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Migraine: Pattern of Prescription & Adverse Drug Reaction Profile in A Tertiary Care Teaching Hospital

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Abstract:

Introduction:
Migraine is commonest of different types of headache presenting to neurologists & also the most common cause of primary paediatric headache.

Aims & objective:
Due to lack of well defined research in India regarding its clinical symptomatology & anti migraine drugs used, more research in this field is required. Our study has aimed to focus on the pattern of prescription of drugs in the management and prevention of migraine & also adverse drug reactions (ADRs).

Materials & Methods:
This was a cross-sectional observational study of migrainers attending both neurology and paediatric outpatient departments of IMS & SUM Hospital, Bhubaneswar over 1 year. Clinico-epidemiological data & ADRs were obtained from patients or their attendants and from records using standard case-report form & CDSCO form respectively.

Observations & results:
Migraine was reported in a predominantly female population with frequent onset in 2nd and 3rd decade. Medications were used for the acute migraine in 1540 patients. Unilateral headache (59.8%) was common as compared to bilateral type (40.2%). NSAIDs alone were prescribed in 44.6% and combined with ergots and triptans in 33.8% cases. For prophylaxis, monotherapy was used most commonly (55.3%) followed by dual and poly therapy. Beta-blockers were most commonly used (57.1%) followed by antidepressants and calcium channel blockers. There were lots of limitations to the use of NSAID due to GI side effects. Amitriptyline showed drowsiness, dry mouth, blurred vision, and constipation.

Conclusion:
Further large clinical as well as epidemiological studies must be conducted in our country to confirm and further enlighten our observations.

Key words:
Migraine, headache, clinic- epidemiology, paediatric headache, ADR, CDSCO form

INTRODUCTION:

Headache is a common neurological disorder associated with a significant disease burden. It affects day to day activities, work, social and leisure activities which has a massive impact on a person's quality of life.[1,2] Migraine is a common headache encountered worldwide including India (up to 80% of population).[3] It is an episodic headache, become chronic if not treated promptly & effectively. Most often it is poorly diagnosed & managed in developing countries. It is characterized by unilateral severe pulsating headache accompanied by typical autonomic symptoms such as nausea, vomiting, photo- and phonophobia. First & important step of management of migraine is primary care.[4] In Netherlands, it is mainly managed by primary care and 95% of prescriptions were triptans.[5] Prophylactic therapy are an option for patients with frequent or long-lasting migraine headache.[6-11]

Insufficient data are available regarding the utilization pattern of available drugs for the prevention & management of migraine. Also ADR profile of the prescribed drugs both in paediatric and adult population are poorly documented. Rational prescriptions should be the aim of neurologists in the prophylaxis & management of migraine to increase proper & satisfactory control of headache. Desired headache control may be achieved by the pharmacological management in most of the patients. In those who fail to respond, other treatment modalities may be considered, ranging from behavior modification to major invasive medical techniques. It is hoped that this paper highlights the current outpatient therapeutic options and demonstrates a rational approach to the management of the patient with migraine both in adult & paediatric population.

MATERIALS & METHODS:

This study was carried out over one year period (from April 2013 to March 2014) in the outpatient Department of Neurology & Paediatric in collaboration with the department of Pharmacology, IMS & SUM HOSPITAL, BBSR. This was a cross-sectional observational study. All the prescriptions issued during this period were recorded on case record forms. Our study was conducted on a patient pool of 1652. Diagnosis will be made on the basis of medical history and physical examination, and, if necessary, tests to rule out other diseases or conditions causing the headache were done.

A diagnosis of migraine is usually made on the basis of repeated attacks (at least 5) that meet the following criteria:[12](ICHD-2)

- Attacks of headache last for **4 - 72 hours**
- Headache having **atleast 2** of the following characteristics: Location on one side of the head; throbbing pain; moderate or severe pain intensity; pain worsened by normal physical activity (such as walking or climbing stairs)

- During the headache, the patient has **one or both** of the following characteristics: Nausea or vomiting; extreme sensitivity to light or sound
- The headache **cannot be** attributed to another disorder

The study was approved by the institutional ethics committee and informed consent was obtained from all the study subjects.

