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# EVALUATION & ESTIMATION OF OUTCOMES OF HEADACHE WITH TREATMENT MODULATION & IMPACT ON QUALITY OF LIFE IN GENERAL POPULATION

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# Abstract

**Introduction:** Headache was defined as recurrent (two or more) primary episodes of pain in the head area, not secondary to any initial organic disease and, when occurring, experienced as disturbing daily life during the preceding six months. Primary headaches are the most prevalent disorders. The objective of this study was to evaluate the therapeutic outcomes and the impact on quality of life.

**Evaluation:** Analysis is completed or ongoing activities that determined the support management, accountability, effectiveness and efficiency using criteria governed by a set of standards.

**Treatment Modulation:** It is a type of therapeutic approach used to acquire better outcomes of the treatment for a condition or a disease.

**Study method:** A prospective observational study. The assessment included a specially structured headache questionnaire, Visual analog pain scale (VAS), Headache attributed lost time (HALT) and Headache and Assessment of Response to Treatment (HART).

**Sample size:** A total of 387 patients with headache completed an assessment protocol as a part of outcome study.

Study site: The study was conducted at Neurology units of tertiary care teaching hospital

**Results:** Out of 387 patients with headache 93(24.3%) were at the age group of 31-40 yrs. Gender wise 255(65.9%) were females. 327(84.4%) patients were migraineurs. Stress is the major reason for developing headache 255(70.7%). Most of the patients 283(73.12%) reported minimal impact on quality of life, the Mean lost productivity time is  $4.7\pm5.8$  days. 66.4% of patients showed average response to the given treatment.

**Conclusion:** Our study concluded that most of the people suffering with headaches are of females due to the biological changes and physical effects and educational stress. The treatment regimen indicated for headache shows better effect to the people.

Keywords: Headache, Therapeutic outcomes, Impact on quality of life.

# **Introduction:**

Headache is a sensation of pain in any region of head and which may range from sharp pain to dull pain. It is a very common symptom. It can occur on one side or both sides of the head (1).

Headache was defined as recurrent (two or more) primary episodes of pain in the head area, not secondary to any initial organic disease and, when occurring, experienced as disturbing daily life during the preceding six months(2). Primary headaches are the most prevalent disorders with 10-14% prevalence rates of migraine & 40% rates of Tension type headache(TTH)(3). Headaches are mostly seen in children & teenagers. At the age of 7, 40% of children are suffering from headaches, with 2.5% having frequent nonmigraine types & 1.4% having migraine. At the age of 15, 75% are suffering from headaches, with 15.7% of frequent tension type headaches, 5.3% of migraines, and 54% of infrequent non migraine headaches(3).In Asia, the prevalence of migraine is more seen in young people when compared to adults. In lower age groups, it is more in males than in females. It is found that prevalence rates of migraine decreases after age 50(4). The prevalence rates of migraine did not show any co-relation to age while tension type headache decreases as age increases (5).

Abrupt drug withdrawal is the treatment of choice for MOH. Drug withdrawal strategies vary. Most physicians prefer inpatient programmes. Treatment recommendations for the acute phase of drug withdrawal vary considerably between studies. They include fluid replacement, analgesics, tranquillizers, neuroleptics, amitriptyline, valproate, intravenous dihydroergotamine, oxygen, and electrical stimulation (55). Valproate has beneficial effects in the prophylactic treatment of chronic daily headache complicated

by excessive analgesic intake (57). A double-blind study showed a single subcutaneous dose of Sumatriptan to be better than placebo in the treatment of ergotamine-withdrawal headache but the headache reappeared within 12 h. A short hospital stay is recommended if MOH has lasted more than 5 years when there is additional tranquillizer, barbiturate, or opioid intake (58). Fluids should be replaced by infusion if frequent vomiting occurs. Vomiting can be treated with antiemetics e.g., metoclopramide or domperidone. The withdrawal headache can be treated with non steroidal anti-inflammatory drugs e.g., naproxen 500 mg twice daily (55). Beta-blockers will improve withdrawal symptoms such as restlessness, tachycardia, or tremor. Patients who have chronic tension-type headache may be started on a tricyclic antidepressant 4 weeks before detoxification (58). If a patient experiences more than three migraine attacks a month after withdrawal, medical and behavioral prophylaxis should be started. Clinical experience shows that many patients respond to prophylactic treatment with betablockers, flunarizine, or valproic acid after drug withdrawal (55).

