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Pattern of Drug Utilization and Pharmacovigilance Survey on Drugs used in Uncomplicated Malaria in Dewas District of Madhya Pradesh

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ABSTRACT

Adverse drug reactions (ADRs) contribute to ill-health or life-threatening outcomes of therapy during management of infectious diseases. Pharmacovigilance study deals with the complete drug monitoring. It will give idea about the safe use of the drugs and also suggest the drug monitoring and possible adverse drug reactions of any drug in various patients, in various age groups and at different dose regimen. Malaria is a very common and frequent disease in a developing country like India. Approximately every year nearly 40-45% of human beings suffer from the disease and among then nearly 15-18 % have ADRs, The present investigation was carried out in the Department of Malaria, Government District Hospital, Dewas, Madhya Pradesh, India, The study was made to the patient who got treatment from the hospital and drug treatment and results were evaluated. From the data obtained it was concluded that age 11-20 were mostly affected by the malaria and first drug choice is chloroquinine followed by artesunate. As far as ADR is concerned, nausea is most occurring ADR followed by vomiting. As per the assessment about 53.88% of ADRs have been recovered.

Keywords: Adverse drug reactions, Pharmacovigilance, Malaria, Chloroquinine, Artesunate

INTRODUCTION

Malaria continues to be a major public health problem, in spite of enhanced control efforts, mostly in Africa and parts of Asia. In 2008, approximately 243 million people fell sick with malaria, with a majority of cases in the African region (85%), causing death of nearly one million people, 85% of whom were

children under 5 years of age.[1] Malaria and poverty are connected. In the countries where malaria has an impact on public health, it is also severely hampering economic development .[2] As a consequence of increasing resistance of the malaria parasite to previously effective monotherapies including chloroquine (CQ) and sulphadoxine-pyrimethamine (SP), the World Health Organization (WHO) held a technical consultation in 2001 endorsing the potential of artemisinin-based combination therapy (ACT) for drug-resistant malaria.[3] Antimalarial combination therapy is the simultaneous use of two or more blood schizontocidal drugs with independent modes of action and thus unrelated biochemical targets in the parasite.[4] The objective of a national antimalarial treatment policy in India is to enable the population at risk of malaria infection to have access to safe, good quality, effective, affordable and acceptable antimalarial drugs.[5] By 2009, most malaria-endemic countries had introduced ACT in their national drug policy, as first-line treatment for uncomplicated *Plasmodium falciparum* malaria. The detection of adverse drug reactions (ADR) mainly depends on detailed and elaborate drug history of the patient. The diagnosis of ADR is by exclusion of other disease and assessment of the causal relationship.[6] Inappropriate treatment, incorrect dosing, drug-drug interaction, administration in populations suffering from or being treated against concomitant diseases like HIV/AIDS, tuberculosis, malnutrition and anemia can all impact negatively on drug safety and efficacy.[7,8] In general, safety information can be collected through two main pharmacovigilance channels: (a) spontaneous reporting and (b) systems using pharmacoepidemiological methods through phase IV clinical trials or cohorts.[7-9] While spontaneous reporting is essential for signal detection of rare events, the pharmacoepidemiological methods provide additional information on both, the utilization and the extent of consumption that will permit the determination of frequency of ADRs in the studied population or the safety comparison between two or more products.[9] Although ACT is generally considered safe, there is still little structured information about their use in real-life settings and the published data are mainly from clinical trials.[10] The World Health Organization defines pharmacovigilance as “the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.” The adverse drug reaction reporting has been going on in India for a long time. The current Pharmacovigilance Programme of India started in 2010 and has organized nearly 30 workshops on pharmacovigilance in the last two years. More than 32,000 ADR reports have been collected through ADR monitoring centers housed in 60 medical colleges across the country. However, pharmacovigilance has been associated with a national health programme for the first time in the country. ADR reporting barely existed for antimalarial drugs before the start of this project. The objectives are to monitor ADRs to antimalarial medicines and guide pharmacovigilance capacity building in the country through cohort event monitoring for antimalarial drugs. Good pharmacovigilance practices based on knowledge and

attitude are the key to safeguard against seven individual behavioral variations and societal barriers which lead to underreporting of ADRs.[11-12] Studies on knowledge and attitude of healthcare professionals (HCPs) have shown high variation. In India, such data is limited to tertiary care hospitals.[13-15] However, 69% of Indian population lives as agrarian society in nearly 6.4 Lakh rural units.[16] Thus, the objectives of the present investigation was to find out the possible drug therapy given for the treatment of malaria and potentially relevant ADR.

