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Evaluation of acute management of migraine at University of Maiduguri Teaching Hospital, Maiduguri, Nigeria

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Research Article

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Abstract

Objective: Migraine is mostly mis-diagnosed, and even when correctly diagnosed does not receive desired attention. This study is aimed at evaluating patients with migraine and to provide physicians and allied health care professionals with guidelines for the diagnosis and acute management of migraine in clinical practice.

Methods: One hundred consecutive adult (18 years and above) migraineurs that attended the Neurology Clinic of the Department of Medicine, University of Maiduguri Teaching Hospital from May, 2009 to December, 2010 and from whom informed consent was obtained were evaluated for this disorder. The success of acute antimigraine therapy was prospectively studied.

Results: Among the seventy patients that took sumatriptan for their acute migraine, 47 (67%) were improved, 17 (24%) moderately improved and 6 (9%) did not improve. On the other hand, 6 (20%) were improved, 15 (50%) moderately improved and 9 (30%) showed no improvement in the migraine symptoms among the thirty (30) patients that took Dihydroergotamine + caffeine (Cafergot®) for their acute migraine head pain. Statistical analysis showed that sumatriptan tablets relives acute migraine better than Cafergot® tablets ($p<0.05$) among the patients studied.

Conclusion: Therefore, improved diagnosis and timely use of sumatriptan to be followed by appropriate prophylactic therapy may be useful in migraine headache, which will lead to reduction in suffering, increased productivity and decreased economic burden.

Key words: Acute Migraine, disability, sumatriptan

Introduction

Migraine is a highly prevalent headache disorder that has a substantial impact on the individual and society [1]. Migraine is a common condition affecting 18% of women and 6% of men in the United States [2]. The basic causes of migraine headache are not yet known, however, it appears to be a combination of environmental and genetic factors that causes specific biologic or physical abnormalities [3]. Risk factors for migraine headaches include inherited gene, medical conditions like epilepsy, fibromyalgia and infections (such as *Helicobacter pylori*, *Candida albicans*, *Bacillus cercius*) [3]. The reduced flow of blood from the occipital lobe triggers the aura that some individuals who have migraines experience because the visual cortex is in the occipital area [4]. According to Moskowitz [5] the release of neuropeptides (substance P, neurokinin A and calcitonin gene-related peptide) does act as neurotransmitters effecting plasma extravasation and vasodilation.

The goals of managing migraine are 2-fold: to prevent attacks from occurring and to effectively and rapidly end them when they do occur [6]. There are numerous options for acute migraine relief, and patients vary in their responses to different medications. While less medication is certainly preferable, aggressive therapy at the onset of a migraine attack often reduces the overall quantity of medication(s) utilized [6]. When migraines occur too frequently, last too long, cause too much disability, and/or acute medications are costing the patient too much, prophylactic therapy should be considered [7].

The goal of prophylactic therapy is not to cure headaches but to try to decrease their frequency, severity, duration and/or disability [8]. Ergot derivatives (ergotamine and dihydroergotamine) and triptans (sumatriptan) are classes that were found to be effective antimigraine agents in clinical practice and they continue to be a class of therapeutic agents used for the acute relief of migraine worldwide. Their interaction with 5-$HT_{1B/1D}$ could account for their antimigraine actions [9].

Non-pharmacologic therapies include educating the patient about this disorder, changes in lifestyle and avoidance of migraine triggers. However, these have not been practiced much in our community, and certainly there is no record to assess the outcome. This study was therefore embarked upon in order to evaluate the

effectiveness and safety of current drug management of migraine as being practiced in other part of the world.

Methodology

One hundred (100) consecutive adult migraine patients that attended the Neurology Clinic of the Department of Medicine, University of Maiduguri Teaching Hospital, Maiduguri From May, 2009 to December, 2010, were prospectively studied with their consents.

The study protocol has been approved by the UMTH's ethics committee on human research. Patients with clinical evidence of an organic disease known to cause migraine and those having a socioeconomic factor (culture and poverty) as well as pregnant mothers were excluded.

