# Prescribing trends of antimigraine drugs amongst general physicians and neuro physicians in southern Pakistan: A comparative approach

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## ABSTRACT

**Objective:** To evaluate the prevalence of migraine and compare the prescribing practices of different General Physicians and Neuro Physicians to choose different anti migraine drugs.

**Study Design:** A Prospective cohort study.

**Place and Duration:** Study performed during the period of 12th October, 2017 to 5th September, 2018 at Outpatient Departments (General Physicians and Neurology) of different hospitals of Karachi.

**Methodology:** Data was obtained by a qualified clinical pharmacist in the form of duplicate prescriptions and also from migraine patients with their consent. Variables which were compared in prescribing practices of different GPs and NPs included, different class of drugs prescribed, polytherapy, mean cost of drugs per prescription, prescribed drugs by its generic name, ratios of antimigraine drugs dosages. Besides, another variable was the estimation of prevalence of migraine among males and females.

**Results:** Among total of 319 reviewed prescriptions analgesics were the most prescribed medications in migraine therapy by both Practitioners i.e. General Physicians (88.8%) and Neuro Physicians (82.3%). The average number of drugs per prescriptions by General Physicians and Neuro Physicians was 6.10 and 3.98 respectively. The cost of treatment (per prescription) was much higher by Neuro Physicians (Rs. 88.4) than General Physicians (Rs. 58.9). The prescribing ratio of generic drugs is comparable between General Physicians (48.09%) and Neuro Physicians (34.10%). Naproxen (1.45 vs 0.97) and Ergotamine (1.24 vs 1.1) were prescribed in higher doses by General Physicians than Neuro Physicians. This study also indicated that the incidence ratio of migraine among females (58.9%) was much higher than males (41.0%).

**Conclusion:** Polypharmacy and discrepancies in daily dosages of anti-migraine drugs were more found in prescribing pattern of General Physicians. However, cost effective treatment by General Physician was noticed due to higher ratio of generic drugs. Higher incidence ratio of migraine was observed among female.

**Keywords:** Migraine, Treatment, Prescribing practices, General physicians, Neuro physicians, Clinical settings, Cost of treatment, Generic name.

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## INTRODUCTION

Migraine is a genetically influenced chronic headache disease designated by neurological and non-neurological symptoms including severe headache, nausea, vomiting, phonophobia and photophobia. Migraine is a serious public health care issue, affecting social and economic aspects of life by reducing patient's working ability and worsens the overall quality of life. It is the third most prevalent and sixth most common disabling illness in the world. The World Health Organization (WHO) estimates that 324 million populations worldwide have suffered from different types of migraine[1]. According to Global Burden of Disease (GBD) study conducted in 2000 reported that migraine contributes 1.4% of all years lost to disability (YLDs) while in 2010 this value reached up to 2.7% of YLDs worldwide[2]. The annual years of healthy life lost per 100,000 people from a migraine in Pakistan have increased by 14.6% since 1990, an average of 0.6% a year[3].

Pain-relieving and prophylactic drugs are used to treat

migraine. Pain-relieving drugs (analgesic, triptans, ergot alkaloids and anti-emetics) are used during the migraine attacks while prophylactic drugs (calcium channel blockers, beta-blockers, anti-seizures, pizotifen, tricyclic antidepressants and methysergide) are taken on regular basis to reduce the severity and frequency of migraine episodes[4]. Various clinical guidelines for migraine treatment have been constructed to achieve better clinical and therapeutic effects[5]. Although, factors related to medication and patient might lessen the realization of treatment goals such as unwanted adverse drug reactions, utilization of ineffective drugs, poor patient compliance and abortive drug of choice[6]. Good prescribing behavior is important to improve the overall treatment strategy such as right drug to right patient at right dose. However, irrational use of drugs might increase the rate of mortality and morbidity in clinical practice.

Numerous studies on assessment of use of drugs for migraine treatment have been conducted worldwide for the betterment of rational drug therapy in clinical settings[7-10]. It has been reported that such studies related to evaluation of prescription pattern showed positive outcome in healthcare system[11-13]. To date, many epidemiological studies have assessed migraine incidence, prevalence, age and gender but no single study has investigated to compare the treatment rationalism among GPs and NPs across the country. This study may help to create the basic for the patients in selection of appropriate practitioners among GPs and NPs for their chronic migraine pain therapy. Therefore in this study we assess incidence ratio of migraine among gender and prescription assessment in migraine treatment to compare the prescribing practices among GPs and NPs in different hospitals of Karachi-Pakistan. The objective of this study was to evaluate the prevalence of migraine and compare the prescribing practices of different General Physicians and Neuro Physicians to choose different anti migraine drugs.

