



Hydroxychloroquine partially prevents endothelial dysfunction induced by anti-beta-2-GPI antibodies in an in vivo mouse model of antiphospholipid syndrome

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Background

Antiphospholipid syndrome is associated with endothelial dysfunction, which leads to thrombosis and early atheroma. Given that hydroxychloroquine has anti-thrombotic properties in lupus, we hypothesized that it could reduce endothelial dysfunction in an animal model of antiphospholipid syndrome. We evaluated the effect of hydroxychloroquine in preventing endothelial dysfunction in a mouse model of antiphospholipid syndrome.

Methods

Antiphospholipid syndrome was induced by an injection of monoclonal anti-beta-2-GPI antibodies. Vascular reactivity was evaluated in mesenteric resistance arteries isolated from mice 3 weeks (APL3W) after receiving a single injection of anti-beta-2-GPI antibodies and after 3 weeks of daily oral hydroxychloroquine treatment (HCQ3W) compared to control mice (CT3W). We evaluated endothelial dysfunction by measuring acetylcholine-mediated vasodilation. A pharmacological approach was used to evaluate NO synthase uncoupling (tetrahydrobiopterin) and the generation of reactive oxygen species (Tempol).

Results

Impaired acetylcholine-mediated dilation was evidenced in mice 3 weeks after anti-beta-2-GPI antibodies injection compared to CT3W, by reduced maximal dilation ($p < 0.0001$) and sensitivity (pKd) ($p = 0.01$) to acetylcholine. Hydroxychloroquine improved acetylcholine-dependent dilation, on pKd ($p = 0.02$) but not maximal capacity compared to untreated mice. The addition of tetrahydrobiopterin ($p = 0.02$) and/or Tempol ($p = 0.0008$) improved acetylcholine-mediated dilation in APL3W but not in HCQ3W.

Conclusions

We demonstrated that endothelial dysfunction in mouse resistance arteries persisted at 3 weeks after a single injection of monoclonal anti-beta-2-GPI antibodies, and that hydroxychloroquine improved endothelium-dependent dilation at 3 weeks, through improvement of NO synthase coupling and oxidative stress reduction.

Résumé en anglais

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