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THE ROLE OF ADJUNCT THERAPIES IN THE RATIONAL TREATMENT OF UNCOMPLICATED MALARIA

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ABSTRACT

Objective: To determine the role of adjunct therapies in the rational treatment of uncomplicated malaria.

Methods: Retrospective patient record review. Six hundred Patients were selected through both stratified and systematic sampling methods. Diagnosis was by both clinical symptoms and treatment. Records were analysed for drug use indicators and rationality of management. Data was collected between September-November 1999.

Results: Four hundred and eighty six (81%) records met the operational definition. Average drug use per patient was 4.0 ± 1.4. Injections were administered to 27.4% and antibiotics received by 25.1%. Only 22% of patients were rationally (well) treated. The most frequently prescribed classes of drugs were anti-malarials (24.8%), analgesics (25.7%), multivitamins (20.4%) and antihistamines (13.2%). These classes of drugs (adjunct therapies) make up about half of all drugs prescribed. Many of the drugs were unjustified and were harmful. A positive and significant relationship was established between the number of complaints given by patients and the number of drugs prescribed by the physician (r= 0.29, p=0.000), indicating symptomatic treatment.

Conclusion: Adjunct therapies contribute significantly to irrational treatment of malaria while patients' complaints and expectations influence physician prescribing.

KEY WORDS: ***Adjunct therapies, rational treatment, anti-malarials, analgesics.***

INTRODUCTION

Malaria is one of the commonest causes of fever in Nigeria. The presenting symptoms of fevers, chills, body aches necessitate the use of anti-pyretics and analgesics drugs along with anti-malarials.[1]

Drug use studies in Nigeria show a high level of use of antipyretics and analgesics drugs such as paracetamol and dipyrone[2,3,4]. Dipyrone was found to constitute up to 25% of all injections prescribed at Primary Health Care centres[2].

More disturbing is the ready disposition of health care workers to use parenteral forms of drugs as opposed to the oral forms[2,3,4]. In one study, patients received from one to four injections per visit for the treatment of malaria[2].

It is then very likely that these adjunct therapies contribute significantly to the high level of irrational drug use observed in Nigeria[3,5]. However, the contributions of these drugs have not been fully assessed in specific clinical context such as malaria.

The present study was conducted to investigate the use of adjunct therapies such as analgesics, antihistamines and multivitamins preparations in the treatment of uncomplicated malaria.

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METHODS

Background

The General Hospital Ikeja was selected as the site of the study. It is a multipurpose secondary care facility. Only doctors treat and prescribe drugs. The majority of patients are seen at the general outpatient department clinics where the study was conducted.

Study design and instrument

The study was conducted as a retrospective case record review of outpatients presenting with malaria in the first quarter of 1999. Record selected were those of patients who came to the clinic for the first time.

Patients' records were included on either of the following categories presenting symptoms of fever, chills or rigours, prescription of anti-malarial drug or if the attending physician wrote a diagnosis of malaria. These symptoms have been reported to be predictive of malaria[6]. Subjects with clinical signs of severe malaria or those that required hospitalization were not eligible for inclusion in the study.

A study specific data collection form was designed for the study. Information recorded on patients' cards was transcribed to the form. Such information included age, sex, presenting

complaints, diagnosis and drugs prescribed.

Sampling techniques

It has been shown that for drug use studies[7] as this, a minimum of 600 cases collected from 20 health facilities or at least 100 cases from one facility would meet statistical requirements for validity (± 7.5%). Studies in Nigeria have validated these recommendations[2,3]. These guidelines were followed in this study.

Six hundred patient case notes were planned to be included for the study. The ratio of adult and children cases to be included was determined from the Medical Records Department (using the attendance for the period) and found to be a ratio of 2:1 while adult male to female ratio was equal. Thus 200 adult males, 200 adult females and 200 children were recruited. Systematic sampling with an interval of one in twenty records was used to select patient records.

Data Analysis

The author to determine if the patients were presenting with malaria and if the treatments received were in agreement evaluated all records. Records who were found not to meet this standard or where there were doubts over the probability of the diagnosis being malaria were eliminated from analysis. Furthermore, pharmacological classification of drugs was determined.

Data was analysed in a computer using Epi-info Version 6.04b statistical software. Drug prescribing indices[7] such as average number of drugs per visit, average number of injections, percentage of patients managed according to treatment guidelines (rational management) were determined. All treatments were compared to a standard reference manual for doctors on treating malaria[1] and classified as rational when in conformity and irrational when at variance with it.

RESULTS

Four hundred and eighty six (81%) patient records met the operational definition. They included 239 females (49.2%) and 247 (50.8%) males. Adults made up 72.8% while children constituted 27.2%. Malaria parasite smears were not requested for in all the patients.

