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The outbreak and control of Ebola viral haemorrhagic fever in a Ugandan medical school

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SUMMARY Uganda has just experienced the largest outbreak of Ebola haemorrhagic fever (EHF) ever recorded[1]. Mbarara UniversityTeaching Hospital (MUTH) is responsible for training approximately one-third of Uganda's doctors. Mbarara is located in South West Uganda, 614 km from Gulu, the main epicentre of the outbreak. On 23 October a patient was admitted to the medical ward of MUTH with an acute fever. He soon exhibited haemorrhagic symptoms and died. He was later confirmed to have suffered Ebola. Three more patients subsequently contracted the disease. All died. There were no further cases in Mbarara. No members of staff or medical student was infected.

We give details of the clinical features of those patients who contracted the disease, the setting up of an Ebola isolation unit, the case surveillance and the search for the source of the outbreak. The implications for similar institutions in East Africa are discussed.

Introduction

Ebola haemorrhagic fever (EHF) is caused by the Ebola virus, a member of the Filoviridae family[2]. There are four known subtypes, three of which have caused EHF, namely *Ebola Zaire*, *Ebola Côte d'Ivoire* and *Ebola Sudan*. *Ebola Sudan* was identified in an outbreak in Sudan in 1976 and this has been responsible for further outbreaks in Sudan (1979) and now Uganda (2000)[1].

The Ugandan epidemic, with 425 cases was the largest recorded outbreak of EHF[1]. The outbreak was confirmed on 15 October, in the Northern district of Gulu and this was where the vast majority of cases occurred[1]. Five cases were reported in Mbarara and 27 cases in Masindi District[1].

Mbarara University Teaching Hospital (MUTH) is part of Mbarara University of Science and Technology (MUST) and is situated in the South Western town and district of Mbarara, approximately 624 km away from Gulu, using the preferred route by road via Kampala. Opened in 1989, the University and Medical School is responsible for educating approximately one-third of Uganda's doctors, with 50–60 graduates per year. The hospital is a 318-bedded single storey complex serving a population of approximately 1 million.

On Wednesday 1 November 2000 a patient, who had recently died at MUTH was confirmed as having been infected with the Ebola virus. Three more patients contracted the disease and all died. There were no further cases confirmed or suspected. No member of staff or student contracted the disease.

We describe the outbreak, the case histories, management of the patients, the setting up of the isolation unit, contact and active case surveillance, management of suspects, the search for the source of Mbarara's outbreak, the experiences of those members of staff and students who were exposed to the infection and finally the implications of such an outbreak for a Medical School and Teaching Hospital in East Africa.

Case histories

Patient 1

Patient 1 was a 20-year-old soldier assigned to look after sick soldiers admitted to MUTH. He had previously been well and had not travelled outside Mbarara district for at least 3 months. He presented to the hospital on the 23 October, having been unwell for 7 days with fever, a frontal headache, arthralgia, myalgia and vomiting. He denied any episodes of haematemesis but he had had an episode of epistaxis 2 days prior to coming to the hospital. He had taken tablets of Fansidar (pyrimethamine with sulfadoxine) with no improvement. On examination he had had an axillary temperature of 39.2 °C but no localizing signs of infection. He was admitted to a medical ward and treated for malaria with intravenous quinine, however, a subsequent thick blood film was negative for

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malaria parasites and spirochaetes. The following day (day 8) he had developed non-bloody diarrhoea associated with abdominal pain. By day 9 his condition had deteriorated, despite adequate quinine treatment. He complained of severe abdominal pain and on examination was noted to have high fever, erythema involving the hard and soft palate, reddened conjunctiva and a faint macular rash affecting the trunk. His abdomen was diffusely tender but soft and had no organomegaly. A blood culture was taken and ciprofloxacin was added to cover Gram-negative infection. At this stage measles and a ricketsial illness were considered.

That night be began to vomit blood, pass bloody stool and he had epistaxis. He also became confused and at one point got into the neighbouring bed. The following morning (day 10) a final year medical student, worried about possible viral haemorrhagic fever, informed the senior medical staff. The patient was immediately isolated in a side room and the medical superintendent and deputy district medical officer (DMO) were informed. The case was discussed with the Ugandan Ebola Task Force and it was arranged for a serum sample to be collected and sent to the mobile level four laboratory, which had been set up in Gulu. The patient was then transferred to the isolation ward. He was transfused one unit of O negative (samples taken were not processed by our laboratory following advice from Gulu) and he was started on oral doxycline. He deteriorated becoming tachypnoeic, shocked and confused and had 5 cm tender hepatomegaly. There was no jaundice, no skin petechiae or ecchymoses but he continued to ooze blood from nose and mouth and had sub conjunctival haemorrhages. Despite intravenous fluids, more blood and sedation he died on the morning of day 11. His body was sealed in body bags and immediately buried by army burial personnel wearing protective clothing. The possessions he had had with him were burnt and his room was thoroughly sprayed with chlorine solution.