Exclusion criteria's:

- ✓ Subjects with major neurological disorders (e.g. epilepsy, space occupying lesions, neurodegenerative disorders)
- ✓ Those with chronic daily headache (undiagnosed or mixed type)
- ✓ Substance abuse disorders

Information was also collected from a family member regarding headache of the patient. All the information was recorded on a proforma. Demographic profile of the patient (age & gender), type, etiology of headache, drug data (group & name of the drug, mono or polytherapy, number of drugs / prescription, formulation) and associated ADRs were recorded.

OBSERVATIONS & RESULTS:

The study enrolled 1652 patients from April 2013 to March 2014. Among the total study populations, 1124(68.1) were females and 528(31.9) were males.(Table 1). The youngest and oldest patient in our study was 4 and 72 years old, respectively. There is wide variability of the duration of headache i,e from 15 days to 37 years, average being 6.54 years.

Table 1: Demographic profile of the study population with percentage (n=1652):

Features	Male (no with %)	Female (no with %)	Total
Gender	528(31.9)	1124(68.1)	(n=1652)
Mean age (± SD, yr)	23.7 (± 11.2)	30.2(± 9.3)	26.5 (±10.9)
Mean age of onset(± SD, yr)	20.1 (± 8.02)	24.6 (±7.24)	22.3 (±7.82)
0-10	21(3.9)	54(4.8)	75(4.5)
11-20	102(19.3)	262(23.3)	364(22.03)
21-30	280(53.03)	405(36.03)	685((41.4)
31-40	76(14.3)	230(20.4)	306(18.5)
41-50	29(5.4)	93(8.2)	122(7.3)
51-60	18(3.4)	68(6.04)	86((5.2)
>60	2(0.3)	12(1.06)	14(0.8)

Table 2: Characteristics of migraine headache in study population (n=1652):

Parameter	Number n=1652	Percentage
Location:		
Strictly Unilateral	442	26.7
Unilateral Changing sides	547	33.1
Bilateral	663	40.2
Pulsatile	1182	71.5
Constricting	94	5.6
Associated features		
Photophobia	1360	82.2
Phonophobia	945	57.2
Nausea	1260	76.2
Vomiting	1022	61.8
Aura	324	19.6
Vertigo	852	51.5
Transient diminution of vision	113	6.84
GI symptoms	54	3.2
Sensory problems	24	1.4
Motor problems	36	2.1
Dysarthria	22	1.3
Sweating	35	2.1
Transient diplopia	12	0.7

Various characteristics of migraine were noted in the study population (Table 2).

Table 3: Distribution of precipitating factors for headache (n= 1652)

Precipitating factor	No of patient (n=1297)	Percentage (%)
Travel	1012	78.02
Tension/anxiety	888	68.4
Hunger/skipped meal	702	54.1
Lack of sleep	632	48.7
Depression	628	48.4
Watching TV/computer	318	24.5
Physical activity	305	23.5
Catamenial	215	16.5
Pollution	202	15.5
Dust	146	11.2
Summer/hot condition	94	7.2
Humidity	91	7.01
Bath	63	4.8
Cola drinks	44	3.3
Cold air	41	3.1
Chocolates	33	2.5
Smell/odour	27	2.08
Crowd	26	2.0

Headache was severe enough to hamper daily work in 1042 cases (63.07%), while rest was mild. Migraine without aura was the commonest presentation 1328(80.4%) while only 324(19.6%) had migraine with aura. 32(1.9%) patients initially presented with status migrainosus.

