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Original Research Article

Patients experiences on the use of dihydroartemisinin piperaquine as an alternative first line artemisinin-based combination treatment for uncomplicated malaria in Northern Ghana

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ABSTRACT

Background: Three different artemisinin-based combination therapies (ACTs) namely; artesunate-amodiaquine, artemether-lumefantrine and dihydroartemisinin-piperaquine (being the latest to be introduced) are concurrently being used for the treatment of *falciparum* malaria in Ghana. This study assessed patients' experience, perceptions and willingness to use dihydroartemisinin-piperaquine, brand name duo-cotecxin as an alternative first line ACT for the treatment of *falciparum* malaria in Northern Ghana.
Methods: This was a qualitative study using phenomenology approach where sixty in-depth interviews were conducted with two groups; thirty patients who were given duo-cotecxin, one group and thirty interviews with patients who were given other ACTs (artesunate-amodiaquine, artemether-lumefantrine) as another group. The interviews were conducted between August and November, 2015 Purposive sampling technique was used to select study participants. The interviews were transcribed and coded into themes using QSR NVivo 11 software for thematic content analysis.
Results: All patients who used duo-cotecxin reported that the drug was very good in treating uncomplicated malaria compared to other ACTs they had used in the past. Some of the patients who used other ACTs could not complete their doses because of the side effects. However, none of the patients who used duo-cotecxin reported side effects. The findings revealed high acceptance and preference to use duo-cotecxin to treat uncomplicated malaria compared with other ACTs. All the participants were also willing to recommend duo-cotexcin to their relatives and friends to use.
Conclusions: Duo-cotecxin as an alternative first line ACT for treatment of uncomplicated malaria is highly accepted, preferred and there was willingness to use it compared with other first line recommended ACTs.

Keywords: Dihydroartemisinin piperaquine, First line, Artemisinin-based combination treatment, Uncomplicated malaria, Northern Ghana

INTRODUCTION

Malaria is a major public health problem in the world especially in sub-Sahara Africa. In 2016, about 216 million malaria cases with 445,000 deaths were reported globally.[1] About 90% of these malaria cases with 91% deaths were recorded in Africa alone.[1] Malaria remains endemic in Ghana where about 3.5 million clinical cases

are reported every year.[2] The malaria burden in the Kassena-Nankana districts of Northern Ghana is seasonal with the high transmission period occurring between June to October coinciding with the rainy season.[3,4] The malaria treatment policy in Ghana requires that artemisinin-based combination therapies (ACTs) be used for treating uncomplicated malaria.[5] This follows the recommendation by World Health Organization (WHO) in 2001 for malaria endemic countries to use ACTs for the treatment of uncomplicated malaria.[6] Though, research studies that evaluated the performance of ACTs reported side effects such as severe headache, body weakness, dizziness and vomiting,[7-10] these ACTs are very effective in treating *falciparum* malaria.[11] Dihydroartemisinin-Piperaquine is highly efficacious and there is lower risk of recurrent parasitaemia compared with other ACTs.[12-14]

Ghana changed her anti-malarial drug policy selecting Artesunate-Amodiaquine combination as the first line drug for the treatment of uncomplicated malaria in 2004.[5] However, due to certain challenges related to adverse drug reactions, two additional ACTs (Artemether-Lumefantrine and subsequently Dihydroartemisinin-Piperaquine) were introduced to cater for those who could not bear the side effects of artesunate-amodiaquine combination therapy.[5] Since then, Ghana has been using these ACTs concurrently for the treatment of uncomplicated malaria.[5,9] Evidence exist that dihydroartemisinin piperaquine is very efficacious in treating uncomplicated malaria.[15] However, data on the effectiveness of the drug has not been systematically collected. Little evidence exists on patients' acceptability and the effectiveness of using dihydroartemisinin piperaquine as the third first line ACT in treating uncomplicated malaria in real-life settings. This study assessed patients' experiences, perceptions and willingness to use duo-cotecxin as an alternative first line ACT for the treatment of uncomplicated malaria in rural Kassena-Nankana districts of Northern Ghana. The study provides information for policy direction on patients' acceptability and willingness to use duo-cotecxin in treating uncomplicated malaria compared with other ACTs.

METHODS

Study design

This was a descriptive qualitative study using phenomenology approach where in-depth interviews (IDIs) were conducted with study participants. This approach to research allows researchers to collect data on a particular phenomenon of interest as experienced by the individuals. Since this study explored experiences on the use of ACTs for the treatment of uncomplicated malaria, phenomenology was more appropriate qualitative strategy for participants to share their experiences and views in more details about the use of these ACTs to treat uncomplicated malaria.

