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Título	Impact of intravascular hemolysis on functional and molecular alterations in the urinary bladder: implications for an overactive bladder in sickle cell disease
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Resumo	Patients with sickle cell disease (SCD) display an overactive bladder (OAB). Intravascular hemolysis in SCD is associated with various severe SCD complications. However, no experimental studies have evaluated the effect of intravascular hemolysis on bladder function. This study aimed to assess the effects of intravascular hemolysis on the micturition process and the contractile mechanisms of the detrusor smooth muscle (DSM) in a mouse model with phenylhydrazine (PHZ)-induced hemolysis; furthermore, it aimed to investigate the role of intravascular hemolysis in the dysfunction of nitric oxide (NO) signaling and in increasing oxidative stress in the bladder. Mice underwent a void spot assay, and DSM contractions were evaluated in organ baths. The PHZ group exhibited increased urinary frequency and increased void volumes. DSM contractile responses to carbachol, KCl, α-β-methylene-ATP, and EFS were increased in the PHZ group. Protein expression of phosphorylated endothelial NO synthase (eNOS) (Ser-1177), phosphorylated neuronal NO synthase (nNOS) (Ser-1417), and phosphorylated vasodilator-stimulated phosphoprotein (VASP) (Ser-239) decreased in the bladder of the PHZ group. Protein expression of oxidative stress markers, NOX-2, 3-NT, and 4-HNE, increased in the bladder of the PHZ group. Our study shows that intravascular hemolysis promotes voiding dysfunction correlated with alterations in the NO signaling pathway in the bladder, as evidenced by reduced levels of p-eNOS (Ser-1177), nNOS (Ser-1417), and p-VASP (Ser-239). The study also showed that intravascular hemolysis increases oxidative stress in the bladder. Our study indicates that intravascular hemolysis promotes an OAB phenotype similar to those observed in patients and mice with SCD.
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