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ORIGINAL ARTICLE

Prevalence of Potent Drug Interactions in Malarial Patients and its Related Physiology

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ABSTRACT

Objective: To find the prevalence of drug-drug interaction in malarial patients.
Study Design: Retrospective study
Place and Duration of Study: Department of Pharmacology, Watim Medical & Dental College, Islamabad Rawat from 1ST May 2021 to 30th November 2021.
Methodology: Eighty malarial patients were enrolled. The patients were divided into two groups with 40 patients in each group. Group A had patients only suffering from malaria while Group B was malarial patients who were also having co-morbidity. There drug-drug interaction was analyzed and prevalence determined.
Results: The mean age was 22.1±3.2 years. There was greater than 5 days' hospital stay in 62.5% cases with malaria in addition to co-morbidities. The drug interaction was present in 8 cases out of 40 in group A while 20 in group B.
Conclusion: The potential of drug-drug interaction is as high as 35% in malarial patients
Key words: Malaria, Drug interaction, Diabetes mellitus, Comorbid

INTRODUCTION

Malaria is an old infectious disease causing global health burden. World Health Organization in 2019 elaborated that cases of malarial infection ranges around 228 million in worldwide with an estimated number of mortality as 405k as recorded by 2018 statistics.[1] The number of malarial cases in Pakistan is reported as 705000 in year 2018.[2] This infectious disease remains one of the common cause of mortality and morbidity all over the globe.[3] There is a gender variance in which males are more prone towards malaria and men are noticed to be more at the effect of catching infection especially those who are in their early teenage and are living in a rural setting than urbane.[4]

Although most of the cases of malaria do not need hospitalization still those who are admitted to the hospital are for managing co-morbid illnesses.[5] The recommended drugs against malaria infection includes anti-malarial drugs, anti-pyretic medications as well as analgesics.[6] In situations where co-morbidity causes secondary infections various other medication is also given for controlling the co-morbidities of malaria.[7] Unfortunately, the usage of various drugs might result into drug-drug interactions also known as DDIs which further effect the pharmaco-kinetic factors in addition to pharmaco-dynamic profiles.[8,9]

Drug-drug interactions can result into negative health outcomes as long term hospitalization, reduction in therapeutic efficacy of the malarial drugs, toxic effects or other side effects.[10] Kohler et al[11] suggested that drug interaction causes about twenty to thirty percent of side effects in malarial patients with around 1-2% having life intimidating while 70 percent required clinical assistance for timely management of these adverse effects.. Other research has also described that patients who are already hospitalized due to liver diseases, immunocompromised condition or diabetic and additionally suffer from malaria had higher frequency of DDIs in them.[12-15] This study was conducted for identifying the frequency of DDIs in malarial patients and assesses their effects on their overall health and recovery. The data of this study will assist in better understanding of drug-drug interactions and facilitates in designing new approaches for health benefits.

MATERIALS AND METHODS

This retrospective study was performed at Department of Pharmacology, Watim Medical & Dental College, Islamabad Rawat from 1st May 2021 to 30th November 2021. Malaria patients are mostly observed in monsoon season in Pakistan therefore the months between July to September were targeted as maximum number of patients were admitted in the hospital during this time. A total of 80 patients suffering from malaria with an age between 20-40 years were enrolled. These patients were further divided into two groups. In group A there were 40 those patients who were healthy other wise and were only suffering from malarial infection. While in group B those 40 patients were enrolled who had previously been suffering from either liver impairment (10 cases), diabetes mellitus (10 cases), carcinoma (10 cases) and rest 10 cases with hypertension. *Plasmodium vivax* and *Plasmodium falciparum* are the major types of malaria causing parasite. The study design was approved from the institutional board. Micromedex Drug-Reax software was study for assessing the DDIs severity level as from minor-moderate-major-contraindicated levels. The most relevant DDIs were reported and their frequency was analyzed through clinical symptoms and laboratory testing. The variance in doses was used for stratification of clinical characteristics if drugs which were interacting. The cut-off points used for identifying raised daily dose was as following: products with calcium ≥ 600 mg per 3 L, rifampin: ≥ 450 mg ceftriaxone: ≥ 3 g; isoniazid: ≥ 300 mg acetaminophen: ≥ 1 g quinine: ≥ 1350 mg dexamethasone: ≥ 24 mg ciprofloxacin: ≥ 800 mg metronidazole: ≥ 1500 mg. The laboratory tests as complete blood count, renal functions test and albumin creatinine test in addition to liver function test was analyzed in each patient. Raised values of leukocytes, blood urea nitrogen, serum creatinine and alkaline phosphate above 11k/uL, 20mg/dl, >1.06mg/dl and >126U/L respectively were considered significant for determining DDIs. Data was analyzed by SPSS version 25.0 where independent t test was used for statistical analysis. P-value less than 0.05 was considered as significant.

