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Effective Inhibition of Platelet Deposition by cGMP-Mediated Agents vs Aspirin and Nifedipine at Sites of Vascular Injury in Rats

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Abstract

Platelets play an important role in thrombosis and arterial thromboembolism and have been implicated in atherosclerosis. Platelet adhesion occurs at sites of vascular injury, followed by activation, recruitment, aggregation and formation of thrombus. In this study, we demonstrated that cGMPmediated agents have the unique property of inhibiting platelet deposition in a rat model of vascular injury (VI). Rats were anesthetized with Inactin and injected with 0.5 ml of In-111 labeled platelets (25 pCi/rat). Thirty minutes later, a fishing nylon was introduced into the abdominal aorta via the femoral artery and advanced to the level of the renal artery. The filament was then withdrawn scratching along the aorta. The entire procedure was repeated twice to produce vascular injury (VI). Individual drug infusions were started 15 min before priming with In-111 platelets and continued throughout the study. Fifteen minutes after VI, the abdominal and thoracic aorta were removed for gamma counting. The results were expressed as ratios of the In-111 activity in the injured abdominal aorta over non-injured thoracic aorta and summarized below.

VI caused a 3.5 fold increase in In-111 activity ratio (vehicle control vs sham control), indicating marked platelet deposition on the injured abdominal aorta. Great reduction in platelet adhesion occurred in the presence of 8-Br-cGMP, zaprinast and dipyridamole (cGMP PDE inhibitor), and Na nitroprusside (a stimulator pf guanylyl cyclase). The results were confirmed with electronmicroscopic examination. In comparison, aspirin and nifedipine failed to exert significant effect on platelet adhesion. The study demonstrates that cGMP mechanism is highly effective in preventing platelet adhesion to injured vessel wall in vivo.