EUROPEAN ACADEMIC RESEARCH
Vol. XI, Issue 8/ November 2023

Impact Factor: 3.4546 (UIF)
DRJI Value: 5.9 (B+)

ISSN 2286-4822
www.euacademic.org

The Outcome of Acute Organic Brain Syndrome due to Falciparum Malaria Treated with Quinine, Haloperidol, and Diazepam Therapies

KAMAL ELDIN AHMED SAILH
Endemic Diseases Centre
Faculty of Medicine and Health Sciences
Sinnar University

Abstract

Background: *Malaria is a major health problem worldwide. It is currently endemic in tropical and subtropical areas in Africa, Asia, and South America. The Republic of Sudan has the highest malaria incidence rate in the Eastern Mediterranean Region (EMRO), contributing to 56% of estimated cases (1). The dominant malaria specie in Sudan is Plasmodium falciparum (87.6%) (7). Falciparum malaria may be complicated by acute organic brain syndrome, agitation, delirium with hallucinations, transient amnesia, and schizophrenic features have also been described. Long-lasting personality disorders and even dementia might develop, albeit rather uncommonly (8-9).*

Methods: *This study was carried out in Sinnar Teaching Hospital, in the period from the first of October 2008 up to the end of October 2012. The data was collected from 61 patients. All of them fulfilled the ICD-10 criteria for the diagnosis of acute organic brain syndrome, and infection with Plasmodium falciparum was confirmed by thick and thin blood films. The other causes of acute organic brain syndrome were excluded by history, physical examination and appropriate investigations. The entire patient received standard quinine therapy for one week. The patients with hyperactive and mixed types all of them received haloperidol IM when needed it, within the first week and then orally to those who needed it. Aggressive patients received diazepam IV. They were followed up weekly up to 29th day by physical and mental assessments and thick and thin blood films for Plasmodium falciparum.*

Result: *51 (83.6%) of the patients fully recovered, 8(13.1%) had incomplete recovery from acute organic brain syndrome, 2(3.3%) passed away. All the patients with hyperactive type 33(54.1) and mixed types11 (18%) received haloperidol IM within the first week. Diazepam IV was needed within the first week in all patient with hyperactive type 33(54.1%), and 5 (8.2%) with mixed type.*

Conclusion: *Quinine as antimalarial drug in standard dose plus haloperidol, and diazepam when are indicated are a suitable therapies for patients with acute organic brain syndrome due to falciparum malaria with good outcome, specially in Situation of Low Health Services of Sudan where other type of antipsychotic and benzodiazepine drugs are not easily available.*

Keywords: Acute organic brain syndrome, falciparum malaria, quinine, haloperidol, and diazepam.

INTRODUCTION

Malaria is a major health problem worldwide. It is currently endemic in tropical and subtropical areas in Africa, Asia, and South America. World Health Organization (WHO) estimated that in 2020 there were 241 million malaria cases in the 85 malaria endemic countries, leading to 627,000 deaths. 96% of these cases occurred in Africa (1). Estimated malaria and malaria related morbidity and mortality had increased by 6%

and 12% respectively, from2019 to 2020, partly due to disruptions to malaria prevention and treatment services caused by COVID-19 pandemic (1-2-3) From 2000 to 2020, malaria incidence in the Eastern Mediterranean Region (EMRO) decreased from 21 to 11 cases per 1000 population at risk. This decline coupled with population growth, led to drop in cases from 7 million to 5.7 million cases . The Republic of Sudan has the highest malaria incidence rate in the EMRO region, contributing to 56% of estimated cases (1).Inspite of the declining malaria incidence in the region, cases in Sudan nearly doubled between 2015 and 2019 (1- 3 -4). The alarming increasing is the result of many intertwined factors. In the past 3 years (2018-2020) Sudan had experienced unusually heavy rainy seasons that caused flash floods (5). The overall economic difficulties that the country is facing ,as well as ongoing political instability , conflicts and on growing size of population living in humanitarian setting in the country , contribute to the complex epidemiological situation in Sudan(5-6). The two main dominant malaria species in Sudan are Plasmodium falciparum (87.6%), and Plasmodium vivax(8.1%), with Plasmodium ovale and confections of both Plasmodium falciparum, and Plasmodium vivax representing the remaining infections in the country(7).

Falciparum malaria may be complicated by acute organic brain syndrome, agitation, delirium with hallucinations, transient amnesia, and schizophrenic features have also been described. Long-lasting personality disorders and even dementia might develop, albeit rather uncommonly (8-9). On occasions, psychiatric problems may be the presenting feature in patients with acute uncomplicated malaria (8-10). It must, of course, be remembered that neuropsychiatric manifestations can also be caused by side effects of antimalarial drugs (11).

