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A Study of Cost Effectiveness of Artemisinine Combination Therapy (Act) Among Paediatric Patients at a Tertiary Medical Centre in South West Nigeria

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Abstract - This retrospective study was to compare the cost effectiveness of oral ACT as a first line of treatment of malaria with non-oral ACTs in paediatric patients aged 5 years and below. The study was carried out at Children Outpatients Clinic of Federal Medical Centre, Abeokuta Ogun State in Nigeria between April and September 2005. Clinical case notes of paediatric patients aged 5 years and below were used. Three hundred and fifty (350) patients were randomly selected with only 328 patients meeting the inclusion criteria. The number consisted of 153 (46.6%) males and 175 (53.4%) females. The mean age of patients was 2.3 years (SD 1.4). Oral Chloroquine/Sulphadoxine and Pyrimethamine (CQ/SP) was administered to 127 (38.7%) patients, 113 (34.5%) patients had Quinine/Sulphadoxine and Pyrimethamine (QSP) while 88 (26.8%) patients had Arthemisine/ Sulphadoxine, Pyrimethamine (ASP). The cure rate for CQ/SP, Quinine/SP and Arthemisine/SP were (11.0%), (22.1%) and (97.7%) respectively. It was only Artemisinine/SP that met the 7.5% efficacy rate recommended by WHO. Data on the therapeutic efficacy of the treatment given to the patients were collected and analyzed using descriptive statistics of frequency distribution and percentages with statistical package Microsoft SPSS 10.0 window version.

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Oral Chloroquine/Sulphadoxine and Pyrimethamine (CQ/SP) was administered to 127 (38.7%) patients, 113 (34.5%) patients had Quinine/Sulphadoxine and Pyrimethamine (QSP) while 88 (26.8%) patients had Arthemisine/ Sulphadoxine, Pyrimethamine (ASP). The cure rate for CQ/SP, Quinine/SP and Arthemisine/SP were (11.0%), (22.1%) and (97.7%) respectively. It was only Artemisinine/SP that met the 7.5% efficacy rate recommended by WHO. Data on the therapeutic efficacy of the treatment given to the patients were collected and analyzed using descriptive statistics of frequency distribution and percentages with statistical package Microsoft SPSS 10.0 window version.

In the economics analysis, Chloroquine/SP, Quinine/SP and Artemisimine/SP had average cost effectiveness ratio (ACER) of 5.19, 3.45 and 1 respectively. The incremental cost effective ratio (ICER) for changing from Chloroquine/SP to Artemisinine was 1 while for changing from Chloroquine/SP to Quinine/SP was 3.68.

The study indicated that ACTs represented by Artemisinine/SP was more cost effective than the non-ACTs represented by Chloroquine/SP and Quinine/SP since the ACER for Artemisinine/SP was the lowest among the three comparators. ACTs was also more clinically effective than the non-ACTs in the treatment of malaria in paediatric patients aged 5years and below ($p<0.05$).

Keywords : ACTs, Non ACTs, Chloroquine, Quinine, Sulphadoxine, Pyrimethamine.

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I. Introduction

Despite the recent introduction of the use of Artemisinine combination therapies (ACTs) in the management of malaria into the National guideline on malaria treatment, most cases of malaria are still treated with old drugs that often fail.(1, 2,3) Most physicians are reluctant to change to ACTs because of the cost. Physicians believed that ACTs is more expensive, (4) therefore cost has proven to be a major obstacle to the widespread use of ACTs. Physician who is the primary decision maker within the health care system have responsibility for controlling health care costs while providing the best possible care for patient.(4) There is need for economic evaluation of pharmacotherapy that will provide prescribers awareness about the costs associated with the treatment they select for their patients.

The pharmacists in a hospital setting are acknowledged as experts on drugs and therefore should maintain a reliable but economic drug delivery system in order to ensure that cost effective drugs are available. (4, 5)

The increase in number of new drugs combined with increase in list of drugs provides a great challenge to manage care organizations (MCOs) as they struggle to deliver quality care while minimizing cost. Pharmacy and therapeutic (P&T) committees are the MCO responsible for evaluating these new drugs and determining their potential value to organization. (5)

