VASCULAR HYPOREACTIVITY IN SEPSIS: INVOLVEMENT OF NITRIC OXIDE, GUANYLATE CYCLASE AND POTASSIUM CHANNELS

Jamil Assreuy, Daniel Fernandes, Regina de Sordi, Ângela Bet, Bettina Heckert and Geisson Nardi

Department of Pharmacology, Universidade Federal de Santa Catarina

Activation of guanylate cyclase (sGC) and potassium channels (KC) are thought to be important mediators accounts for several of nitric oxide (NO) effects in vessels. Therefore, we investigated the roles of sGC and KC on the NO-mediated hypotension and hyporeactivity in sepsis. Vasoconstrictive responses to phenylephrine (Phe) were reduced by 40-50% in all time periods. Twelve hours after surgery, none of potassium channels blockers reversed the hyporeactivity to Phe. Tetraethylammonium (TEA; a non-selective KC inhibitor) and glibenclamide (GLB; a selective blocker of ATP-dependent KC) reversed hyporesponsiveness to Phe 24 h, but not 12 h, after CLP. Methylene blue (MB; an inhibitor of sGC) given 8 h after CLP, reduced survival rate (from 50% to 20%). On the other hand, if injected 20 h after surgery, MB improved survival (CLP 25%; CLP + MB 55%). KC do not seem to be important for hypotension nor in the hyporeactivity to Phe 12 h after CLP procedure. Blockage of NOS1 improved the hyporeactivity towards Phe. Thus, NOS1-derived NO is important for vascular chnages in sepsis. In addition, inhibition of sGC activity and of KC operation may be useful therapeutic strategies if administered at the proper window of opportunity.

Keywords: Sepsis, nitric oxide, guanylate cyclase, potassium channel.
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