Study site

The study was conducted in the Kassena-Nankana East and West Districts by the Navrongo Health Research Centre (NHRC). The districts cover an area of 1,675 square kilometres of Sahelian savannah with a population of about 153,000.[16] The main languages spoken in the study area are Kasem and Nankani. The population is predominantly rural with subsistence farming as the mainstay of the districts' economy. The districts have one referral hospital, eight health centers, two private clinics, which provide curative and preventive health care services to patients. There are 28 Community-based Health Planning and Services (CHPS) compounds located in various communities and villages providing health care services to people.[17,18]

The study drug

The dihydroartemisinin-piperaquine brand name duo-cotecxin that was in the market and being prescribed was used in the study. Treatment doses of duo-cotecxin is as follows: for children, 20/160 mg (duo-cotecxin) dose is given as one tablet per day for those 5 kg to <10 kg; two tablets per day for those 10 kg to <20 kg and for the adults the dosage is 40/320 mg (duo-cotecxin) administered as two tablets per day for those between 20 kg to <40 and 3 tablets per day for those ≥40 kg and all the treatment doses are taken once daily for three days.

Sampling of health facilities

The study area have been demarcated into five zones (North, South, East, West and Central) based on their geographical locations by the Navrongo Health Demographic Surveillance System.[16] Two zones (Central and South) were conveniently selected for the study. There are 10 health facilities in the two zones selected for the study. Therefore, simple random sampling technique was used to select six health facilities for the interviews. This was done by writing the names of the ten health facilities on a piece of paper each and concealed by wrapping the paper. Five people randomly selected the first five facilities, which were used to recruit the study participants for the in-depth interviews.

Sampling of respondents

Two groups (patients with malaria who received duo-cotecxin and those who received other ACTs) were selected and interviewed in this study. All qualified individuals who visited the selected health facilities, who were confirmed to have had uncomplicated malaria and were given duo-cotecxin or other ACTs during the period of data collection were selected for the in-depth interviews. These patients shared their experiences and perceptions on duo-cotecxin and other ACTs that they used during their last malaria episode.

The data collectors spent two days in each of the selected facilities and all patients with malaria who received dihydroartemisinin-piperaquine-duo-cotecxin or other ACTs (Artesunate-Amodiaquine and Artemether-Lumefantrine) were identified and followed-up at home for the interviews. All participants who were selected consented to be part of the study. The longest duration for taking ACT is three days. Therefore, all recruited participants were followed-up for the interviews on the fourth day when they were expected to have completed the full treatment of these ACTs including duo-cotecxin.

Data collection

Addresses of all qualified individuals were obtained to enable the data collectors trace them for the interviews at home. The data collectors visited the study participants and booked an appointments with them a day before the interviews were conducted. A total of 30 in-depth interviews each were conducted with individuals in each of the groups. The interviews were tape recorded after informed consent was obtained from study participants. They were conducted in Kassem, Nankani and English depending on the preferred language of the participant. The interviews were conducted between August and November, 2015.

Training of data collectors

Two university graduates with some level of experience in conducting qualitative interviews were recruited and trained for one week. Role plays were done during the training session where trainees interviewed each other in both English and the local languages and received feedback from the research team. A pre-test was conducted to evaluate their performance and to also help finalize the interview guide before the actual data collection.

Data processing and analysis

We utilized the principle of saturation for data collection in this study. Data saturation is reached where no new or additional information is being found from the interviews. Data collection, management and analysis were done concurrently. All interviews were audio-recorded and later transcribed verbatim after repeatedly listening to the recordings. The transcripts were then uploaded onto QSR NVivo 11 software to facilitate data management and coding. To ensure a fair interpretation of the data, the transcripts were initially coded by two researchers independently. Guided by the objectives of the study, the coding process involved a critical review (line-by-line) of each transcript to identify emerging themes from the data. The two independent coders then met to review the themes and agreed on the best fit interpretation of the data. The results are presented by the major and sub-themes below, supported by relevant quotes from the transcripts.

Ethical consideration

Ethical approval for the study was received from the Navrongo Health Research Centre Institutional Review Board and the Ghana Health Service Ethics Committee. Written consent was obtained from each study participant prior to being interviewed. The interview moderators read and translated the consent form into the preferred local language of each participant on the purpose of the study, study procedure, right to withdraw and confidentiality. All children from 12 to 17 years old gave assent while their parents/caretakers gave consent before the interviews were conducted. To ensure confidentiality, personal identification numbers were assigned to participants instead of their names. Consent was also obtained from study participants for the findings to be published in a peer review journal.

