ejpmr, 2018,5(2), 537-543

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

THE EFFECT OF DIRECTLY OBSERVED TREATMENT FOR INTERMITTENT PREVENTIVE TREAMENT OF MALARIA USING SULPHADOXINE-PYRIMETHAMINE TO PREVENT ANAEMIA IN PREGNANCY AT SELECTED PRIMARY HEALTHCARE FACILITIES, PLATEAU STATE, NIGERIA

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Article Received on 22/12/2017 **Article Revised on 11/01/2018** **Article Accepted on 01/02/2018**

ABSTRACT

Malaria in pregnancy is a major public health problem in Nigeria which impacts on maternal and neonatal morbidity and mortality. Malaria induced anaemia has been found to be a complication which leads to maternal mortality. This study was aimed at determining the effect of directly observed treatment for intermittent preventive treatment of malaria using Sulphadoxine-Pyrimethamine on malaria induced anaemia. It was a quasi-experimental study conducted among 243 recruited pregnant women (119 in intervention and 124 in the control groups) attending antenatal clinics in four primary healthcare clinics of two selected LGAs of Plateau State Nigeria. The findings revealed higher education and lower parity as predictors for improved uptake of Intermittent Preventive Treatment with Sulphadoxine-Pyrimethamine. It also revealed that it was 34 times more likely to have malaria among participants who did not receive the intervention than those who did (CI = 4.56-255.93) and there was a statistically significant difference among participants who received the intervention and having a normal PCV (p=<0.001). This study concluded that through the intervention, there was a lower incidence of maternal malaria infection at delivery and therefore malaria induced anaemia when compared to the control group to ensure a healthy mother and child.

KEYWORDS: Malaria in pregnancy, malaria induced anaemia, directly observed treatment, Intermittent preventive treatment in pregnancy.

INTRODUCTION

Malaria infection during pregnancy is a significant public health problem with substantial risks for the pregnant woman, her foetus, and the newborn child.[1] Sub-Saharan Africa (SSA) has an estimate of about 30 million pregnant women who are at risk for malaria.[2] The global prevalence of malaria in pregnancy is estimated to be about 28% with about 125 million pregnancies at risk for malaria every year, and up to 200,000 babies die as a result.[2,3]

The prevalence of Malaria in Pregnancy (MiP) in different regions of Nigeria ranges from 19.7% to 72%.[4] It is an important cause of perinatal mortality, infant mortality, low birth weight, and is associated with severe maternal anaemia and placental parasitaemia, particularly in *P. falciparum* infection.[3] The effects of malaria during pregnancy include spontaneous abortion, preterm delivery, still births, low birth weight, congenital infection, severe maternal anaemia and maternal death.[5] Malaria in pregnancy still accounts for 11% of maternal deaths due to severe maternal anaemia and parasitaemia impacting on higher maternal mortality and morbidity indices.[1]

Furthermore, the Nigeria Demographic and Health Survey (NDHS) 2013, indicates that despite the stated policy of the National Malaria Elimination Program, the proportion of pregnant women who take the recommended two doses of Sulphadoxine-Pyrimethamine (SP) for Intermittent Preventive Treatment (IPTp) was only 15% even though there was a slight improvement over the 5% figure reported in the 2008 NDHS and an improvement in ANC utilization impacting on parasitaemia and therefore anaemia.[6]

Directly Observed Treatment (DOT) which has been successful in improving adherence for the management of diseases such as Tuberculosis would be valuable in increasing the uptake of IPTp-SP, increasing compliance and would result in improved effectiveness in reducing maternal morbidity due to malaria parasitaemia and anaemia.[7] This study therefore hopes to use the DOT strategy to ensure adherence of pregnant women in the

use of IPTp for the prevention of maternal malaria and anaemia. Also, findings from this study would provide valuable information to guide planning of programmes to improve the utilization of IPTp.

