The Professional Medical Journal
www.theprofesional.com

DOI: 10.29309/TPMJ/18.4008

ORIGINAL PROF-4008

CERBRAL MALARIA;

PHYSICIAN DILEMNA, QUININE DIHYDROCHLORIDE VS ARTEMISININ.

Muhammad Rasheed Khan Durrani[1], Tahreem Shafi[2], Zinnia Ali[3], Muhammad Danial Iqbal[4]

1. MBBS, MCPS, FCPS
Associate Professor,
Department of Medicine,
Medical Unit II Jinnah Post Graduate Medical Centre, Karachi.
2. Final Year Medical Student,
at Jinnah Sindh Medical University, Karachi.
3. MBBS,
House Officer,
Medical Unit II Jinnah Post Graduate Medical Centre, Karachi.
4. MBBS,
Resident of Medicine,
Medical Unit II Jinnah Post Graduate Medical Centre, Karachi.

Correspondence Address:
Dr. Rasheed Durrani
Associate Professor,
Department of Medicine,
Medical Unit II Jinnah Post Graduate Medical Centre, Karachi.
drrasheeddurrani@gmail.com

Article received on:
28/04/2017
Accepted for publication:
15/09/2017
Received after proof reading:
02/01/2018

ABSTRACT… Cerebral malaria is a disease entity which we commonly come across and that it should be suspected in every patient with impairment of conscious level and high spiking fever especially with no history of trauma. Early treatment is crucial and can be lifesaving. There are two treatment option in which one is conventional Quinine Dihydrochloride and other artmisinin infusion. **Objectives:** To study the outcomes of Quinine dihydrochloride and artemisinin practice in patients with cerebral malaria in terms of acceptance and response. **Study Design:** Descriptive cohort study. **Place and Duration of Study:** Department of Medicine, Unit. II, Jinnah Postgraduate Medical Centre (JPMC), Karachi from January1st2015 to December 31st, 2015. **Methodology:** A total of 78 patients fulfilled the inclusion criteria of Glasgow Coma scale (GCS) were of less than 6 for more than 6 hours Defervescence time were 2 to 3 hours after start of treatment Strength of our study is that patients traditional prompt response, with coma multi-organ dysfunction tends to recover and discharge in 4 days. **Result:** There were total of 78 patient. Out of them 32 (41.0%) were positive for Malaria with 29 (37.1%) were positive for Plasmodium Falciparum and 3 were having Plasmodium Vivax .all were offered treatment with 57 (73.0%) were given Quinine infusion and 21 (26.94%) were treated with artemisinin infusion. Cure rate was 44 (56.4%) with 46 (58.9%) in quinine group and 14 (17.9%) artemisinin group and (19.2%) and 07 (8.9%) respectively making total mortality of 18 (23.0%). There were 9 (11.5%) patients who left against the medical advice. Average age was 26 ±, majority were male. In addition laboratory derangements like alanine amino transferases (ALT), bilirubin, creatinine, electrolytes as potassium and arterial blood gases(ABGs) were also considered. It has been estimated that recovery time of patients was maximum of 72 hours (time of discharge) for both artimisinin and Quinine dihydrochloride. Late responders were also observed. Occasionally persistent of treatment is needed with no fear of drugs resistance. **Conclusion:** Quinine infusion is generally safe and effective conventional treatment option, whose benefits and acceptance is well known and we are also documenting this.

Keywords: Artimisinin; Quinine dihydrochloride; dilemma; cerebral malaria; conventional treatment.