Table 1 shows the various symptoms observed as recorded in the patient case notes. Fever was the most common symptom. Patients seen had an average of 2.85 complaints ± 1.24, with a range varying from one to six. The median and modal number of complaints was three.

Table 1: **Symptoms of Malaria**

SYMPTOM	N(N=486)	%
Fever	419	86.2
Headache	218	44.9
Joint pains	170	35.0
Vomiting	73	15.0
Loss of appetite	48	9.9
Cough	40	8.2
Diarrhoea	13	2.7
Other symptoms	241	49.6

Drug use indicators are shown on Table 2. Patients received on the average four drugs though the range was one to nine, with a median number of three drugs while four drugs per patient was the most frequently prescribed number.

About a quarter of patients received injections and the same proportion received antibiotics. Antibiotic prescribing was generally limited to one per patient (n=122) though some received up to three. Only 22% of patients were deemed to have been properly managed.

Table 2: **Drug Use Indicators in the Treatment of Malaria**

Indicator	Value
Average number of drugs per patient (SD)	4.0 (1.4)
Percentage of patients who received at least one injection	27.4
Percentage of patients who received at least one antibiotic	25.1
Percentage of patients managed according to treatment guidelines	22.0

Table 3 shows the pharmacological groups of drugs prescribed. Tables 4-6 give a frequency distribution of analgesics, antihistamines and multivitamins. Of note is the use of both oral and intramuscular (i.m) forms of the drugs.

Table 3: **Pharmacological Classification of Drugs**

Classification	N	%
Analgesics	501	25.7
Anti-malarials	483	24.8
Multivitamins	397	20.4
Anti-histamines	257	13.2
Antibiotics	155	7.9
Haematinics	51	2.6
Anti-helminthics	23	1.2
Gastro-intestinal	19	0.9
Cough syrups	11	0.6
Others	52	2.7
	1949	**100.0**

Table 4: **Analgesics**

Name	N	%
Paracetamol	308	69.4
I.m. Dipyrone	59	13.3
Oral Dipyrone	5	1.1
I.m Dipyrone + Paracetamol	42	9.4
Non-steroidal anti-inflammatory drugs	19	4.3
Non-steroidal anti-inflammatory drugs + Paracetamol	8	1.8
Other combinations	3	0.7
	444	**100.0**

Table 5: **Antihistamines**

Name	N	%
Oral chlorpromazine	128	55.4
Oral promethazine	4	1.7
I.m. Promethazine	79	34.2
I.m. chlorpromethazine	4	1.7
Oral & i.m. chlorpromethazine	1	0.4
Oral & i.m. promethazine	5	2.2
I.m Promethazine + oral chlorpheniramine	10	4.3
	231	**99.9**

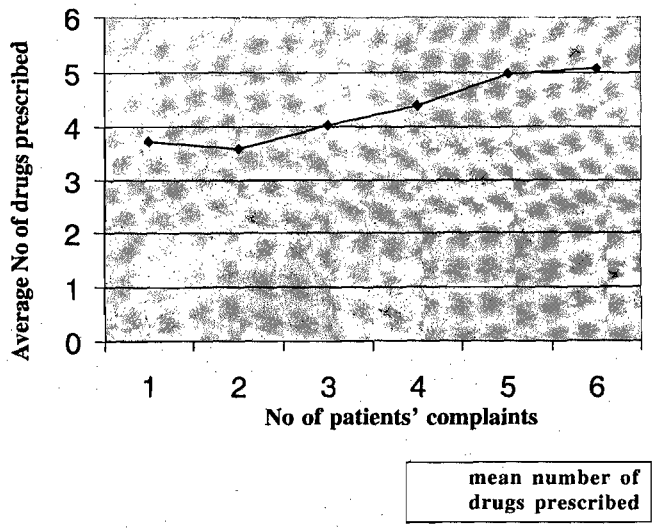
Table 6: **Multivitamins**

Name	N	%
Oral vitamin B complex	237	70.9
Oral Vitamin C	9	2.7
Multivitamin syrup	24	7.2
I.m Vitamin B complex	5	1.5
Combination of multivitamins	59	17.7
	334	**100.0**

Figure 1 shows the relationship between number of complaints given by patients and the average number of drugs prescribed. The values vary from 3.7 drugs for one complaint to 5.1 drugs for 6 complaints on the average.

The correlation coefficient (r) was found to be 0.29 and this was significant (t test=6.67, p=0.00000) while the regression coefficient was 0.32, Y-axis intercept=3.08. A significant association was found between the number of patient complaints and the average number of drugs prescribed ($X^2 = 51.08$, degrees of freedom=5, p value=0.0000).