This study was therefore aimed at determining the effect of DOT of IPTp-SP on malaria induced anaemia among women accessing Antenatal Care in selected Primary Healthcare clinics (PHCs) in Jos, Plateau State, Nigeria.

MATERIAL AND METHODS

Study Design

The study was a quasi-experimental study for 243 pregnant women enrolled and was carried out in Pre-intervention, intervention and post intervention phases.

Study Area

Jos North and Jos South Local Government Areas (LGAs) are two of the seventeen LGAs selected purposively as both LGAs have similar characteristics for the study.

Study Population

This consisted of pregnant women accessing ANC at gestational age greater than 13 weeks and less than 28 weeks who were HIV negative and excluded Pregnant women who had known adverse drug reaction to SPs, and known haemoglobinopathies (such as sickle cell disease) in the selected PHCs of the LGA selected for the intervention and control groups.

Sample size determination

The minimum sample size of 72 was determined using the formula for determining the sample size for interventional studies.[8] An attrition rate of 20% was considered, bringing the estimated sample size to 87, and this was rounded up to 100. The same minimum sample size was used for both the intervention and control groups.

Sampling method

A multistage sampling technique was used: In the first stage Jos North and Jos South LGAs were purposively selected. The second stage was the selection of four PHCs (2 per LGAs) by balloting and the selection of participants in stage 3 by systematic sampling technique using the ANC monthly register as the sampling frame. An interval of 1 in 5, 1 in 2, 1 in 3 and 1 in 2 was calculated and used in PHC Nassarawa, PHC Angwan Rogo, PHC Bukuru central and PHC Vom Vwang respectively.

A total of 119 pregnant women were recruited into the intervention and 124 in the control group.

Data collection

A pretested semi-structured adapted interviewer administered questionnaire was used.[29] Information on the socio-demographic characteristics, obstetric history, knowledge and attitude of pregnant women to malaria, IPTp use and perception of its relevance to malaria prophylaxis was collected.

Rapid Diagnostic Test (RDT) multispecies kits were used to detect the presence/ absence of malaria parasites at baseline, after 2nd dose of SP and at delivery in peripheral blood by finger pricks. ACTs (Coartem®) was used for participants with slide-positive parasitaemia, free of charge for a three-day period, which was the approved drug for the treatment of uncomplicated malaria..

A Heitch spin PCV 2400 Centrifuge and haematocrit reader was used for Packed Cell Volume (PCV) to determine anaemia at baseline and at delivery (PCV< 30%)

Post intervention, Health education (on malaria in pregnancy, its effects on mother and child and the role of IPTp in malaria prevention) was given to all women in both intervention and control groups.

Data analysis

All the quantitative data generated was entered and analysed using the SPSS version 20 statistical package.

Chi square test was used to test associations between categorical variables and logistic regression analysis was then used in determining the strength of associations.

At 95% confidence interval, a p-value of ≤ 0.05 was considered statistically significant.

Ethical Consideration

Ethical clearance was obtained from the JUTH Health Research Ethics Committee before the commencement of the study and informed written consent was obtained from the participants before enrolment into the study. Assurance of anonymity and confidentiality of their information was also given.

RESULTS

Table-1.

Socio- demographic characteristics	Intervention (%) n =119	Control (%) n =124
Age group(years)		
<20	31 26.1	7 5.6
21-25	36 30.3	31 25.0
26-30	36 30.3	43 34.7
31-35	14 11.8	33 26.6
>35	2 1.7	10 8.1
Gestational age (months)		
>3-6	60 50.4	54 43.0
>6	59 49.6	70 56.5
Parity		
Primigravidae	43 36.1	41 33.1
Multiparous	48 40.3	65 52.4
Grand multiparous	28 23.5	18 14.5

Table 2: Proportion of women who received and used IPTp-SP while pregnant in both intervention and control groups.

