P-1086 - IMPACT OF ANTIPSYCHOTICS ON THROMBOXANE PRODUCTION IN-VITRO

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Introduction: Thromboxane (TX) A2 and the activation of its receptor have been shown to modulate vasoconstriction, platelet aggregation, but also dopaminergic and serotonergic signaling. As dopaminergic and serotonergic systems play a crucial role in the pathophysiology of schizophrenia and as these systems are main targets of antipsychotics, we hypothesized that antipsychotics might also influence TXA2 production.
Methods: We measured levels of TXB2, the metabolite of the very unstable molecule TXA2, in the stimulated blood of 10 healthy female subjects in a whole blood assay using the toxic shock syndrome toxin-1 (TSST-1) and the monoclonal antibody against the surface antigen CD3 combined with the protein CD40 (OKT3/CD40) as stimulants. Blood was either supplemented with antipsychotics (chlorpromazine, clozapine, and its metabolite N-desmethylclozapine with four different concentrations each) or not.
Results: Under TSST-1 as well as OKT3/CD40 stimulation, mean TXB2 concentrations were significantly ($p < 0.05$) decreased by clozapine over all of the applied concentrations. N-desmethylclozapine led to a decrease in TXB2 levels under TSST-1 stimulation only. Chlorpromazine did not show any significant influence on TXB2 production.
Conclusions: Clozapine might, complementary to serotonin and dopamine receptor binding, act on the dopaminergic and serotonergic system via a modulation of TXA2 production. Additionally, side effects of clozapine such as orthostatic hypotension may be a result of the reported TXA2 changes.

https://doi.org/10.1016/S0924-9338(12)75253-7 Published online by Cambridge University Press