A number of precipitating factors were observed (Table 3). 1297 patients (78.6%) had one or more aggravating factors, 355 patients (21.4%) had none. Amongst these, commonest were travel, mental tension & hunger. Some patients reported, precipitation of attacks by certain foods (fish, cheese, cold drinks), perfumes, agarbatti, petrol, phenyl & cigarette smoke.

Familial hemiplegic migraine was seen in one patient. Seizures were associated in 43(2.6%) cases. Prior history of head trauma was noted in 63(3.8%) patients. Connective tissue disorders and allergic disorders were a/w 32 (1.9%) and 44 (2.6%) patients, respectively. 18(1.08%) patients also had previous H/O stroke. None of the patients were found to have other progressive neurological deficits like ataxia, pyramidal or extrapyramidal symptoms. Neuroimaging was done in 326(19.7%) patients. Nonspecific T2/FLAIR hyper intensities in sub cortical white matter were seen in 83(25.4%) patients.

In our set up medications were used for acute relief of headache in 1540 patients (93.2%).

Table 4: Drug treatment for acute pain relief (n=1540)

Drugs	Number with%
NSAID alone	688(44.6)
Ergotamine preparations alone	152(9.8)
Triptan alone	172(11.1)
NSAIDS with Ergotamine	262(17.01)
NSAIDS with Triptan	266(16.8)
Anti emetics in combination	430(27.9)
Steroid	48(3.1)

Total 2546 drugs were used. The drug used per patient was 1.65. Sometimes drugs in combinations were also used.

NSAIDS commonly used were paracetamol, ibuprofen, naproxen sodium, indomethacin, diclofenac sodium, mefenamic acid & aspirin. NSAIDs Combination ontaining aspirin, caffeine, & acetaminophen were used. The triptans used were sumatriptan (Oral, Intranasal, Subcutaneous), almotriptan (Orally), rizatriptan (Oral), zolmitriptan (Oral, intranasal). Combination of triptans and NSAIDs: Sumatriptan 85 mg/naproxen 500 mg was also used. Ergotamine preparation used was dihydroergotamine (IV, IM, Oral). Antiemetics used were metoclopramide, prochlorperazine, ondansetron.

The prophylactic therapy in patients with migraine headache was initiated in 882(53.3%) patients with following indications [13]:

- ✓ Contraindications or intolerance to acute therapies
- ✓ Headache symptoms occurring > 2 days/week
- ✓ Headaches that severely limit quality of life despite acute therapy
- ✓ Presence of uncommon migraine conditions (hemiplegic migraine, basilar migraine, migraine with prolonged aura, or migrainous infarction)

Table 5: Prophylactic therapy in migraine: % of mono, dual and polytherapy (n=882)

Monotherapy	488(55.3)
Dual therapy	323((36.6)
Polytherapy	71(8.1)

In dual therapy, combinations used were Beta blockers+ Antidepressant 152(47.05%), Beta blockers + Calcium channel blockers 81(25.07%) etc.

Table 6: Groups of drugs for prophylaxis of migraine with % of side effects noted:

Types of drugs	No of prescription (n=882)	Side effects & % (n=132)
βBlockers: Propranolol, Metprolol, Atenolol	504(57.1)	31(6.1)
Antidepressants: Amitriptyline,Nortriptyline	291(32.9)	47(16.1)
Calcium Channel Blockers: Flunarizine, Verapamil	196(22.2)	15(7.6)
Anticonvulsants: Valproic acid	183(20.7)	22(12.02)
Topiramate	109(12.3)	10(9.1)
Gabapentine	26(2.9)	3(11.5)
Serotonergic Agents: Cyproheptadine	22(2.4)	2(9.09)
Onabotulinumtoxin A injection	16(1.8)	2(12.5)

Table – 7: Analysis of prescriptions for prophylactic therapy in migraine (n=882)

Number of prescriptions	882(53.3%)
Total no. of drugs prescribed	1347
Total no. of drugs prescribed through oral route	1331
Average no. of drugs prescribed per prescription	1.5
Number of fixed dose combinations	87(6.5)

