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Título	Heme-induced corpus cavernosum relaxation and its implications for priapism in sickle cell disease: a mechanistic insight
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Resumo	<p>Background: Patients with sickle cell disease (SCD) experience intravascular hemolysis, leading to elevated plasma heme levels. This phenomenon has been associated with increased priapism in men with SCD. The heme group can be metabolized by heme oxygenase (HO), generating carbon monoxide (CO), which is known to promote smooth muscle relaxation via soluble guanylyl cyclase (sGC)-cyclic guanosine monophosphate (cGMP). However, the effects of heme on the relaxation responses of corpus cavernosum (CC) have not been investigated. Objectives: To evaluate the functional and biochemical effects of the heme group on mouse CC smooth muscle in vitro.</p> <p>Materials and methods: Male C57BL/6 mice were used. CC tissues were mounted in organ baths. Measurement of cGMP in mice CC was evaluated. Results: The cumulative addition of heme concentrations promoted the relaxation of CC. HO inhibitor (1J, 100 μM) or sGC inhibitor (ODQ, 10 μM) blocked the relaxing effect of the heme group. Pre-incubation of CC with heme (100 μM) enhanced relaxation induced by acetylcholine, sodium nitroprusside, and nitrenergic relaxation (electrical field stimulation), which was abolished by 1J or ODQ. The heme group increased the cGMP production in CC, which was abolished by 1J or ODQ. cGMP levels were significantly higher in CC treated with heme, and pre-incubation with compound 1J or ODQ abolished the effect of heme in raising cGMP levels. Discussion and conclusion: The HO-CO-sGC-cGMP pathway appears to play a crucial role in promoting CC relaxation. Our study provides novel insight into the role of group heme in CC relaxation and its potential contribution to priapism in SCD. Heme may serve as a pharmacological target for new therapies to prevent priapism.</p>
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