

Delayed gastric emptying time in adult cerebral falciparum malaria

M.K. Mohapatra¹, P.C. Dash², S.C. Mohapatro³ & R.N. Mishra³

¹V.S.S. Medical College, Burla; ²S.C.B. Medical College, Cuttack; ³M.K.C.G. Medical College, Berhampur, Odisha, India

ABSTRACT

Objective: We hypothesize that upper gastrointestinal symptoms in cerebral malaria are due to gastric motor dysfunction. But gastric motility studies in cerebral malaria are scarce.

Methods: We determined gastric emptying half-time (GET_{1/2}) of liquid meals quantitatively by radio isotope scintigraphy in 25 patients of cerebral malaria and 10 healthy controls.

Results: GET_{1/2} was prolonged (46.5 ± 4.8 min) significantly ($p < 0.001$) in patients of cerebral malaria compared to healthy controls (27.6 ± 5.3 min).

Conclusion: Cerebral malaria can cause prolongation of gastric emptying time of liquid foods.

Key words Gastric motility; gastroparesis; scintigraphy; severe malaria

INTRODUCTION

Falciparum malaria when complicated affects single or multiple organs of the body and manifests clinically with respective organ dysfunction alone or in combination^{1,2}. Hence, the manifestations of severe malaria cover a wide range of clinical entities related to different systems that include cerebral malaria, renal failure, jaundice, anaemia, etc. But affect on gastrointestinal system has not been investigated adequately.

It is known that apart from fever, gastrointestinal symptoms like nausea, vomiting, and epigastric discomfort are common in malaria³. Due to vomiting, patients of severe malaria develop dehydration, electrolyte disturbances, hypotension, and pre-renal azotemia. Further, during treatment, we encountered intolerance to nasogastric feeding in the form of regurgitation and vomiting among patients of cerebral malaria. We hypothesize that abnormal gastric motility may be the cause of these upper gastrointestinal symptoms in cerebral malaria. But gastric motility studies in malaria are rare. One study in uncomplicated falciparum malaria showed that there was no alteration in gastric emptying time⁴. However, no study is available on gastric motility in cerebral malaria. Therefore, this study was undertaken to study gastric emptying time in cerebral malaria by radionuclide imaging technique.

MATERIAL & METHODS

The present study was undertaken in the Department of Medicine of MKCG Medical College Hospital,

Berhampur, Odisha from January 2006 to December 2007 and gastric emptying time was studied in the Nuclear Medicine Department of the Hospital. After taking clearance from the Institutional Ethical Committee, 25 patients of cerebral malaria and 10 healthy controls within the age group of 18 to 35 yr were enrolled in this study. The diagnosis of falciparum malaria was made with the detection of asexual form of the parasite in the peripheral smear with Giemsa stain.

Cerebral malaria was diagnosed when a patient of malaria had unarousable coma with exclusion of other encephalopathies³. We performed lumbar puncture and CSF analysis to exclude febrile encephalopathy. CT scan was also done in cases with history of convulsion. Metabolic encephalopathy was excluded by appropriate biochemical investigations as described below. Patients of cerebral malaria with jaundice, renal failure and multi organ dysfunction were excluded from the study because uraemia, hepatic dysfunction, and electrolyte abnormalities are important metabolic causes of gastroparesis⁵. Patients of diabetes mellitus, chronic kidney diseases, chronic liver disease including cirrhosis of liver and any patient with history of taking any antimalarial, antimotility, and antiulcer drugs before admission were also excluded.

Patients were evaluated through a detailed clinical history, physical examination, and investigations according to the proforma of the study. The investigations included estimation of haemoglobin, differential count, total leukocyte count, platelet count, fasting blood glucose, blood urea, serum creatinine, S. bilirubin, SGOT, SGPT, S. sodium and S. potassium. The parasitic count was done

from the peripheral blood smear and expressed as numbers of asexual parasites per micro litre of blood and was calculated from the numbers of parasitized cells per 200 leukocytes in a thick film, i.e. No. of parasites 'x' total leukocyte count/200. Patients were treated with Inj artesunate at the dose of 2.4 mg/kg body weight on admission, then at 12 h, 24 h, and thereafter once daily until he can take oral medication^{6,7}.

