

Interactions between hormonal contraception and single or intermittently dosed rifampicin: a pharmacokinetic modelling and simulation study

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Abstract

Aim Scale up of rifampicin-based prevention regimens is an essential part of the global leprosy strategy. Daily rifampicin may reduce the effectiveness of the oral contraceptive pill (OCP), but little is known about rifampicin's effects at the less frequent dosing intervals used for leprosy prophylaxis. Since many women of reproductive age who are eligible for rifampicin-based regimens rely on OCP for family planning, additional information characterising the interaction would enhance scalability and acceptability of leprosy prophylaxis. **Methods** We used a semi-mechanistic pharmacokinetic model to predict the expected induction effect of rifampicin on OCP oral clearance (CL/F) when used for leprosy prophylaxis. Rifampicin dosing schedules were selected based on WHO-recommended and investigational leprosy prophylaxis regimens. Uncertainty in the model was explored using a scenario analysis. **Results** Hormonal contraceptive CL/F with rifampicin given as a single 600mg dose, a single 1200mg dose, or as 600mg once every four weeks was predicted to increase by a maximum of 12%, 14% and 14%, respectively, and return to baseline before the next dose. Hormonal contraceptive CL/F was predicted to increase by >20% with once-weekly and once-daily dosing of 600mg rifampicin. Using a threshold of 20%, rifampicin used for leprosy prophylaxis does not have a clinically relevant interaction with OCP. **Conclusion** These modelling study findings suggest that women using OCP can expect efficacy to be maintained with coadministration of rifampicin-based leprosy prophylaxis and should provide reassurance to stakeholders that leprosy prophylaxis need not be accompanied by any additional specific recommendation about use of OCP.

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