Table 8: Drugs showing ADRs used for acute therapy in migraine n=203 (7.9%):

Drugs	n=2546	No of ADR with %	ADRs
NSAID	1216(47.7)	88(7.2)	Nausea, vomiting (NV), constipation, acid peptic disease, GI bleeding, drowsiness, hypertension
Ergotamine preparations	414(16.2)	47(11.3)	NV, stomach pain, diarrhea, chest pain, dizziness, weakness, drowsiness, seizure, confusion., pedal edema, burning, tingling extremities
Triptan	438(17.2)	40(9.1)	NV, jaw, neck or chest tightness, tachycardia; fatigue; numbness-tingling (especially face); burning, pain, or soreness in nose (nasal spray), taste change (nasal spray), dizziness, dry mouth, muscle cramps.
Anti emetics	430(16.8)	22(5.1)	Constipation, dizziness , headache, arrhythmia
Steroid	48(1.8)	6(12.5)	↑ BP, hyperglycemia, easy bruising, stretch marks, muscle weakness, mood and behavioral changes, gastric ulcers, infection, acne, blurred vision

ADR noted in 203(7.9%) patient with 2546 drug prescribed.

Table 9: Drugs showing ADRs in for prophylactic therapy of migraine 132(14.9%):

Name of the group of drugs	No of ADRs (%)	Side effects noted
Antidepressants: Amitriptyline, Nortriptyline	47(35.6)	Drowsiness, head reeling, dry mouth, blurred vision, constipation
β Blockers: Propranolol, Metprolol, Atenolol	31(23.4)	Asthenia, tiredness, postural hypotension, sleep disturbance, depression
Anticonvulsants: Valproic acid, divalprox sodium	22(16.6)	Sedation, dizziness, tremor, ↑appetite, ↑ bleeding time, alopecia, and ↑LFTvalues
Calcium Channel Blockers: Flunarizine, Verapamil	15(11.3)	Weight gain, tiredness, depression
Topiramate	10(7.5)	Parenthesis and weight loss, kidney stone, sedation, cognitive dysfunction
Gabapentine	3(2.2)	Dizziness and sedation
Serotonergic agents: Cyproheptadine	2(1.5)	Drowsiness, weight gain.
Onabotulinumtoxin A inj	2(1.5)	Muscle weakness at the site of injection; bruising, bleeding, pain, redness, or swelling, fever, cough, sore throat, runny nose, flu symptoms, dizziness, drowsiness

DISCUSSION:

In our set up, the commonest complaint with which patient comes to the neurology OPD was headache. The study population had female preponderance (68.1%). The Female to male ratio is 2.1: 1. The literature from various studies from western society also suggests, migraine is more frequent in the female population.[14]Another study regarding the sex distribution in India, showed the female to male ratio as 2.5:1.[15] The mean age of onset of migraine was 22.3±7.82 years and majority of cases had onset in 3rd and 2nd decade [1049(63.4%)]. There was decrease in frequency of migrainers as age advances irrespective of the gender. 14(0.8%) patients were more than 60 years in our study group. Also it was seen in different studies on Indian population that migraine is a disease of the young. It has been observed that the prevalence of migraine increases at the time of puberty without significant differences between the genders, with a subsequent increase in prevalence in females after puberty.[16] The majority of the patients in our study sample suffered from migraine without aura with a prevalence of 80.4%. Migraine without aura is the commonest presentation in both Indian and western studies.[15]

Trigger factors are important for migraine as these may be helpful as indicators to treat the cause & severity of migraine attack. The most common precipitants in this study were travel (78.02%), tension, hunger/ skipped meal/ fasting, insomnia, depression etc. Some interesting but unrelated stress factors also were observed during our study period such as fish, vegetables, fast foods etc and changing weather (even taking a bath). Certain other factors associated with migraine include frequent & more television, strong light, computer, eating citrus fruits. [16 ,17]