Article Citation: Durrani MR, Shafi T, Ali Z, Iqbal MD. Cerbral Malaria; Physician delima quinine dihydrochloride vs artemisinin. Professional Med J 2018;25(1):45-49. **DOI:**10.29309/TPMJ/18.4008

INTRODUCTION

In 2016 The World Health Organization (WHO) had reported that in 2015, 95 countries and areas (tertiary) are having active malarial disease with its transmission. About half billion of the world's population is at risk of having disease i.e. in between 2000 and 2015.The incidence of malaria declared was 37% while there was a 60% decline in mortality from malaria.[1,2]

Malaria remains a major global health problem due to a number of factors including global warming, urbanization, overcrowding, drug resistance etc. There has been a recent rush in its occurrence and concentration.[3] This is also true for Pakistan.[4] Malaria epitomizes a unique health challenge. Malaria has a huge influence on health facilities and is considered to be public and economic burden. It is generally benign but may demonstrate virulent behavior in severe and complicated cases. Most common and dreadful complication is cerebral malaria.[5]

Although any one can acquire the disease but children are more at risk especially for Plasmodium Falciparum Malaria (PF).

Progression to complicated and severe malaria can occur not only with Plasmodium Falciparum Malaria but also with Plasmodium Vivax (PV).In a significant percentage of cases, PV being the most prevalent type. The management of malaria depends upon several factors including poverty, provision of health facilities, drug resistance, proper maintenance of records etc.[6,7]

Patients with cerebral malaria generally present with impaired consciousness, respiratory distress, seizures, prostration, shock, bleeding, and jaundice etc.[8]

Laboratory tests are generally positive for severe anemia, hypoglycemia, acidosis and renal dysfunction besides hyper parasitaemia.[9]

Quinine dihydrochloride is unique as it is well tolerated by patients with very good outcome compared to other treatment modalities like artmisinin and quinidine. It can be associated with significant side effects but is generally well tolerated.[10] The situation changes when, there are multiorgan dysfunction, where there are theoretical risk of increase infrequency and intensity of side effect.

Keeping this in mind the aim of study was to document the usual extremely effective response of Quinine infusion and its acceptance and tolerability in cerebral malaria especially in absence of renal and metabolic complications. Therefore, artimisinin with less side effects and toxicity may be a better alternative but since life is too precious to put under trial, in emergency situations quinine may remain the prime option.[11,12]

RESULT

There was incredible response and patients generally regained consciousness in 8-12 hours. The majority of our patients were male. All were given treatment regardless of test numbers. These patients were treated for cerebral malaria despite negative reports, on the basis of strong clinical suspicion. The average age of patients was 26 years ±.

In this study only 32(41%) patients showed MP positive report on peripheral film. Patients had complete urea, creatinine, liver function test and other metabolic test as acute renal failure is not uncommon. The complications like renal failure with metabolic acidosis, electrolyte imbalance can occur in complicated malaria and these patient were subjected to artimisinin with same degree of response and mortality.

There were total of 78 patient, where, there was strong suspicion of cerebral malaria. Out of them 32 (41.0%) were positive for Malarial Parasite with 29 (37.1%) were positive for PF and 3 were having PV. They all were offered treatment either with quinine infusion 57 (73.0%) or artemisinin 21 (26.94%). The cure rate was 44 (56.4%) with 46 (58.9%) in quinine group and 14 (17.9%) artemisinin group and (19.2%) and 07 (8.9%) respectively making total mortality of 18 (23.0%). There were 9 (11.5%) patient who left against the medical advice. Among them there were no pure case of simple cerebral malaria. They all have a proportion of other system dysfunction and there were difference in outcome, cure, mortality or side effect in both drugs.

Treatment	Quinine DiHcl	Artimisinin	Total
No. of Patient	57(73.0%)	21(26.9%)	78
Current Rate	34(56.4%)	14(66.6%)	48(56.0%)
Mortality	16(56.4%)	7(33.3%)	24(30.7%)
Left against the medical advice(LAMA)			9(11.5%)
Treatment Outcome			

DISCUSSION

With the global increase in incidence of malaria, the incidence of cerebral malaria (the most dreaded complication of falciparum malaria and sometimes vivax malaria) has also increased. Quinine infusion remains the time tested, still most effective and well tolerated medicine with phenomenal response. It is the most effective intervention in presence of artimisinin and quinidine. Considering there is huge cry over the

drug resistance especially when life is at stake. Quinine infusion can be risky in cerebral malaria associated complications such as metabolic acidosis, renal failure etc and in that conditions Artemisinin infusion is better substitute.[13] Here consideration should also be given in cases which may be reported late that will has effect on the drug efficacy and final outcome.

