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Child age or weight: difficulties related to the prescription of the right dosage of antimalarial combinations to treat children in Senegal

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ABSTRACT

Less than a year after the introduction of amodiaquine (AQ)/sulfadoxine-pyrimethamine (SP) as the first-line antimalarial treatment in Senegal, our study aimed to assess patients' drug intake and check its correspondence with nurses' prescription-adherence, the national guidelines regimen and theoretical dosage. The study was conducted at five health centers. Children aged 2–10 years who were prescribed AQ/SP by the nurse were recruited. At day 3, caregivers were questioned about treatment adherence. We collected information about nurses' prescriptions and conducted in-depth interviews on prescription patterns. Among the 289 children who were recruited, 35.3% took less than 80% of the prescribed doses. Nevertheless, 47.7% and 83.7% respectively for AQ and SP received a dosage higher than the theoretical dosage. Age-weight discrepancy leads to overprescribing drugs: nurses acknowledged using the child's age more often than weight to determine the dosage if the child has a low weight. Under and overdosing are not only due to patient practices but causes related to national guidelines and health staff practices. For successful implementation and utilization of antimalarial combinations in Africa, countries should really focus on nurses' training. National guidelines should also be based on national average weight instead of international tables.

1. Introduction

The emergence of chloroquine resistance led malaria-endemic states to change their antimalarial treatment policies by discontinuing use of chloroquine and adopting artemisinin-based combination therapy (ACT), as recommended by WHO.[1] In 2004, Senegal temporarily adopted amodiaquine (AQ)/sulfadoxine-pyrimethamine (SP) combination therapy prior to transitioning to ACT in May 2006. Combining different antimalarial molecules with different modes of action improves the drugs' effectiveness compared to drugs used individually,[2] and it decreases the risk of the emergence of resistance.[3]

Nearly all high-burden African countries have seen an unprecedented change in national drug policies in recent years; their first challenge was to provide drugs to the population, making affordable treatment available throughout the country. However, before broad utilization of ACT becomes successful throughout the African continent, the correct use of drugs must be carefully considered, particularly in terms of dosage.[4] Drug intake at a dosage below the threshold defined in effectiveness studies would expose parasites to insufficient drug concentrations,[3,4] which could contribute to an increased rate of therapeutic failures while later leading to the emergence of parasites that are resistant to these new antimalarial drugs. On the other hand, the use of excess dosages of drugs, which thus

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far are not well known, in the general population could involve side effects and contribute to the population's poor perception of the drugs, consequently risking failure of the new strategies. Until the development of a co-formulation that would considerably reduce the number of tablets to be taken, correct adherence to therapeutic regimens remains a complex phenomenon. The combination AQ/SP requires taking two drugs with different durations (1 day and 3 days of treatment respectively for SP and AQ). The ACT available in Senegal since May 2006 (Falcimon) requires an adult to take eight tablets once a day for 3 days. The population's ability to follow such a prescription is further exacerbated by the prescription's inherent difficulty, and how it corresponds to the national guidelines and the theoretical dosage determined by the pharmaceutical industry. Nurses are confronted with a new treatment for which they received very little information.[5] Will they prescribe the treatment as advised? Our study aimed to assess patient drug dosages and check the correspondence between the nurses' prescription, the national guidelines regimen and theoretical dosage.

2. Methods

2.1. Study area and population

The study was conducted in five health centers in rural areas in Mbour and Thiès departments, 90 km south-east and east of Dakar, respectively. Malaria is endemic with seasonal outbreaks. The annual rainy season is short (July–October) with malaria transmission mainly restricted to August–November. The annual average rainfall was 463 mm from 1988 to 1999. The study took place in 2004 during the rainy season.

During the study period, all children aged 2–10 years who had a fever (axillary temperature >37.5 °C) and a presumptive diagnosis of mild malaria at the consultation were identified by nurses. We received the identification form from the nurse and recruited the children the day after the last treatment dose on day 3 (D3) when we visited mothers/guardians at home to explain the study and collect their written consent. A questionnaire was addressed to each child's caregiver and accompanying adult at D3 with questions related to adherence (daily dosage, treatment duration, frequency of daily administration), how they administered drugs to the child and difficulties. In-depth interviews were also conducted with nurses to define their prescription patterns and how they used the national guidelines defined by the Senegalese National Malaria Control Program.

2.2. Definition of variables analyzed

We defined four variables: theoretical dosage, national guidelines, prescribed dosage and intake dosage.

Theoretical dosage is a function of weight and is determined by the pharmaceutical industry. Combination AQ/SP therapy consists of a single dose of SP (25 mg sulfadoxine/kg; 1.25 mg pyrimethamine/kg) on day 0, and one daily dose of AQ for 3 days (10 mg/kg/day).

The national guidelines defined five categories based on the child's age and weight: 2–11 months or 5–10 kg; 1–2 years or 10.1–14 kg; 3–5 years or 14.1–15 kg; 6–8 years or 15.1–20 kg; 9–11 years or 20.1–30 kg. A dosage has been determined for each category. Each provider received a chart showing the appropriate dosage by weight and age, as defined by the Senegalese National Malaria Control Program (Table 1).

We calculated the total dosage prescribed for 3 days from the nurses' consultation form, which they completed during the consultation.

Using questionnaire answers we calculated the children's intake dosage, i.e. the entire declared drug intake for the duration of the treatment. To measure adherence, we compared the caregiver's administration of the drugs with the nurse's prescription. We defined two adherence indicators. Firstly, we considered those who took 80% of the prescribed dose of the two drugs as adherent.[6] We totalled the entire stated drug intake and compared the total dose with the total dose prescribed by the nurse. Secondly, strict full adherence (SFA) described a patient as fully adherent to the prescription including dose, duration and frequency. Patients were required to take the daily exact dose of AQ prescribed for 3 days and the exact dose of SP prescribed on the first day.

The tablets available in Senegal at the time of the survey contained 500 mg of sulfadoxine and 25 mg of pyrimethamine for SP and 153 mg of AQ base for AQ. For syrup, one teaspoon of approximately 5 ml contained 50 mg of AQ base.

The presentation of findings is illustrated using verbatim quotations translated into English and anonymous identification of individuals (both nurses and patients) is given as source.

Table 1
Age-specific dosing schedule for sulfadoxine-pyrimethamine (SP) and amodiaquine (AQ) in Senegal

Age group	Weight (kg)	SP tablets[a]	AQ tablets[b]		
		Day 0	Day 0	Day 1	Day 2
2–11 months	5–10	0.5	0.5 or 2 tsp	0.5 or 2 tsp	0.5 or 2 tsp
1–2 years	10.1–14	0.75	0.75 or 3 tsp	0.75 or 3 tsp	0.75 or 3 tsp
3–5 years	14.1–20	1	1 or 4 tsp	1 or 4 tsp	1 or 4 tsp
6–8 years	20.1–30	1.5	1.5	1.5	1.5
9–11 years	30.1–40	2	2	2	2
12–13 years	40.1–50	2.5	2.5	2.5	2.5
>14 years	>50	3	3	3	3

[a] SP: one tablet contains 500 mg of sulfadoxine and 25 mg of pyrimethamine.
[b] AQ: one tablet contains 153 mg of amodiaquine and one teaspoon (tsp = 5 ml) contains 50 mg of amodiaquine.