MATERIALS AND METHODS

Selection of diseases

Malaria is a very common and frequent disease in a developing country like India. Approximately every year nearly 40-45% of human beings suffer from the disease and among then nearly 15-18 % have ADRs, therefore the present disease was selected.

Selection of study area

Dewas district of Madhya Pradesh, India is selected for the present investigation due to Department of Malaria treatment centre in it, Also, the disease in very frequent in and around Dewas district due to various factors among which un hygienic is one of the prime cause and as per that data obtained from the Dewas Government Hospital 3-8 patients were reported to have malaria every days, hence for the present investigation Dewas was chosen.

Selection of study period

The present study was conducted for a period of 3 months (April' 2017 to June' 2017) in Government District Hospital, Dewas, Madhya Pradesh, India.

Selection of study population

Three hundred eighty three (383) patients were selected for the present investigation hospitalized in medical ward receiving anti-malarial drugs for the treatment were enrolled in this study.

Study design & design of questioner

The study was hospital based prospective observation study. Patients were followed up for the period of one month after receiving the drug treatment. For proper and orderly study Suspected ADR reporting form were filled for the each patient.

In this study the following parameters were reveled out.

- Demographic responses
- ADR and Non ADR status
- No. of Male and Female Patients
- Age wise distributions of ADR in male and female
- Anti-malarial treatment in male and female

- Incidence of ADR of individual drugs

Study tools

ADRs reporting as per standard mentioned in Indian Pharmacopoeial Commission was use to collect the data. One separate questionnaire regarding social-demographic characteristics was developed and was used in the present study.

Inclusion and exclusion criteria

During the course of present investigation, patient receiving anti-malarial therapy and developed atleast one ADRs were included for the present investigation and patient having other disease along with the malaria were excluded from the present investigation.

Data collection

The present study was based on Cohort Event Monitoring (CEM) system. It records all clinical events but not suspected ADRs. It is prospective, observational, cohort study of adverse events associated with one or more drugs/medicine.

Data analysis

Information received from the patient was recorded and was assessed using the causality WHO-UMC Causality Assessment scale for classifying the adverse events. Also, severity assessment was assessed using hartwing scale and Schumock and Thornton preventability scale were used in the present investigation.

RESULTS AND DISCUSSIONS

Malaria is a very common and frequent disease. Dewas district of Madhya Pradesh was chosen for the present investigation and data regarding the present study was obtained after a proper questioner developed as per Pharmacovigilance ADRs report form Dewas District hospital. Total 383 questionnaires i.e., case sheet were administered out of which 267 were returned completely filled. Out of 267, 193 ADRs were found and reported from 89 female patients and 104 male patients during the study period for present investigation. Table 1 reveal the demographic responses of ADR in study population and Figure1 demonstrated the Socio-demographic characteristics of study population. Different age groups of patient were pointed out in the present investigation for both the sexes (male and female). The data so obtained are presented in table 2. The results obtained indicate that the majority of the ADRs observed in the age group of 11-20 in male and females. The drugs viz., Quinine, Chloroquine, Artesunate, Proguanil, Mefloquine, Sulphadoxine + Pyrimethamine, Atavaquone + Proguanil were prescribed to the 193 patients and the drug distribution over male and female were presented in table 3. The data obtained indicate that the most prescribed drug is Chloroquine followed by Artesunate. The class of drugs viz.,

Quinine, Chloroquine, Artesunate, Proguanil, Mefloquine, Sulphadoxine + Pyrimethamine, Atavaquone + Proguanil after treatment offered to the patient was studied for ADRs. The most common ADRs observed were nausea, anorexia, vomiting, bitterness of mouth, gliddiness and dizziness Figure 2-8. From the data revealed in table 4 it was observed that most commonly occurred ADRs is nausea (79 %), followed by vomiting (24%), Anorexia (34%), bitterness of mouth (24%) and others (11%). The ADRs observed were assessed for their causality using Naranji algorithm propability scale. It was observed from the data obtained that 37.30% were probable, 25.90% were possible 19.68% were certain and 17.09% were unlikely Table 5. The ADRs observed were assessed for their severity using a modified Hartwig severity scale, which is standard scale for severity assessment as per the standard. It was observed 79.27% were mild, 16.58% were moderate and 4.14% were severe Figure 9. The ADRs observed were assessed for their preventability using modified Schumock and Thornton preventability scale. It was revealed that 32.64% were recovering, and 53.88% were recovered Figure 10.

