IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

COMPARITIVE EVALUATION OF SAFETY AND EFFICACY OF METOPROLOL VERSUS AMITRIPTYLINE IN MIGRAINE PATIENTS

SAMPAT KUMARI*
[1]Research Scholar, Maharishi Arvind Institute of Pharmacy, Jaipur, India- 302020.

ABSTRACT:

Migraine affects more than one billion individuals each year across the world, and is one of the most common neurologic disorders, with a high prevalence and morbidity, especially among young adults and females. Migraine is associated with a wide range of comorbidities, which range from stress and sleep disturbances to suicide. The complex and largely unclear mechanisms of migraine development have resulted in the proposal of various social and biological risk factors, such as hormonal imbalances, genetic and epigenetic influences, as well as cardiovascular, neurological, and autoimmune diseases. This review presents a comprehensive review of the most up-to-date literature on the epidemiology, and risk factors, as well as highlighting the gaps in our knowledge.

Keywords: migraine, epidemiology, risk factors, comorbidity, narrative review

INTRODUCTION:

Migraine may be considered as a prolonged neurological condition with periodic exacerbations. It is highly prevalent, with the symptoms of pain and disability. Pain is associated with autonomic symptoms, the mostly common being nausea, vomiting, phonophobia and photophobia, (the International Classification of Headache Disorders (ICHD), the edition, published in 2013). The complaint is categorised by events of moderate to severe cranium pain, which is frequently one-sided and throbbing, and characteristically aggravated by monotonous physical activities. The period of unprocessed migraine occurrences is slightly long, from 4 hours to 3 days (median duration 18 hours).

Other indications, such as osmophobia, fatigue, pallor, difficult in attentiveness, blurry vision, or diarrhoea, may be existent. In numerous patients, the headache stage is headed by predictive symptoms (or prodromes) which can last from a few hours to 24 hours, and are categorised by yawning, fatigue, fluid retention, sensory hypersensitivity, mood changes, food cravings, or increased thirst. Similar psychological, overall and autonomic symptoms can also describe the determination phase of an attack (postdrome).[1]

In up to 25% of migraine patients, the headache phase can be headed by transient focal neurological symptoms, usually long-lasting from 4 minutes to 1 hour, described as migraine aura. The utmost aura indications are ocular disturbances (hemianopia, scintillating scotomata, blind spots), sensory disturbances (numbness, unilateral

paraesthesia affecting the face and limbs) or speech/language disturbances (aphasia, dysarthria). Uncommon aura occurrences include ataxia, weakness, vertigo, or loss of perception. The median migraine attack incidence is one per month, though about 30% of subjects in the common people report three or more attacks per month.

NEED OF THE STUDY.

Apart from efficacy, the safety of migraine medication is another predominating factor that must be considered by physicians when selecting an appropriate intervention. As suggested by previous studies, migraine patients treated by antiepileptic drugs may experience several side- effects.[27]

Most studies have evaluated the efficacy of such drugs alone; however, there are some studies with metoprolol and tricyclic agents in association with other drugs[28].

The clinical experience with combination therapy or monotherapy for migraine seems to be a rational approach when migraine is refractory.

The study was intending to probe into the best medication for prophylaxis of migraine in terms of safetyandefficacy with careful

RESEARCH METHODOLOGY

Study Design and Duration:

This study was prospective, comparative, single-center study for 24 weeks duration Patients was considered the study after informed consent

Sample size:

120 patients was enrolled in the study

Sample size calculation:

By using Fischer's exact test

In group 1: 60 patients
In group 2: 60 patients

$n = 2 (Zpower + Z1- \alpha_2)$

$(\mu 1- \mu 2/\partial)^2$

where:

Z (i.e. power = 80%) = 0.8416

Z1- α2 = 1.96

(μ1- μ2) = 0.10 or 10 %

∂ = 0.2 or 20 %

Calculating through above formula, a value of 120 study participants is obtain, assuming 20% dropouts rate from the study.

Inclusion Criteria:

- Patient was considered as per International Headache Society Criteria for Migraine with Aura.
- Patient was considered as per International Headache Society Criteria for Migraine without Aura.