Personal interviews using a structured questionnaire were conducted individually with the 100 patients. The socio-demographic profile of each patient, clinical presentation, aggravating/relieving factors and history of drug use (within the previous months) was obtained. In addition, haematological, immunological and biochemical pathological analysis were done on each study subject to exclude other organic disease known to cause migraine.

Those patients that did not meet the inclusion criteria were given analgesics and were not enrolled for the study. Seventy (70) and thirty (30) patients enrolled in this study were given Sumatriptan and Dihydroergotamine + caffeine (Cafergot® tablets) respectively. Thirty-eight (38) patients were given 50 mg of sumatriptan, while the remaining 32 received 100 mg of sumatriptan. On the other hand, 15 patients were given 1 mg of Cafergot® and the remaining 15 patients took 2 mg of Cafergot®. Responses to acute migraine therapy with the drug's respective adverse effects were noted and recorded after the drug's administration.

All the one hundred patients enrolled in this study took appropriate prophylactic therapy (propranolol, atenolol, topiramate, paroxetine, pizotifen and amitriptyline) two weeks after the symptomatic treatment. Responses to symptomatic therapy followed by prophylactic treatment and assessment of disability to the quality of life were recorded with subsequent two-weekly and monthly hospital visit.

Statistical analysis

The data was analyzed using statistical analysis software (SAS) system version 16. Chi-square, Fisher's Exact Test and Student t-test were used to determine significance of association between categorical and non-categorical variables. P values less than 0.05 were considered significant.

Results

Age and Sex Distribution

Twenty-eight percent (28%) of the studied population were male while seventy-two percent (72%) were female. The mean ages for male and female were 32.5 ± 9.9 and 31.8 ± 10.1 years respectively (Table 1). The ages of the patients studied ranged from 19-69 years with largest number of patients falling within the group 20-29 years. There was no statistically significant difference between the mean ages for male and female.

Table1: Age and sex distribution of migraine patients

Age (years)	*No. / %*		
	Male	*Female*	*Total*
10 – 19	1	6	7
20 – 29	12	33	45
30 – 39	11	18	29
40 – 49	1	10	11
50 – 59	2	2	4
60 – 69	1	3	4
Total	*28*	*72*	*100*

Improvement and Sustained Freedom from Pain at Two Hours

The percentage of patients with improvement in head pain and those with sustained freedom from pain at 2 hrs after acute therapy with no rescue medication and with no recurrences of headache within 24 hrs are shown in Table 2. These values were higher with sumatriptan (50 mg and 100 mg) than with Cafergot® (1 mg and 2 mg). Sixteen (42%) and sixteen (50%) of the patients that took sumatriptan 50 mg and 100 mg respectively had sustained freedom from pain when compared with two (13%) and one (6.7%) that took Cafergot® 1 mg and 2 mg respectively. On the other hand 4 (26.7%) patients that took Cafergot® (1 mg and 2 mg) had improvement in head pain at 2 hrs, while 14 (36.8%) and 9 (28.1%) of patients that took sumatriptan 50 mg and 100 mg respectively had improvement in head pain (Table 2).

Response to Acute Therapy (sumatriptan / Cafergot®) among Migraineurs

Fourty-seven (67%) and 6 (20%) of the patients that took sumatriptan and Cafergot® tablets respectively improved

from therapy, while 17 (24%) and 15 (50%) that took respective drugs above showed a moderate improvement to acute therapy. The remaining 6 (9%) and 9 (30%) among those that took sumatriptan and Cafergot® tablets respectively did not get improvement (Table 3). However, there was statistical significant difference in response to acute migraine therapy among patients with different type of migraine headache ($p<0.05$).