Table 1 Demographic responses of ADR of study population (n=383)

Characteristics	ADR	Non-ADR	Total	Percentage
ADR Status	193	74	267	69.71
Percentage	72.28	27.21	-	100
Male Patient	104	43	147	55.05
Female Patient	89	31	120	44.94

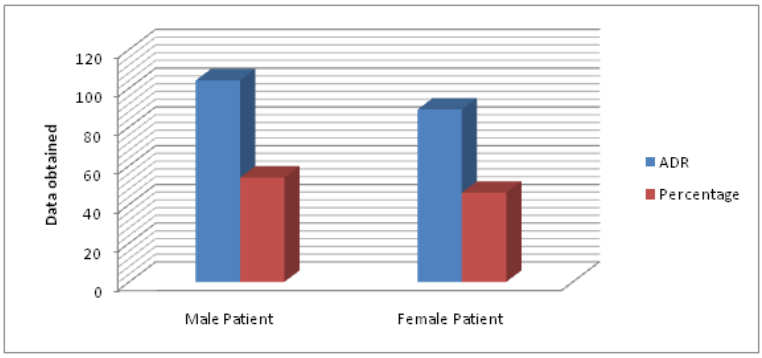

Figure 1 Socio-demographic characteristics of study population

Table 2 Age wise distribution of ADRs (n=193)

Age Groups (Years)	Male	Percentage	Female	Percentage	Total Percentage (M+F)
0-10	28	14.50	21	10.88	25.38
11-20	41	21.24	32	16.58	37.82
21-40	19	9.84	12	6.21	16.05
41-80	12	6.21	18	9.32	15.53
≥80	4	2.07	6	3.10	5.17

Table 3 Anti-malaria drug treatment in hospital (n=193)

Treatment Given	Male	%	Female	%	Total	Percentage
Quinine	18	9.32	15	7.77	33	17.09
Chloroquine	32	16.58	29	15.02	61	31.60
Artesunate	27	13.98	21	10.88	48	24.87
Proguanil	6	3.10	3	1.55	9	4.66
Mefloquine	11	5.69	13	6.73	24	12.43
Sulphadoxine + Pyrimethamine	7	3.62	6	3.10	13	6.73
Atavaquone + Proguanil	3	1.55	2	1.03	5	2.59

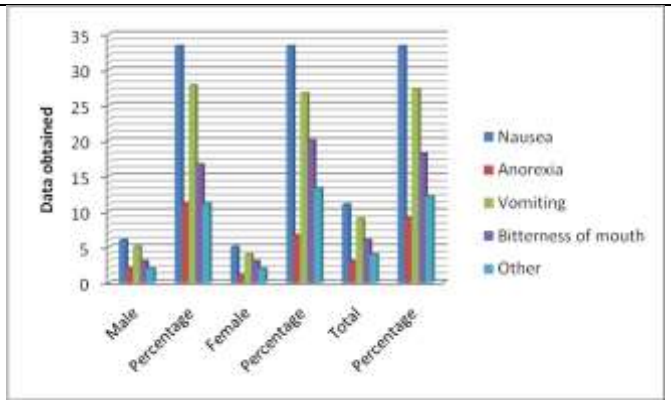

Figure 2 ADR reports of Quinine (n=33; M=18; F=15)

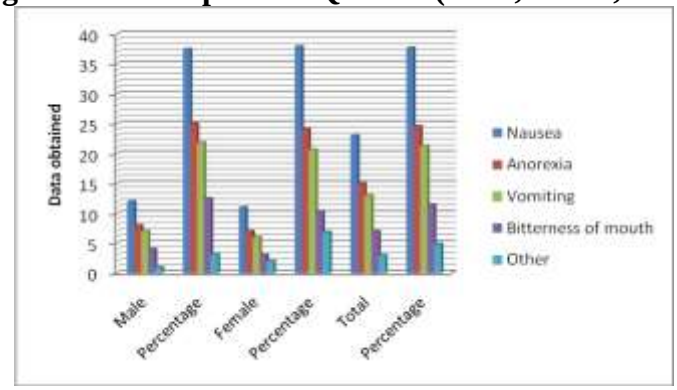

Figure 3 ADR reports of Chloroquine (n=61; M=32; F=29)

