Title : PLATELET INHIBITION BY NITROPRUSSIDE AND NITROGLYCERIN

Authors : F.B.Allen, M.D., J.I.Gerson, M.D., F.R.Davey, M.D.

Affiliation: Departments of Anesthesiology and Clinical Pathology; SUNY Upstate Medical Center, Syracuse, New York, 13210

Introduction. A recent study by Fahmy[1] compared nitroprusside (SNP) to nitroglycerin (NTG) for the induction of controlled hypotension during total hip replacement. He reported significantly more blood loss in the group given SNP than in the group given NTG. Fahmy suggests that this is due to the slightly lower central venous pressure observed with NTG. However, recent evidence indicates that SNP is a potent inhibitor of human platelet aggregation at clinical doses and thus may significantly compromise normal hemostatic mechanisms.[2,3,4] No published data exist that describe the effect of clinical concentrations of NTG on platelet function. Therefore, we have undertaken to compare the effects of NTG and SNP on platelet aggregation in vitro.

Methods. SNP (Nipride^{R}, Hoffmann-La-Roche) and NTG for injection (Lilly) were diluted in 0.9% saline solution and protected from light. With the approval of the Committee for the Protection of Human Subjects at our institution and after obtaining informed consent, platelet-rich plasma was obtained from 7 volunteers. Plasma samples from each volunteer were incubated with various concentrations of SNP and NTG, or saline. Following incubation, aggregation studies were performed by exposure to epinephrine, adenosine diphosphate (ADP) or collagen. Results were expressed as percent aggregation compared with saline control values and plotted as dose-response curves. Individual points were compared using a paired t-test.

Results. SNP markedly inhibited ADP-induced aggregation at every concentration, to a greater extent than did NTG (TABLE 1). At the highest concentration tested, SNP significantly inhibited epinephrine-induced aggregation. This inhibition was significantly greater than that produced by NTG. No inhibition of collagen-induced aggregation was seen using either drug, in contrast to published studies of SNP[2,3,4]

Discussion. No published data exist regarding plasma levels of either SNP or NTG during intravenous infusion in man. We estimate a clinical steady state plasma level of SNP of 32 to 950 nanograms/ml by extrapolation from work in a baboon by Rodkey and Collison.[5] NTG 0.3mg sublingually achieves a peak plasma level of about 1 nanogram/ml.[6] The NTG concentrations tested, selected to equal the SNP levels, may be higher than clinical plasma levels. If so, this would tend to exaggerate any deleterious effects of NTG on aggregation.

Conclusions. We conclude that SNP has a greater deleterious effect on ADP and epinephrine-induced platelet aggregation than does NTG, at similar concentrations. This may explain Fahmy's finding of decreased blood loss using NTG when compared to SNP. In vivo testing would be necessary to confirm this.

References.

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TABLE 1: PLATELET AGGREGATION AS PERCENT OF CONTROL, MEAN± S.D.

CONC.of SNP or NTG (nanogram/ml)	SNP	NTG	N	SNP vs NTG SIGNIFICANCE
AGGREGATING AGENT: ADP				
1000	32.1±20.2	75.8±19.7	7	P .05
100	51.2±27.5	82.4±18.5	7	P .05
10	64.4±26.8	83.6±14.0	7	P .05
AGGREGATING AGENT: EPINEPHRINE				
1000	62.8±37.6	95.2± 5.1	7	P .05
100	82.0±34.7	97.0± 5.0	7	NS
10	83.9±29.5	100.4± 8.3	7	NS
AGGREGATING AGENT: COLLAGEN				
1000	93.4±12.2	100.9± 8.8	7	NS
100	100.1± 7.3	94.9± 7.3	7	P .05
10	97.1± 3.7	98.5± 5.6	7	NS