Pregnant women	Groups		Fishers exact	p-value
	Intervention (%) n= 119	Control (%) n=124		
Received IPTp				
Yes	119(100.0)	122(98.4)	0.498	0.496
No	0 (0.0)	2 (1.6)		
Used IPTp				
Yes	119 (100.0)	121(99.2)	1.000	1.000
No	0 (0.0)	1 (0.8)		
Dosage of IPTp used				
1 dose only	0(0.0)	91(75.2)	0.001	<0.001
2 doses (Full)	119(100.0)	30(24.8)		
Use of IPTp under supervision(DOT)				
Yes	119(100.0)	6 (4.6)	0.000*	<0.001
No	0 (0.0)	115(95.4)		

***** *Fishers exact*

Table 3: Logistic regression showing predictors for the uptake of full dose of IPTp-SP among pregnant women in the control group.

Predictors	OR	95% C.I.	P-value
Educational status			
None/Arabic	1		
Primary	5.333	0.248 -1.166	0.483
Secondary	6.667	0.213 -1.022	0.283
Tertiary	1.650	0.979 -4.684	1.000
Parity			
Primigravidae	16.190	6.354 -18.981	0.001
Multigravidae	3.208	1.214- 5.834	0.003
Grand-multigravidae	1		

Table 4: The effect of IPTp-DOT on malaria incidence among participants in intervention and control groups.

Malaria Parasite(MP) results	Groups		χ^2	p-value
	Intervention (%) n =117	Control (%) n =123		
Maternal MP (after 2nd month)				
Present	11(9.4)	28(22.8)		
Absent	106(90.6)	95(77.2)	7.867	0.005
Total	117(100.0)	123(100.0)		
Maternal MP (At delivery)				
Present	1 (0.9)			
Absent	116(99.1)	19 (15.7) 102 (84.3)	16.965	0.001
Total	117(100.0)	123(100.0)		

Table 5: Comparison of the effect of IPTp-DOT on maternal outcome among pregnant women in intervention to the control group.

Packed Cell Volume (PCV)	Group		χ^2	p-value
	Intervention (%) n =119	Control (%) n =124		
Maternal PCV(baseline)				
<30%	3(2.6)	32 (26.0)	26.476	<0.001
≥30%	116(97.4)	92 (4.0)		
Total	119(100.0)	124(100.0)		
Maternal PCV (at delivery)				
<30%	1(0.9)	17(13.8)		
≥30%	116(99.1)	106(86.2)	14.532	0.001
Total	117(100.0)	123(100.0)		

Table 6: Logistic regression analysis of the association between IPTp-DOT and malaria parasitaemia and anaemia among women in intervention group.

Anaemia	OR	95% C.I.	p- value
Maternal PCV (at delivery) >30%			
Control group	1		
Intervention group	13.363	3.964-45.040	0.001

RESULTS

The study participants comprised of 119 pregnant women in the intervention group and 124 in the control group with an attrition rate of 2.8%. Majority of the participants in the intervention and control groups (98% and 96% respectively) were married. The pregnant women in the intervention group were between the ages of 16 and 36 years with a mean age of 25.03 ±5.17 years. Those in the control group were between the ages of 18 and 38 years with a mean age of 28.62±5.05 years.

In both groups, the gestational age of about half of the women 59 (49.6%) in the intervention group and 70 (56.5%) in the control group was 20 to 26 weeks. The difference between both groups was not statistically significant, p =0.498. There were 41(33.1%) primigravidae in the intervention group and 43(36.1%) in the control group; 65(52.4%) were multiparous in the intervention group and 48 (40.3%) in the control group. Others were grand multiparous -18(14.5%) in the intervention group and 28 (23.5%) in the control group. In terms of parity, there was no statistically significant difference between both groups, p = 0.096. (Table 1).