Pharmacoeconomics analysis are categorized by the method used to access outcomes. If the outcomes are assumed to be equivalent, the study is called a cost minimization analysis (CMA). If the outcomes are measured in monetary terms such as dollar and naira, the study is called cost benefit analysis (CBA). If the cost are measured in natural unit such as cures, years of life and blood pressure, the study is called a cost effectiveness analysis (CEA) and if the outcomes takes into account patient's preferences such as utilities, the study is called cost utility analysis (CUA). Pharmacoecomics study categorized cost into four. These are direct medical cost, direct non medical cost,

indirect cost and intangible cost. Direct medical cost are the most obvious costs to measure. These are the medically related inputs used directly to provide treatment such as costs associated with pharmaceutical products, physician visits, emergence room visits and hospitalization. Direct non medical costs are cost directly associated with treatment but are not medical in nature. These includes travelling to and from the physician's office, travelling to and from physician's office to hospital, baby sitting for the children of a patient and food and lodging required for the patient and their family during out- of -town treatment.

Indirect costs involve costs that result from the loss of productivity due to illness or death. This economic term "indirect costs" is different from accounting term "indirect costs."

Accounting term indirect costs is used to assign over head. Intangible costs include the costs of pain, suffering, anxiety or fatigue that occur because of an illness or treatment of an illness. It is difficult to assign values to intangible costs. Treatment of illness such as malaria may include all four types of costs. (3, 5)

As used in this study, pharmacoeconomics is the process of identifying, measuring and comparing costs, risks and benefits of programs, services or therapies and determining the alternative that produces the best health outcome for the resources invested based on long term benefits. It involves weighing the cost of providing a practical product or service to determine which alternative yields the optimal outcome for a specific sum and the information obtained can assist clinical decision makers in choosing the most cost effective treatment options. (3, 5)

The objective of this study is to determine the cost effectiveness of artemesinine combination therapies (ACTS) among peadeatric patients attending federal medical center Abeokuta Ogun State in Nigeria with the goal of providing and promoting pharmaceutical care.

II. Patients And Methods

This is a Retrospective pharmacoeconomics analysis in which paedaitric malaria patients who aged 5years and below that attended the Children Outpatient Clinic of Federal Medical Centre, Abeokuta were used for the study. This is a 100-bed tertiary hospital located in South-Western part of Nigeria. It is about 70-kilometers from Lagos. It has 120 medical doctors comprising of Consultants in Paediatrics, Surgery, Family Medicine, Internal Medicine, Cardiology and Gynecology. The outpatient unit of the Pediatrics Department attends to over fifty patients aged 12 years and below daily. The criteria for inclusion were: Patient must be a confirmed malaria patient through symptomatic or diagnostic test and Patient must attend follow up clinic within one week of first visit in order to assess the effectiveness of treatment.

Between the six-month period of April 1st and September 30th 2005, 350 case notes of patients with malaria aged 5 years and below that attended Children Outpatient Clinic were randomly selected from the Medical Record Unit and the mode of treatment with ACTs and non ACTs for each patient was thoroughly studied. Twenty two (22) patients did not meet the inclusion criteria, therefore a total of 328 patients who came back within one week of initial visit for check up were used for the study. This comprise of 153 (46.6%) males and 175 (53.4%) females.

One hundred and twenty seven (127) patients were treated with Chloroquine and Sulphadoxine pyrimethamine (CQ/SP), 113 patients were treated with Quinine, Sulphadoxine and pyrimethamine (QSP), while 88 patients were treated with Artemisinine, Sulphadoxine and Pyrimethamine (ASP).

Clinical success was defined as the complete clinical cure of the malaria confirmed by absence of symptoms or a negative malaria parasite test.

The treatment cost of each comparator included direct medical cost such as drug cost, cost of drug prescribed to treat side effects, cost of laboratory investigation and consultation fee.

The direct non-medical costs were those associated with receiving therapy including follow up visits and the only expenses included under this was the transportation expenses and an estimate of N100 (One Hundred Naira) was used. The average cost effectiveness ratio and the incremental cost effectiveness ratio were then determined using the cost and therapeutic outcomes.

Since only 328 patients (93.72%) reported back within the stipulated one week of treatment for follow-up clinic, the remaining 22 patients (6.28%) that did not come back for follow up clinic may serve as a potential source of bias.