RESULTS

The mean age was 22.1±3.2 years. There were 52.5% males and 47.5% females among those patients who were only suffering from malaria. While 62.5% males and 15% females in those malarial patients who were also suffering from co-morbidities (Table 1).

The present study showed that prolonged hospitalization was higher in cases having malaria in addition with other co-morbidities. There was greater than 5 days' hospital stay in 62.5% cases with malaria in addition to co-morbidities. Acute gastroenteritis was also formed in 12.5% cases during their malarial infection (Table 2).

The drug interaction was seen in 35% cases within which it was present in 8 cases out of 40 only malaria patients while in 20 those having malaria with co-morbidities. The individual prevalence of DDIs in hypertension and liver disorder including cirrhosis was

similar as 21%. The categorization of DDIs presenting as major DDIs in 45% of total malarial patients (Fig. 1).

There were various drugs used which interacted between each other during malarial treatment. It was seen that drugs used in low dosage has more prevalence of interacting for calcium containing drug-drug interactions (Fig. 2).

Table 1: Gender and age distribution among malarial patients (n=80)

Variable	Group A		Group B	
	No.	%	No.	%
Gender				
Male	21	52.5	25	62.5
Female	19	47.5	6	15.0
Age (years)				
≤ 20	9	22.5	16	40.0
21–40	18	45.0	13	32.5
> 40	13	32.5	11	27.5

Table 2: Hospital stay in malarial patients (n=80)

Variable	Group A		Group B	
	No.	%	No.	%
Hospital stay (days)				
4 – 5	16	40.0	15	37.5
> 5	24	60.0	25	62.5
DDIs in Co-morbidities				
Hypertension (n=10)	-	-	2	20.0
Diabetes mellitus (n=10)	-	-	6	60.0
Hepatitis (n=10)	-	-	1	10.0
Acute gastroenteritis (n=40)	5	12.5	1	2.5
Carcinoma (n=10)	-	-	6	60.0

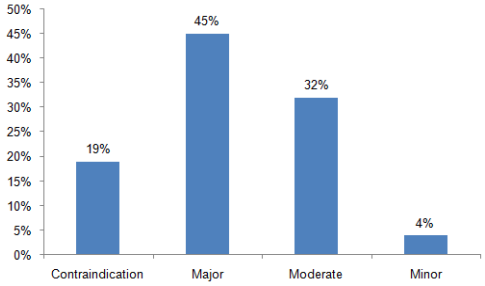

Fig. 1: Categorization of DDI

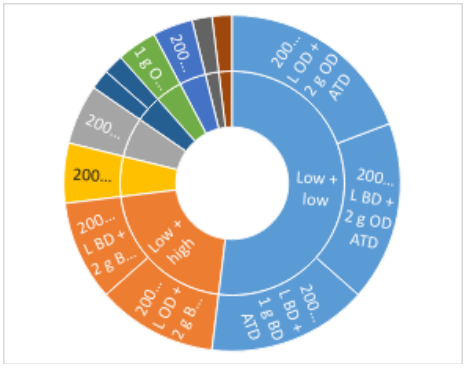

Fig. 2: Calcium containing product drug-drug interactions

DISCUSSION

Drug-drug interactions persist as a major therapeutic challenge in various diseases including malaria. The data available on DDIs in malaria patients is still limited. The reported DDIs were as 35% in total malarial patients. The results of this study were in coordination with previously reported result from Pakistan which reported 37.2% drug-drug interaction.[16] The prevalence of hypertension and liver cirrhosis and immunocompromised patients DDIs is reported earlier as 21.1%, 21.5% and 33.5% respectively with much higher prevalence of diabetes mellitus and transplant patients suffering from drug-drug interactions.[17]

The higher frequency reported in the current study might be due to regional variance. Pakistani population had a different drug prescribing protocol than the western countries. Moreover, the software applied in this study may also create result variance than reported earlier.[18,19] The present study highlights the fact that drug-drug interaction can cause lethal outcomes especially in patient who have any other persistent disease. This is justified by the statement that patient having co morbidity are already immune compromised and sensitive towards combinational drugs.[20]

Another important finding of this study is that diabetes mellitus cases had higher DDIs than other co morbidities. This is further explained by the fact that the drugs which are prescribed in patients suffering from diabetes mellitus are the most potent drugs for interacting with malarial prescribed drugs. Therefore, escalating the prevalence of DDIs in diabetes patients. Similar results have been observed for cancer patients where as well the cancer treating drugs highly interact with malarial drugs increasing the frequency of DDIs in such patients.[21]

CONCLUSION

The potential of drug-drug interaction is as high as 35% in malarial patients where its frequency becomes higher in diabetic and cancer patients.

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