Fig 1: **Number of Patients' Complaints and Average Number of Drugs Prescribed**



DISCUSSION

To our knowledge, this is the first study to examine in detail the contribution of adjunct therapies to rational treatment especially in the clinical context. The drug use indicators observed in our study are high but in keeping with the average figure of four drugs per patient observed in other Nigerian studies, (4.4 in Edo state[3]), but lower than the figures from primary health care centres (4.9 &7.7)[2,5].

However, more revealing is the fact that the anti-malarial drugs constitute only one quarter of drugs prescribed and when this group is added to the analgesics, about half of the drugs prescribed were not essential to the treatment of malaria. Thus it is clear that many of the drugs here were prescribed for reasons other than their medical indications. For example, multivitamins and anti-histamines made up a third of the drugs while cough syrups, anti-helminthics, anxiolytics and antispasmodics were also prescribed. This pattern of polypharmacy has also been observed in Ghana[8].

Moreover, the prescribing rates of multivitamins (20.4%) and those of analgesic (25.7%) in this study are much lower than the rates observed amongst doctors in private practice (57.2% and 64.3% respectively)[3] suggesting that different factors such as economic gains which is important to the latter group may not be important to doctors working in the public sector.

We found that parenteral forms of antihistamines were used in more than a third of patients and dangerous drugs such as dipyrone and expensive drugs such as non-steroidal drugs (for example diclofenac) were also used. These drugs were used in situations where cheaper and safer alternatives exist.

Dipyrone has been withdrawn from the market in several countries on account of agranulocytosis associated with it[9] but it continues to be the leading parenteral analgesic at this hospital. A study in South Africa found that analgesic use was much higher (40.4%)[10] than was observed in our study (11%).

Furthermore, this study firmly established a significant relationship between the number of complaints made by the patients and the number of drugs prescribed by the attending physician (r=0.29, p=0.000). As the number of complaints increased, doctors wrote more medicines probably to cover as many of the symptoms the patients gave.

This is reflected in the use of drugs like dipyrone, diclofenac, chlorpheniramine, hyoscine and cough syrups. If the regression model constructed for the number of patient complaints and the number of drugs prescribed was to be followed, a patient presenting with as many as ten symptoms will receive at least over six drugs.

The number of complaints given by patients is an indirect measure of patient expectation and pressure and we can state categorically that these doctors were influenced by patient expectations. This has been found to be true in other studies[11,12] and one study showed that physician opinion about patient expectations was the strongest determinant of prescribing[12].

We observe that physician guidelines for treating malaria[1] recommend only an anti-malarial and an analgesic, this advice was not followed most of the time. It may well be that the doctors are not comfortable with prescribing as few as two drugs. Some reports have shown that irrational prescribing is associated with

young medical interns and less qualified personnel[8,13] but we were unable to establish the cadre or work experience of the prescribers in or study as doctors are only required to append their signatures to case notes without details of names or status.

Furthermore though this hospital has facilities for malaria parasite smears to be performed, the test was not requested for. The non-use of this test may be related both to the time it takes to perform or more likely to the time it takes for the test results to be returned to the doctor.

The high patient attendance would also put considerable pressure on the laboratory if the test was ordered for every suspected case of malaria. Thus it is likely that some of the patients may not have had malaria or had malaria in addition to other ailments. Nevertheless, the diagnostic accuracy of doctors in diagnosing malaria on clinical grounds alone has been reported to be as high as 86%[6].

However, there are some limitations to the malaria parasite smear, as patients have been known to be asymptomatic though positive[15] for the test while subpatent malaria has been reported amongst patients who had negative smears[16].

It should not be thought that all of the polypharmacy observed here is bad. For instance the wide spread use of anti-histamines is probably to prevent chloroquine induced pruritus which is common[14] while it is also now known that antihistamines reverse chloroquine resistance[17].

In addition, the polypharmacy may be a reflection of inadequacy of diagnostic facilities in the hospital and of diagnostic uncertainty on the part of the doctor. An additional reason may be the pressure of work whereby the doctor has to attend to so many patients that he ends up prescribing the same pattern of medicines to different patients once the symptoms are similar.

In conclusion, up to half of the drugs used to treat malaria in this study are not necessary and reflect symptomatic treatment by the doctors. Suggestions to improve drugs use include wide availability of treatment guidelines, continuing medical education and availability of rapid diagnostic tools such as the quantitative buffy coat and Parasight F tests[18,19]. Doctors should also give more time to counseling patients rather than prescribe drugs to cover as many symptoms patients present with.

The study suffers from the usual limitations of retrospective studies, that of incomplete data. Furthermore, the treatments administered cannot be linked to any particular doctor or cadre of doctors. However, the findings of the study are applicable to the generality of physician prescribing behaviour in the hospital.

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