# **MATERIALS & METHODS**

Place of Study: Department of Neurology" OP at Narayana Hospitals, Nellore, a 1440 bedded multidisciplinary hospital

**Study design:** The study was a prospective observational study conducted in neurology department of tertiary care teaching hospital.

Study population: This study was done in 387 patients who are suffering with different types of headaches.

Study duration: This study was conducted for 9 months (August, 2020 to May 2021)

Study criteria/Patient enrollment: Patients are enrolled in the study based on inclusion and exclusion criteria;

## **Inclusion criteria:**

All the patients suffering with different types of headaches

Patients age in between 10-80

Patients of both sexes

### **Exclusion criteria:**

Pregnancy women

Lack of interest to give information

Pediatrics

Whose verbal communication was poor

Unconscious patients

Sample Size:

## Calculation of sample size:

n = Z 2 / d2 x p q

Where Z = risk of type I error (value of Z2 is 1.962) d = absolute precision p

= assumed prevalence q = 1-p

From a previous study conducted by Abbas Ghorbaniet al. The prevalence was reported as 58.7% (82). Assuming this as prevalence and taking precision of 5% with a level of significance of 95% the minimum sample size required for the study is 373.

# **Study materials:**

Patient informed consent form

A specially designed headache questionnaire

Visual analogue scale

Headache Attributed Lost Time Index (HALT)

Headache and Assessment of Response to treatment (HART)

**Study method:** This study will be initiated after obtaining the permission from the institutional ethical committee. The patients will be enrolled in the study after taking informed consent from them. The enrollment of patients will be done on the basis of inclusion and exclusion criteria.

The data for the present study will be collected by **"Patient Interview &Chart Review Method"**, which is well suited to identify all the necessary and relevant baseline information, which will be collected on a specially designed patient data collection Proforma and Headache questionnaire. Which includes patient demographics like age, socio-economic status, family income, educational status, high risk factors, past and present medical/medication history, lab investigation data, radiographic data, physician medication order form, nurse's medication administration record (drug chart) and any other verbal communication data. The prospective observational study was carried out during the study period of 6months (August 2018 to January 2019), at Neurology department OP of Narayana Hospitals, Nellore.

A total of **387 Headache Patients** were recruited under inclusion criteria and were followed for the present study. The collected Headache patient's data were analyzed based upon the following parameters;

Based on Age, Gender, Marital status, Educational status and Hygienic conditions wise distribution.

Based on Previous Medical history.

Based on Reasons for Headache.

Based on Duration of Headache.

Based on severity Of Headache.

Based on Symptoms associated with Headache

Based on Prevalence of different

## Type of Headache.

Based on Medication history for Headaches.

Based on drug therapy for Headache patients.

Based on Impact on quality of life.

Based on Therapeutic Outcomes.

# Table 1: Shows age wise distribution of Headache patients

Age wise distribution of Headache patients: Out of 387 patients 38(9.7%) were at the age group of 10-20, 47(12.1%) were at 21-30, 93(24.3%) were at 31-40, 93(24.3%) were at 41-50, 61(15.8%) were at 51-60, 38(9.7%) were at 61-70 and 17(3.6%) were at 71-60. The mean age of the patients was  $43.91\pm14.70$ 

Age Group	No. of Cases	Percentage (%)
11-20	38	9.7
21-30	47	12.1
31-40	93	24.3
41-50	93	24.3
51-60	61	15.8
61-70	38	9.7
71-80	17	3.6

# Table 2: Shows gender wise distribution of Headache patients

**Gender wise distribution of Headache patients:** Out of 387 patients 132(34.1%) were males and 255(65.9%) were Females

Gender	No. of Cases	Percentage (%)
Male	132	34.1
Female	255	65.9

# Table 3: Shows marital status of Headache patients.

**Marital & Educational Status wise Distribution:** Out of 387 patients 325(84.1%) were married, 62(15.8%) were Unmarried.