## METHODOLOGY

This Prospective Cohort study was performed at Outpatient Department (Neurology and General Physicians) of different hospitals of Karachi-Pakistan i.e. Jinnah Postgraduate Medical Center, Civil Hospital and Abbasi Shaheed Hospital during the period of 12th October, 2017 to 5th September, 2018. All patients selected for this study had fulfilled the following eligibility criteria including, a confirmed diagnosis of migraine identified from patient history, during last one month at least one episodes of migraine and filled consent form. However, children, pregnant women, patients who used homeopathic medications and patients who performed hajama were excluded from the study. This study was performed without prior knowledge of different GPs and NPs for the assessment of their real prescribing practices. The population used for this study was raised using convenient sampling technique. The sample size was calculated using the statistical software Open Epi (Version 2.3.1), keeping anticipated frequency of 71% and was found to be 317 at 95% Confidence Interval (CI)[14].

The assessment and comparison of prescribing pattern among different GPs and NPs was performed in terms of percentage

of different class of drugs prescribed by both NPs and GPs for the treatment of migraine; average number of drugs in each prescription; mean cost of drugs per prescription; percentage of prescribed drugs by its generic name and ratios of antimigraine drugs dosages. The mean daily drug dosages for the treatment of migraine was calculated using WHO criteria. It is defined as the ratios of actual prescribing dose of each drug for the treatment of migraine and the actual recommended dose by WHO for each drug[14]. Besides these, prevalence of migraine among males and females was also estimated.

A qualified clinical pharmacist collects the duplicates of prescriptions and also demographic data by the migraine patients with the consent. Demographic and disease data of patients were collected from the previous case profiles of patients without interviews. The study was approved by the board of advance studies and research (BASR) of University of Sindh-Pakistan.

**Data Analysis:** All collected data of this study were reported in percentages and as the means ± standard deviation (S.D). The significance of study was evaluated by performing inferential analysis using SPSS (version. 23). Independent t- test was used to compare the prescribing pattern of different GPs and NPs with respect to different variables. The collected findings were compared and analyzed between GPs and NPs at a significance level of 0.05.

## RESULTS

A total of 319 prescriptions of migraine patients were collected in which the age group was in a range of 15 years to 81 years with mean age of 39.6 years. One hundred and eighty nine (59.2%) prescriptions belonged to GPs (Table-I) and 130 (40.7%) prescriptions related to NPs (Table-II). This study indicated that the incidence ratio of migraine among females (n=188, 58.9%) was much higher than males (n=131, 41.0%) as reflected in both Table-I and II. It is also observed that the population aged between 26-40 years were more affected with migraine. Table-I represents the medications prescribed by GPs.

Table-II belongs to NPs for the treatment of migraine. Analgesics were the most prescribed medications in migraine therapy by both practitioners i.e. GPs (n=168, 88.8%) and NPs (n=107, 82.3%) in which Naproxen (n= 64, 38.0% vs n=34, 32.3%) was the first choice of drug among all analgesics. It was also observed that the selective serotinin reuptake inhibitors (n=99, 52.3%) and Tricyclic antidepressants (n=56, 43.0%) were the second most utilized drugs by GPs and NPs respectively.

It has been also observed that GPs prescribed (6.10 ± 0.21) average number of drug per prescription to a patient whereas NPs pescribed (3.98 ± 0.12) drugs as mentioned in Table-III. The same table represents the cost of prescribed medications in each prescription for migraneurs in the two different prescribing practices. The mean price per prescription for GPs was 58.9 ± 2.47 while for NPs the cost of drugs per prescription was 88.4 ± 3.45 (in Pakistan rupees). Moreover, it is found that 48.09% (n=90) and 34.10% (n=44) of drugs prescribed with their generic names by GPs and NPs respectively.

