Effect of Modulation of Nitric Oxide on Rat Diaphragm Isometric Concentration and Fatigue Resistance in Hyperoxic and Hypoxic Conditions

Abstract:

The role of nitric oxide (NO) in ventillatory muscle contractile function has been under debate for several years. Moreover littleis known about NO role under hypoxicconditions and the contribution of inducible nitric oxide synthetase (iNOS) in its generation. The aim of this study was to investigate the effect of NO on the force generation and fatigue resistance of the rat diaphragm muscle under acute in vitro hypoxiaand to compare these effects to those under hyperoxic conditions. The effects of the NOS inhibitor *NG*-monomethyl-L-arginine (L-NMMA), the NO scavenger hemoglobin,and the NO donor Na nitroprusside on the maximal twitch force (Ft), submaximal tetanic force (F_{30}), maximal tetanic force (F0) and isotonic endurance time under Hyperoxic and hypoxic conditions were evaluated. Also diaphragm *iNOS* activity and nitrotyrosin level as a marker of peroxynitrite were measured. Inhibition of NO production and its scavenging using L-NMMA and Hb respectively had no effect on the diaphragm isometric contraction, the recruitment of its muscle fibers and fatigue resistance under hyperoxic condition. Hypoxia significantly reduced Ft, F_{30}F0 and fatigue resistance with increased diaphragm iNOS activity and nitrotyrosine level. Hypoxia significantly reduced ft and F0 in L-NMMA group compared to hyperoxic control one. While L-NMMA significantly increased F_{30} and decreased isotonic fatigabilityduring hypoxia concomitant with reduction ofiNOS activity and nitrotyrosin level compared to hypoxic control group. Moreover Hb induced similar results with additional significant improvement of Ft and F0. The effects of L-NMMA were prevented by co-administrationwith the NOS substrate L-arginine. On the other hand, excessive exogenous No production by Na nitroprousside markedly decreased isometric contractile and fatgue properties during both hyperoxic and hypoxia .in conclusion theseresults of this study showed that the iNO is activated in the diaphragm under hypoxia and may contribute partially to NO generation in hypoxica. Also they indicate that NO has a more prominent role in rat diaphragm under in vitro hypoxia compared to hyperoxic condition and that it contributes to the depression of force generation in the hypoxic diaphragm in vitro. Inhibition of NO generation during hypoxia may have a protective effect which could be a target in clinical conditions.

Key words: NO-diaphragm- iNO-fatigue.