Marital Status	No. of Cases	Percentage (%)
Married	325	84.1
Unmarried	62	15.8

## Table 4: Shows educational Level of Headache patients

Educational level of headache patients 197(51.2%) have primary education, 146(37.8%) have secondary education and 44(10.9%) have tertiary education.

Educational level	No. of Cases	Percentage (%)
Primary 🖉 🛁	197	51.2
Secondary	146	37.8
Tertiary 🔍 🔍	44	10.9

# Table 5: Shows nutritional status of Headache patients.

The nutritional status out of 387 patients 119(30..4%) have excellent status, 234(60.9%) have good status and 34(8.5) have poor cleanliness status.

Nutritional status	No <mark>. of Cases</mark>	Percentage (%)
Excellent	<mark>119</mark>	30.4
Good	234	60.9
Poor 🔪 🧹	34	8.5

# Table 6: Shows cleanliness of Headache patients.

The cleanliness status out of 387 patients 127(32.9%) have excellent status, 236(60.9%) have good status and 24(6.0) have poor cleanliness status.

Cleanliness	No. of Cases	Percentage (%)
Excellent	127	32.9
Good	236	60.9
Poor	24	6.0

## Table 7 Shows previous medical history of patients with headache

**Previous Medical history of Headache patients:** 217 (56.07%) patients have Hypertension, 122(31.5%) patients have Diabetes mellitus, 146(37.7%) patients have Hypothyroidism, 130(33.5%) have arthritis, 79(20.4%) patients have Stroke, 23(5.9%) patients have seizures, 8 (2.06%) patients have anemia and 12(3.15%) patients have Lung disease.

Previous medical history	No. of patients	Percentage (%)
Hypertension	217	56.07
Diabetes mellitus	122	31.5
Lung disease	12	3.15
Anemia	08	2.06
Arthritis	130	33.5
Thyroid	146	37.7
Seizures	23	5.9
Stroke	79	20.4

# Table 8 Shows the reasons for admission of patients with headache

**Reasons for Headache:** 269 (70.7%) patients have headache due to stress, 84(21.9%) due to sleep deprivation, 33(8.5%) due to common cold, 10(2.4%) due to dental issues, 35(8.5%) due to hypertension, 20(4.8%) due to head injury, 79(20.7%) due to irregular menstruation, 37(9.7%) due to drug abuse, 104(26.8%) due to fatigue, 10(2.4%) due to stroke.

Reason for Headache	Number of patients	Percentage (%)
Sleep Deprivation	84	21.9
Common cold	33	8.5
Dental issues	10	2.4
Hypertension	35	8.5
Head injury	20	4.8
Stress	269	70.7
Irregular menstruation	79	20.7
Drug abuse	37	9.7
Fatigue	104	26.8
Stroke	10	2.4

# Table 9 Shows the Duration of headache with patients

Out of 387 patients 10(2.4%) patients suffer 10-30 mins daily from headache, 132(48.7%) for 30mins-1 hr., 30(7.7%) for 1-2 hrs. 12(3.1%) for 2-4 hrs. 28(7.2%) for 4-6 hrs. 25(6.45%) for 6-12 hrs. 35(9.04%) for 12-24hrs., 23(5.9%) for 1day, 92(24.3%) suffer from headache attacks thought the day.