Association of migraine with allergic and psychiatric disorders was seen in our study population, such as migraineurs with significantly more asthma and chronic musculoskeletal pain compared to non- migraineurs (5%versus 3.2% and 39% versus 25%, respectively).[18]

Unilateral type of headache (59.8%) was much more common than bilateral type (40.2%). Headache was throbbing (71.5%) in nature in a majority of migraneurs which was consistent with various previous studies.[19, 20] Some other studies from India showed strictly unilateral pain in 40.5% patients and 1/5th of them was suffered from true hemicranial headache (oculo-fronto-temporoparietal or fronto-temporoparietal). [21] The above finding was in contrast to the previous finding in the west which showed [22]hemicranial headache in 71.2% of subjects with episodic migraine and > 60% of those with chronic migraine. Our study showed photophobia, phonophobia, nausea, and vomiting as the most common accompanying symptoms as the previous reports.[23]Other reported symptoms were dizziness, allodynia, and neck stiffness.

Association of migraine with psychiatric disorders like generalized anxiety and depressive disorder was 228/1652(13.8 %). In female, the association most commonly seen with mixed dissociative disorders (fits and fainting). Migraine is more commonly associated with anxiety disorder than with depression.[20,24]

It was observed that migraine was under diagnosed & management was insufficient affecting quality of life. Avoidance of trigger factors is important in management of migraine.

In our study, for acute attack, NSAIDs alone were prescribed in 44.6% of cases and in combination with ergots and triptans 33.8% cases. For acute therapy ergotamine and sumatriptan alone were used in 9.8% and 11.1% cases, respectively. NSAIDs are a usual first-line therapy for mild to moderate migraine. A 2007 meta-analysis of ibuprofen for moderate to severe migraine showed that 200mg and 400mg doses were effective for short-term pain relief.[25] Ketorolac, a parenteral NSAID, was found to be effective in reducing headache even more than sumatriptan. [26] The practice parameters by the American Academy of Neurology recommend sumatriptan, ergotamine and its derivatives to be more effective than NSAIDs for acute attack.[27] Higher use of NSAIDs in this study could be due to easy availability and less cost. Triptans are considered first-line therapy for moderate to severe migraine or mild to moderate attacks unresponsive

to analgesics.[28] 32(1.9%) patient initially presented with status migrainosus and 98(5.9%) during the course of the disease in our study. Steroid was being used in 48(3.1%) cases. In two meta-analyses, dexamethasone was added to other standard therapies, showed that about 10 patients needed treatment to prevent headache recurrence within 24 to 72 hours.[29,30]

In prophylaxis of migraine, monotherapy was used most commonly in 55.3% patients followed by dual therapy and poly therapy. Beta-blockers were most common dugs (57.1%) followed by, antidepressants and calcium channel blockers. Studies have shown Beta blocker (60-80%) were effective in reducing attack frequency by more than 50%.[31]Although propranolol is the most commonly prescribed drug in this class, there is no evidence of difference in efficacy between propranolol & other ß-blockers (atenolol, metoprolol or bisoprolol).[32] Among antidepressant, amitriptyline was most commonly used. Some clinical trials suggest that amitriptyline is at least as good as propranolol if not better in reducing headache frequency. [31]

OnabotulinumtoxinA injection was used in 1.8% cases, mostly in resistant headache. It is also approved for prevention of migraine but is best for chronic (not episodic) migraine. As prophylaxis is not sufficient to prevent the attacks, patients must use acute medication concurrently.

In a large European study, by order of frequency, the prophylactic treatments administered were topiramate (43%), β-blockers (18%), flunarizine (17%), amitriptyline (14%). β-blockers and flunarizine were used much more frequently in men and antidepressants were more in women.[33] A France study (2000), revealed dihydroergotamine and β-blockers were most commonly used in migraine prophylaxis.[34] There are no literatures about the management of migraine in relation to various drugs from India.