**Table-I: Frequency of different classes of drugs prescribed by General Physicians (N = 189)**

| Class of drugs | All Patients (n* = 189) | Age <= 25 (n = 28 ) | Age 26-40 (n = 71) | Age 41-55 (n = 53) | Age >55 (n = 37) | Male (n = 79) | Female (n = 110) |
|---|---|---|---|---|---|---|---|
| Analgesics | 168(88.8%) | 26(92.8%) | 65(91%) | 40(75.4%) | 37(100%) | 71(89.8%) | 97(88.1%) |
| SSRIs | 99(52.3%) | 10(35.7%) | 31(43.6%) | 30(56.6%) | 28(75.6%) | 32(40.6%) | 67(60.9%) |
| Benzodiazapines | 91(48.1%) | 5(17.8%) | 20(28.1%) | 35(66.0%) | 31(83.7%) | 40(50.6%) | 51(46.3%) |
| TCA** | 85(44.9%) | 4(14.2%) | 21(29.5%) | 36(67.9%) | 24(64.8%) | 31(39.2%) | 54(49.0%) |
| Antihistamines | 52(27.5%) | 11(39.2%) | 25(35.2%) | 9(16.9%) | 7(18.9%) | 22(27.8%) | 30(27.2%) |
| Triptan | 41(21.6%) | 8(28.5%) | 17(23.9%) | 10(18.8%) | 6(16.2%) | 20(25.3%) | 21(19.0%) |
| Anti-emetics | 34(17.9%) | 4(14.2%) | 12(16.9%) | 9(16.9%) | 9(24.3%) | 7(98.8%) | 27(24.5%) |
| Antiserotonin | 20(10.5%) | 2(7.1%) | 8(11.2%) | 7(13.2%) | 3(8.1%) | 8(10.1%) | 12(10.9%) |
| Antiepileptics | 13(6.8%) | 1(3.5%) | 1(1.4%) | 5(9.4%) | 6(16.2%) | 5(6.3%) | 8(7.2%) |
| Beta Blockers | 10(5.2%) | 0(0%) | 1(1.4%) | 3(5.3%) | 6(16.2%) | 3(3.7%) | 7(6.3%) |
| Ca Antagonists | 8(4.2%) | 0(0%) | 0(0%) | 1(1.8%) | 7(18.9%) | 3(3.7%) | 5(4.5%) |
| Ergotamine | 7(3.7%) | 1(3.5%) | 0(0%) | 3(5.3%) | 3(8.1%) | 2(2.5%) | 5(4.5%) |
| Others Medications | 104(55.0%) | 11(39.2%) | 35(49.2%) | 32(60.3%) | 26(70.2%) | 33(41.7%) | 71(64.5%) |

*Number of Patients
**Tricyclic antidepressants

**Table-II:** Frequency of different classes of drugs prescribed by Neuro Physicians (N = 130)

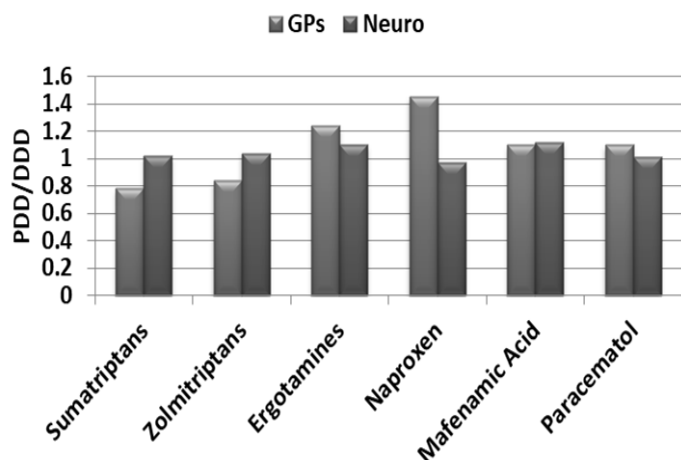| Class of drugs | All Patients (n* = 130) | Age <= 25 (n = 17) | Age 26-40 (n = 49) | Age 41-55 (n = 38) | Age >55 (n =26) | Male (n = 52) | Female (n = 78) |
|---|---|---|---|---|---|---|---|
| Analgesics | 107(82.3%) | 15(88.2%) | 41(83.6%) | 29(76.3%) | 22(84.6%) | 40(76.9%) | 67(85.8%) |
| TCA** | 56 (43.0%) | 5(29.4%) | 13(26.5%) | 20(52.6%) | 18(69.2%) | 19(36.5%) | 37(47.4%) |
| Triptans | 49 (37.6%) | 9(52.9%) | 19(38.7%) | 12(31.5%) | 9(34.6%) | 20(38.4%) | 29(37.17%) |
| Anti-epileptics | 47 (36.5%) | 4(23.5%) | 12(24.4%) | 15(39.4%) | 16(16.2%) | 20(38.4%) | 27(34.6%) |
| Anti-emetics | 27 (20.7%) | 5(29.4%) | 11(22.4%) | 7(18.4%) | 4(15.3%) | 8(15.3%) | 19(24.3%) |
| Ca Antagonists | 22 (16.9%) | 2(11.1%) | 3(6.1%) | 9(23.6%) | 8(30.7%) | 7(13.4%) | 15(19.7%) |
| Beta Blockers | 15 (11.5%) | 0(0%) | 2(4.0%) | 6(15.7%) | 7(26.9%) | 6(11.5%) | 9(11.5%) |
| SSRIs | 15 (11.5%) | 3(17.1%) | 5(10.2%) | 5(13.1%) | 2(7.6%) | 5(9.6%) | 10(12.8%) |
| Benzodiazapines | 11 (8.4%) | 1(5.8%) | 3(6.1%) | 2(5.2%) | 5(11.5%) | 4(7.9%) | 7(8.9%) |
| Ergotamine | 8 (6.1%) | 1(5.8%) | 2(4.0%) | 2(5.2%) | 3(7.6%) | 3(5.7%) | 5(6.4%) |
| Antihistamines | 7 (5.3%) | 0(0%) | 2(4.0%) | 3(7.8%) | 2(7.6%) | 4(7.9%) | 3(3.8%) |
| Anti-serotonin | 2 (1.5%) | 0(0%) | 1(2.0%) | 1(2.6%) | 0(0%) | 0(0%) | 2(2.5%) |
| Others Medications | 87 (66.9%) | 7(41.1%) | 25(51.0%) | 23(60.5%) | 32(123.0%) | 34(65.5%) | 53(67.9%) |