- Patients age between18-65 years was considered.
- Both male and female gender patients was considered.

Exclusion criteria

- Patients 65 years
- Patient having chronic incapacitating illness eg. AIDS, cancer, TB.
- Patient whose primary headaches were other than migraine headaches e.g. With a clinical history of stroke or Transient Ischemic Attack (TIA)

Methodology:

Patients was group into 2 for the treatment.

Group1 :Dose of metoprolol was 25mg BD for the first two weeks , 25 mg TDS for the next two weeks and Finally 50 mg BD for the consecutive 8 weeks.

Group 2: Dose of Amitriptyline was 10 mg once for the first two weeks , 25 mg once for the next two weeks and Finally 50 mg once for the consecutive 8 weeks at bed time.

Follow-up and outcome:

Patients were followed for a three months period during which they was instructed to maintain a headache diary with the following information:
presence of headache and intensity of headache by Visual Analogue Pain Scale.

This also include the need for analgesic for headache.
Patients was asked to return on days 30, 60 and 90.

The primary outcome evaluate the proportion of patients in each group that achieved a 50% reduction in the number of days with headache.

Secondary outcomes reduce of MIDAS, the number of days with headache per month, frequency of side effects, and the proportion of patients abandoning the study before the end of medication. The causes of noncompliance and side effects was individually registered

Migraine disability assessment (MIDAS)

The MIDAS was developed to assess headache-related disability with the aim of improving migraine care. It is self-administered questionnaire designed to quantify headache-related disability over a 3-month period. This questionnaire consists of five questions that focus on time or productivity lost, as well as the limited ability to participate in work or school, household activities and family, and social or leisurely activities. The total MIDAS score can be used to define four grades of migraine-related disability with grade I for "little or no disability" (0–5); grade II for "mild disability" (6–10); grade III for "moderate disability" (11–20); and grade IV for "severe disability" (≥ 21). The MIDAS also include a migraine severity global question, with subjects' responses ranging between 0 (no pain at all) to 10 (very severe pain). Two additional questions included in the MIDAS provide the physician with supplementary clinical information about headache frequency and severity/intensity (scale from 0 to 10) of headaches over the previous three months. The MIDAS is a reliable and valid instrument with moderately high test- retest reliability in persons with migraine and correlates to clinical judgment regarding the need for medical care.[29]

Statistical Analysis

After collection all the data was checked and edited. Then data were entered into the computer with the help of software SPSS for windows.

Categorical variables were compared by chi-square test. Quantitative data of parameters and adverse-effects was analysed by using the students unpaired 't'-test for difference between means.

IV. RESULTS AND DISCUSSION

RESULTS

1. In both the groups, maximum number of patients were in the age group of 18-25 years and least number of patients were 46-65 years of age.

Table 7.1 Comparison of Mean Age in Groups

Age-Group	**Group 1**		**Group 2**	
	Number	Percentage	Number	**Percentage**
18-25 years	37	61.6%	34	**56.6%**
26-45	20	33.3%	25	**41.6%**
46—65	3	5.0%	1	**1.6%**
Total	60	100	60	**100**
Mean±SD	27.21±7.71 years		**28.01±7.65 years**	
p-value	**0.609**			

Mean age in group 1 patients were **27.21±7.71** and in Group 2 patients were **28.01±7.65**. There was no statistically significant difference in mean age of patient from Group 1 and Group 2 patients with **Unpaired t test.**

Table 7.2: Gender difference between Group 1 and Group 2

	Group 1		**Group 2**		**Chi- Square test p=value**
	n=60	(%)	n=60	(%)	
Male	19	31.6	21	35.0	**0.112**
FEmale	41	68.3	39	65.0	
Total	**60**	**100**	**60**	**100**	

The table 7.2 reflects those 120 migraine patients in Group 1: 19 were male (31.6%) while 41 were female patients (68.3%). In Group 1 consisted of 21 male patients (35%) and 39 female patients (65%). There was no statistically

significant difference in number of patients from Group A1and Group 1 patients (0.112) when we applied with **Chi-square test**. **Table 7.3 : Comparison of Frequency of migraine Attack between Group 1 and Group 2**