The cost of treating 100 patients was calculated and the percentage effectiveness of the treatment was also calculated.

$$\text{Cost of treating 100 patients} = \text{Unit cost of therapy} \times 100$$

$$\%\text{Effectiveness} = \frac{\text{No of Patients successfully treated}}{\text{No of patient that had the treatment}} \times 100$$

Average cost effectiveness ratio (ACER) was calculated as the average cost per patient treated successfully and done by dividing the total cost and patients successfully treated.

$$ACER = \frac{\text{Healthcare cost (A)}}{\text{Clinical outcome (B)}}$$

Incremental cost effectiveness ratio (ICER) was calculated as the incremental change in cost divided by the incremental change in effectiveness.

$$ICER = \frac{\text{Cost A} - \text{Cost B}}{\text{Outcome A} - \text{Outcome B}}$$

The data obtained were analyzed using SPSS (Statistical Package for Social Science) Version 10.0

1. Descriptive statistics of frequency distribution and percentages were used as appropriate.
2. Chi – square test was used to test hypothesis.

III. Results

Table 1 : The age distribution showed that 22.0% of the patients were less than 1 year old, 29.0% were between 1 & 2 years old, 14.0% were between 2 & 3years old, 15.0% were between 3 & 4 years old while 20.0% were between 4 & 5 years of age.

Table 1 : Patients' Age Distribution

Age	Frequency	Percentage
< 1 YEAR	72	22.0
>1 year- 2 years	95	29.0
>2 years – 3 years	47	14.0
>3 years – 4 years	50	15.0
>4 years – 5years	64	20.0
TOTAL	328	100

Table 2 : The percentage effectiveness of CQ/SP was 11.20%, Quinine/SP was 22.12% and Artemisinine/SP was 97.72%. The average cost effectiveness ratio for CQ/SP was 5.19, Quinine/SP was 3.45 and Artemisinine/SP was 1. The ICER for changing from CQ/SP to Quinine/SP was 3.68, while for changing from CQ/SP to Artemisinine/SP was 1.

Table 2 : Cost Effectiveness Comparison Table

COMPARATORS	COST (A) NAIRA(=N=)	DOLLAR($)	%EFFECTIVENESS (B)
CQ/SP	51000	340.0	11.02
QUININE/SP	68000	453.40	22-12
ARTEMISININE	87000	580.0	97.72
AVERAGE COST EFFECTIVENESS RATIO			
COMPARATOR	AVERAGE COST NAIRA(=N=)	DOLLAR($)	RATIO
CQ/SP	4627.94	30.85	5.19
QUININE/SP	3074.14	20.50	3.45
ARTEMISININE/SP	890.29	5.94	1
INCREMENTAL COST EFFECTIVENESS RATIO			
COMPARATOR	ICER NAIRA(=N=)	DOLLAR($)	RATIO
CQ/SP to QUININE/SP	1531.53	10.2	3.68
CQ/SP to ARTEMISININE/SP	415.22	2.77	1

Table 3 : The drug prices were the local prices in Naira (which was converted to US dollars) paid by patients at the point of purchase at the pharmacy. The adverse effect treatment only covered the price of Chlopheniramine prescribed to treat pruritus in patients.

Table 3 : Treatment Cost Treatment

	CQ/SP NAIRA(N) DOLLAR($)		QUINI/SP NAIRA(N) DOLLAR($)		ARTEMISI/SP NAIRA(N) DOLLAR($)	
Drug Price	100	0.67	270	1.8	570	3.41
Laboratory Test	100	0.67	100	0.67	100	0.67
Consultation	100	0.67	100	0.67	100	0.67
Adverse Effect Treatment	110	0.73	110	0.73	NIL	
Direct Non-Medical Cost (Transport Fare)	100	0.67	100	0.67	100	0.67
Total	510	3.41	680	4.54	870	5.42

Table 4 : The cure rate of Chloroquine, Sulphadoxine and Pyrimethamine was 11.0%, Quinine, Sulphadoxine and pyrimethamine was 22.1% and Artemisinine and Sulphadoxine – pyrimethamine was 97.7%.

