Seasonal malaria chemoprevention: history, rationale and challenges

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Introduction

Seasonal malaria chemoprevention (SMC) is recommended in the Sahel: three-day courses of sulfadoxine-pyrimethamine and amodiaquine (SP-AQ) are administered to children aged 3-59 months once per month during the high transmission rainy season. Clinical trials showed a decrease in malaria incidence of up to 75% in areas receiving SMC. Despite high SMC program coverage, malaria continues to overwhelm health structures in Magaria District of Niger. We performed a series of studies in 2015 and 2016 to respond to concerns about the protective effectiveness of SMC (PE_{SMC}) in field conditions. Main results of three studies will be presented; this abstract focuses on a case-control study.

Methods

We conducted a prospective case-control study in two different areas, one receiving SMC with directly-observed (DOT) first doses and the other with non-directly-observed first doses. Cases of clinical malaria, defined as fever and a positive pLDH RDT, were enrolled at health centres. Three age-matched healthy controls were enrolled in the case's village of origin on the same day. Three additional age-matched RDT-negative controls were enrolled in the same health centre within 72 hours of the case's enrolment. Caregivers were asked about receipt of SMC, access to health care, demographics, diet and socio-economic status. Thick and thin smears were prepared and blood was collected to measure plasma levels of amodiaquine. Conditional logistic regression was used to compare cases and controls; PE_{SMC} was estimated as (1-OR)x100%.

Results

577 cases, 1700 community controls and 1233 health centre controls were enrolled between 1 August and 2 December 2016. When comparing cases to community controls, among children with a card proving receipt of SMC, PE_{SMC} against clinical malaria was 85.1% [95%CI: 78.7-89.6]. When also considering children with verbally-reported receipt of SMC, PE_{SMC} was 50.2% [27.6-65.7]. PE_{SMC} was significantly higher in the first-dose DOT zone than in the first-dose non-DOT zone, both when considering card-proven and card-or-orally-reported receipt of SMC: (with card: 96.8% [93.1-98.5] vs 59.1% [34.5-74.4]; with card or verbal report: 88.6% [77.7-94.2] vs 20.5% [-30.5-51.5]). Similar trends were seen for PE_{SMC} against microscopy-confirmed malaria. Point estimates of PE_{SMC} remained above 70% for 4 weeks after each SMC distribution.

Conclusion

SMC was efficacious, but seemed to be more efficacious in zones where the SP and the first dose of AQ were directly-observed than in the zones were no doses were directly observed. The observational nature of this study limits the strength of our conclusions, but the trends were pronounced. Analysis of plasma amodiaquine levels is ongoing and will provide important information about adherence to treatment.

Overall, SMC was efficacious, but important differences in PE_{SMC} were seen with different distribution strategies. As SMC is scaled up across the Sahel, ensuring high-quality implementation will be essential.