	Group 1 Mean±SD		**Group 2 Mean±SD**		**p-value**
Frequencyof Attack	Period 1 (Metoprolol)	Period 2 (Amitriptyline)	Period 1 (Amitriptyline)	Period 2 (Metoprolol)	P= 0.016
	4.41±1.22	4.01±0.92	3.93±0.97	4.21±1.02	

In **Table 7.3**, the mean Frequency of Attack of migraine in **Group 1** at period 1 was 4.41 with SD of 1.22 and period 2 was 4.01 with SD 0.92. In **Group 2** during period 1 was 3.93 with SD of 0.97 and in period 2 mean 4.21 with SD 1.02. These was statisticallysignificant difference in **Group 1 and Group 2** (p=0.016) with **Unpaired t test**.

Bar Graph 7.1: Comparison of Frequency of migraine Attack between Group 1

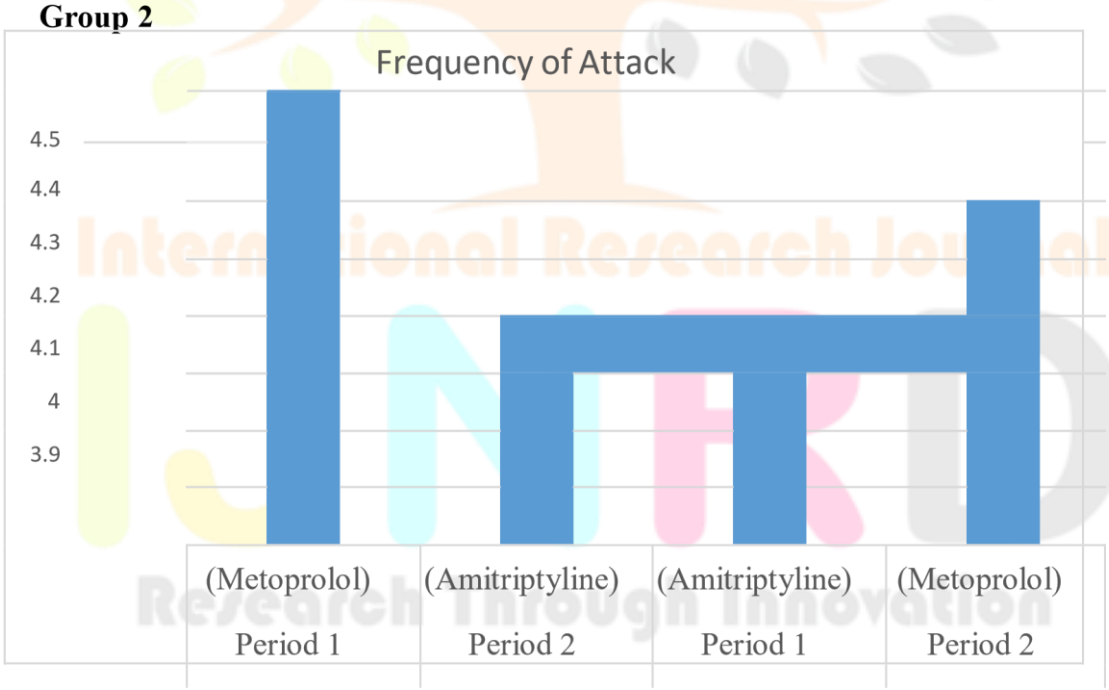


Table 7.4: Comparison of severity of Attack of migraine between Group 1 and Group 2

	Group 1 Mean±SD		Group 2 Mean±SD		p-value
Severity of Attack	Period 1 (Metoprolol)	Period 2 (Amitriptyline)	Period 1 (Amitriptyline)	Period 2 (Metoprolol)	P=0.023
	2.91±0.84	2.11±0.64	2.03±0.71	2.76±0.81	

In **Table 7.4**, the mean severity of Attack of migraine in **Group 1** at period 1 was 2.91with SD of 0.84 and period 2 was 2.11 with SD 0.64. In **Group 2** during period 1 was 2.03 with SD of 0.71 and in period 2 mean 2.76 with SD 0.81. These was statisticallysignificant difference in **Group 1 and Group 2** (p=0.023) with **Unpaired t test**.

