Antimalarial Prescriptions for Children Presenting with Uncomplicated Malaria to a Teaching Hospital in Nigeria after the Change of National Guidelines for Malaria Treatment

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Abstract: Malaria is still a major public health problem in Nigeria. It is the leading cause of infant and childhood mortality in Nigeria. The cornerstones of its management are prevention, early and appropriate diagnosis and prompt, adequate and appropriate treatment. The conformity of the prescribed antimalarials for the children that presented to the paediatric outpatient clinic to the World Health Organisation’s recommendation and the national guidelines for malaria treatment in Nigeria was the aim of this research. The case files of children that presented to the paediatric outpatient clinic of the Lagos State University Teaching Hospital between March and September, 2006 were studied prospectively. The case files were coded and selected randomly. A total of 3500 case files were studied. Information of the patients with regards to their ages, gender, weights, body temperatures, diagnosis of malaria (provisional or confirmatory) and the types of antimalarials prescribed were extracted from the case files. Antimalarials constituted the highest group of drugs prescribed as indicated in 2824 (80.1%) of the case files. Children aged 12 to 72 months constituted the highest percentage (47.6%) and those with ages 0 to 1 month constituted the least (1.3%) patients treated for malaria. Artemisinin based combination drugs constituted 26.2% of all the antimalarials prescribed followed by Sulphadoxine+Pyrimethamine 564 (20.0%). Artemether+lumefantrine was the least 40 (1.4%). Majority of these drugs were prescribed based on provisional diagnosis rather than on diagnostic investigations. Most of the prescriptions including Sulphadoxine+Pyrimethamine were written in their brand names and were associated more with underdosage errors. It was concluded that more efforts should be geared towards malaria prevention than chemotherapy. Nigeria policy for malaria treatment should include continuous surveillance of rational prescription of the available drugs, especially the artemisinin combined drugs and implementation of the new guidelines.

Key words: Antimalarial drugs • uncomplicated malaria • outpatient prescriptions • teaching hospital • Nigeria

INTRODUCTION

Malaria is a tropical disease transmitted by the female Anopheles mosquito of which Anopheles gambiae is the most efficient vector [1]. It is a public health problem of global concern because of its high economic burden on the nation, high mortality in children, pregnant women and non-immune individuals. Malaria is a major cause of morbidity and mortality in Nigeria where it is holoendemic. It is the leading cause of death in children and accounts for over 60% of outpatient visit in Nigeria and other Sub-Saharan African countries [2, 3]. Also, it is responsible for 25% infant mortality and 30% of childhood mortality [3, 4]. Plasmodium falciparum accounts for 98% of malaria infection in Nigeria and associated with significant morbidity and mortality [4]. Every year about 12 million children die before attaining age five and many during their first year of life. Up to 1% of these children die of uncomplicated malaria, 50% of such children die within the first 24 hours from complications of severe malaria [5].

Until recently malaria was majorly and effectively treated with chloroquine and sulphadoxine-pyrimethamine but due to the emergence of resistance to these drugs they were no longer effective. Recent drug therapeutic efficacy trials conducted in the six geo-political zones in Nigeria have shown a high level of resistance to these drugs ranging from 23 to 96% [6]. The World Health
Organization (WHO) has recommended that an antimalarial agent may not be used as first line when the level of resistance is above 25% in an area [7], hence the change in the Nigerian national guidelines for malaria treatment in the year 2005 [6]. The guidelines stated that the treatment of choice for uncomplicated malaria should be artemisinin based combination therapy (ACT). This consists of the use of an artemisinin derivative and another effective antimalarial drug and by WHO’s definition, these drugs should be administered simultaneously, have schizonticidal effects and independent modes of action and different biochemical targets on the parasites. The basis of this combination therapy is to reduce duration of treatment and theoretically to improve cure rates and the speed at which resistance would develop. In tropical African countries, WHO has pushed for artemether+lumefantrine and artesunate+amodiaquine combinations as the first choice of antimalarial therapy. Other ACTs available in Nigerian market include artemunate+mefloquine and dihydroartemesinin+piperazine+trimethoprim and are as effective as those recommended by WHO [8]. Emerging evidence has shown that malaria incidence amongst children less than three months (<5 kg) is increasing. However, enough studies are not available to support the use of ACTs in this group; hence quinine is recommended for the treatment of malaria in this group.

The correct use of antimalarial drugs is the key not only to therapeutic success but also to deterring the spread of drug resistance malaria [9]. Most cases of malaria are treated based only on the clinical features and it is inevitable that some patients without malaria may be treated with antimalarial drugs. However, in areas with stable malaria or high transmission season like Nigeria, a recent history of fever is enough criterion for diagnosis of uncomplicated malaria [8]. It is on this premise that the new antimalarials are prescribed for empiric treatment of malaria without confirming the diagnosis by laboratory investigations [10]. A grievous consequence of this is early emergence of resistance to these novel drugs. The objective of this study was to evaluate the prescribing patterns of antimalarials to children presenting to the general paediatric outpatient clinic of the Lagos State University Teaching Hospital, Ikeja so as to know if they conform to the World Health Organisation’s recommendations and the Nigerian national guidelines for malaria treatment. The information provided by this study is also expected to aid in interventions that would improve the prescribing practices of doctors attending to children presenting to this hospital with uncomplicated malaria so as to stem the tide of early emergence of resistance to these drugs.