We performed radioisotope scintigraphy to study the gastric emptying time. ^{99m}Tc sulfur colloid was prepared as per the protocol of BARC, Mumbai. 500 µci of ^{99m}Tc sulfur colloid was mixed with 500 ml 5% glucose water and fed to the patients through the nasogastric tube⁸. Each control was asked to take the liquid meal orally within 1 min. Then the patient was positioned in a supine position under a Gamma camera, fitted with a parallel hole, low energy all purpose (LEAP) collimator. Serial images were recorded at an interval of 10 min, till 50% of test meal is emptied from stomach. Then the images were taken at 30 min interval. However, for drawing the curve images were taken at 10 min interval till 120 min in few patients. The per pixel count was determined and the values plotted to get the gastric emptying time (GET) curve. The half time ($t^{1/2}$) of GET was determined. Student's *t*-test was used to compare the mean value of GET with the controls. Correlation between GCS and GET^{1/2} was calculated. *P*-value of <0.05 was considered significant.

RESULTS

Out of 25 patients of cerebral malaria, there were 17 males and 8 females and all were in the age group of 18 to 35 yr. All the patients had loss of consciousness and the mean GCS was 6.5 ± 2.2 . Fever was intermittent in 18 and continuous in 7 cases. Myalgia and headache was present in 10 and 15 cases respectively. Gastrointestinal (GI) symptoms were present in 12 patients. It included nausea and vomiting, abdominal pain, abdominal bloating, and diarrhoea in 11, 5, 6 and 2 cases respectively.

The parasitic count was $5244.4 \pm 728.1/\mu\text{l}$. The base line investigations were: haemoglobin 7.4 ± 1 g/dl; total leukocyte count: $6045.4 \pm 628.1/\text{mm}^3$; platelet count: $158230.7 \pm 5893/\text{mm}^3$; fasting blood glucose: 96.7 ± 11.1 g/dl; blood urea: 27.9 ± 2.9 g/dl; S. creatinine: 0.9 ± 0.3 mg/dl; S. bilirubin: 1.1 ± 0.3 mg/dl; SGOT: 33.9 ± 5.3 IU/l; SGPT: 32.9 ± 6.8 IU/l; S. alkaline phosphatase: 77.8 ± 9.9 IU/l; S. sodium: 138.5 ± 2.9 mEq/l; and S. potassium: 3.8 ± 0.2 mEq/l.

The mean GET in falciparum malaria and control was 93.8 ± 9.8 and 55.6 ± 10.3 min respectively ($p < 0.001$). The mean GET^{1/2} in falciparum malaria and control was

46.5 ± 4.8 and 27.6 ± 5.3 min respectively ($p < 0.001$). GET curve plotted is shown in Fig. 1. The photographs of scintigraphy showing delayed GET of a patient are provided in Figs. 2 and 3. Among the patients of falciparum malaria, 19/25 patients had delayed (47.8 ± 4.7 min) and 6/25 had normal (24.6 ± 5.3 min) GET^{1/2}. GET^{1/2} was more in female (49.8 ± 6.7 min) patients than

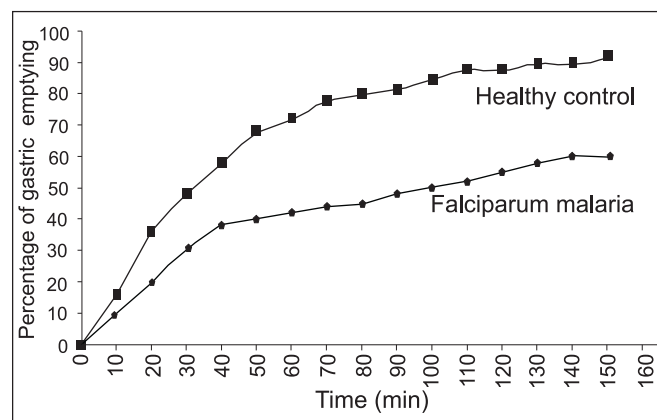


Fig. 1: Gastric emptying time curve.