Bar graph 7.2: Comparison of severity of Attack of migraine between Group 1 And Group 2

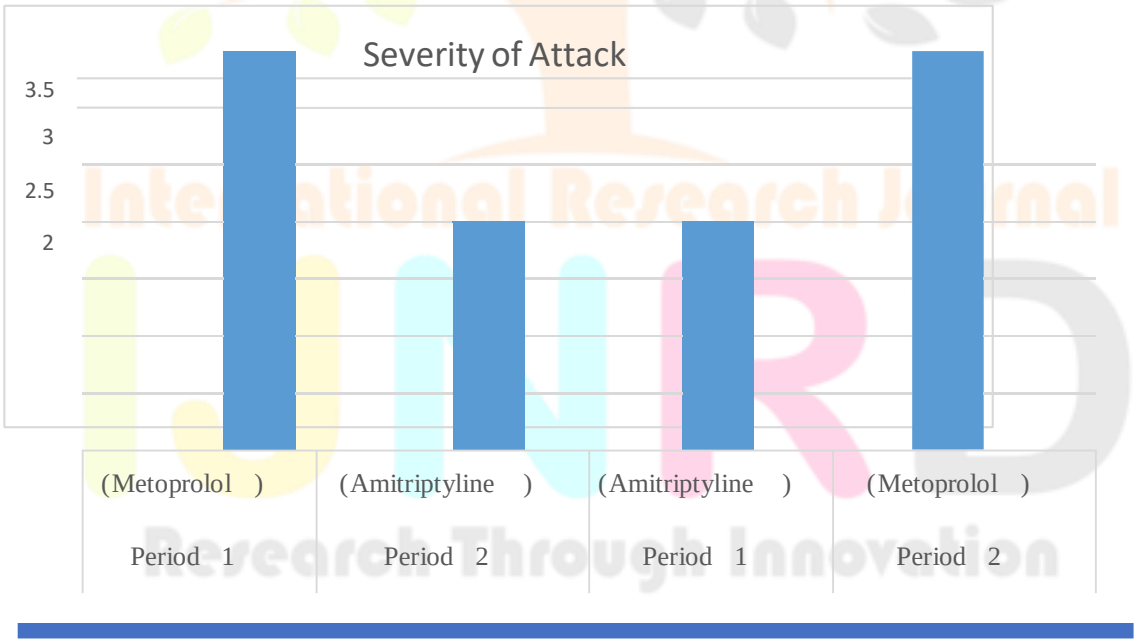


Table 7.5: Comparison of Duration of Attack of migraine between Group 1 andGroup 2

	Group 1 Mean±SD Group 2 Mean±SD p-value				
Duration ofAttack (hours)	Period 1 (Metoprolol)	Period 2 (Amitriptyline)	Period 1 (Amitriptyline)	Period 2 (Metoprolol)	P= 0.038
	16.01±2.60	13.51±2.22	13.63±1.56	15.83±2.00	

In **Table 7.5**, the mean duration of Attack of migraine in **Group 1** at period 1 was 16.01 hours with SD of 2.60 and period 2 was 13.51 hours with SD 2.22. In **Group 2** during period 1 was 13.63 hours with SD of 1.56 and in period 2 mean 15.83 hours with SD 2.00. These was statistically significant difference in **Group 1 and Group 2** (p=0.038) with **Unpaired t test**.