Duration of headache	Number of patients	Percentage(%)
10-30 minutes	10	2.4
30 minutes-1 hr.	132	48.7
1-2 hrs.	30	7.7
2-4 hrs.	12	3.1
4-6hrs	28	7.2
6-12 hrs.	25	6.45
12-24hrs	35	9.04
1 day	23	5.9
Constant	92	24.3

Table 10 Shows the Severity of headaches: Out of 387 headache patients 127(32.9%) patients have mild intensity headache, 196(51.2%) have moderate intensity, 64(15.8) have severe intensity. The mean of VAS pain scale at first time visit is  $7.36\pm1.84$  and the mean score of VAS pain scale at Follow up is  $3.09\pm2.43$ .

Severity of headache	Number of patients	Percentage (%)
Mild	127	32.9
Moderate	196	51.2
Severe	64	15.8

**Table-11 Shows symptoms associated with headache**: 150(38.7%) patients have nausea, 63(16.2%) have vomiting, 153(39.5%) have vertigo, 147(37.9%) have photophobia and phonophobia, 97(25.06) have visual changes, 24(6.2%) have sleep disturbances, 52(13.4%) have nasal congestion.

Symptoms associated with headache	No. of patients	Percentage (%)
Nausea	150	38.7
Vomitings	63	16.2
Vertigo	153	39.5
Photophobia	147	37.9
Phonophobia	147	37.9
Visual changes	97	25.06
Speech disturbances	24	6.2
Nasal congestion	52	13.4

# Table 12- Shows Diagnosis of Different Types of Headache:

Out of 387 headache patients 327(84.4%) were diagnosed with Migraine, 47(12.1%) with Tension type headache, 9(2.3%) with cluster headache and 4(1.03%) with Hypnic headache.

Diagnosis of patients	No. of patients	Prevalence(%)
Migraine	327	84.4
Tension type headache	47	12.1
Cluster headache	09	2.3
Hypnic headache	04	1.03

 Table 13 Shows self-medication for headache

Self-medication for headache	No of patients	Percentage (%)
NSAIDs	89	62.7
Paracetamol	33	23.2
Acetaminophen/Propyphenazone/Caffeine	21	13.9

### Table 14 Drugs advised of the pharmacist

Drugs advised of the pharmacist	No of patients	Percentage (%)
Paracetamol	181	74.3
Naproxen	63	25.6

## Table 15 Categories of drugs used for headaches

**Drug therapy for Headaches:** A total of 387 patients of Headache were enrolled in the study, out of which there were 255 female and 132 males. Among 387Headache patients, these were taken treatment for disease including Antidepressants (20.41%), Analgesics (60.7%), Anti-emetics (54.5%), and Anti-migraine (17.05%).

Categories of drugs used for headaches	No of patients	Percentage (%)
Antidepressants	79	20.41
Analgesics	235	60.7
Anti-emetics	211	54.5
Anti-migraine	66	17.05

# Table 16 Classes of drugs used for headaches

Different classes of drugs prescribed for the headache, 211(54.5%) were of NSAIDs, 26(6.71%) were of SSRIs, 9(2.32%) were of GABA agonists, 53(13.6%) were of tricyclic antidepressants, 24(6.2%) were of paracetamol, 170(43.9%) were of beta blockers, 87(22.4%) were of triptans.

Classes of drugs used for headaches	No. of patients	Percentage (%)
SSRIs	26	6.71
Tricyclic Antidepressants	53	13.6
GABA agonists	09	2.32
NSAIDs	211	54.5
Paracetamol	24	6.2
Beta blockers	170	43.9
Triptans	87	22.4

# **Table 17 Therapeutic outcomes**

**Therapeutic outcomes due to drugs:** Out of 387 patients 63(16.2%) showed poor response to the therapy, 257(66.4%) showed average response and 67(17.3%) showed good response to the given treatment.