Clinical Features of Acute Organic Brain Syndrome

According to ICD-10 acute Organic Brain Syndrome is a term that refers to mental disorders that caused by physical or physiological conditions. It is not specific diagnosis, but generally a category that includes various types of cognitive impairment, mood disorders and psychotic symptoms. It presents with acute onset of impaired awareness, easy distractibility, confusion, and disturbances of perception (e.g., illusions, misinterpretations or visual hallucinations). Recent memory is usually deficient, and the patient is typically disoriented to time and place. Abnormalities of congition and behavior may fluctuate dramatically over brief periods. Three types have been described (12). Hyperactivity type is characterized by increased psychomotor activity, agitation and sometimes aggression. Hypoactive type is characterized by generalized slowing so that the patient seem calm or even apathetic (13). Mixed type there is swinging across the spectrum of psychomotor disturbance ranging from agitation (hyperactivity) at one end and low drive (hypoactivity).

Diagnosis

The diagnosis of acute organic brain syndrome depends on clinical grounds (History and physical examination). History is to be taken from the patient and his relatives. The etiology and precipitating factors are then sought. Reaching the etiology and precipitating factors is essential for treatment. The basic diagnostic investigations include the followings:-

1-Laborotary (complete blood count, CRP, glucose, hepatic and renal function tests, electrolytes, TSH, urine analysis, and thick and thin blood films for malaria in endemic areas or traveler to endemic areas).

2-CSF studies.

3-ECG.
4-Echocardiography.
5- Chest x-ray.
6-Brain CTscan.

The treatment of Acute Organic Brain Syndrome

The cause of acute organic brain syndrome should be treated, if possible. For example fluid and electrolytes imbalances should be corrected, bacterial infections cured with antibiotics, malaria cured with antimalarial and anticholinergic discontinued. Patients with hyperactivity are usually treated with antipsychotic drugs. Haloperidol is administered in 1 mg dose every two to four hours. In the elderly haloperidol should be started in lower doses (0.25 to 0.5 mg every four hours). Patients should be watched for cardiac arrhythmias with prolongation of QT interval, especially in the elderly (14-15). Treatment of acute organic brain syndrome with benzodiazepines is cotraversal (16), as these drugs may cause paradoxical reaction, respiratory depression, and over sedation. Nevertheless for patients with severe psychomotor agitation, the administration of benzodiazepines and antipsychotic drugs is an important component of the treatment. When the cause of acute organic brain syndrome is falciparum malaria it should be treated by Artesunate or **Quinine. Quinine is usually used when Artesunate not available (17).** Initial treatment with **Quinine** should be in infusion, preferably in 5% Glucose or 5% glucose in normal saline. The dose is 10 mg salt/kg body weight administered 8-hourly over four hours duration, for at least 2 days and shift to the oral quinine as soon as the patient can take oral medication to complete the 7 days.

IV Artesunate is a short-acting antimalarial drug that clears Plasmodium parasites more rapidly than conventional antimalarials. The drug acts against both the sexual and asexual stages of the parasite. The dose of Artesunate is 2.4 mg/kg body weight (3.0mg/kg in children less than 20kg) given by IV injection on admission (time = 0), repeated at 12 hours and 24 hours, then once a day. After at least 24 hours of IV treatment and if the patient can tolerate oral medication, should complete the treatment with a full course of oral artimether and lumefantrine.

Development of coma, seizures, and post treatment hypoglycaemia were each less common in patients treated with Artesunate (18). Also it decreased the risk of death compared with quinine for the treatment of severe malaria in adults and children (19).

Problem

Malaria is a major medical and economical problem in Sudan that affects all society (1). This study tries to touch on acute organic brain syndrome as one of the serious falciparum malaria complications (8-9).

Patients and Methods

This study was carried out in Sinnar Teaching Hospital, in the period from the first of October 2008 up to the end of October 2012. The data was collected from 61 patients, all of them fulfill the ICD-10 criteria for the diagnosis of acute organic brain syndrome, and infection with Plasmodium falciparum was confirmed by thick and thin blood films. Also the following investigations were done for all the patients (complete blood count, glucose, hepatic and renal function tests, electrolytes, urine analysis, ECG and chest x-ray).Echocardiography and CT scan were not available in Sinnar State during the study period. All the patients received standard dose of quinine infusion according to

their weights at least for 48 hours or continued infusion until they became able to take it orally to complete the course for one week. The only medication available for treatment of severe falciparum malaria in Sinnar State during the study period was quinine. The patients with hyperactive and mixed types of acute organic brain syndrome received haloperidol, the minimum dose was 5mg per day and maximum was 10 mg per day in divided doses IM within the first week and then orally to those who needed it. Aggressive patients received diazepam IV, with the minimum dose is 10mg per day and maximum is 20 mg per day in divided doses within the first week only. Thick and thin blood films for Plasmodium falciparum were repeated on the eighth day after the last dose of quinine and weekly up to the 29th day. Physical and mental assessments were repeated on eighth day on discharge and weekly up to 29th day.