Bar graph7.3: Comparison of Duration of Attack of migraine between Group 1 and Group 2

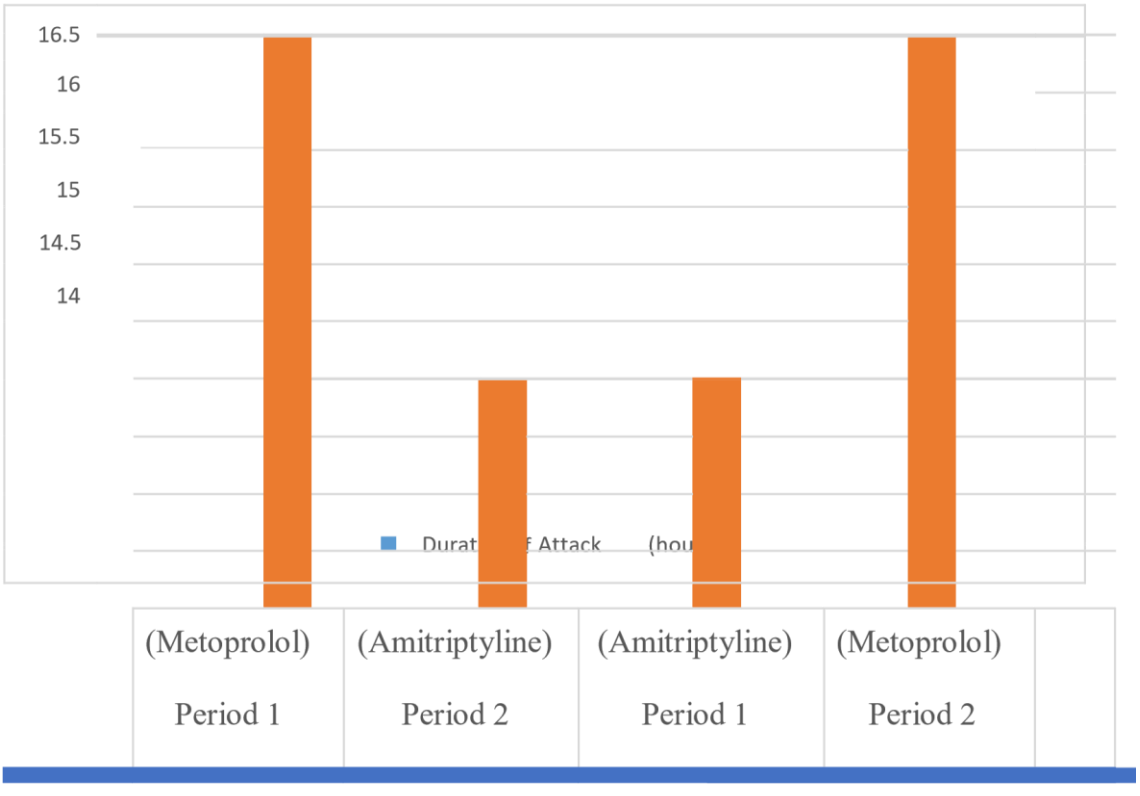


Table 7.6: Comparison of ADRs during treatment with Group 1 and Group 2:

Type of reaction	Group 1		Group 2		
	Period 1 (Metoprolol)	Period 2 (Amitriptyline)	Period 1 (Amitriptyline)	Period 2 (Metoprolol)	p=value
Xerostomia	2	6	7	1	0.02
Dizziness	6	3	2	7	0.03
Weight gain	3	4	3	2	0.09
Somnolence	2	7	6	1	0.01
Constipation	1	3	2	1	0.04

In table 7.6 : Most common adverse drug reaction reported in two groups were includes.In the Group 1: In period 1 maximum ADR was Dizziness and least one constipationwhereas in during period 2 highest incidence of ADR was Somnolence and least was Dizziness and constipation. On the other hand, in group 2 during period 1 maximum ADR was Xerostomia and least constipation. Moreover, in during period

2 more ADR were dizziness and followed by weight gain and xerostomia, somnolence and constipation.