We studied ADRs of various drugs. In acute migraine therapy we have noted ADR in 203 patients (7.9%). Steroid and ergotamine preparations were implicated for more frequent ADR 6(12.5%) and 47(11.3%) respectively.

During prophylaxis we have encountered 14.9% ADRs with antidepressant & β blockers having frequent ADR with 35.6 & 23.4% respectively.

There were lots of limitations regarding the use of NSAID in migraine patients due to GI side effects which may be minimized by Metoclopramide use.[35,36] ADRs related to ergot alkaloids include nausea, vomiting, diarrhea and vertigo [37, 38, 39] chronic ergotism (severe peripheral vasoconstriction & gangrene in the extremities) which may prevent ergotamine use for migraine prophylaxis. The triptans may produce dizziness, paresthesias, somnolence, fatigue, flushing, myalgias and transient increases in blood pressure. Other effects, including chest and neck symptoms.[40]The intranasal route may cause local reactions & taste disturbances.[41, 42]

β blockers in our study showed various ADRs such as asthenia, tiredness, postural hypotension, sleep disturbance, depression which was comparable to other studies and were well tolerated.[43] Amitriptyline was showing different ADRs such as drowsiness, head reeling, dry mouth, blurred vision, constipation similar to other studies.[43]ADRs change the focus of physicians for alternative drugs such as SSRIs. [44] Anticonvulsant such as valproic acid use in our study experienced with ADRs such as sedation, dizziness, tremor, alopecia, and ↑liver function test values which should be avoided in patients with a H/O pancreatitis or hepatic disorder, such as cirrhosis or chronic hepatitis.[31] Gabapentin was associated with dizziness and sedation which was similar to other studies.[45] In our study topiramate showed weight loss, kidney stone, sedation, cognitive dysfunction whereas some studies showed lots of GI side effects.[46]

Management & prophylaxis of migraine in children: Most cases only mild analgesics & homemade remedies are sufficient. The American Academy of Neurology's practice guidelines for children and adolescents recommend the following drug treatments [47]:

- Children ≥6yrs, ibuprofen, acetaminophen (acetaminophen works faster, ibuprofen longer)
- For adolescents (≥12 years), sumaptriptan nasal spray is recommended

Non-medicinal methods like muscle relaxation techniques may be helpful in prevention of migraine in children. If failed, preventive drugs may be used (effectiveness is not proved).

CONCLUSION:

The treatment options for episodic migraine are varied and depending upon the individual patient. Physicians should be well aware of the different groups of drugs, efficacy and side effect profile of the drugs they choose, but not basing on their clinical experience only. Patient education is the most important measure for effective migraine treatment program. Although more high quality clinical studies into migraine preventative agents are needed this must be correlated by our patient's response. Important areas for future research include:

- Identification of associations between symptoms, signs, and pathology
- Mechanism based treatment strategies
- Comparison of polytherapy, dual therapy treatments with monotherapy;
- Last but not the least, conducting pharmacogenomic studies

REFERENCES:

1. Leonardi M, Steiner T J, Scher A T & Lipton R B. The global burden of migraine: measuring disability in headache disorders with WHO Classification of Functioning, Disability and Health (ICF). J Headache Pain, 2005; 6: 429–440.
2. Linde M. & Dahlöf C. Attitudes & burden of disease among self-considered migraineurs: a nation-wide population-based survey in Sweden. Cephalalgia 2004; 24: 455–465.
3. Stovner LJ, Hagen K, Jensen R, Katsarava Z, Lipton RB, Scher AI, Steiner TJ, Zwart J-A The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia, 2007; 27:193–210
4. Freitag FG: The cycle of migraine: patients' quality of life during and between migraine attacks. Clin Ther, 2007; 29:939-949.
5. Dekker F, Wiendels N, de Valk V, van der Vliet C, Knuistingh Neven A, Assendelft WJJ etal: Triptan overuse in the Dutch general population: A nationwide pharmaco-epidemiolology database analysis in 6.7 million people. Cephalalgia 2011; 31:943-952.