Exclusion: Any patients with possible cause of acute organic brain syndrome other than falciparum malaria like cerebrospinal meningitis, drugs addiction and trauma were excluded from the study.

Objective

Study outcome of acute organic brain syndrome due to falciparum malaria treated by quinine, haloperidol, and diazepam therapies.

RESULTS

Table (*1*) Explain the frequency of gender.

	No	%
Male	28	45.9
Female	33	54.1
Total	61	100

Table (*2*) Explain the frequency of age.

Age	No	%
18-27	36	59
28-37	11	18
38-47	8	13.1
48-57	3	4.9
More than 57	3	4.9
Total	61	100

Table (3) Clinical types of acute organic brain syndrome.

Types	No	%
Hyperactive	33	54.1
Hypoactive	17	27.9
Mixed	11	18
Total	61	100

Table (4) Symptoms at presentation.

Symptoms	No	%
Visual hallucinations	48	78.7
Delusion	11	18
Disorientation to time	30	49.2
Disorientation to place	29	47.5
Disorientation to person	23	37.7
Impaired of recent memory	57	93.4
Impaired of remote memory	43	70.5

Impaired attention and concentration	61	100
Echolalia	2	3.3%
Echparaxia	2	3.3%

Table (5) The patients who needed haloperidol IM within the first week.

Types	No	%
Hyperactive	33	54.1
Hypoactive	Zero	zero
Mixed	11	18
Total	44	72.1

Table (6) The patients who needed haloperidol orally after the first week.

	No	%
Needed	8	13.1
Not needed	51	83.6
Pass away	2	3.3
Total	61	100

Table(7) The need for diazepam IV within the first week.

	No	%
Hyperactive type	33	54.1
Hypoactive type	Zero	Zero
Mixed	5	8.2
Not need	23	37.7
Total	61	100

Table(8) Outcome of the treatment

	No	%
Cured	51	83.6
Incomplete recovery	8	13.1
Pass away	2	3.3

T able (9) Symptoms that persist up to the 29th day

Symptoms	No	%
Visual hallucinations	6	9.8
Delusion	2	3.3

DISCUSSION

This study has been conducted in Sinnar Teaching Hospital in the period from the first of October 2008 up to the end of October 2012..The data was collected from 61 patients presented with the features of Acute Organic Brain Syndrome due to falciparum malaria. 28(45.9%) were male and 33(54.1%) were female (Table 1) These patients categorized age wise into 5 groups. Most frequent group is 18-27 years old composed of 36 (59%), the second group is 28-37 years old composed of 11 (18%), the third group is 38-47 years old composed of 8 (13.1%), the fourth group include two groups, 48-57 years old composed of 3 (4.9%) and more than 57years old composed of 3 (4.9%) (Table 2).

The thick and thin blood films were positive for Plasmodium falciparum in all patients, on admission, and negative in all of them after quinine therapy, which were done weekly up to the 29th day.

Concerning clinical types of acute organic brain syndrome, hyperactive is 33 (54.1 %) hypoactive is 17 (27.9%), and mixed is 11 (18%) (Table3).

The study showed that the symptoms of presentation were as the following; visual hallucinations was 48(78.7%), delusion was 11(18%), disorientation to Time was 30(49.2%), disorientation to place was 29 (47.5%), disorientation to person was 23

(37.7%), impaired of recent memory was 57 (93.4%), impaired of remote memory was 43 (70.5%), impaired attention and concentration was 61 (100%), echolalia was 2 (3.3%), and echoparaxia was 2 (3.3%) (Table 4). 44 (72.1%) patients received haloperidol IM within the first week, all the patients with hyperactive type 33(54.1) and mixed types11(18%) received haloperidol IM within the first week (Table 5). Haloperidol was needed to be continued orally after the first week in 8 (13.1%) (Table 6) Diazepam IV was needed within the first week in all the patient with hyperactive type 33(54.1%), and 5 (8.2%) with mixed type (Table 7). Concerning the outcome 51 (83.6%) of the patients fully recovered, 8(13.1%) had incomplete recovery from acute organic brain syndrome, 2(3.3%) passed away (Table 8). The symptoms that persisted up to the 29th day were visual hallucinations in 6 (9.8%) and delusion in 2 (3.3%) patients (Table 9).