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Therapeutic outcomes	No of patients	Percentage (%)
Poor /	63	16.2
Average	257	66.4
Good	67	17.3

## Table-18 shows Impact on Quality of Life

**Impact on quality of life:** Out of 387 headache patients, 283(73.12%) had minimal impact, 64(16.53%) mild impact, 29(7.5%) moderate impact and 11(2.85%) had severe impact on quality of life. The mean lost productivity time is  $4.7\pm5.8$  days

HALT SCORE	Impact on Quality of Life	No. of Cases	Percentage
0-5	Minimal	283	73.12
6-10	Mild	64	16.53
11-20	Moderate	29	7.5
20+	Severe	11	2.85

# **DISCUSSION:**

Out of 387 patients, 132 (34.1%) were males & 255 (65.8%) were females of age group 10-80 were included with marital status of 325 (34.1%) and unmarried were 62 (15.8%), the educational status of the patients were mostly of primary 197(51.2%), secondary 146 (37.8%) and last of tertiary 44 (10.9%), the hygienic conditions of the people were good of 234 (60.9%) and last was poor of 34 (8.5%) and most of the patients living environmental conditions were also good 294(76.8%) and last poor of 34 (8.5%). The cleanliness in patients was of approximately 236 (60.9%) which were good and last was poor 24 (6.0%). The reasons for headache are mainly stress in all the patients' 269 (70.7%), fatigue104 (26.8%) sleep deprivations 84 (21.9%) and the last was due to dental and stroke issues 10(2.4%). The maximum period of head ache onset in the people was found to be maximum of 30 min to 1 hour i.e., of 132 (48.7%) and the last is 10 to 30(2.4%) and the constant headache is also observed in people of 92 (24.3%) which in relation to affect the quality of life and was severe imbalance in the life style. Based on the observation of the patient condition the severity was assessed and the maximum were moderate 194 (51.2%), mild 127(32.9%) and severe 64 (15.8%) was observed by using different

questionnaires. The self-medication practices followed by the patients with knowingly or unknowingly were on NSAID therapies were maximum period of 89 (62.7%), only on paracetamol 33 (23.2%) and Acetaminophen/Propyphenazone/Caffeine 21 (13.9%) people were observed in our study. In some stances, the patient underwent the treatment by the guidance of pharmacist were mainly of 2 categories of drugs they are of paracetamol 181(74.3%) & Naproxen sodium 63 (25.6%). To relieve from symptoms of headache they used different categories of drugs which are mainly of Analgesics 235 (60.7%), Anti emetics 211(54.5%), Antidepressants 79 (20.41%) and minimum with anti-migraine 66 (17.05%) categories of drugs are used for the treatment to relieve from headache & its complications. To relieve from headache, the maximum classes of drugs used were NSAIDs 211 (54.5%), Beta Blockers 170 (43.9%), Triptans 87 (22.4%) & last were benzodiazepines 09 (2.32%). After the treatment the outcomes were established by observing and assessing the patient's condition and it was categorized into poor 63 (16.2%), Average 257(66.4%), and Good 67(17.3%) in which maximum were of good. Due to headaches, the changes in the quality of life & burden on the patient was analyzed with scales of Quality of life given by WHO & headache scales & observed that the most of the patients had minimal impact on quality of life after treatment 283(73.12%), mild impact 64 (16.53%), moderate impact 29(7.5%)& minimum had severe impact on quality of life 11(2.85%). In the study it is to assessed that the symptoms associated with different type of headaches were mostly of vertigo 153 (39.5%), Nausea 150 (38.7%), Photophobia 147 (37.9%), Phonophobia 147 (37.9%), sleep disturbances 24 (62%) & symptoms relapsed after treatment. The Past medical history of patients also analyzed in the study out of which, the most of the patients were of Hypertension 217(56.07%), Thyroid 146 (37.7%), Arthritis 130 (33.5%), Stroke 79 (20.4%), Seizures 23 (5.9%) and the last was lung diseases 12(3.15%). Out of them, all the diagnosis of headaches & therapy of headaches were based on its confirmation as migraine 327 (84.4%) & last was hypnic headaches 04 (1.03).

