Low-dose primaquine for falciparum malaria

Article (Accepted Version)


This version is available from Sussex Research Online: http://sro.sussex.ac.uk/id/eprint/82270/

This document is made available in accordance with publisher policies and may differ from the published version or from the version of record. If you wish to cite this item you are advised to consult the publisher’s version. Please see the URL above for details on accessing the published version.

Copyright and reuse:
Sussex Research Online is a digital repository of the research output of the University.

Copyright and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable, the material made available in SRO has been checked for eligibility before being made available.

Copies of full text items generally can be reproduced, displayed or performed and given to third parties in any format or medium for personal research or study, educational, or not-for-profit purposes without prior permission or charge, provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.
Low-dose primaquine for falciparum malaria: authors’ reply

We read with interest the Correspondence by Kapil Goyal and colleagues1 on primaquine resistance and Eyal Meltzer and Eli Schwartz2 on primaquine metabolism by CYP2D6 in relation to our report on primaquine for transmission reduction of Plasmodium falciparum.3 The development of resistance has two discrete phases: de-novo emergence and subsequent spread. Resistance arises during asexual reproduction and not in non-replicating gametocytes. Although primaquine has been used widely for more than 60 years, including in mass drug administrations of single-dose formulations,4 no conclusive evidence exists of primaquine resistance5 in P. falciparum gametocytes. Goyal and colleagues state that drug sensitivity assays are needed to monitor gametocyte resistance to primaquine and refer to an in-vitro screening system for gametocytocidal drugs.6 This approach is unfeasible and uninformative for primaquine because the active metabolites of primaquine are unknown and the parent compound has very little activity in vitro.6 Moreover, the assay relies on a small number of gametocyte-producing laboratory parasite isolates that are unlikely to represent those in natural infections.

Primaquine might exert a strong selective advantage to the small proportion of surviving gametocytes. Meltzer and Schwartz use the term failure rate for these surviving gametocytes, linking this to the slow drug metabolism by CY2D6 in some individuals. The densities of surviving gametocytes were markedly lower than those before primaquine,1 and the drug might further affect their viability.7 Further evidence of this finding with mosquito infectivity assays would allow the investigation of primaquine failure. We agree that more data are needed for the geographical differences in CYP2D6 metaboliser phenotype, and we are establishing CYP2D6 status in our Ugandan cohort to inform primaquine policy considerations.

We declare no competing interests.

Teun Bousema, Alice C Eziefula, Helmi Pett, Chris Drakeley*
chris.drakeley@lshtm.ac.uk