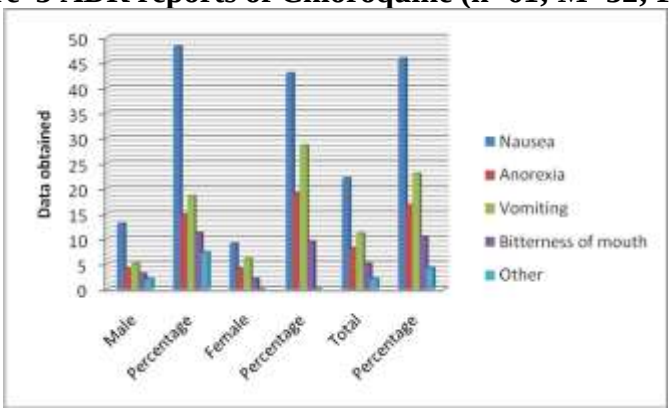

Figure 4 ADR reports of Artesunate (n=48; M=27; F=21)

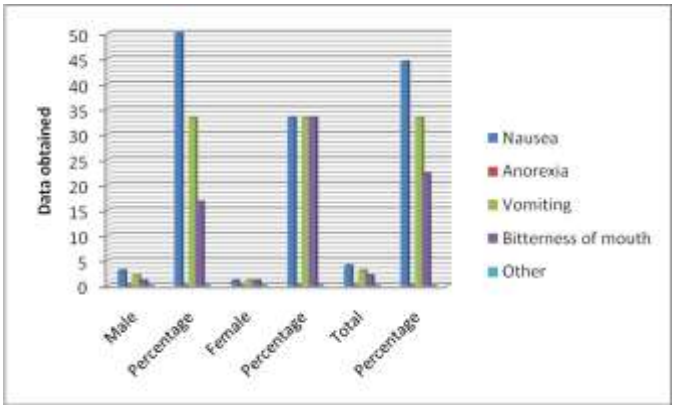

Figure 5 ADR reports of Proguanil (n=9; M=6; F=3)

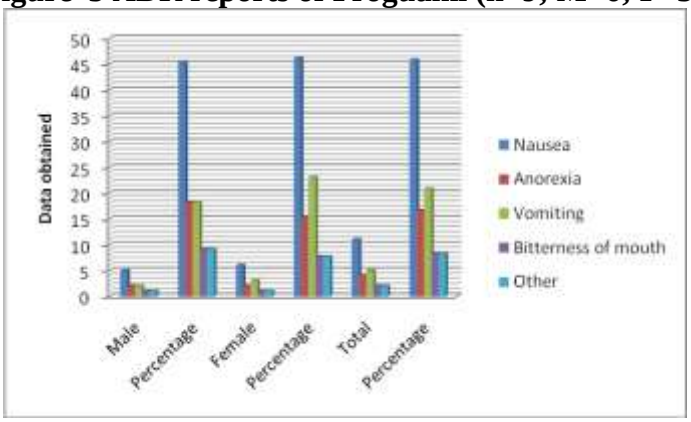

Figure 6 ADR reports of Mefloquine(n=24; M=11; F=13)

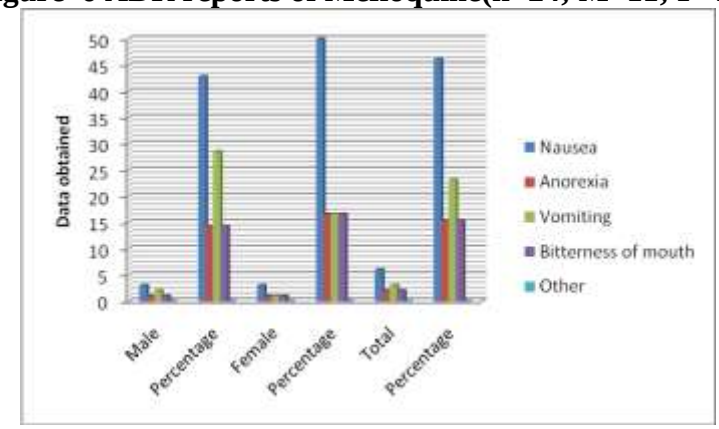

Figure 7 ADR reports of Sulphadoxine + Pyrimethamine(n=13; M=7; F=6)

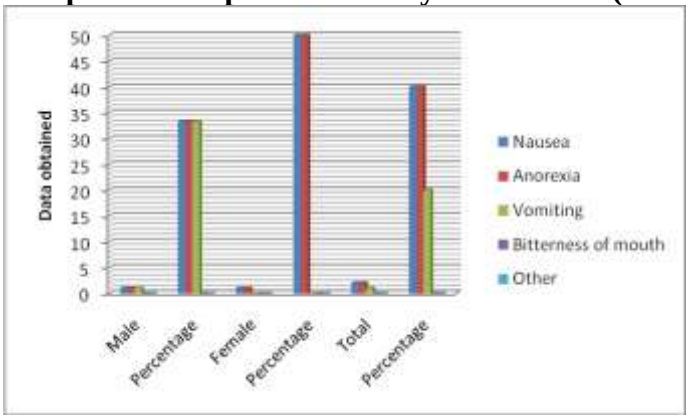

Figure 8 ADR reports of Atavaquone + Proguanil(n=5; M=3; F=2)

