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1: Thromb Res. 1999 Jun 1;94(5):307-16.

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ELSEVIER SCIENCE FULL-TEXT ARTICLE

L-arginine modulates aggregation and intracellular cyclic 3,5-guanosine monophosphate levels in human platelets: direct effect and interplay with antioxidative thiol agent.

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Platelet nitric oxide is involved in the control of aggregability via cyclic 3',5'-guanosine monophosphate synthesis. Since L-arginine provides a guanidino nitrogen group for nitric oxide synthesis through nitric oxide synthase activity, we tried to clarify whether an increased availability of this amino acid can directly modulate the response of human platelets. In our conditions, L-arginine (at 100-6000 micromol/L) was able to influence the response of human platelets stimulated with adenosine 5-diphosphate and collagen both in PRP and in whole blood. The anti-aggregating effect was not present when D-arginine was used. Permeabilized platelets exhibited an increased sensitivity to L-arginine. Also, an increased availability of Ca2+ enhanced L-arginine effect. L-arginine (at 120-500 micromol/L) increased cyclic 3',5'-guanosine monophosphate levels in resting platelets; the amino acid also determined an increase of cyclic 3',5'-guanosine monophosphate in platelets at the end of adenosine 5-diphosphate-induced aggregation. Nitric oxide synthase inhibitor N(G)-monomethyl-L-arginine prevented L-arginine effects on aggregation and cyclic 3',5'-guanosine monophosphate synthesis. Phosphodiesterase III inhibitor milrinone and antioxidative thiol N-acetyl-L-cysteine enhanced the effect of L-arginine on cyclic 3',5'-guanosine monophosphate. In conclusion, L-arginine exerts inhibitory effects on human platelet response through a nitric oxide-dependent synthesis of cyclic 3',5'-guanosine monophosphate. A positive interplay on platelet response between L-arginine and milrinone or antioxidative thiol N-acetyl-L-cysteine was evidenced.

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