# **Conclusions:**

Our study concluded that most of the people suffering with headaches are of females due to the biological changes and physical effects and educational stress. The treatment regimen indicated for headache shows better effect to the people and the symptoms and the conditions shows the average outcome. If the clinical pharmacist support & guidance to the students & public and also educating them will help the headache free society and decreases the effects obtained due to the changes. The impact on quality of life can be made normal by educating the people As we the clinical pharmacist should provide the information about the conditions and complications and side effects to the people will enhance the quality of life and reduce the burden on the family, the government should take measures to get rid of the attacks and disharmony of headache issues and complications.

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# **References:**

1.Headache Mayo Clinic. 2018. Available from: https://www.mayoclinic.org/symptoms/headache/basics/definition/sym-20050800 2.Sillanpää M, Saarinen MM. Long term outcome of childhood onset headache: A prospective community study. Cephalalgia. 24];38(6):1159–66. Available 2018 May 22 [cited 2019 Jan from: http://www.ncbi.nlm.nih.gov/pubmed/28828903

3.Evans, Randolph W.; Mathew NT. Handbook of headache. 2nd ed. Evans, Randolph W.; Mathew NT, editor. Lippincott Williams & Wilkins; 2004. 400 p.

4. Manzoni GC, Stovner LJ. Epidemiology of headache. Handbook of Clinical Neurology. 2010.

5.Rasmussen BK, Jensen R, Schroll M, Olesen J. Epidemiology of headache in a general population-A prevalence study. J Clin Epidemiol. 1991;44(11):1147–57.

6.BS S, WF S, Simon D, RB L. Epidemiology of tension-type headache. JAMA. 1998 Feb 4;279(5):381– 3. Available from: http://dx.doi.org/10.1001/jama.279.5.381

7.Fischera M, Marziniak M, Gralow I, Evers S. The incidence and prevalence of cluster headache: A metaanalysis of population-based studies. Cephalalgia. 2008;

8.Pietrobon D, Moskowitz MA. Pathophysiology of Migraine. Annu Rev Physiol 2013 Feb 10;75(1):365–91. Available from: https://doi.org/10.1146/annurev-physiol-030212-183717

9. Ophoff RA, Terwindt GM, Vergouwe MN, van Eijk R, Oefner PJ, Hoffman SM., et al. Familial Hemiplegic Migraine and Episodic Ataxia Type-2 Are Caused by Mutations in the Ca2+ Channel Gene CACNL1A4. Cell 1996 Nov 1;87(3):543–52. Available from: https://www.cell.com/cell/fulltext/S0092- 8674(00)81373-

2?\_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867400813732%3Fshowall%3Dtrue

 Hargreaves R, Shepheard S. Pathophysiology of Migraine — New Insights. Can J Neurol Sci / J Can des Sci Neurol. 1999 Aug 2;26(03):12–9. Available from:

http://www.journals.cambridge.org/abstract\_S0317167100000147

11. Olesen J, Tfelt-Hansen P WK. Headache. Goadsby PJ, editor. JAMA 2nd ed. 2006 Feb 15;295(7):830. Available from: http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.295.7.830-

Cutrer FM. Pathophysiology, clinical manifestations, and diagnosis of migraine in adults. UpToDate. 2016;
 Goadsby PJ, Lipton RB, Ferrari MD. Migraine — Current Understanding and Treatment. N Engl J Med. 2002;

14. Goadsby PJ. Mechanisms and management of headache. J R Coll Physicians London. 1999;33(3):228-34.

15. Ferrari MD. Migraine. Lancet. 1998 Apr;351(9108):1043-51. Available from:

http://linkinghub.elsevier.com/retrieve/pii/S0140673697113708

16.Flaherty KN, Dishler EL. Headaches. In: Arcangelo VP., Peterson AM, Wilbur V, Reinhold JA, editors. Pharmacotherapeutics for Advanced Practice: A Practical Approach. 3rd ed. Lippincott Williams & Wilkins; 2013.

17.Fumal A, Schoenen J. Tension-type headache: current research and clinical management. Lancet Neurol.