RESULTS

Background characteristics of the study participants

The age of the study participants was grouped into four categories. Most of the participants (25) were between 31-40 years while only seven were 41 years and above. Majority of the participants (34) were females and most of them (33) were from the Kassem ethnic group. In terms of the level of education, most of the study participants (29) had between primary to junior high education while only eight (8) of them had secondary to tertiary education (Table 1).

Table 1: Background characteristics of participants.

Category	Frequency
Age of respondents (years)	
10-20	11
21-30	17
31-40	25
41+	7
Sex	
Male	26
Female	34
Educational status	
No education	23
Primary/JHS	29
Secondary/Tertiary/Higher	8
Religion	
Traditional	13
Christian	41
Muslim	6
Ethnicity	
Kassem	33
Nankam	27
Occupation	
Trader/housewife	17
Civil/public servant	8
Farming	32
Other	3

Completion of dosage

Most of the individuals who used other ACTs reported of having completed the full treatment course given them. The reason for completion of the dosage was that they wanted their condition to get better. However, some of them said that they were not able to complete the full treatment course because of the side effects such as body weakness dizziness and lack of appetite after they had initiated the treatment. The bitter taste of the medications was also reported by participants as another factor accounting for their inability to complete the full treatment course. A 39 year old male patient shared his views this way on the issue:

R: No, it was not easy to complete it because when you take it, you become weak unless after sometime before you become okay again.

Q: What drug were you given?

R: I was given artesunate amodiaquine and I could not take all the tablets because my whole body was weak) (IDI-39 year old female patient who used other ACTs.

However, patients who used duo-cotecxin reported that it was very easy to use the drug. Almost all the individuals who took duo-cotecxin reported of having completed the full treatment course. For instance, only one person reported that he could not use all the doses with the reason that he felt better after he had taken the initial dosage. The participant shared his views this way on the issue:

Q: why didn't you take all the tablets?

R: the simple reason is that I was fine and that was why I had to stop using the drug. (IDI-28 year old male patient who used duo-cotecxin).

Experiences on the effectiveness of using ACT in treating malaria

Most of the participants who used artesunate-amodiaquine reported that the drug was very good in treating uncomplicated malaria. All respondents who completed their treatment using artesunate-amodiaquine reported feeling well on the second day of using the drug. Some of them reported that they preferred to use artesunate-amodiaquine in treating malaria as compared with artemether-lumenfantrine. The reason they gave was that though the artesunate-amodiaquine had side effects, it was very good in treating malaria compared with artemether-lumenfantrine. They added that though the artemether-lumenfantrine does not have side effects but it was less effective in treating their malaria. They also complained of the many tablets that a patient had to take when using artemether-lumenfentrine compared to artesunate-amodiaquine.

"Yes, I asked for it (artesunate-amodiaquine) because it is very effective even though it makes you weak but after the treatment you will be cured as compared with the lumenfantrine. Apart from that you take two tablets daily unlike the lumefantrine where you have to take four tablets at a go, two times daily which I don't like. I prefer fewer tablets"(IDI-29 year old female patient-who used other ACTs).

Very few participants however reported that their condition was not better after they had used artesunate-amodiaquine to treat malaria. A 47 year old female patient had this to say:

"For that one I can't say because the way I am sitting down like this I am still not feeling well and for that reason I don't know whether the drug (refers to artesuante-amodiaquine) is good or not. (IDI-47 year old female patient who used other ACTs).

All individuals who used duo-cotecxin to treat their last malaria episode before the interview reported that the drug was very good in treating their malaria. They said symptoms such as headache, cold, high temperature and general body pain that they had experienced before using the drug were all gone within the second day after they had initiated the treatment. Some of them even reported that they felt better within the first day after using the drug.

"No, no, no, I did not go to any other place for treatment, this drug has worked very well for me and so I did not take any other drug. If I have malaria again in future, I am going to look for this same drug and buy once I have the pack, I will not go to the clinic again"(IDI-45 year old male patient who used duo-cotecxin)

"Yes because of the benefits I got from using the drug. The drug is good because it has cured my malaria very well. Malaria has been my illness for a very long time and each time I treated it, it would come back but when I took this drug (duo-cotecxin), I have realized that the drug is good because I am now fine"(IDI-32 year old female patient who used duo-cotecxin).