Majority of the pregnant women in both intervention and control groups received IPTp-SP tablets at the selected PHCs - 119(100%) and 122(98.4%) respectively. All 119(100%) women enrolled in the intervention group used the IPTp-SP under supervision (DOT) by the researchers and received the full dose (2 doses of 3 tablets each) of the IPTp-SP but only 30(24.8%) took the full dose at home in the control group. Also, supervision was reported by only 6(4.6%) pregnant women in the control group of those who used the SPs which was provided by their husband or other relatives. (Table 2).

Participants in the control group with primary education were 5 times more likely than those with no/Arabic education to adhere to the uptake of the full dose of IPTp-SP, secondary 7 times more likely and tertiary 2 times higher probability of adherence; while women who were pregnant for the first time have 16 times a higher likelihood of completing the recommended 2 doses of IPTp-SP; and multigravidae were 3 times more likely to adhere to the SPs than grand multi-gravidae which was found to be statistically significant (p- 0.001 and 0.003) (Table 3).

After the 2nd month, the cumulative incidence of malaria among pregnant women in the intervention group was 9/100 [11(9.4%)] and <1/100 [1(0.9%)] at delivery while incidence in the control group was found to be higher with 23/100 [28(22.8%)] and 16/100 [19(15.7%)] respectively. This was found to be statistically significant at both times with p-values of 0.005 and 0.001 respectively (Table 4).

The mean PCV was 35.74±3.5 for pregnant women in the intervention group and 35.2±5.2 in the control group. Thirty-two (26%) of the participants in the control group had mild anaemia at baseline with PCV <30% (range of 29% to 27%) whereas, only 3(2.6%) were mildly anaemic in the intervention group. This difference was statistically significant with a p value of <0.001. At delivery, there was also a statistically significant difference in the proportion of women in the intervention group who had mild anaemia 1(0.9%) and those in the control group 17(13.8) with p = 0.001. (Table 5).

Table 6 shows that it was 13 times more likely for participants in the intervention group compared to women in the control group to have a normal PCV ≥ 30% by using the DOT administration of the SPs.

DISCUSSION

Uptake and utilization of Sulphadoxine-Pyrimethamine for Intermittent Preventive Treatment in Pregnancy

IPTp-SP is said to be achieved when a complete dose of SP (3 tablets each i.e. 1500mg/75mg) is taken twice one month apart between 13 and 36 weeks' gestation of pregnancy (i.e. a two-dose course).[9,10] Studies in Tanzania and Uganda recorded only 43.6% and 31.3% of unsupervised pregnant women studied who received a full two-dose course of IPTp.[11,12]

This was corroborated by studies conducted in Ekiti and Kano States of Nigeria, where only 27.3% and 36.8% of the women studied received the full dose of IPTp-SP respectively at ANC.[13,14] This is in keeping with findings in the control group of this study where less than one-third of the women in the control group attending ANC in PHC Bukuru central and Vom Vwang, who claimed to have used IPTp, had a full-course of IPTp-SP despite the availability of the SPs and very few were supervised implying that the availability of SPs do not infer utilization of the full course when clients take them home.

This study revealed educational status as a predictor for utilization of IPTp-SP suggesting an increased probability of uptake and utilization of the full dose of IPTp-SP among those who had higher educational status – (secondary and tertiary education)- compared to those with none/Arabic or primary education among pregnant women in the control group. This was similar to findings in a cross sectional study of six districts in Tanzania where women with secondary or higher education were almost twice as likely as those who had never been to school to have received optimal SP doses during pregnancy (OR = 1.93, 95% CI: 1.04-3.56).[11] And in keeping with another study in urban Kano Northern Nigeria which revealed that higher educational attainment was associated with improved adherence of pregnant women attending ANC in PHCs to IPTp-SP (OR=3.2, 95%CI: 1.32-6.72).[14] However in a study of determinants of use of IPTp in Jinga, Uganda, pregnant women with lower educational status were more likely to receive the full course of SP (RR=1.56, 95%CI: 1.03-2.38) citing improved provider level factor targeting women with lower educational status as the possible reason.[12]

Studies have also shown a relationship between parity and uptake/ adherence to IPTp-SP. One of such is a study conducted among Tanzanian women where the likelihood of taking the complete dose of IPTp was higher among women who were having their 1st pregnancy compared to multigravidae and grand multigravidae.[15] This study was not different revealing that adherence to the uptake of IPTp-SP by women in the control group was associated with lower parity as more primigravidae had a higher likelihood of taking the complete dose of SP. This may be attributed to the belief by multigravidae of having more experience in pregnancy and may not think they need IPTp or require supervision.