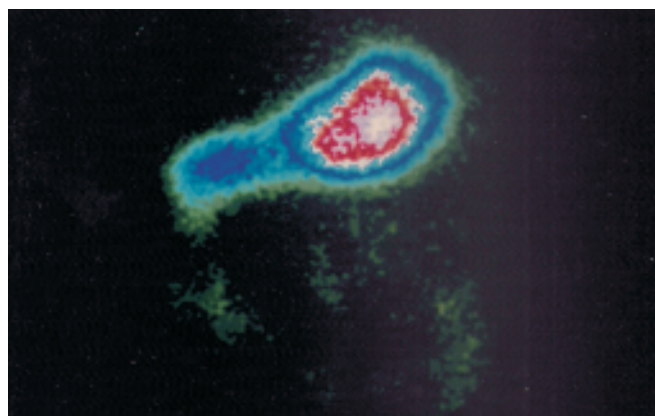


Fig. 2: Delayed gastric emptying showing activity in the stomach at 1 h.

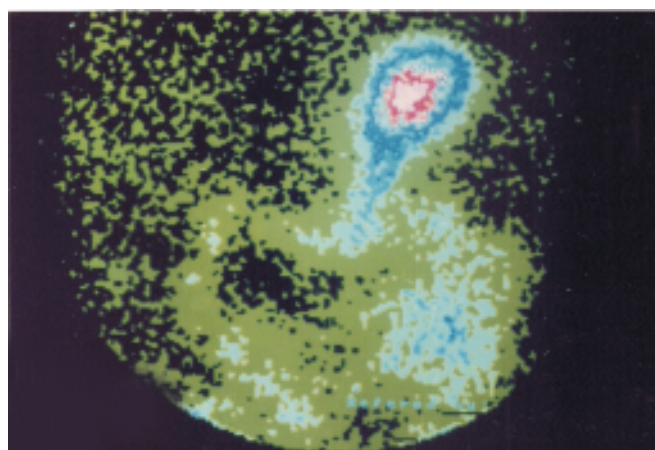


Fig. 3: Delayed gastric emptying showing activity in the stomach at 2 h.

in males (44.8 ± 4.7 min) ($p < 0.01$). A significant negative correlation was found between GCS and GET $\frac{1}{2}$ ($-r = 0.33$, $p < 0.01$). Out of 19 patients with delayed GET $\frac{1}{2}$, 12 patients had GI symptoms and the rest 7 patients had asymptomatic gastroparesis.

DISCUSSION

The present study showed that GET was abnormal in majority (76%) of the patients with cerebral malaria. Patients with low GCS have prolonged GET. There is a gender variation in GET showing prolonged GET among female patients compared to the males.

Except anaemia, all the biochemical and haematological investigations were within normal limits in this study because we have excluded cases of cerebral malaria with metabolic complications. Though high parasite density has been correlated with severe malaria, a high parasitic count from peripheral blood smear may not be obtained in the patients of severe malaria⁵. It is due to sequestration of parasites in internal organs and destruction of the parasitized red blood cells^{1,5}. Therefore, parasitic count in malaria with anaemia is less than that observed in other complications¹. In this study, anemia (mean Hb 7.4 ± 1 g/dl) was present in all the patients causing a decrease in the parasitic count.

Paracetamol absorption test did not show any significant change in gastric emptying during acute uncomplicated malaria and convalescence⁴. But the usefulness of paracetamol absorption test for gastric motility study is controversial⁹. Gastric emptying is determined by different gastric motility studies that include manometry, electrogastrography, paracetamol absorption test, and radio isotope scintigraphy¹⁰. The latter test, if available is better than other methods because it is easy to perform, physiological, non-invasive, and reproducible.

Delayed GET in the absence of mechanical obstruction is known as gastroparesis. It may be acute or chronic, and acute causes are potentially reversible. The common causes of acute gastroparesis are head injury, cytomegalo virus and herpes simplex virus gastritis¹⁰. But cerebral malaria as a cause of gastroparesis has not been described due to lack of research.

Pathologically cerebral malaria is an acute encephalopathy diffusely affecting the central nervous system. Cerebral malaria may evoke dysmotility affecting the motor apparatus of the gut through central nervous system (CNS) and autonomic supply. It is known that CNS abnormalities directly or through autonomic nervous system affect the motor functions of stomach adversely¹¹. In this study, we observed an inverse relation with GCS and

emptying time (patients with low GCS had increased GET) indicating the role of coma (CNS dysfunction) in the control of gut function. Similar observation was made among patients of head injury with coma¹¹. In normal population and in conditions like head injury, females have delayed GET in comparison to their male counterparts^{10,11}. Similar gender variation in cerebral malaria is also found in this study.