Six days after his death, the Gulu laboratory confirmed that this patient's serum was positive for Ebola antigen and IgG (using enzyme linked immunosorbent assay (ELISA): reverse transcriptase polymerase chain reaction (rtPCR) was also positive).

Patient 2

Patient 2 was a 27-year-old male prisoner who had been instructed by the prison service to look after sick prisoners admitted to MUTH. He had been sleeping on the male medical ward, in the bed next to Patient 1. On the night of the 25 October the confused Patient 1 had got into the bed of Patient 2. That night Patient 2 was exposed to body fluids including bloody vomitus, stool and sweat of Patient 1.

Five days later, Patient 2 became unwell with high fever and severe myalgia. On day 3, when Patient 1 was confirmed to have had EHF, Patient 2 reported to the nurse on duty that he was still unwell and that he had been in close contact with the deceased Patient 1. There was no history of bleeding. He was immediately isolated, initially in a side room and later on the isolation ward. Examination revealed a fever of 39.5 °C an erythematous pharynx, but no rash.

He became progressively unwell complaining of high fever, odynophagia, abdominal pain (particularly epigastric and right upper quadrant) diarrhoea which was occasionally associated with blood and chest pain. He bled from his nose occasionally. On examination he had high axillary temperatures (up to 40.2 °C), red conjunctiva and a tender hepatomegaly. Ebola was confirmed by serological testing (antigen, IgG and rtPCR positive). Despite supportive treatment he became very weak and confused and incontinent of urine and faeces. By day 10 he had become tachypnoeic. The following morning he was shocked and had an axillary temperature of 37.5 °C. He died later that day and his body was buried by the recently trained burial team and his possessions and room were handled as for Patient 1.

Patient 3

Patient 3 was a 27-year-old soldier who had been a close friend of Patient 1. He had been in close contact with Patient 1 on the 23 October, 4 days prior to his death – they had been sharing the same crowded accommodation. He became unwell on 30 October with fever and myalgia. On 3 November he admitted himself to the Ebola Isolation Unit (EIU) having developed a severe headache and abdominal pain. There was no history of bleeding. On examination he had an axillary temperature of 38.4 °C and a tender but soft epigastrum and right upper quadrant. No hepatomegaly was recorded at this time. There was no jaundice, no rash and the eyes and oropharynx were normal.

He soon became very unwell with high fever, odynophagia, severe epigastric and right upper quadrant pain, diarrhoea which was intermittently bloody and bouts of confusion. Despite symptomatic and supportive care he continued to deteriorate and Ebola was confirmed by serological testing (antigen IgG and rtPCR positive). By 6 November he had become tachypnoeic, his jugular venous pressure was not raised and no focal chest signs were elicited. He became very confused, on three occasions leaving his isolation room within the EIU and on one occasion having to be stopped from leaving the ward, after which he was restrained and sedated. He had a temperature of 38 °C. He died later that day and his body, possessions and room were managed as above.

Setting up of the Ebola Isolation Unit

MUTH has managed three cholera epidemics in recent years. The ward, previously known as 'The Cholera Ward' was quickly converted to the EIU, initially using guidance provided by the Ugandan Ministry of Health and later extensive advice, guidelines and resources[4] provided by consultants from Gulu, the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDCP) and Médecins Sans Frontières (MSF). The EIU had six rooms, four of which were kept for patients, each containing two beds, and also one as a changing room, and another as an office. The unit had an adjacent dedicated toilet facility in which chlorine-treated clinical waste was disposed of. Other waste including sharps was burnt in a special pit dug for the purpose. Training was given to a team of cleaners and a team of soldiers for burial duty. Protective gear for the carers (three doctors and three nurses) and ancillary staff (two cleaners and four-man burial team) was provided by the hospital stores and later by MSF, the Ministry of Health and the German Embassy.