Mean Age	34 Years
Gender	Male 49 (62.8%) Female 29(37.3)
MultiorganFailure	24 (30%)
Recovery Event:	
Days of defervescence	4
Day toll recovery from coma	3
Parasite negativity	12-36 h
Sodium , 125	40
Potassium , 3.5	21
Urea >	22
Creatinine> 3	15
Dialysis	4
Hemoglobin <5	6
Ph , 7.1	4

Table depicts the main findings.

Quinine infusion related severe side effect which is even worse in presence of other associated complication like DIC, renal failure, metabolic derangement. Role of artimisinin in increased which has less side effect and better tolerability in this situation. But quinine infusion remains the gold standard treatment with several advantages; some are unique as in our study drugs resistance seems to be minimal. There is still a potential threat (for plasmodium falciparum and plasmodium vivax) to become resistance to one or more medicine in complicated malaria especially cerebral malaria. Generally, there is full recovery and there were no residual neurological, renal deficits etc. Quinine infusions in cerebral malaria need careful monitoring of dosage and any side effects. Response is often remarkable and parasite become negative in about 24-36 hours. Patients regain consciousness in 24 hours. Studies are in favor of Quinine infusion as preferred treatment option in cerebral malaria.[14]

Data is retrospective review of 78 consecutive patients who were started on quinine infusion without waiting for result of reports for diagnosis. All patients were followed with multidisciplinary medical teams when required. Patients had regular follow-up including laboratory tests and were examined for GCS. Quinine infusion was given according to WHO criteria i.e. 20 mg/kg loading dose, followed by 10 mg/kg over the next 24 hours q 8 hourly. If further parental treatment was required, dose was reduced to 5 mg/kg considering the side effects and tolerability. Otherwise, patients were generally switched, to oral quinine once they were able to take the drug orally. Major side effects noted were hypotension and hypoglycemia. Correction of this is not associated with regain of consciousness and arrhythmia, which make of mandatory the use of ICU monitoring of patient. The other option of artimisinin and quinidine is not considered in pure cerebral malaria. There are multiple reasons for preference of Quinine infusion, it is a conventional treatment option and also with infinite experience of use in Pakistani population.[15]

Cerebral malaria generally present as a part of severe and complicated malaria, therefore associated multiorgan dysfunction makes side effect of quinine almost incompatible Quinine infusion generally has a astonishing response when life of the patient is at risk and there is no place for experiment. Here the artemisinin with fewer side effects is better, but the efficacy is doubtful. Drug like artimisin are mentioned in presence of growing concern about drugs resistance and side effect and their results are comparable to Quinine dihydrochloride.[15]

Treatment response in the form of sophisticated response measurement such as parasite clearance time, fever clearance time, consciousness regaining time, oral intake and mobilization time, sitting time are indefinite parameters which are difficult to monitor, chase and calculate. Over all patient responded 72 hours and discharge subsequently.[16]

In our study the response with Quinine dihydrochloride and artimisinin is almost same but high incidence of mortality makes situation

uncertain, as contribution of side effect and drugs resistance cannot be measured.

Cerebral malaria is a major health problem and common cause of admission in tertiary care centre. In our study we have contradictory outcome; on one hand conventional Quinine dihydrochloride has predictable response but there is a concern of drug resistance, on other hand artimisinin is newer drug which is effective but its efficacy is doubtful and it is associated with less severe side effect, making it effective tool in presence of severe and complicated malaria with multi-organ and metabolic dysfunction where Quinine dihydrochloride with its severe side effect may have limited role. This is also happening in scenario where cerebral malaria may be overwhelmed in intensity and associated complications. We tried to cover this controversial management in our study.