*Number of Patients
**Tricyclic antidepressants

**Table-III**: **Comparison and statistical analysis of prescribing practices between GPs and NPs (N = 319)**

| Variables | General Physicians (n = 189) | Neuro Physicians (n = 130) | p-value |
|---|---|---|---|
| Average number of drug | 6.10 ± 0.21 | 3.98 ± 0.12 | 0.018 |
| Mean price per prescription (PKR) | 58.9 ± 2.47 | 88.4 ± 3.45 | 0.011 |
| Drug with generic name (%) | 48.09 | 34.10 | 0.008 |

*P ≥ 0.05

The define daily dosages (DDDs) ratios of different drugs prescribed by two practitioners are presented Figure-1 in which Naproxen (1.45 vs 0.97) and Ergotamine (1.24 vs 1.1) were prescribed in higher doses by GPs than NPs. Whereas, sumatriptans (0.78 vs 1.02) and zolmitriptans (0.84 vs 1.04) were prescribed in lower doses by GPs as compared to recommended doses by WH

**Fig-1: Daily dosages ratios (means ± SD) of six direct acting anti migraine drugs used as monotherapy or poly therapy (N = 319)**
*DDD=Defined Daily Dose.
**PDD=Prescribed Daily Dose.

## DISCUSSION

In our study, we have found that the incidence ratio of migraine is high in women than men i.e. 58.9% and 41.0% respectively. Similarly, a study was conducted in Aga Khan University Hospital Karachi in which the prevalence of migraine in women (68.4%) and in men (31.6%) was reported and another study indicates the same situation in India[15-16]. It has been reported that levels of estrogen in women may potentiate the migraine tendency[17]. Hence this could be the reason of greater migraine frequency in women as compare to men.

In this study we have evaluated that the ratio of nonsteroidal anti-inflammatory drugs (NSAIDs) prescription was high among both GPs and NPs i.e. 88.8% and 82.3% respectively. The uses of NSAIDs by migraneurs are very much similar with the study in Finland reported that is 71% in women and 62% in men and also Kefeel and Rukh et al reported that paracetamol was primarily used drug in Karachi[18]. Because, NSAIDs have early symptomatic effect. Furthermore, the acceptability of treatment by migraine patients due to early pain relief. However, NSAIDs cause serious adverse effects like gastrointestinal, renal, hepatic, and respiratory. On long term use and taking inappropriate high dose may cause high risk.