The time and work required to set up such a unit at the start of an outbreak was significant, which may have affected our ability to provide the best possible clinical care. In addition, a capacity of only four separate rooms soon caused the team serious concern, particularly about

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Fig. 1 Photograph of a member of the Ebola Case Management Team in protective gear

putting a suspected case in the same room as a confirmed patient. At one point converting the 50-bedded tuberculosis ward into an EIU was considered.

Contact tracing and active case surveillance

A contact list for each patient was immediately established, contact being defined as those who had had direct physical contact with an EHF patient or his body fluids, clothing or linen. All contacts were classified by village or institution and a trained health worker was assigned contacts in a specified village or institution for active surveillance.

Those contacts who were members of staff or students of MUTH were asked to record their temperature at least once daily. If a fever greater than 38 C was recorded or they became unwell they were asked to immediately consult their designated surveillance health worker or a member of the Ebola Case Management Team (ECMT). The other contacts were checked daily for any symptoms, especially fever. Surveillance was continued for 21 days from the last possible date of contact.

From a total of 68 contacts followed up, two contacts had become unwell by the time the surveillance had started (Patients 2 and 3). One had already been isolated and the other was isolated soon afterwards. No other contact developed significant symptoms or fever.

In addition to this contact surveillance, all suspected cases in the district of Mbarara were reported to a community alert system or by other healthcare workers. Each case was assessed by the mobile response unit (MRU), which included the viral haemorrhagic fever (VHF) coordinator of MUTH or they were brought directly to the EIU, where they were assessed in a safe place outside the unit.

Suspect management

A suspect was defined as

- any person suffering from a feverish illness who then suffered bleeding from any orifice
- any contact of a known case of Ebola who then developed a feverish illness
- anyone from the barracks or who had recently travelled from Gulu and later Masindi, who now had a feverish illness

These criteria were based on guidelines provided by the workers from Gulu.

During the outbreak 30 'suspects' were seen by the ECMT. Seven patients were admitted to the EIU. Four were confirmed negative and discharged. One patient was human immunodeficiency virus antibody positive and severely immunosuppressed. He had developed epistaxis and fever while on high dose Fansidar for presumed toxoplasmosis. He had been on the ward when Patient 1 had been admitted. Although there was no history of direct contact with Patient 1 (their beds were not close) he was transferred to the EIU. The Fansidar was stopped, as suspected bone marrow suppression could not be investigated. He was treated with ciprofloxacin and amoxicillin to cover neutropenic sepsis and his nose was packed. Despite the cessation of any bleeding and becoming apyrexial within days of admission to the unit he gradually deteriorated, became increasingly confused and eventually died. His serum was eventually tested and found to be positive for Ebola IgG, but negative for antigen and Ebola virus RNA. Members of the team thought that, clinically, this patient was unlikely to have suffered EHF. This may have been a false positive result or evidence of previous infection[3]. However, this patient was later considered to have fulfilled the diagnostic criteria[1] set by the Ugandan Ebola Task Force and subsequently confirmed as a case. Two other patients who were isolated on the EIU because they fulfilled the clinical criteria unfortunately died but their serum was later confirmed to be negative for Ebola.

An outbreak of a dysenteric illness in and around Mbarara town added to our workload. However, using the criteria mentioned above it was possible to differentiate most cases from an EHF-like syndrome. Admitted cases were cared for in isolation rooms on the general ward and closely monitored by the ECMT. All cases soon responded to oral ciprofloxacin. Two nurses from the medical ward were seen with an acute febrile illness. Although both were unsure as to whether they had been caring for the first confirmed case, careful questioning revealed no history of contact and both recovered fully from their respective illnesses.

Management of hospital staff and students of MUTH

Meetings were called in which members of the ECMT were able to inform members of MUTH and students of MUST about the situation in Mbarara and answer any questions. A WHO produced educational video was shown, describing the important features of EHF, the management of an outbreak and effective personal protection methods. These helped to reduce some of the rumours, anxieties and fears related to EHF.

One member of the ECMT was appointed VHF coordinator for the hospital. This member was responsible for the provision of guidelines for all departments

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including suspect diagnostic criteria and management guidelines, keeping the hospital updated on the number of confirmed cases and in liaison with the infection control sister (also a member of the ECMT) ensuring that adequate infection control practices were followed around the hospital. He was also responsible for training the EIU cleaners and burial team (as above) and was a member of the district's MRU.