6. D'Amico D, Solari A, Usai S, Santoro P, Bernardoni P, Frediani F,etal: Improvement in quality of life and activity limitations in migraine patients after prophylaxis. a prospective longitudinal multicentre study. Cephalalgia 2006; 26:691-696.
7. Silberstein SD, Winner PK, Chmiel JJ: Migraine preventive medication reduces resource utilization. Headache 2003, 43:171-178.
8. Goadsby PJ: Recent advances in diagnosis & management of migraine.BMJ 2006; 332:25-29.
9. Peres MF, Silberstein S, Moreira F, Corchs F, Vieira DS, Abraham N, Gebeline- Myers C: Patients' preference for migraine preventive therapy. Headache 2007; 47:540-545.
10. Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF: Migraine prevalence, disease burden & need for preventive therapy. Neurology 2007; 68:343-349.
11. Goadsby PJ, Sprenger T: Current practice and future directions in the prevention and acute management of migraine. Lancet Neurol 2010; 9:285-298.
12. Headache Classification Committee of the International Headache Society, The international classification of headache disorders. Cephalgia 2nd, 9–160
13. Migraine headache. AAN summary of evidence-based guideline for clinicians. St. Paul, Minn.:American Academy of Neurology; 2009. Accessed December 14, 2010.
14. Stewart W F, Lipton R B, Celentano D D & Reed M L. Prevalence of migraine headache in the US. Relation to age, income, race & other sociodemographic factors. JAMA, 1992; 267, 64–69.
15. Panda S & Tripathi M. Clinical profile of migraineurs in a referral centre in India. J Assoc Physicians India, 2005; 53, 111–115.
16. Bener A etal. Genetic & environmental factors associated with migraine in schoolchildren. Headache, 2000; 40, 152–157.
17. Stewart WF, Linet MS, Celentano DD, Van NM & Ziegler D.Age & sex-specific incidence rates of migraine with & without visual aura. Am J Epidemiol, 1991; 134, 1111–1120.
18. Terwindt G M. et al. The impact of migraine on quality of life in the general population: the GEM study. Neurology, 2000; 55, 624–629
19. Kudrow, L. Current aspects of migraine headache. Psychosomatics, 1978; 19, 48–57.
20. Merikangas K R, Risch N J, Merikangas JR, Weissman M M. & Kidd K K. Migraine & depression: association & familial transmission. J Psychiatr Res, 1988; 22, 119–129.
21. Chakravarty A, Mukherjee A & Roy D. Migraine pain location in adult patients from eastern India. Ann Indian Acad Neurol, 2008; 11, 98–102.
22. Kelman L. Migraine pain location: a tertiary care study of 1283 migraineurs. Headache, 2005; 45, 1038–1047.
23. Bokhari F A, Sami W, Shakoori T A, Ali S A & Qureshi G A. Clinical characteristics of 226 college-going female migraineurs in Lahore, Pakistan - putting ICHD-2 to the road test. Neuro Endocrinol. Lett. 2008; 29, 965–970.
24. Breslau N, Davis G C & Andreski P. Migraine, psychiatric disorders & suicide attempts: an epidemiologic study of young adults. Psychiatry Res, 1991; 37, 11–23.
25. Suthisisang C, Poolsup N, Kittikulsuth W, Pudchakan P, Wiwatpanich P. Efficacy of low-dose ibuprofen in acute migraine treatment: systematic review and meta-analysis. Ann Pharmacother. 2007;41(11):1782-1791
26. Meredith JT, Wait S, Brewer KL. A prospective double-blind study of nasal sumatriptan versus IV ketorolac in migraine. Am J Emerg Med. 2003; 21(3):173-175.
27. Silberstein SD for US Headache Consortium. Practice parameter: Evidence-based guidelines for migraine headache. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2000; 55:754-763.