Table 2: Improvement and sustained freedom from pain among migraineurs

Acute drug therapy	*Number (percentage of patients improved at 2 hrs)*	*Number (percentage of patients with sustained freedom from pain at 2 hrs)*
Cafergot® 1 mg (N = 15)	4 (26.7)	2 (13.3)
Cafergot® 2 mg (N = 15)	4 (26.7)	1 (6.7)
Sumatriptan 50 mg (N = 38)	14 (36.8)	16 (42.1)
Sumatriptan 100 mg (N = 32)	9 (28.1)	16 (50)

P = 0.038* (Significant) (χ^2)

Table 3: Distribution of responses to acute (Sumatriptan & Cafergot®) therapy

Response to therapy	*Acute therapy (Number / Percentage)*		*Total*
	Sumatriptan (50 mg and 100 mg)	Cafergot® *(1 mg and 2 mg)*	
Improved	47 (67)	6 (20)	53
Moderate improvement	17 (24)	15 (50)	32
No improvement	6 (9)	9 (30)	15
Total	*70*	*30*	*100*

$p<0.05$ (χ^2)

Responses to Prophylactic Therapy

At the end of the study patients that took monotherapy prophylactic agents including β-blocker (35%), amitriptylline (43%), pizotifen (44%), paroxetine (46%) and topiramate (30%) showed a good response. There was a significant difference between those that used combination therapy and those that used monotherapy prophylactic agents ($p<0.05$). The combination prophylactic agents used in this study with their percentage responses were as follows: β-blocker + amitriptylline (100%), β-blocker + pizotifen (100%), β-blocker + topiramate (50%), amitriptylline + topiramate (64%), and pizotifen + topiramate (86%). Seven (41%), 7(50%), 1(12%), 6(46%) and 4(40%) of patients on β-blocker, amitriptylline, pizotifen, paroxetine and topiramate respectively showed moderate improvement to therapy, while 4(24%), 1(7%), 4(44%), 1(8%) and 3(30%) of patients on β-blocker, amitriptylline, pizotifen, paroxetine and topiramate did not show signs of improvement at the end of the study (Table 4). Patients that improved due to combined prophylactic treatment were statistically significantly different from those that did not improve ($p<0.05$) (Table 4).

Table 4: Responses to prophylactic therapy

Prophylactic therapy	*Response to therapy (Number / percentage)*			*Total*
	Improved	*Moderate improvement*	*No improvement*	
β-blocker	6 (35)	7 (41)	4 (24)	17
Amitriptylline	6 (43)	7 (50)	1 (7)	14
Pizotifen	4 (44)	1 (12)	4 (44)	9
Paroxetine	6 (46)	6 (46)	1 (8)	13
Topiramate	3 (30)	4 (40)	3 (30)	10
β-blocker + Amitriptylline	5 (100)	0 (0)	0 (0)	5
β-blocker + Pizotifen	6 (100)	0 (0)	0 (0)	6
β-blocker + Topiramate	4 (50)	3 (38)	1 (12)	8
Amitriptylline + Topiramate	7 (64)	3 (27)	1 (9)	11
Pizotifen + Topiramate	6 (86)	1 (14)	0 (0)	7
Total	*53*	*32*	*15*	*100*

Discussion:

In this study, migraine headache was found to be present in both males (28%) and females (72%) (Table 1). It has also been observed that sixty-seven percent (67%) and 29% of the studied migraine patients had common and classic migraine attack respectively. More females (73% and 69%) were afflicted with both common and classic migraine respectively than males (27% and 31%). Russel *et al* [10] and Bille [11] had shown earlier that 75% of

migraineurs experienced common migraine and about 33% of migraineurs experience both types of attack during their life time. The predominance of females over males observed in this study agrees with reports of several other studies [12, 13, 14, 2] in which females were afflicted more with the disease. The changes in the level of oestrogen in female subjects during menstruation, ovulation and pregnancy may be the underlining cause. It is also evident that approximately three quarter of the patients (74%) were in their 20s and 30s which correspond to a large segment of the productive age. The data showed that 4% each of the studied migraineurs were in their 50s and 60s, which is in agreement with other related studies that showed migraine tends to decrease with age [15, 2].