Admitting interns and outpatient personnel of MUTH were encouraged to use universal precautions and, if worried about a possible suspect, to contact the ECMT immediately, without further touching the patient. Medical students were taken off the wards during the two weeks of the outbreak. They were later brought back but restricted to supervised clinical contact. Student work in the admissions room was postponed until the end of the outbreak.

The search for Mbarara's index case

It was obviously enormously important to discover how a patient, who had not travelled outside Mbarara for at least 3 months, had contracted EHF. Had it come from Gulu or was this an unrelated separate outbreak[1]?

The case surveillance team searched through the medical notes of all the patients that had been cared for by Patient 1, immediately prior to his becoming unwell with EHF. Fifteen patients were identified, one of whom had become unwell within 16 days of returning from Gulu. In Gulu he and his wife had visited Kabedo Opong, in which some inhabitants had been confirmed to have contracted EHF. He presented to MUTH on the 12 October with a history of fever, haemoptysis and diarrhoea. On examination he was very unwell, hypotensive with a systolic blood pressure of 60 mmhg, had an axillary temperature of 38.7 °C and a 'blood stained oral cavity'. He was admitted but despite treatment with broad-spectrum antibiotics, quinine and intravenous fluids he rapidly deteriorated and died the following day.

Patient 1, who had cared for the above during his short time on the medical ward, became unwell 5 days after his patient's death. No samples were taken to confirm the possibility of EHF in this patient, as the suspicion was retrospective. The wife of the deceased had suffered a febrile illness 5 days prior to her husband becoming unwell. She recovered and was later tested positive for IgG antibodies specific to Ebola.

Contact experience

Twelve members of staff (six doctors, five nurses and one cleaner) and six medical students had direct contact with Patient 1 during the last few days of his life. All of these contacts were made before the clinical syndrome of EHF was thought likely. Eleven of them experienced extreme anxiety on learning of the patients' confirmed diagnosis. Fifteen developed Ebola like symptoms including 71% experiencing 'phantom' fevers (a feeling of fever despite normal body temperature). Fifteen sought help outside their family and friends, including use of the University's medical (anxiolytics were prescribed) and counselling services, and spiritual support.

The development of anxiety and 'symptoms' was closely linked to the risk of exposure. Most contacts regretted not taking more care with infection control methods, when dealing with Patient 1, which, they thought, would have lessened their experienced anxiety. Student contacts experienced a degree of social quarantine and even harassment from their fellow students. This was reduced after education by members of the ECMT. Some members of staff were made to feel unwelcome in town and in some instances were refused entry to some establishments. A local radio station even advised its listeners to 'run away' from all staff members of MUTH. Following an occasion when the burial team was threatened with stones as they approached the burial ground with one of the bodies, subsequent visits were accompanied by armed military escort.

Subsequent serological testing of 12 of these contacts, at least 21 days after their last direct contact with Patient 1, showed no evidence of infection: all cases were negative for Ebola IgG.

Discussion

The outbreak in Mbarara was small and quickly contained. Having been forewarned by the outbreak in Gulu and by the health education provided by the Ministry of Health in the national papers and on radio, we had prepared for the possibility of the outbreak reaching Mbarara. This included the display of diagnostic guidelines and educational posters provided by the Ministry of Health and the organization of protective clothing by the hospital stores manager. We were also fortunate to be relatively well staffed and were soon supported by Ministry of Health and other organizations. Having an isolation facility already in place was essential.

Incubation times of our second two cases were 6 and 8 days, respectively, which correlates with incubation times recorded in other epidemics[5]. It is possible that the incubation period is related to the infective viral load[5]. The overall clinical impression was of a syndrome beginning non-specifically, with high fever, headache and myalgia. This phase continued for 5–8 days, with the patient able to mobilize, try outpatient remedies and even work (Patient 2). Then various characteristic clinical features tended to develop. Symptoms included diarrhoea, abdominal pain (particularly epigastric), bleeding from orifices, (although with the exception of Patient 1 this was not dramatic), odynophagia, chest pain and, later, breathlessness. Signs included persistently high temperature, erythamatous conjunctiva and oropharynx, a rash, tender hepatomegaly and later tachypnoea and confusion. The patients suffered an unremitting course with gradual but progressive deterioration. These findings correlate with previous studies[5] and with what was seen in Gulu[1]. Whilst the breathlessness in the days prior to death was a prominent feature in our patients, the pathogenesis for this is unclear, although lung and cardiac involvement have been postulated. However, auscultation was avoided by most physicians due to fear of infection. Previous workers have noted the absence of chest signs in such patients[5] and have suggested that acidosis secondary to renal failure or lactate accumulation may be the cause. If this is so, would better fluid management reduce mortality?