28. Morey SS. Guidelines on migraine: part 2. General principles of drug therapy. Am Fam Physician. 2000; 62(8):1915-1917
29. Singh A, Alter HJ, Zaia B. Does the addition of dexamethasone to standard therapy for acute migraine headache decrease the incidence of recurrent headache for patients treated in the emergency department? A meta-analysis and systematic review of the literature [Acad Emerg Med 2009; 16(5):435]. Acad Emerg Med 2008; 15(12):1223-1233.
30. Colman I, Friedman BW, Brown MD, et al. Parenteral dexamethasone for acute severe migraine headache: meta-analysis of randomised controlled trials for preventing recurrence. BMJ. 2008; 336(7657):1359-1361.
31. Silberstein SD, Goadsby P. Migraine: Preventative treatment.Cephalalgia 2002; 22:491-512.
32. Rapoport A. Acute and prophylactic treatments for migraine:Present and future. Neurol Sci 2008; 29:S110-22.
33. López Hernández N, Morera Guitart J, Medrano Martínez V, Fernández Izquierdo S & Pérez Sempere A. Prevention of migraine:a pharmacoepidemiological study. Neurologia, 2009; 24, 98–101.
34. Lantéri-Minet, M. et al. [Pharmaco-epidemiological study on the prophylactic treatment of migraine. National inquiry on attitude to prescription practices by primary care physicians and neurologists in Franceø]. Rev. Neurol. (Paris), 2000; 156, 1106–1112.
35. Diener HC, Lampl C, Reimnitz P, et al. Aspirin in the treatment of acute migraine attacks. Exp Rev Neurother 2006;6(4):563–573.
36. Tfelt-Hansen P, Olesen J. Effervescent metoclopramide and aspirin (Migravess) versus effervescent aspirin or placebo for migraine attacks: A double blind study. Cephalalgia 1984; 4:107–111.
37. Siberstein SD. The pharmacology of ergotamine and dihydro ergotamine. Headache 1997;36(Suppl 1):S15–S25
38. Scott AK. Dihydroergotamine: A review of its use in the treatment of migraine and other headaches. Clin Neuropharmacol 1992; 15(4):289–296.
39. Bigal ME, Tepper SJ. Ergotamine and dihydroergotamine: A review. Curr Pain Headache Rep 2003; 7(1):55–62.
40. Durham P, Russo A. New insights into the molecular actions of serotonergic antimigraine drugs. Pharmacol Ther2002;94(1 –2):77–92
41. Dahlof C. Sumatriptan nasal spray in the acute treatment of migraine: A review of clinical studies. Cephalalgia 1999; 19:769–778.
42. Ensink FB. Subcutaneous sumatriptan in the acute treatment of migraine. J Neurol 1991; 238:S66–S69.
43. Snow V, Weiss K, Wall EM, Mottur-Pilson C, American Academy of Family Physicians; American College of Physicians-American Society of Internal Medicine. Pharmacologic management of acute attacks of migraine and prevention of migraine headache. Ann Intern Med. 2002; 137:840–9.
44. Gray RN, Goslin RE, McCrory DC, Eberlein K, Tulsky J, Hasselblad V. Drug treatments for the prevention of migraine. Technical review February 1999.
45. Matthew NT, Rapoport A, Saper J, Magnus L, Klapper J, Ramadan N, et al. Efficacy of gabapentin in migraine prophylaxis. Headache. 2001; 41:119–28.
46. Silberstein SD, Neto W, Schmitt J, Jacobs D. Topiramate in migraine prevention: results of a large controlled trial. Arch Neurol. 2004; 61:490–5.
47. Lewis, D. et al. Practice parameter: pharmacological treatment of migraine headache in children and adolescents: report of the American Academy of Neurology Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society. Neurology 63, 2215–2224 (2004).