2008 Jan;7(1):70–83. Available from: http://linkinghub.elsevier.com/retrieve/pii/S1474442207703253

18. Schoenen J. Depression in tension-type headache sufferers: Bystander or villain? Pain. 2004;

- 19. Gannon LR, Haynes SN, Cuevas J, Chavez R. Psychophysiological correlates of induced headaches. J Behav Med. 1987;
- 20. Manishaben Jaiswal, "CYBERCRIME CATEGORIES AND PREVENTION", International Journal of Creative Research Thoughts (IJCRT), ISSN:2320-2882, Volume.7, Issue 1, pp.526-536, February 2019, Available at: <u>http://www.ijcrt.org/papers/IJCRT1134229.pdf</u>
- 21. Manishaben Jaiswal, "CRYPTOCURRENCY AN ERA OF DIGITAL CURRENCY", International Journal of Creative Research Thoughts (IJCRT), ISSN:2320-2882, Volume.8, Issue 1, pp.60-70, January 2020, Available at :http://www.ijcrt.org/papers/IJCRT2001010.pdf

22. Ashina S, Bendtsen L, Ashina M. Pathophysiology of tension-type headache. Curr Pain Headache Rep. 2005 Dec;9(6):415–22. Available from: http://wapo.st/2h2eeOJ

- 23. Blau JN. Sleep deprivation headache. Cephalalgia. 1990;
- 24. Payne TJ, Stetson B, Stevens VM, Johnson CA, Penzien DB, Van Dorsten B. The Impact of Cigarette
- Smoking on Headache Activity in Headache Patients. Headache J Head Face Pain. 1991;
- 25. Hatch JP, Moore PJ, Cyr-Provost M, Boutros NN, Seleshi E, Borcherding S. The use of electromyography and muscle palpation in the diagnosis of tension-type headache with and without pericranial muscle involvement. Pain. 1992;
- 26. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. Cephalalgia 2004 Jun 1;24 Suppl 1(6):9–160. Available from: http://jnnp.bmj.com/cgi/doi/10.1136/jnnp.2003.031286
- 27. Penzien DB, Rains JC, Lipchik GL, Creer TL. Behavioral interventions for tension-type headache: overview of current therapies and recommendation for a self-management model for chronic headache. Current pain and headache reports. 2004.

- 28. Holroyd KA, O'Donnell FJ, Stensland M, Lipchik GL, Cordingley GE, Carlson BW. Management of chronic tension-type headache with tricyclic antidepressant medication, stress management therapy, and their combination: A randomized controlled trial. J Am Med Assoc. 2001;
- 29. Carlsson J, Fahlcrantz A, Augustinsson LE. Muscle tenderness in tension headache treated with acupuncture or physiotherapy. Cephalalgia. 1990;
- 30. Torelli P, Jensen R, Olesen J. Physiotherapy for tension-type headache: A controlled study. Cephalalgia. 2004;
- Schoenen J. Tension-Type Headache. In: Wall PD, McMahon SB, Koltzenburg M, editors. Wall and Melzack's Textbook of Pain. 5th ed. Amsterdam: Elsevier Health Sciences; 2005. p. 875–86.
- 32. Migliardi JR, Armellino JJ, Friedman M, Gillings DB, Beaver WT. Caffeine as an analgesic adjuvant in tension headache. Clin Pharmacol Ther. 1994;
- 33. Goadsby PJ, Edvinsson L. Human in vivo evidence for trigeminovascular activation in cluster headache nEuropeptide changes and effects of acute attacks therapies. Brain. 1994;
- 34. KUNKLE EC, PFEIFER JB, WILHOIT WM, HAMRICK LW. Recurrent brief headache in cluster pattern. N C Med J 1954 Oct;15(10):510–2. Available from: http://www.ncbi.nlm.nih.gov/pubmed/13224053
- 35. Ekbom K. Nitroglycerin as a Provocative Agent in Cluster Headache. Arch Neurol. 1968;