Our mortality was 100%, considerably worse than the mortality rate seen in Gulu, which was 53% (224 deaths)[1], but our numbers are too small to be of statistical significance. Our management was supportive, with intravenous fluids as the principal supportive measure. We found oral rehydration was unreliable due to frequent vomiting, general fatigue and later confusion (towards the end of the outbreak this view was challenged by other workers who found that a satisfactory oral intake could be achieved, thereby reducing high risk procedures such as

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canulation and maintenance of intravenous drips). Blood loss was not massive and only Patient 1 required a blood transfusion, correlating with the Gulu experience[1] and that of previous outbreaks[5]. Our monitoring was entirely clinical. No specimens were processed for haematological or biochemical indices due to the lack of safe facilities to process such high-risk samples[6]. All three patients showed clinical features which may indicate a poorer prognosis, including right upper quadrant pain, bleeding from mucous membranes and tachypnoea[5]. The severity of their disease may be related to the magnitude of their exposure and possibly infective viral load[7].

Palliation of symptoms was a particular concern. As fever, vomiting, abdominal pain, odynophagia and confusion were the main symptoms suffered by our patient, the ideal palliation would keep the patients free from such symptoms and be safe to administer. Intravenous regimens of morphine and haloperidol, which could be added to the infusion fluids thus avoiding repeated injections or the less reliable oral route in patients who were vomiting, were discussed. Our patients all died in isolation without contact with family or friends, cared for by people wearing masks and goggles. The psychological and spiritual needs of such patients should not be overlooked.

Ebola is a rare disease but presents as a non-specific acute fever. East Africa has experienced several outbreaks and is likely to experience more. The reservoir is unclear[3]. The disease is sporadic[3] until it is amplified by close human contact with body fluids such as in a healthcare setting. With no vaccine available for human use[8], how can hospitals in East Africa prevent further large outbreaks?

Our experience, supported by previous work, indicates that infection with Ebola required a direct contact with an infected patient or their body fluids. The magnitude of direct contact required is not clear. Eighteen members of staff and students had direct contact with our Patient 1 during the last few days of his life and none contracted the disease or showed serological evidence of sub clinical infection. This and previous work[9] may suggest that simple skin to skin contact may not be enough to transmit the virus despite evidence that it becomes abundant in a patient's skin[10]. The implications of this are that basic and affordable infection control methods and facilities may be enough to prevent large outbreaks if strictly adhered to. Infection control in the African hospital is challenged by many obstacles[3]. Hand washing between every patient is difficult, the wards are full and busy and the sink facilities, if available, are limited. In Mbarara, and indeed any medical school, this problem is increased by the fact that the medical students need to apply rigorous infection control as well. Hand washing, however, is essential and hospitals such as ours need to engineer affordable and practical ways to facilitate this act after examining every patient. The use of gloves when in direct contact with body fluids and good sharps techniques and disposal is a basic requirement. Isolation rooms should be available and used when necessary. The availability of an isolation ward has been invaluable in the Mbarara experience. Simple affordable protective clothing should be available in all hospitals in case of future outbreaks and reproducible at short notice[4]. Manuals like that produced jointly by the WHO and CDCP should be widely distributed and available[4].

The diagnosis of Ebola is confirmed by serological detection of Ebola antigen and antibodies[1] and possibly the detection of Ebola RNA by reverse transcriptase polymerase chain reaction (validation awaited at time of writing). Prior to this outbreak there was no testing facility in East Africa, the nearest being the National Institute of Virology in Johannesburg, South Africa. Until a patient has been confirmed as having Ebola the practicalities of implementing the rapid and relatively costly measures required to contain an outbreak may be difficult for a medical superintendent or DMO with lots of other priorities. It is, therefore, essential that such testing is made as available as possible to clinicians working in East Africa. The news that such a testing facility may become available permanently in Uganda is welcome. The prospect of skin biopsy as a means of diagnosis, particularly after death may be of help[10].

Continued education and awareness of all members of the health team is also vital. We hope that this generation of Mbarara's medical students will carry these lessons throughout their careers as doctors and pass them on to others. Ebola was a terrifying experience. It strikes those who care for others. Mbarara was fortunate to survive this outbreak relatively unscathed and we are indebted to those who supported us. We acknowledge and deeply respect the bravery and commitment of our colleagues in Gulu and Masindi, many of who died from Ebola having contracted the disease performing their duty.

