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Prostaglandin F2α modulates atrial chronotropic hyporesponsiveness to cholinergic stimulation in endotoxemic rats

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Introduction: Endotoxemia induces various physiological adaptive responses such as tachycardia. There is evidence to show that inflammatory tachycardia might be linked to a direct action of prostanoids on the cardiac pacemaker cells. Recent reports have indicated that systemic inflammation may uncouple of cardiac pacemaker from cholinergic neural control in experimental animals, however, the exact mechanism of this phenomenon is uncertain. This study was aimed to explore the hypothesis that prostanoids modulate atrial chronotropic hyporesponsiveness to cholinergic stimulation in endotoxemic rats. **Methods:** Male albino rats were given intraperitoneal injection of either saline or lipopolysaccharide (LPS, 1 mg/kg). Three h after saline or LPS injection, the atria were isolated and chronotropic responsiveness to cholinergic stimulation was evaluated in an organ bath. The expression of atrial cyclooxygenases (COX)-1, COX-2 and COX-3 mRNA was assessed by quantitative real-time RT-PCR and cytosolic calcium-dependent phospholipase A_2 ($cPLA_2$) activity was measured in the atria. **Results:** The expression of atrial COX-2 mRNA and $cPLA_2$ activity increased significantly in endotoxemic atria ($P<0.05$). Incubation with prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$, 100 pM) could significantly decrease chronotropic response to cholinergic stimulation *in vitro*. Likewise, LPS injection could induce a significant hyporesponsiveness to cholinergic stimulation, and incubation of isolated atria with either indomethacin (5 μM) or AL-8810 (a $PGF_{2\alpha}$ antagonist, 10 μM) could reverse it ($P<0.01$, $P<0.05$, respectively), while SQ29548 (a thromboxane A_2 antagonist, 10 nM) was failed ($P>0.05$). **Discussion:** Our data showed that $PGF_{2\alpha}$ may contribute to the atrial chronotropic hyporesponsiveness to cholinergic stimulation in endotoxemic rats.

Keywords: Endotoxin, Chronotropic response, Prostaglandin F2α, Systemic inflammation