Dihydroartemisinin-piperaquine: if it works for control, can we use it for elimination?

Historically, antimalarial drugs have been used at a population level in malaria-endemic areas with the objective of decreasing the burden, impact, and transmissibility of malaria. Continuous chemoprophylaxis, once experimented but never seriously considered a feasible wide-scale implementable strategy, has been superseded by the concept of intermittent treatment targeting different population groups, presenting many advantages, including non-interference with the acquisition of natural immunity against malaria. A fundamental premise for the use of any drug as part of population wide distribution efforts, besides its efficacy, is that the drug is sufficiently safe so as to not to risk endangering the healthy individuals that will be exposed to it. The artemisinin-derived combination dihydroartemisinin-piperaquine (DP), registered under the European Medicines Agency in 2011, would appear as an ideal candidate for the treatment of malaria, not only because of its high-demonstrated efficacy, but on account of its excellent tolerability and good safety profile, well reported in the literature. From a preventive point of view, the long half-life of the partner drug piperaquine conveys protection of 22 days for adult patients and around 20 days for paediatric patients, indicating a better post-treatment prophylactic effect than other combination therapies. From a preventive point of view, the long half-life of the partner drug piperaquine conveys protection of 22 days for adult patients and around 20 days for paediatric patients, indicating a better post-treatment prophylactic effect than other combination therapies.

The authors are, however, shy to extend their recommendations for the use of DP for elimination purposes. Indeed, many of the considerations that they ponder for the use of DP as IPT in restricted population groups, including repeated dosing, apply to its wider use in mass drug administration (MDA) campaigns that target the interruption of transmission. It is precisely DP’s longer-lasting post-treatment prophylactic effect that is appealing as an elimination drug, being the basis for massive use in Zambia and Mozambique in ambitious malaria elimination demonstration projects. In elimination settings, careful pharmacovigilance should be coupled to the assessment of the effectiveness of drug deployment, and inform on the occurrence of rarer safety events, so as to help build a more definitive case for the adequacy of the chosen drug for MDA. If transmission is successfully interrupted, legitimate concerns on the risks of fuelling drug resistance should become less pressing.

Pregnant women and very young children are often neglected in the assessment of the efficacy and safety of new drugs, or new uses of already existing drugs. For DP, this is not the case, and a robust portfolio of data has been compiled in recent years, both regarding the treatment and prevention of malaria during pregnancy and infancy including the recent development of a dispersible paediatric formulation (NCT01992900). The safety and pharmacological interactions of IPTp-SP need to be assessed in HIV-positive pregnant women already receiving antiretrovirals, understanding that in this particularly vulnerable group, the use of sulphadoxine-pyrimethamine is incompatible with cotrimoxazole prophylaxis.

Current WHO recommendations for the use of ACTs in pregnancy approach acceptance of ACT use throughout the entire pregnancy, because the risk-benefit ratio still favours the quick elimination of malaria infections
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in vulnerable pregnant populations. In MDA efforts, however, use of ACTs in the first term of pregnancy should not be recommended, as the risks of exposing healthy uninfected pregnant women outweigh the potential community benefits of interrupting transmission. For this reason, adequate pregnancy detection strategies are mandatory in malaria MDA efforts using ACTs.

Debate is necessary for more proactive use of drugs to achieve the immensely ambitious goal of malaria eradication, but for the time being, DP seems to be a good candidate, both for IPT and elimination purposes.

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We declare no competing interests

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