Curcumin inhibits the increase of glutamate, hydroxyl radicals and PGE2 in the hypothalamus and reduces fever during LPS-induced systemic inflammation in rabbits.

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Abstract

Evidence has accumulated to suggest that systemic administration of lipopolysaccharide (LPS), in addition to elevating tumor necrosis factor-alpha (TNF-alpha), interleukin-1beta (IL-1beta), and interleukin-6 (IL-6) as well as fever, induces overproduction of glutamate, hydroxyl radicals and prostaglandin E(2) (PGE(2)) in the rabbit's hypothalamus. Current study was attempted to assess whether Curcumin exerts its antipyresis by reducing circulating pro-inflammatory cytokines and hypothalamic glutamate, hydroxyl radicals and PGE(2) in rabbits. The microdialysis probes were stereotaxically and chronically implanted into the preoptic anterior hypothalamus of rabbit brain for determination of glutamate, hydroxyl radicals, and PGE(2) in situ. It was found that systemic administration of LPS (2 microg/kg) induced increased levels of both core temperature and hypothalamic levels of both glutamate and hydroxyl radicals accompanied by increased plasma levels of TNF-alpha, IL-1beta, and IL-6. The rise in both the core temperature and hypothalamic glutamate and hydroxyl radicals could also be induced by direct injection of TNF-alpha, IL-1beta, or IL-6 into the lateral ventricle of rabbit brain. Pretreatment with Curcumin (5-40 mg/kg, i.p.) 1 h before an i.v. dose of LPS significantly reduced the LPS-induced overproduction of circulating TNF-alpha, IL-1beta, and IL-6, and brain glutamate, PGE(2), and hydroxyl radicals. Both the febrile response and overproduction of both glutamate and hydroxyl radicals in the hypothalamus caused by central administration of TNF-alpha, IL-1beta, or IL-6 could be suppressed by Curcumin. These results indicate that systemic injection of Curcumin may exert its antipyresis by inhibiting the glutamate-hydroxyl radicals-PGE(2) pathways in the hypothalamus and circulating TNF-alpha, IL-1beta, and IL-6 accumulation during LPS fever.