Bar Graph 7.4 : Comparison of ADRs during treatment with Group 1 and Group 2

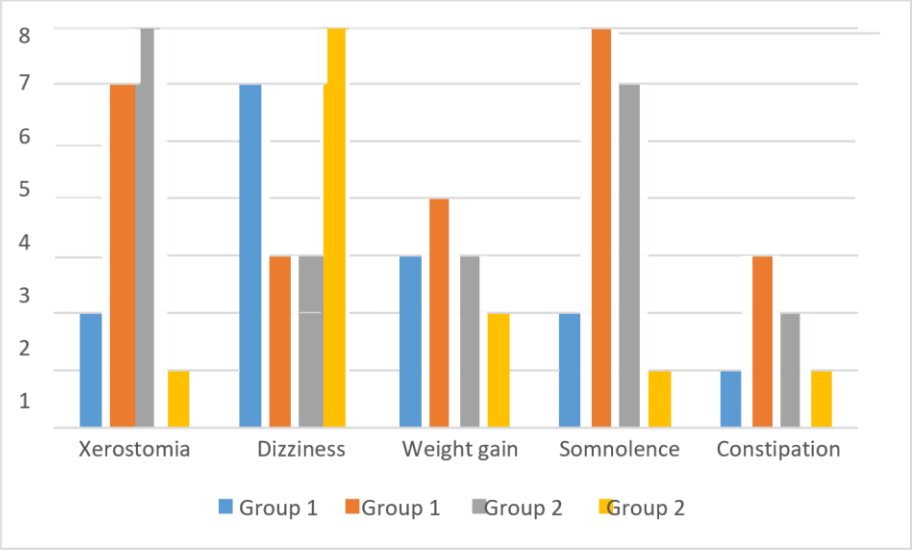


Table 7.7: WHO causality assessment of ADRs

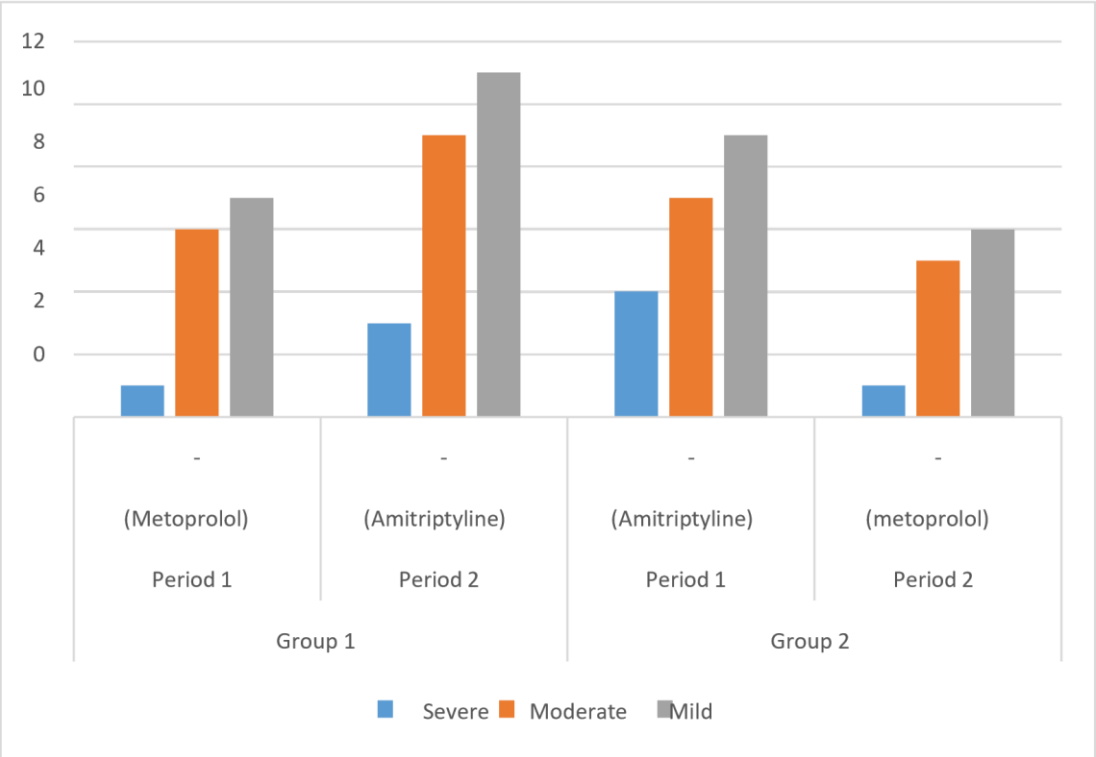
Type of reaction	**Group 1**		**Group 2**	
	Period 1 (Metoprolol)	**Period 2 (Amitriptyline)**	**Period 1 (Amitriptyline)**	**Period 2 (Metoprolol)**
Certain	3	2	4	4
Probable/ likely	4	11	9	5
Possible	6	8	6	2
Unlikely	1	1	1	1
Conditional/ unclassified	-	1	-	-