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Comparative bioavailability of oral sugar-coated and plain formulation of chloroquine phosphate marketed in Tanzania

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SUMMARY The bioavailability of chloroquine from a single oral dose (10 mg/kg body weight) of a sugar-coated (Dawaquin ®) and a plain formulation (Shellyquine ®) of chloroquine phosphate were compared in two groups of 10 volunteers each, following an overnight fast. Whole blood chloroquine concentrations were measured using high-performance liquid chromatography (HPLC) and bioavailability was determined by measuring area under the blood chloroquine concentration curve (AUC ng mL^{-1} h) and the peak blood chloroquine concentration (Cp_{max} ng/mL). The AUC and Cp_{max} for Shellyquine were 4396.3 ± 833 ng mL^{-1} h and 162 ± 14 ng/mL, respectively. The AUC and Cp_{max} for Dawaquin were 2060 ± 339 ng mL^{-1} h and 56.6 ± 5.2 ng/mL, respectively. Shellyquine was significantly more bioavailable than Dawaquin ($P < 0.001$). Although the Cp_{max} for Dawaquin was higher than the required therapeutic level for sensitive *Plasmodium falciparum* of 30 ng/mL, its blood levels may not guarantee a rapid clearance of parasites. The differences between the two formulations point to a problem in the quality of pharmaceuticals marketed in this country, whose extent need to be ascertained further. Failure of chloroquine phosphate in this country has already been declared by the Ministry of Health, and the potential contribution of poorly formulated products remains a subject of debate.

Introduction

Chloroquine is extensively used in the treatment and prophylaxis of malaria in Tanzania in all dosage forms, particularly tablets. The establishment of a free market has witnessed an increase in the number of brands marketed. The marketing of drugs of poor quality is a major concern in most developing countries and has been widely reported in Africa[1–4]. In some countries, because of economic restraints expired drugs have been given to patients and there is a lack of adequate drug information[1]. Climatic conditions in the tropics have been shown to reduce the potency of many drugs such as ergometrine, lignocaine, adrenaline, suxamethonium and ampicillin[2]. Other studies have also shown that between 10–50% of drugs manufactured locally in Kenya and Latin America and those reported from different countries do not meet standard test requirements[3,4]. We have previously shown that one of nine chloroquine brands marketed in Tanzania had a dissolution rate of 39% in 45 min compared to the required minimum of 75%[5], drug dissolution being an important determinant of bioavailability. A chloroquine bioavailability study performed in Sudan found one brand in five had less than half the area under the plasma concentration curve (AUC ng mL^{-1}h) and a significantly lower peak plasma concentration[6]. With the increasing number of sugar-coated chloroquine brands, bioavailability testing becomes a necessity in order to limit the number of brands to those with sufficient bioavailability to effectively treat malaria. Many people prefer the sugar-coated brands as the plain chloroquine has a bitter taste. In order to avoid malaria treatment failures with chloroquine, biopharmaceutical (product-related) and physicochemical (drug-related) factors which may lead to inadequate drug delivery to the systemic circulation – and which may result in reduction of the blood levels of the active free drug below the minimum effective concentrations – have to be considered when formulating the product.

Our finding of one chloroquine brand with low dissolution rate and the popularity of sugar-coated chloroquine brands prompted us to carry out this bioavailability study.

Methods

Subject

Twenty healthy adult volunteers aged 18–45 years participated in the study after giving written informed consent. They all had a negative Haskins' test for chloroquine in urine[7] indicating that the volunteers had not taken any 4-aminoquinoline drugs recently which would have interfered with the study and that were also not on any medication for the past month. All were non-smokers. The study protocol was approved by the College Ethical Committee.

Study design

This was an open randomized study. The volunteers were randomly allocated into one of the two study groups by means of drawing 20 closed envelopes in which the form (brand) of chloroquine preparation is stated (sugar-coated or plain chloroquine). Group A received 10 mg/kg body weight of Shellyquine while group B received 10 mg/kg body weight of Dawaquin (sugar-coated chloroquine). The drugs were administered at 8.00 h with a cup of water after an overnight fast. They were given standard breakfast 3 h after drug administration.

Sampling procedures

Capillary blood samples (100 µL) were drawn pre-dose (0 time), 10, 30 min and 1,2,3,6,8, 24 and 48 h after drug

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