**MATERIALS AND METHODS**

Lagos State University Teaching Hospital (LASUTH) is a tertiary healthcare centre that operates free health care services for all the children in Lagos State. Because of this, patients flow to the paediatric general outpatient clinic was overwhelmingly high and an average of 350 patients is attended to per week. The general outpatient clinic holds everyday except Saturdays, Sundays and public holidays. It is run by a chief medical officer, 2-3 medical officers (from both paediatric and family medicine departments) and a resident in paediatric.

**Study design:** This was a prospective study involving children attended to at the paediatric general outpatient clinic of LASUTH between March and September, 2006. Case files of these patients were retrieved from the medical record office after the clinic had ended on Fridays of every week for random selection and information extraction. Each case file is assigned a code number written in a ballot paper. The ballot papers are folded and kept in a box where a neutral person that is not knowledgeable of this study was employed to pick 125 of these ballot papers randomly. The code in the selected ballot papers are used to retrieve the patients’ case files. A total of 3500 case files were used for the study. Patients who had nothing written on their cards, no diagnosis made or no drugs prescribed were excluded from the study.

**Information extraction:** Information extracted from the case files are: demographic data (age, gender, weight) and body temperature of the patients, diagnosis of malaria (provisional or confirmatory), antimalarials prescribed, prescription of the antimalarials by generic/proprietary names or acronym/abbreviation and adequacy of the prescribed dosages. The recommended dosages of the antimalarials were obtained from the information booklets that accompanied each of the antimalarial drugs from the hospital pharmacy. These recommended values were used to calculate adequacy of the prescribed dose of the antimalarials based on the patients’ weight in kilogramme.

**Data management and analysis:** The data of each case file was collected on a check list, entered into a spread sheet and analysed using SPSS Version 10.
RESULTS

Out of the 3500 case files selected, 1855 (53.0%) prescriptions were written for males, 1446 (41.3%) for females and 199 (5.7%) patients with their gender not indicated. The mean age of the patients is 55.8±37.4 months. Those with ages between 12 to 72 months constituted the highest percentage (47.6%) while those with ages 0 to 1 month constituted the lowest (1.3%). The mean weight and the body temperature of the children were 10.3±5.5 kg and 37.2°C, respectively.

Antimalarials constituted the highest group of drugs prescribed as indicated in 2824 (80.1%) of the case files. Antipyretic-paracetamol 2793 (79.8%) and vitamin B complex 2689 (76.8%) were the two commonly prescribed drugs with the antimalarials. Table 1 showed the pattern of antimalarial drugs prescribed. While Sulphadoxine+Pyrimethamine only 564 (20.0%) was the highest antimalarial prescribed, artemether+lumefantrine was the least 40 (1.4%). Only 23 (0.8%) of the patients were investigated and confirmed to have malaria before prescribed antimalarial drugs. Artemisinin-based combined drugs were the antimalarials prescribed after the confirmation of malaria in the blood film of the investigated patients. Artemisinin based combination drugs constitute 26.2% of all the antimalarials prescribed, majority of which were prescribed, like other antimalarials, empirically based on the symptoms and signs of malaria. Majority of the antimalarial drugs 2785 (98.6%) had their duration of use adequately prescribed. Of the artemisinin-based combined drugs, only artemether+lumefantrine was prescribed as a fixed combined drug. The rest were prescribed as loose combined drugs. Sulphadoxine+pyrimethamine and amodiaquine prescribed together were in loose forms. Table 2 showed the names and forms by which the antimalarials were prescribed. The dosages of the antimalarials were adequately written for 1164 (41.2%) patients. Underdosage and overdosage prescriptions of the antimalarials were associated with 711 (25.2%) and 302 (10.7%) patients respectively. Dosages of the antimalarials were not stated in the case files of 647 (22.9%) patients. The dosage errors were most common with sulphadoxine+pyrimethamine prescriptions and least common with artemisinin, its derivatives, combined forms and amodiaquine.

DISCUSSION

The fact that antimalarials were prescribed for 80.1% of the patients showed that malaria is the most common illness affecting children in Lagos state. This finding therefore supports the earlier reports from Nigeria and other tropical countries that malaria is the leading cause of death in children and accounts for over 60% of outpatient visit in Nigeria and other Sub-Saharan African countries [2, 3]. Children with ages between 12 to 72 months constituted the highest percentage (47.6%) of the patients treated for malaria at this centre and this is because the consequences of delayed or poorly treated malaria in this age group is usually fatal. Such consequences include infant and childhood mortality [3, 4]. Children of ages 0 to 1 month (neonates) constituted the lowest percentage (1.3%) of the patients from this study. Malaria in this age group is called neonatal malaria and is considered rare and largely asymptomatic or mild [11]. The prevalence of neonatal malaria (1.3%) obtained from this study was lower than 9.1% previously reported in Nigeria [12]. Most of the cases occurred within the first three to four weeks of life as a result of increased immunity, thus implying that majority of the cases were mosquito-borne. The prescription of paracetamol (79.8%) and vitamin B complex (76.8%) along with the antimalarials has been