Preferred ACT in treating uncomplicated malaria

All patients who received duo-cotecxin reported that they were ready and willing to use the drug again in future when they had malaria. The main reason participants gave was that the drug was very good and they did not experience any side effects as compared with other ACTs they had used in the past. They said that their condition was better when they used the drug and for that reason they would use it again if the same drug was given to them by health workers in future. They also mentioned that they would recommend the duo-cotecxin to their relatives and friends to use and treat their malaria.

"Yes I will use it again because it is fast action (very effective) as compared to the others that will take like a

week before you see anything changes in your condition" (IDI-18 year old patient who used duo-cotecxin)

"if you take artesunatee amodiaquine, you become very weak and might even be sent back to the hospital. And because of that, I will not select that one…. I will choose the blue one (refers to duo-cotecxin) because that one is very good because my child has recovered" (IDI-35 year old mother whose child used duo-cotecxin).

Other participants reported that they were willing to buy it at any price. They were of the view that it was better to use a drug that would work and cure your illness rather than to use a drug that would not work well for you.

DISCUSSION

It is difficult for some patients to complete their medications including ACTs because of various reasons. It was reported in previous studies that 53% of patients who used ACTs could not complete their dosages.[19] In this study, most of the individuals who used other ACTs did not complete their treatment regimen as compared to only one patient who could not complete the full treatment course using duo-cotecxin. Though some individuals were not able to complete their doses in our study, majority of the patients completed the full treatment course because they wanted their health condition to get better. Side effects such as body weakness, dizziness as well as the taste of the drug being bitter accounted for the inability of some of the patients who used other ACT to complete the full treatment course. However, those who used duo-cotecxin said that their illness or condition was better after using the initial dosage and that is the reason why they did not use the rest of the tablets. Duo-cotecxin (that was used as the study drug) had worked very well for them and that is why they had to stop using it half way through the treatment regimen. Earlier studies reported that patients who could not contain the side effects of these ACTs affected their ability to complete the treatment regimen.[7,19,20]

In Ghana, the malaria treatment policy requires that artesunate-amodiaquine, artemether-lumefantrine and dihydroartemisinin-piperaquine should be used to treat uncomplicated malaria.[5] Though, it is demonstrated that ACTs are very effective in treating uncomplicated malaria.[11] There is the need to explore perceptions of patients on the use of these ACTs for the treatment of uncomplicated malaria in real-life settings. The artesunate-amodiaquine though is effective in treating uncomplicated malaria, patients however complain about the severity of the side effects.[8,10,21] However, individuals who use both duo-cotecxin and other ACTs said that duo-cotecxin works much better than the other ACTs that they have used in the past. They perceived that the drug was effective and very easy to use compared with other ACTs.

It is reported that dihydroartemisinin-piperaquine is highly efficacious and operationally preferable to artemether-lumefantrine because of the less intensive dosing requirements.[15] There is also lower risk of recurrent parasitaemia and no side effects have been reported for those who took dihydroartemisinin-piperaquine.[7,13,22] Our findings collaborate with findings from earlier studies that demonstrated that there was minimal or no side effects using dihydroartemisinin-piperaquine in treating uncomplicated malaria compared with other ACTs especially artesunate-amodiaquine.[13]

It is therefore not surprising that all the individuals in this study who used duo-cotecxin and also used other ACTs to treat uncomplicated malaria in the past said they would prefer to use duo-cotecxin in treating their malaria. Apart from the fact that the drug has no side effects as reported by these individuals in this study, it has no bitter taste compared to the other ACTs. All the patients who took the duo-cotecxin expressed their readiness and willingness to use it to treat their malaria should they get it again. They also prefer to recommend the drug to their relatives and friends to use. Surprisingly, these individuals said they are willing to buy the drug at any price in the market and use.

Though, the other ACTs are equally good and effective in treating uncomplicated malaria, some patients are not able to complete their doses because of the severity of the side effects associated with them especially the artesunate-amodiaquine. Patients also complained of the bitter taste and the many tablets that they are usually supposed to take to complete the full treatment course as extremely difficult for them. This is not the case for the individuals who used duo-cotecxin to treat their last malaria episode. For them the drug has worked very well and has cured their illness. Therefore, duo-cotecxin as an alternative first line ACT for treatment of uncomplicated malaria is highly accepted, preferred and there was willingness to use it compared to the other first line recommended ACTs

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