In this study, use of selective serotonin reuptake inhibitors (SSRIs), benzodiazepines and tricyclic antidepressants (TCA) are frequently prescribed medicines after NSAIDs by GPs while NPs prescribed TCA, triptans and antiepileptic drugs with or without NSAIDS. According to US National Surveillance Studies (2009), triptans are primary prescribed drugs while sumatriptan showed major share among all triptans which is also comparable to our study[19]. Depression is one of the associated factor of migraine hence, these medications are considered better choice after NSAIDs.

It has been evaluated that GPs are prescribing more medications as compared to the NPs which indicates polypharmacy which is the use of multiple medications for a single patient. This practice can be used to treat multiple comorbidities where no alternatives exist for such conditions. Increase number of drugs also increases the chances of adverse drug reactions and could be responsible to lower quality of life and insignificant health outcomes[20]. Hence these facts are sufficient to hypothesize that decrease in polypharmacy will contribute to a positive healthcare outcome[21]. Incorporation of multivitamins has also been observed in this research and studies suggested that use of Riboflavin showed superior results when compared with placebo and reducing the frequency of migraine attacks in the prophylactic treatment[22]. Hence, polypharmacy increase the treatment cost and also directly related to decrease compliance to treatment therapy.

The variation observed in mean cost of treatment per prescription in treatment of NPs (Rs. 88.4) as compared to GPs (Rs. 58.9); the previous study conducted in Germany reported the similar outcomes[7]. Prescriptions with low quality or irrational drugs due to their low costs are more associated with serious adverse reactions during treatment[23]. Apart from this, costly treatment might lead to decrease patient's adherence to treatment.

The percentages of drugs prescribed with their generic names by GPs (48.09%) are much higher than NPs (34.10%). It indicates that prescribing practices of GPs are more focused on cost effective therapy by prescribing drugs with their generic names. It is also reported that there is a significant price difference in marketed brands of same generic which possessed same pharmaceutical quality[11]. The outcome of this comparison provides the space in term of choice to patients to purchase cost effective drugs which may also leads to the improvement patient's compliance.

Our study results showed the major discrepancies in GPs drugs prescribing dosages as compared to NPs. The usage of Sumatriptans (0.78) and Zolmitriptans (0.84) in very low doses by GPs. Conversely, Naproxen is the most prescribing analgesic in the treatment of migraine in Pakistan but it was prescribed by GPs at much higher doses (1.45) as compared to its actual DDDs. More significantly, it was also revealed that no alteration of drug dosages observed with respect to patients gender, age or prescribed as a monotherapy or polytherapy. This type of dosing variability of drugs was also reported in previous study for the treatment of epilepsy[24]. So far, low dose is highlighting issue which may cause sub-therapeutic effect of these drugs which ultimately reduce the patient satisfaction towards treatment if the intensity of migraine does not reduced. Similarly, high dose of the drugs causes toxicities like, the utilization of analgesic in higher doses may cause renal or gastrointestinal toxicities.

Furthermore, statistical findings of independent t-test of this study results indicates that there is a significant difference (P = 0.018; S.D = 0.606) found in average number of prescribed drugs in each prescriptions between GPs and NPs prescriptions practices. Similarly, there are differences observed in mean price per prescription (P = 0.011; S.D = 5.121) and in percentage of drug prescribed with its generic name (P =

0.008; S.D = 3.805) between GPs and NPs prescriptions practices.

The current investigations have some limitations. Firstly, there was no valid information was obtained regarding duration and frequency of migraine or the pain related to attacks of migraine. This lack of information taken into account when initiating a prophylactic treatment may explain the minimum use of prophylactic medicines or, otherwise, there is a huge room for an improvement of treatment of migraine in Pakistan. Secondly, in this study there is no information related to outcomes of migraine therapy.

## CONCLUSION

Polypharmacy and discrepancies in daily dosages of anti-migraine drugs were more found in prescribing pattern of General Physicians. However, cost effective treatment by General Physician was noticed due to higher ratio of generic drugs. Higher incidence ratio of migraine was observed among female.

## CONTRIBUTION OF AUTHORS

**Khan K:** Literature search, Literature review, Data collection, Manuscript writing
**Arain MI:** Conceived idea, Supervised the study, Designed research methodology
**Ghoto MA:** Formulated data, Data analysis, Manuscript writing
**Dayo A:** Supervised the study, Manuscript final reading
**Zehravi M:** Literature search, Literature review, Manuscript writing
**Rehman AA:** Literature search, Study design, Manuscript writing
**Asghar MA:** Data interpretation, Statistical analysis, Manuscript writing

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