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Hydroxychloroquine and the human placenta: a systematic review and preliminary studies

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Objectives Hydroxychloroquine (HCQ), a toll-like receptor antagonist, is prescribed for inflammatory obstetric conditions such as antiphospholipid syndrome, lupus and placental lesions. Despite its use in pregnancy, understanding of the placental effects of HCQ is limited. This study aimed to collate current knowledge of the effects of HCQ on the human placenta. Further to this, it examined the effects of HCQ on amino acid transport, human chorionic gonadotrophin (hCG) secretion, syncytiotrophoblast turnover and cytokine secretion in term placental villous explants.

Methods A systematic review of literature was performed using Medline (November 2016). Placental villous explants were cultured (7 days) and treated with HCQ at therapeutically relevant concentrations (250–1,500 ng/ml) on days 4–7 or 5–7. Cell turnover was assessed by proliferation, apoptosis and syncytiotrophoblast integrity (immunohistochemistry), endocrine function by human chorionic gonadotrophin secretion (hCG; enzyme-linked immunosorbent assay (ELISA)) and nutrient transport by uptake of 3H-taurine (day 7). Cytokine release was quantified by ELISA of conditioned medium.

Results Three prior studies were identified, revealing modest protective effects in BeWo cells and primary trophoblasts. No previous studies had examined the effects of HCQ on human placental tissue. In terms of villous explants, HCQ had no adverse effects on cell turnover, nutrient transport or endocrine function, but increased secretion of interleukin 10 (IL-10).



Conclusions The systematic review identified no damaging effects of HCQ on trophoblast function, but a significant gap in knowledge regarding the effects of HCQ on the placenta remains. Our own explant studies demonstrated no adverse effects of HCQ, and suggested that HCQ may have beneficial effects by promoting the secretion of anti-inflammatory cytokine IL-10.