Table 4 : Clinical Result Derived From The Treatment

DRUG	CLINICAL OUTCOME SUCCESS	FAILURE	TOTAL
Chloroquine And Sulphadoxine-Pyrimethamine	14 11.0%	113 89%	127 100.0%
Quine And Sulphadoxine-Pyrimethamine	25 22-1%	88 77.9%	113 100.0%
Artemisinine And Sulphadoxine Pyrimethamine	86 97.7%	2 2.3%	88 100.0%
Total	125 38.1%	203 61.9%	328 100.0%

IV. Discussion

The increasing number of therapeutic failure after treatment of *falciparum* malaria with conventional drugs are alarming and there is an urgent need to find effective drugs or drug combination suitable for immediate use when patients first seek medical care. ACTs are more expensive than the other drugs, however, as resitance to these drugs is increasing, there is need to switch to ACTs in all areas with high transmission of drug resistance *P. falciparum.* (6, 7)

The lower the average cost effectiveness ratio (ACER), the less expensive the treatment and the more efficient the therapy. The incremental cost effectiveness ratio (ICER) showed that changing from CQ/SP to Quinine/SP had an ICER of 3.6, while changing from CQ/SP to Artemisinine/SP had 1. The larger the ICER, the more money is required to buy each unit of outcome and intervention becomes less cost effective with increase in the ICER. Although ACTs are more expensive than other malaria drugs which are not ACTs, but in the long term, it proved to be most cost effective option in the treatment of malaria especially multidrug *P.falciparum* infection. (8, 9)

The drug cost analysis would identify CQ/SP as the best alternative based on price, but decisions based solely on these figures are not valid since they do not reflect the true cost picture. In the cost of therapy analysis, Artemisinine/SP emerged as the most cost-effective alternative because of its high clinical success rate. Using the ACER, which is the average cost per patient successfully treated CQ/SP had a ratio of 5.19, Quine/SP had 3.45 and Artemisinine/SP had 1.

This result confirmed the assertion that ACTS are more than 95% likely to be cost effective under most condition. In terms of cost effectiveness, Artemisinine has a potent gametocidal effect on immature early stages of stages I-IV of *falciparum* gametocytes in bone marrow and an effect on complete prevention of gametocytes that have just matured to stage V and this activity which has not been shown in any other antimalarial except Primaquine is significant for the control of infection source and reduction in the transmission of parasites from an infected person to another via mosquito bite. This will in turn reduce the number of people that will get infected with malaria and this markedly reduces the cost of malaria management on the long run. (9, 10, 11, 12)

For each drug in a cost – effectiveness analysis, the major cost factor is not primary success, but primary failure because of the necessity of using two or more treatment regimens. The cost of failure includes the cost of drugs that consist the second and third line drugs, cost of consultation and diagnosis. ACTs will reduce the overall cost of malaria treatment by eliminating initial treatment due to the present high resistance to most of the antimalarials currently in use. The direct non-medical costs include transport expenses and the indirect cost includes the loss of productivity via absence from duty by the patient's parent. Cost of failure also include loss of confidence in public health system since the patient will need to come back to complain about the same ailment. (5)

The clinical result of this study showed that the cure rate for CQ/SP was 11.0%, Quinine/SP was 22.1% and Artemisinine/SP had 97.7% cure rate. This result supports the assertion that Chloroquine containing combinations no longer provide adequate protection against *P.falciparum.* Artemisinine rapidly reduces parasitemia and SP has a long term effect in clearing residual parasites. Owing to the short elimination half life of Artemisinine (1.57hours), the chances of developing resistance appear to be low. While the short half life of Artemisinine necessitates repeated drug administration or combination therapy, it is probably the most crucial pharmacokinetic feature for delaying the development of resistance. (13, 14, 15, 16)

The result also showed that ACTs represented by Artemisinine, Pyrimethamine and Sulphadoxine met the 75% efficacy rate recommended by WHO. This result is consistent with those obtained from previous studies since it was reported from the studies leading to the adoption of ACTs as first line drugs for treatment of malaria covered only children less than 5 years of age and therefore lacked basis for generalization for the whole population.(6,8,17, 18) Artemisinine is an effective partner drug in ACTs because it is a more active therapy than the other antimalarials, reducing the number of parasites by approximately 100, 000 per asexual cycle and therefore reducing the number of parasites that are exposed to the partner drug alone. A report produced by Medicine san Frontier (MSF) strongly endorses the use of ACTS to combat malaria in Africa. (18, 19, 20, 21) Result obtained from the hypothesis test showed that there was a statistically significant difference in therapeutic effectiveness of ACTs and non-ACTs based on the results from the study since p value is less than 0.05. The hypothesis test showed that ACTs represented by Artemisinine is more therapeutically effective than the non-ACTs represented by CQ/SP and Quinine/SP.

V. Conclusion

Pharmacoeconomics evaluation has demonstrated that a more expensive per unit drug can be most effective therapeutic alternative.

VI. Aknowledgement

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