RECOMMENDATIONS

After enumeration of study results, there are some ideas which could help further the field of research and are better to be recommended as follows:

- Falciparum malaria can present with acute organic brain syndrome that causes distress to patients and relatives.

-Quinine therapy plus haloperidol and diazepam when needed are corner stone in treating acute organic brain syndrome due to falciparum malaria.

-Patients of acute organic brain syndrome due to falciparum malaria should be followed until mental symptoms disappear.

CONCLUSIONS

This study has been conducted in Sinnar Teaching Hospital in 61 patients with features of acute organic brain syndrome due to falciparum malaria. The goal of the research is to study the outcome of acute organic brain syndrome due to falciparum malaria treated with quinine, haloperidol, and diazepam therapies. All the patients fulfill the ICD-10 criteria for the diagnosis of acute organic brain syndrome; all of them received the standard dose of quinine. Also all the patients with hyperactive type 33(54.1%) and mixed types11 (18%) received haloperidol IM within the first week, 8 (13.1%) of them needed to continue haloperidol orally after the 29th day. Diazepam IV was needed within the first week in all patient with hyperactive type 33(54.1%), and 5 (8.2%) with mixed type. 51 (83.6%) of the patients fully recovered, 8(13.1%) had incomplete recovery from acute organic brain syndrome, 2(3.3%) passed away.

REFERENCES

1-8WHO. *World malaria report 2019* (2019).

2-Weiss, D. *et al.* Indirect effects of the covid-19 pandemic on malaria intervention coverage, morbidity, and mortality in Africa: a geospatial modelling analysis. *Lancet Infect. Dis.* **21**, 59–69. https://doi.org/10.1016/S1473-3099(20)30700-3 (2020).

Article PubMed Google Scholar

3-WHO. *World malaria report 2020: 20 years of global progress and challenges* (2020).

4-WHO. *World malaria report 2019* (2019).

5- Ahmed, A. *et al.* The impacts of climate change on displaced populations: a call for action. *J. Clim. Change Health* **3**, 100057 (2021).

Article Google Scholar

6-Mohamed, N. *et al.* Malaria epidemic in humanitarian crisis settings the case of South Kordofan state, Sudan. *J. Infect. Dev. Ctries.* **15**, 168–171. https://doi.org/10.3855/jidc.13122 (2021).

7-Ahmed Elagali, et *al.* Spatiotemporal mapping of malaria incidence in Sudan using routine surveillance data. Scientific Reports 12. https://drive.google.com/14114 (2022)

8- Blocker WW, Kastl AJ, Daroff RB. The psychiatric manifestations of cerebral malaria. Am J Psychiatry. 1968;125:192–196. [Google Scholar]

9- Kochar DK, Shudhakaran, Kumawat B. Neurosychiatric manifestations in malaria. J Assoc Physicians India. 1998;46:886–890. [Google Scholar]

10-Arun Prakash MV, Stein G. Malaria presenting as a typical depression. Br J Psychiatry. 1990;156:594–595. [PubMed] [Google Scholar]

11- Weinke T, Trautmann M, Held T, et al. Neuropsychiatric side effects after the use of mefloquine. Am J Trop Med Hyg. 1991;45:86–91. [PubMed] [Google Scholar]

12- Lawlor PG, Gagnon B, Mancini IL, et al. Occurrence, causes, and outcomes of delirium in patients with advanced cancer. Arch Intern Med. 2000;160(6):786–794. [PubMed] [Google Scholar]

13- Singler B. Das postoperative Delir. Geriatrie Journal. 2010;2:41–42. [Google Scholar]

14- Ozbolt LB, Paniagua MA, Kaiser RM. Atypical antipsychotics for the treatment of delirious elders. J Am Med Dir Assoc. 2008;9:18

15- Lonergan E, Luxenberg J, Areosa Sastre A, Wyller TB. Benzodiazepines for delirium. Cochrane Database Syst Rev. 2009;(1) CD006379. [PubMed] [Google Scholar]

16- American Psychiatric Association Quick reference to the American Psychiatric Association practice guidelines for the treatment of psychiatric disorders. American Psychiatric Association, Arlington. 2006. [Google Scholar]

17- WHO. Guidelines for the treatment of malaria. 3rd Edn. Geneva, World Health Organization, 2015.

18-Dondorp AM, Fanello CI, Hendriksen IC, et al. Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. *Lancet*. 2010 Nov 13. 376(9753):1647-57. [QxMD MEDLINE Link]. [Full Text].

19-Sinclair D, Donegan S, Isba R, Lalloo DG. Artesunate versus quinine for treating severe malaria. *Cochrane Database Syst Rev*. 2012 Jun 13. 6:CD005967. [QxMD MEDLINE Link].