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Induction of cell cycle arrest and apoptosis in JAR trophoblast by antimalarial drugs

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ABSTRACT

Chloroquine, quinine, artemisinin, and pyrimethamine are generally considered safe drugs for treatment of malaria during pregnancy; however, high doses of these drugs are detrimental with adverse outcome of pregnancy. Since antimalarial drugs interaction with placental cells has not been addressed, in this study, we employed a non-radioactive proliferation assay and lactate dehyrogenase (LDH) release assays to investigate the effect of these drugs on JAR trophoblastic cell survival. All drug treatment resulted in inhibition of cell proliferation in a dose-dependent fashion (p < 0.05) with IC50 at 6.96, 6.49, 6.69, and 6.89 μ g/mL for chloroquine, quinine, artemisinin and pyrimethamine, respectively. In addition, the inhibition of cell proliferation was accompanied by increased cytotoxicity. Analysis of the progression of the cell cycle showed that these drugs triggered G0/G1 and S phase arrest. Furthermore, these antimalarial drugs induced apoptotic cell death as visualized by DNA fragmentation analysis techniques. Findings in this study revealed that cytotoxicity of these drugs on human placental trophoblast is mediated by both cell cycle arrest and induction of cell death and this could have important implications for the use of antimalarial drugs for treating malaria drugs pregnancy.

[PDF (1105K)] [References]

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