Table 4 ADR reports of prescribed anti-malarial drugs (n=193)

Adverse effects	No. of Patients	Percentage
Nausea	79	40.93
Anorexia	34	17.61
Vomiting	45	23.31
Bitterness of mouth	24	12.43
Other (Giddiness & Dizziness	11	5.69

Table 5 Casuality assessment among patient suffering from malaria shows ADR (n=193; M=104; F: 89)

Assessment of Causality	No. of Patient	Percentage	Male	Percentage	Female	Percentage
Probable	72	37.30	38	36.53	34	38.20
Possible	50	25.90	29	27.88	21	23.59
Certain	38	19.68	20	19.23	18	20.22
Unlikely	33	17.09	17	16.34	16	17.97

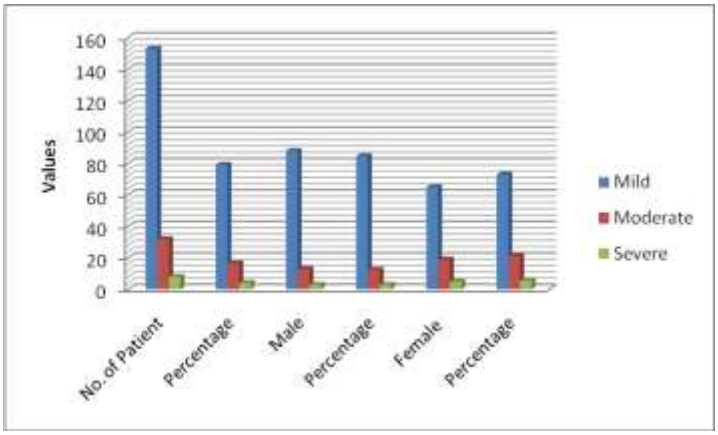

Figure 9 ADR assessment among patient using anti-malarial drug using Hartwig severity scale (n=193; M=104; F: 89)

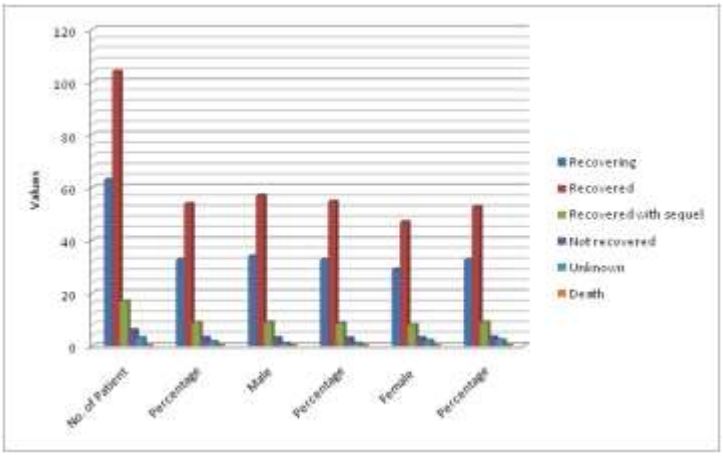

Figure 10 ADR assessment among patient using anti-malarial drug using Schumock and Thornton preventability scale (n=193; M=104; F: 89)

CONCLUSION

The World Health Organization defined ADRs as a response of drug which in noxious, unintended and harmful which occur at a specific dose administered to the patient. These definitions exclude overdose and drug abuse. ADRs are one of the most important because it leads to morbidity and mortality and also increases the cost of hospital. Approximately overall ADRs estimated is 6.5% and 28% of these ADRs as preventable as per WHO assessment. The present investigation was carried out in the Department of Malaria, Government District Hospital, Dewas, Madhya Pradesh, India, The study was made to the patient who got treatment from the hospital and drug treatment and results were evaluated. From the data obtained it was concluded that age 11-20 were mostly affected by the malaria and first drug choice is chloroquinine followed by artesunate. As far as ADR is concerned, nausea is most occurring ADR followed by vomiting. As per the assessment about 53.88% of ADRs have been recovered.

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