Gastroparesis and related symptoms are prominent features of any disorder with autonomic dysfunction and described in a variety of diseases affecting autonomic nervous system that include diabetes mellitus, scleroderma, head injury, spinal cord, Parkinson's disease, etc¹⁰. Experimentally, inhibition of gastric emptying and antral motility due to cold was observed in rats and it was mediated through sympathetic system¹². Autonomic dysfunction has been detected in falciparum malaria which may inhibit GET¹³.

Acute stressful condition like sepsis inhibits gastric motor activity. Corticotrophin-releasing factor (CRF) acts through CRF-2 receptors of medulla to inhibit such stress related delay in GET¹⁴. The pathogenesis of cerebral malaria is also similar to sepsis¹⁵. Hence, there may be a role of CRF for inhibition of GET in cerebral malaria.

In a nutshell, central nervous system control of gut function is lost in cerebral malaria causing gastroparesis. It may cause upper G.I. manifestations in cerebral malaria. This observation is important because nutrition is maintained mainly through naso-gastric tube in patients of cerebral malaria. Such patients are at risk of pulmonary aspiration of gastric contents due to gastroparesis. Hence, pro kinetic drugs may help to prevent gastric dysmotility and further complications.

REFERENCES

1. Mohapatra MK. The natural history of complicated falciparum malaria—A prospective study. *J Assoc Physicians India* 2006; 54: 848–53.
2. Mohapatra MK, Das SP. The malaria severity score: A method for severity assessment and risk prediction of hospital mortality for falciparum malaria in adults. *J Assoc Physicians India* 2009; 57: 119–26.
3. Idro R, Jenkins NE, Newton CR. Pathogenesis, clinical features, and neurological outcome of cerebral malaria. *Lancet Neurol* 2005; 4: 827–40.
4. Wilairatana P, Looareesuwan S, Kaojarern S, Vanijanonta S, Charoenlarp P. Gastric emptying time in acute falciparum malaria. *J Trop Med Hyg* 1995; 98: 22–4.
5. Ali H, Ashan T, Mahmood T, Bakht SF, Farooq MU, Ahmed N. Parasite density and the spectrum of clinical illness in falciparum malaria. *J Col Phys & Surg Pak* 2008; 18: 362–8.
6. South East Asian Quinine Artesunate Malaria Trial (SEAQUAMAT) group. Artesunate versus quinine for treatment

- of severe falciparum malaria: A randomised trial. *Lancet* 2005; 366: 717–22.
7. *Guidelines for the treatment of malaria*. Geneva: World Health Organization 2006; p. 1–182.
 8. Dash PC, Mohapatro SC, Meher LK, Mishra RN, Patnaik SR. Scintigraphic evaluation of gasytric emptying time in diabetic gastroparesis. *Int J Diab Dev Countries* 2000; 20: 65–7.
 9. Willems M, Quartero AO, Numans ME. How useful is paracetamol absorption as a marker of gastric emptying time? A systematic literature study. *Dig Dis Sci* 2001; 46: 2256–62.
 10. Quigley EMM. Gastric motor and sensory function and motor disorders of the stomach. In: Feldman M, Friedman LS, Brandit LJ, editors. Philadelphia: Lippincott-Raven 2006; p. 999–1028.
 11. Kao CH, Chang Lai S-P, Chieng P-U, Yen T-C. Gastric emptying time in head-injured patients. *Am J Gastroenterol* 1998; 93: 1108–12.
 12. Koo MWL, Ogle CW, Cho CH. The effect of cold restraint stress on gastric emptying in rats. *Pharmacol Biochem Behav* 1985; 23: 969–72.
 13. Mohapatra MK, Das SP. The nature and course of cardiac involvement during and after falciparum malaria: A prospective study. *Indian Med Gaz* 2006; CXL: 293–7.
 14. Beglinger C, Degen L. Role of thyrotrophin releasing hormone and corticotrophin releasing factor in stress related alterations of gastrointestinal motor function. *Gut* 2002; 51: i45–8.
 15. Lou J, Lucas R, Grau GE. Pathogenesis of cerebral malaria: Recent experimental data and possible applications for humans. *Clin Micro Rev* 2001; 14: 810–2.

Correspondence to: Dr M.K. Mohapatra, Professor of Medicine, V.S.S. Medical College, Qr. No. C/1, Doctors Colony, Burla, Sambalpur–768 017, India.
E-mail: mohapatra.manoj@rediffmail.com

Received: 20 February 2012 *Accepted in revised form:* 22 September 2012