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Resumo	Sickle cell disease (SCD) is a genetic disorder that has been associated with priapism. The role of hydroxyurea, a common SCD therapy, in influencing the nitric oxide (NO)-cGMP pathway and its effect on priapism is unclear. To investigate the effect of hydroxyurea treatment on smooth muscle relaxation of corpus cavernosum induced by stimulation of the NO-cGMP pathway in SCD transgenic mice and endothelial NO synthase gene-deficient (eNOS-/-) mice, which are used as model of priapism associated with the low bioavailability of endothelial NO. Four-month-old wild-type (WT, C57BL/6), SCD transgenic, and eNOS-/- male mice were treated with hydroxyurea (100 mg/Kg/day) or its vehicle (saline) daily for three weeks via intraperitoneal injections. Concentration-response curves for acetylcholine (ACh), sodium nitroprusside (SNP), and electrical field stimulation (EFS) were generated using strips of mice corpus cavernosum. The SCD mice demonstrated an amplified CC relaxation response triggered by ACh, EFS, and SNP. The corpus cavernosum relaxation responses to SNP and EFS were found to be heightened in the eNOS-/- group. However, the hydroxyurea treatment did not alter these escalated relaxation responses to ACh, EFS, and SNP in the corpus cavernosum of the SCD group, nor the relaxation responses to EFS and SNP in the eNOS-/- group. In conclusion, hydroxyurea is not effective in treating priapism associated with SCD. It is likely that excess plasma hemoglobin and reactive oxygen species, which are reported in SCD, are reacting with NO before it binds to GCs in the smooth muscle of the corpus cavernosum, thus preventing the restoration of baseline NO/cGMP levels. Furthermore, the downregulation of eNOS in the penis may impair the pharmacological action of hydroxyurea at the endothelial level in SCD mice. This study

	emphasize the urgency for exploring alternative therapeutic avenues for priapism in SCD that are not hindered by high plasma hemoglobin and ROS levels.
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