CONCLUSION

Quinine DiHcl is a safe and effective conventional treatment option, whose benefits are time tested. In a patient who are dying, prompt start of quinine infusion, without delaying and waiting for laboratory tests is time effective and lifesaving. Despite conventional treatment there is a strong concerns regarding the side effects and resistance? In these situations, artimisinin is a better alternate especially in multi-organ dysfunction with renal, metabolic and electrolyte imbalance where safety of quinine infusion is undefined.

REFERENCES

1. Warrell DA, Looareesuwan S, Warrell MJ, et al. **Dexamethasone proves deleterious in cerebral malaria: a double-blind trial in 100 comatose patients.** New England Journal of Medicine. 1982 Feb 11; 306(6):313-9.

2. Moline ME, Taylor TE, WirimaJJ, et al. **Clinical features and prognostic indicators in paediatric cerebral malaria: a study of 131 comatose Malawian children.** QJM. 1989 May 1; 71(2):441-59.

3. Idro R, Jenkins NE, Newton CR. **Pathogenesis, clinical features, and neurological outcome of cerebral malaria.** The Lancet Neurology. 2005 Dec 31; 4(12):827-40.

4. Chaparro-Narváez PE, Lopez-Perez M, et al **Clinical and epidemiological aspects of complicated malaria in Colombia, 2007–2013.** Malaria Journal. 2016 May 10; 15(1):1.

5. Chima RI, Goodman CA, Mills A. **The economic impact of malaria in Africa: a critical review of the evidence.** Health Policy. 2003 Jan 31; 63(1):17-36.

6. Molyneux ME, Taylor TE, Wirima JJ, et al **Clinical features and prognostic indicators in paediatric cerebral malaria: a study of 131 comatose Malawian children.** QJML 1989 May 1; 71(2):441-59.

7. Kochar DK, Das A, KocharSK,et al. **Severe Plasmodium vivax malaria: a report on serial cases from Bikaner in northwestern India.** The American journal of Tropical Medicine and Hygiene. 2009 Feb 1; 80(2):194-8.

8. Trampuz A, Jereb M, Muzlovic I, et al **Clinical review: Severe malaria.** Critical Care. 2003 Apr 14; 7(4):1.

9. Petti CA, Polage CR, Quinn TC, et al. **Laboratory medicine in Africa: a barrier to effective health care. Clinical Infectious Diseases.** 2006 Feb 1; 42(3):377-82.

10. Malaria SE. **Artesunate versus quinine for treatment of severe falciparum malaria: a randomized trial. The Lancet.** 2005 Sep 2; 366(9487):717-25.

11. Van Agtmael MA, Eggelte TA, van Boxtel CJ. **Artemisinin drugs in the treatment of malaria: from medicinal herb to registered medication. Trends in Pharmacological Sciences.** 1999 May 1; 20(5):199-205.

12. Achan J, Talisuna AO, Erhart A, et al Quinine, **An old anti-malarial drug in a modern world: role in the treatment of malaria.** Malaria Journal. 2011 May 24; 10(1):1.

13. Barnes KI, Mwenechanya J, Tembo M, et al **Efficacy of rectal artesunate compared with parenteral quinine in initial treatment of moderately severe malaria in African children and adults: a randomized study.** The Lancet. 2004 May 15; 363(9421):1598-605.

14. Pasvol G. **The treatment of complicated and severe malaria. British Medical Bulletin.** 2005 Jan 1; 75(1):29-47.

15. Lalloo DG, Shingadia D, Pasvol G, et al **HPA Advisory Committee on Malaria Prevention in UK Travellers. UK malaria treatment guidelines. Journal of Infection. 2**007 Feb 28; 54(2):111-21.

16. Guerin PJ, Olliaro P, Nosten F, et **al Malaria: current**

status of control, diagnosis, treatment, and a proposed agenda for research and development. The Lancet Infectious Diseases. 2002 Sep 30; 2(9):564-73.

Impossible is just an opinion.

– Paulo Coelho –

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	M. Rasheed Khan Durrani	Concept, data collection and main writing.	
2	Tahreem Shafi	Data interpretation	
3	Zinnia Ali	Literature review of article	
4	M. Danial Iqbal	Data interpretation review. article.	