Effect of directly observed treatment administration for Intermittent Preventive Treatment on the incidence of malaria

In 2013, The WHO evidence review group on IPTp of malaria in pregnancy stated that several randomised control studies conducted in Cote d'Ivoire, Malawi and Uganda revealed that there was a reduced incidence of clinical malaria and peripheral and placental parasitaemia among participants who received the two doses of SP as DOT.[10,16]

Although malaria parasitaemia was similar in both groups at baseline, at the second month, it was found to be less than half the baseline results- 9/100 (9.4%) among the pregnant women studied in the intervention group while incidence of malaria was 23/100 (22.8%) for women in the control group and this indicated a positive effect of DOT administration on MiP with a p-value of 0.005. At the point of delivery, when placental blood was tested for parasitaemia in both groups, incidence was <1/100 (0.9%) in the intervention group while it was 16/100 (15.7%) in the control group (p= 0.001).

This is similar to a study conducted in Uganda where reported malaria parasitaemia decreased from 39.1% at recruitment to 13.1% at delivery among women who accessed IPTp-SP via DOT at health units and found to be statistically significant.[17] However, in another study in Cote d'Ivoire, there was no statistical significant difference in malaria parasitaemia at delivery as *Plasmodium falciparum* was seen in placental impression smears for 9.8% women who had received at least two doses of SP as IPT-SP using DOT administration and for 8.2% women who did not receive IPT-SP via DOT (p = 0.39).[16] This difference may be attributed to the fact that DOT administration of IPTp was not ascertained and was only based on historical report given by the respondents unlike in this study.

Effect of directly observed treatment administration for Intermittent Preventive Treatment on the incidence of anaemia

A low PCV (< 30%) has been identified and considered a clinical indicator of placental infection with malaria parasites; IPTp-SP when administered by DOT improves compliance and ensures clearing of placental parasitaemia reducing the risk of anaemia.[18,19]

More participants in the control group in this study had mild anaemia than those in the intervention group with PCV<30% at delivery. This is similar to a few experimental studies conducted in West Africa, in which anaemia in pregnant women studied was much less, comparatively, with the administration of IPTp-SP via DOT; one of which had a prevalence of anaemia of only 5.7% versus 13.4% in the control.[19, 20]

In a randomised controlled trial conducted in Osun State Nigeria, results were slightly higher with 22.6% and 37.1% women in the intervention and control groups, respectively, having anaemia.[21] Higher values were also observed in a similar interventional study conducted in Korle-Bu Teaching hospital, Ghana with anaemia in 22.8% and 58.4% of pregnant women in the intervention and control groups respectively.[22] These slightly higher values documented may be due to the larger sample size compared to this study.

CONCLUSION

This study has shown that through improved adherence in the uptake of the full dose of IPTp-SP through the DOT administration in the intervention group, there was a lower incidence of maternal malaria infection at delivery and therefore malaria induced anaemia when compared to the control group.

RECOMMENDATION

Regular malaria and packed cell volume tests at antenatal clinic visits may be needed at PHCs by health care workers for pregnant women to aid in early detection and treatment of malaria and anaemia in pregnancy and thereby reduce associated infant and maternal morbidity and mortality.

ACKNOWLEDGEMENT

The Network on Behavioural Research for Child Survival in Nigeria (NETBRECSIN) were helpful in reviewing this research and making helpful input.

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