MELATONIN REVERSES LPS-INDUCED GASTRO-INTESTINAL MOTILITY DISTURBANCES THROUGH THE INHIBITION OF OXIDATIVE STRESS

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A growing number of evidences demonstrate that a pro-inflammatory and oxidative condition is related to the pathogenesis and the progression of endotoxin-induced septic shock in mice and that anti-oxidants may have therapeutic potential in LPS-induced sepsis. Melatonin has show to posses anti-oxidant properties in several models of inflammation in mice and rats. In the present study we focused on the possible protective mechanism of melatonin in preventing gastrointestinal disturbances induced by LPS in mice. In fact, mice treated with LPS showed a reduced gastric emptying of solid beads. Also the geometric centre, representing the relative distribution of the solid beads throughout the whole gastrointestinal tract, was significantly reduced in LPS-treated mice confirming that sepsis leads to a disturbed gastrointestinal motility in mice. Melatonin completely reversed the LPS-induced motility disturbance. This beneficial effect of melatonin is associated with a reduction in lipid peroxidation, MAPK activation, NF-kappaB activation, iNOS transcription and expression and nitrite production in intestinal tissue from septic mice. These results demonstrate that melatonin prevents the LPS-induced gastrointestinal disturbances in mice switching off the pro-oxidant pathways induced by endotoxin. Therefore it is reasonable to propose melatonin as a molecule with therapeutic potential for the treatment of systemic inflammation by interfering at the earliest step of activation of the oxidative and pro-inflammatory cascade.