Table 7.8: Severity of reported ADRs by modified Hartwig & Siegel scale

Type of reaction	**Group 1**		**Group 2**	
	Period 1 (Metoprolol)	Period 2 (Amitriptyline)	Period 1 (Amitriptyline)	**Period 2 (Metoprolol)**
Lethal	-	-	-	-
Severe	1	3	4	**1**
Moderate	6	9	7	**5**
Mild	**7**	**11**	**9**	**6**

In table 7.8: As per the modified Hartwig and Siegel's scale maximum number of ADRs was mild category and lowest in sever type of reaction was observed in this study. No ADRs were found in lethal type of reaction.

Bar graph 7.5: Severity of reported ADRs by modified Hartwig & Siegel scale



REFERENCES

1. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al.Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the global burden of disease study. Lancet. 2013;380:2197–223.

2. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the global burden of disease study 2010.

Lancet. 2013;380:2163–96.

3. Ferrari MD. The economic burden of migraine to society. Pharmacoeconomics. 1998;13:667–76.

4. Stewart WF, Lipton RB, Simon D. Work-related disability: results from the American migraine study. Cephalalgia. 1996;16:231–8.

5. Michel P, Dartigues JF, Lindousli A, Henry P. Loss of productivity and quality of life in migraineurs among French workers: results from the GAZEL cohort.

Headache. 1997;37:71–8.

6. Edmeads J, Findlay H, Tugwell P, Pryse-Phillips W, Nelson RF, Murray TJ. Impact of migraine and tension-type headache on life-style, consulting behavior, and medication use: a Canadian population survey. Can J Neurol Sci.

1993;20:131–7.

7. Adams AM, Serrano D, Buse DC, Reed ML, Marske V, Fanning KM, et al. The impact of chronic migraine: the chronic migraine epidemiology and outcomes (CaMEO) study methods and baseline results. Cephalalgia. 2015; 35(7):563–78.

8. Lipton RB, Hamelsky SW, Kolodner KB, Steiner TJ, Stewart WF. Migraine, quality of life, and depression: a population-based case–control study. Neurology. 2000;55:629–35.

9. Leonardi M, Raggi A, Bussone G, D'Amico D. Health-related quality of life, disability and severity of disease in patients with migraine attending to a specialty headache center. Headache. 2010;50:1576–86.

10. Bagley CL, Rendas-Baum R, Maglinte GA, Yang M, Varon SF, Lee J, et al. Validating migraine-specific quality of life questionnaire v2.1 in episodic and chronic migraine. Headache. 2012;52(3):409–21.

11. Apolone G, Mosconi P. Health-related quality of life (HRQOL) and migraine. J Headache Pain. 2001;2(Suppl 1):s21–4.

12. Antonaci F, Nappi G, Gailli F, Manzoni GC, Calabresi P, Costa A. Migraine and psychiatric comorbidity: a review of clinical findings. J Headache Pain. 2011; 12(2):115–25.

13. Stewart WF, Lipton RB, Dowson AJ, Sawyer J. Development and testing of the migraine disability assessment (MIDAS) questionnaire to assess headache- related disability. Neurology. 2001;56(suppl 1):S20–8.

14. Kosinski M, Bayliss MS, Bjorner JB, Ware JE, Garber WH, Batenhorst A, et al. A six-item short-form survey for measuring headache impact: the HIT-6. Qual Life Res. 2003;12:963–74.

15. Jacobson GP, Ramadan NM, Aggarwal SK, Newman CW. The Henry ford hospital headache disability inventory (HDI). Neurology. 1994;44:837.

16. Ashina M, Saper J, Cady R, Schaeffler BA, Biondi DM, Hirman J, et al. Eptinezumab in episodic migraine: A randomized, double-blind, placebocontrolled study (PROMISE-1). Cephalalgia 2020;40:241-54.