The headache (pain) response at two hours was the primary end point observed in nearly all patients treated with Cafergot® and sumatriptan tablet in this study. There was no significant difference in the percentage of patients with improvement in head pain after 2 hrs between those that took sumatriptan (50 and 100 mg) and those that took Cafergot® (1 mg and 2 mg) for their acute head pain (Table 2) ($p>0.05$). However, the result of this study showed a relatively higher percentage of improvement among those that took 50 mg of sumatriptan (37%) than those taken 100 mg of sumatriptan (28%). Therefore, sumatriptan's effect based on this study was not dose dependent. This also agrees with the findings of Goadsby *et al* [6] in which 50 mg of sumatriptan was better in improving the migraine head pain at 2 hours than 100 mg of sumatriptan. Triptans are known to cause specific vasoconstriction of the cerebral blood vessels [16], which could contribute to the observed effect.

The percentage of patients with sustained freedom from pain (freedom from pain at 2 hours with no rescue medication and with no recurrence of headache within 24 hours) as shown in the table 3 reveals that patients on sumatriptan 50 mg and 100 mg (42% and 50%) had higher percentage when compared to those that took Cafergot® 1 mg and 2 mg (13% and 7%) for their acute head pain ($p<0.05$). The pretreatment exposure to Cafergot® and the non specificity in its action on trigeminovascular system could be responsible for the low percentage of patients with sustained freedom from pain. This again agrees with the reports of Goadsby *et al* [6] in which 50 mg and 100 mg of sumatriptan had 32% and 29% of patients with freedom from head pain at 2 hrs.

At the end of this study fourty-seven (67%) and six (20%) of the patients that took sumatriptan and Cafergot® tablets respectively improved (complete disappearance of migraine symptoms, disability and other investigational findings at the end of the study) from therapy, while 17 (24%) and 15 (50%) that took respective drugs above showed a moderate improvement (incomplete disappearance of migraine symptoms, disability and/or other investigational findings at the end of the study) to acute drug therapy.

There was a statistical significant difference in response to acute migraine therapy among patients with different types of migraine headache ($p<0.05$) (Table 3). Patients on sumatriptan (67%) had better relieve of migraine head pain compared to those that took Cafergot® (20%). Thirty percent (30%) of patients that took Cafergot® for their acute head pain did not improve (the migraine symptoms, disability and other investigational findings persisted at the end of the study), while only nine percent of those that took sumatriptan had no improvement.

The specificity of effect of sumatriptan on the trigeminal nerve and cerebral blood vessels could be responsible for the higher improve rate when compared with Cafergot® [16]. In addition, the pretreatment exposure to Cafergot® is much higher when compared to sumatriptan. This is due to the fact that Cafergot® is available and affordable when compare to sumatriptan that is scarce and expensive. The antimigraine effect of sumatriptan may thus, be attributable to its cerebrovasoconstrictive effect and peripheral neuronal inhibition. The result of these findings agrees with several literature reports [17-19] that confirms the advantage of sumatriptan over Cafergot® in relieving acute migraine head pain.

Result of this study shows that β-blockers, amitriptyline, pizotifen, paroxetine and topiramate reduced the frequency of migraine attack via different mechanisms [20] (Table 4). The result also showed that combination of these prophylactic agents (combination therapy) tends to relieve migraine head pain better than when use alone (monotherapy) ($p<0.05$). This also agrees with the report of Goadsby *et al* [6] in which migraine combination prophylactic therapy was found to prevent attack in patients better than those on monotherapy. The choice of these prophylactic agents depends on the location and type of focal discharge that can alters the cerebral blood vessels leading to the process of migraine. β-blockers did better in patients having over sympathetic activity, topiramate helped those having a possible neurological discharge and amitriptyline was given to migraine patients having sign of depression.

Conclusion

The clinical features presented by the migraineurs studied fulfilled the criteria of IHS [21]. The migraine head pain was found to cause minor, moderate and severe disability among the migraineurs studied resulting in suffering, decreased productivity and social functioning, and increased economic burden. Sumatriptan (a relatively new drug) followed by appropriate prophylactic therapy was able to improve the quality of life of migraineurs and their loved ones better than the Cafergot® (a conventional drug).

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

Not commissioned; externally peer reviewed

CONFLICTS OF INTEREST

The authors declare that they have no competing interests