<table>
<thead>
<tr>
<th>Antimalarial drugs</th>
<th>Numbers prescribed</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>SP</td>
<td>564</td>
<td>20.0</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>560</td>
<td>19.8</td>
</tr>
<tr>
<td>Artesunate+SP</td>
<td>500</td>
<td>17.7</td>
</tr>
<tr>
<td>Artesunate only</td>
<td>360</td>
<td>12.8</td>
</tr>
<tr>
<td>SP+Amodiaquine</td>
<td>316</td>
<td>11.2</td>
</tr>
<tr>
<td>Amodiaquine</td>
<td>284</td>
<td>10.0</td>
</tr>
<tr>
<td>Artesunate+Amodiaquine</td>
<td>200</td>
<td>7.1</td>
</tr>
<tr>
<td>Artemether+Lumenfantrine</td>
<td>40</td>
<td>1.4</td>
</tr>
<tr>
<td>Total</td>
<td>2824</td>
<td>100.0</td>
</tr>
</tbody>
</table>

SP = Sulphadoxine+pyrimethamine
reported in Nigeria [13]. Malaria characteristically presents with fever which together with other symptoms form the basis of diagnosis and empiric treatment without recourse to diagnostic investigations [10, 14]. This may therefore explain the high rate of paracetamol prescription along with the antimalarials. However, the recorded mean body temperature of the patients did not reflect high fever that necessitated the use of antipyretics as practised by the doctors attending to these patients. Therefore this practice is irrational and carries the risk of chronic toxicity of paracetamol.

The prescription of vitamin B complex along with the antimalarials revealed by this study appears to be a routine practice in Nigeria [13, 15, 16]. The justification for this practice is not clear to us. However, some parents and doctors believe that vitamin B complex may induce or enhance the child’s appetite, as such, should be routinely prescribed. Despite the change in the national guidelines for malaria treatment in Nigeria, sulphadoxine+pyrimethamine and chloroquine were the most prescribed antimalarials. Resistance has been reported to these antimalarials in the six geo-political zones in Nigeria [6] and by the new guidelines and WHO’s recommendation; they should not be used as first line treatment of uncomplicated malaria. Instead, artemesinin based combination therapy (ACT) should be used. The consequence of non-compliance to the treatment of uncomplicated malaria is further propagation of resistant malaria, treatment failure, high rate of re-treatment and economic burden to both the parents and the government. Approximately 13.0% of the prescribed antimalarials were artesunate/artemisinin derivatives only. These prescriptions negate both the national treatment guidelines and WHO’s recommendation [6]. This monotherapy is not likely to improve cure rates of uncomplicated malaria or reduce the speed at which resistance could develop. Of the artemisinin combined therapy, artemether + lumefantrine and artesunate + amodiaquine were the least prescribed. These combinations are the first choice of antimalarial therapy recommended by WHO in tropical African countries and the national guidelines for malaria treatment in Nigeria. Majority of the artesunate+amodiaquine combination drugs and artesunate+sulphadoxine/pyrimethamine were prescribed as loose combination drugs. The consequence of this type of prescription is that these drugs may not be taken together at once or due to poor finance or lack of the drugs at the hospital pharmacy for free dispense, only one of the combinations may be taken as monotherapy, thereby further promotes early resistance development.

Error of underdosaging was more common than overdosaging of the antimalarials and is even more associated with prescriptions other than use of generic names. Similar result on dosage error of antimalarials in both public and private hospitals in Lagos, Nigeria has been reported by Oreagba et al. [17]. Most patients on antimalarials are receiving drugs with potential for resistance when under-dosed and must be prescribed according to specific protocols. Even if antimalarial drugs are of good quality, overuse or under-dosing influences resistance. Overuse and over-prescription of sulphadoxine+pyrimethamine places these children at a high risk of adverse drug reactions such as fixed drug eruption and Stevens Johnson syndrome.

This study has been able to highlight the flaws in the management of malaria in a Teaching Hospital in Nigeria. Presumptive treatment of uncomplicated malaria should be full dose chloroquine. Early diagnosis with confirmatory side laboratory test should be ensured before using the artemesinin combined therapy so as to prevent early emergence of resistance to these novel drugs. Preventing malaria by using impregnated nets and other forms of vector control measures will reduce the incidence of malaria cases presenting to the hospital and antimalarial drugs utilization. Thus reducing the risk of adverse reactions to these drugs and further reduces the speed at which resistance are likely to develop to them. The policy for malaria treatment in Nigeria should not be limited only to change in the guidelines, but should also include continuous surveillance of rational prescription of these drugs and implementation of these guidelines to the end. Routine prescriptions of antipyretics and vitamin B complex should be discouraged rather; a strong indication and evidence based medicine should guide their use.

REFERENCES


