | 2 (9.1) | Fisher’s exact test | <0.001*** |
| Dull aching headache | 2 (4.2) | 20 (90.9) | Fisher’s exact test | <0.001*** |

**Significant at 0.01 level, ***Significant at 0.001 level. CTTH – Chronic tension type headache; SD – Standard deviation

| Table 4: Common symptoms of chronic tension type headache (n=22) |
|-----------------------------------------------|
| Symptoms | n (%) |
| Dull aching headache | 20 (90.9) |
| Lethargy | 15 (68.1) |
| Light headedness | 15 (68.1) |
| Mood changes | 14 (63.6) |
| Diffuse or central headache | 14 (63.6) |
| Scalp tenderness | 10 (45.4) |
| Frontotemporal headache | 6 (27.2) |
| Fatigue | 5 (22.7) |
| Dizziness | 5 (22.7) |

| Table 5: Symptom/characters overlapping in chronic migraine and chronic tension type headache |
|-----------------------------------------------|
| Symptoms | Migraine (n=48; 100%), n (%) | CTTH (n=22; 100%), n (%) | χ² | P |
| Headache character | | |
| Severe/ incapacitating | 39 (81.3) | 8 (36.4) | 13.7 | <0.001*** |
| Mild/moderate | 9 (18.8) | 14 (63.6) |
| Headache lateralized | 39 (81.3) | 8 (36.4) | 13.7 | <0.001*** |
| Dizziness | 46 (95.8) | 5 (22.7) | 40.7 | <0.001*** |
| Fatigue | 34 (70.9) | 5 (22.7) | 14.1 | <0.001*** |
| Nausea | 38 (79.16) | 4 (18.1) | Fisher’s exact test | <0.001*** |
| Vomitting | 33 (68.7) | 4 (18.1) | Fisher’s exact test | <0.001*** |
| Scalp tenderness | 21 (43.7) | 10 (45.4) | 0.01 | 1.0 |
| Light headedness | 23 (47.9) | 15 (68.1) | 2.4 | 0.1 |
| Lethargy | 42 (87.5) | 15 (68.1) | 3.7 | 0.05* |
| Mood change | 40 (83.3) | 14 (63.6) | 3.3 | 0.06 |
| Comorbidity (anxiety and depression) | | |
| Present | 34 (70.8) | 13 (59.1) | 0.9 | 0.3 |

*Significant at 0.05 level, ***Significant at 0.001 level. CTTH – Chronic tension type headache
The present study tries to provide a theoretical construct of the common clinical observation that “CDH” patients respond better with a combination of anti-migraine and anti-stress medications, rather than responding either to anti-migraine or anti-stress treatment alone, irrespective of clinical diagnosis of CM or CTTH.

Who are these subgroup of patients, among CDH patients, who responds better to combination drugs? How to identify and diagnose this subgroup? Is there any specific symptom or symptom cluster to identify and isolate this subgroup of CDH patients?

Detail analysis of symptoms and symptom cluster appeared to give a hint toward the presence of such a clinical entity. The subgroup of patients showing the presence of comorbid anxiety and depressive symptoms could form a distinct subgroup of CDH patients, which appear to be fitting perfectly into our clinical observation [Table 6]. Thirty-four (70.8%) participants among our CM patients and 13 (59.1%) of CTTH patients had comorbid anxiety and depressive symptoms. Overall, we found a significant 67.1% (47) of our CDH patients had comorbid anxiety and depressive symptoms. Fourteen (20%) patients form pure “CM” group and rest 9 (12.9%) patients form pure “CTTH group.” Thus, it appears that there are three sub-varieties of CDH seen in daily clinical practice: One, CDH-“migraine” type, two, CDH- “tension headache type,” and three, CDH-“mix headache” type. This “CDH-mix headache” type can be clinically differentiated easily. They form the bulk (67.1%) of the CDH patients in our study. Moreover, this “mix headache” group probably best explains the clinical observation that is seen regularly in headache clinics all over the globe!

Long back in 1982, Saper proposed three types of CDH -predominantly migrainous headache, predominantly muscular or muscular like headache, and a third pattern “chronic mixed syndrome” has both muscular as well as vascular features co-existing.[11] Summarizing, features of “chronic mixed headache syndrome” Saper mentioned about the presence of depression and anxiety in addition to other criteria of CDH.[11] Ours is an attempt to qualify as well as quantify his “mixed headache syndrome” group with more stringent and scientific understanding.

A beginner in the headache clinic can diagnose this subgroup by applying simple bedside psychological instruments, to note the presence of significant depression and anxiety symptoms in patients diagnosed with CDH. An expert in a headache clinic can also do it easily, by giving few more minutes interviewing their patients and searching for the presence of these symptoms!

CONCLUSION

The present study conceptualized to explore and validate the clinically and diagnostically less explored regions in CDH. Our study findings point toward predominant 67.2% (47) subjects of CDH form the special category of “CDH-mix headache” subtype. Rest 20% (14) patients constitute “CDH -migraine” subtype and 12.8% (9) patients have a diagnosis of “CDH-CTTH” subtype. This theoretical proposition perfectly explains the clinical observation why majority of CDH patients responds better with a combination of anti-migraine and anti-stress medications. If the proposition is accepted by wider scientific community associated with headache research, it will have a significant impact on the way, we look and treat CDH patients.

Financial support and sponsorship
Nil.
Conflicts of interest
There are no conflicts of interest.

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