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Cytokine Modulation of Dopamine

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Abstract

Cytokine Modulation of Dopamine

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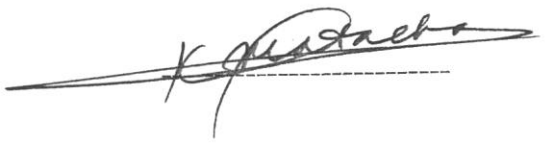
In systemic inflammation, the immune and other cells produce high amounts of pro-inflammatory cytokines that promote and initiate the inflammatory process. In severe cases, such as sepsis, inflammation leads to hypotension and organ failure. As first line vasopressor in the above cases, dopamine is administered. However, some studies have shown the immunomodulatory effects of dopamine. In the present study, more detailed experiments were planned to show the effects of dopamine (with and without dopamine antagonists) on cytokine production from human blood stimulated with different mitogens (Phytohemagglutinin (PHA), Lipopolysaccharide (LPS), or both) and from different mice tissues following administration with LPS, as a mild-moderate septicemia model.

In vitro, the results demonstrated that DA modulated cytokines production in dose dependent manner. DA enhanced significantly IL-6 production at concentrations higher than 1 pg/ml in PHA+LPS stimulated whole blood cells. This latter effect was reversed by Haloperidol stimulated whole blood cells. In addition, IL-10 production was up-regulated in LPS and PHA+LPS stimulated whole blood cells and this enhancing effect was further up-regulated by Haloperidol, Buspirone, and Clozapine. On the other hand, DA

at low concentrations (0.01 and 0.1 pg/ml) reduced IL-8 production in PHA, LPS, and PHA+LPS stimulated whole blood cells.

In vivo, co-administration of DA (0.5-50 mg/kg) with LPS modulated IL-10, IFN-γ and TNF-α production in several organs of mice. DA decreased significantly IL-10 production in blood, brain, and liver and increased its production in the lungs and spleen. D2, D3, and D4 DA receptor antagonists not only reversed DA reducing IL-10 effect in blood, and liver but also increased IL-10 production in the latter tissues, spleen and lungs. This phenomenon was not seen in the brain. DA decreased significantly TNF-α production levels in blood, brain, liver, spleen and lungs. DA antagonists, however, including Haloperidol, Buspirone, and Clozapine reversed DA reducing action on TNF-α production in blood, while Buspirone reversed such effect in spleen. On the other hand, DA decreased significantly LPS production effect of IFN-γ in blood, liver, and lungs, but not in the brain, and even enhanced IFN-γ in the spleen. In the blood, co-administration of Buspirone and Clozapine reversed the reduction effect of DA on IFN-γ production level, whereas in the liver Haloperidol and Clozapine reversed the effect of DA on the IFN-γ production. In the lungs and spleen, Haloperidol reversed the changes in IFN-γ production level that were induced by DA. In the brain, Haloperidol enhanced significantly IFN-γ production level when co-administered with LPS and DA.

The above data indicated that DA action on cytokine production differs between organs because of the differential expression of the DA receptors in these tissues and on T helper, T cytotoxic, B lymphocytes, and monocytes.

Furthermore, these patterns of cytokine modulation draw the attention of utilizing DA or DA agonists as an immunomodulatory agent in managing autoimmune mediated inflammatory diseases that are associated with lungs, spleen and brain.