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DESMOPRESSIN DOES NOT DECREASE BLEEDING AFTER ASPIRIN

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Many patients for opern heart surgery have recently taken aspirin. While desmopressin (D) does not lessen bleeding after routine aortocoronary bypass (ACB) surgery,[1-3] data support its procoagulant effects in patients taking aspirin.[4] Since aspirin exacerbates blood loss after bypass (CPB),[5] we investigated whether D decreased bleeding in those patients who have taken aspirin.

METHODS

With IRB approval and informed consent, 82 patients for surgery utilizing CPB received randomly and in double-blinded fashion either placebo (P) or D, 0.3 μg/kg iv over 30 min following infusion of protamine after CPB. All patients received moderate dose fentanyl or sufentanil ± inhalation supplementation for anesthesia and nondepolarizing muscle relaxant. CPB utilized cold, san guinous cardioplegic arrest, systemic hypothermia to 25°C, nonocclusive roller pumps, and membrane oxygenators. Platelet count, PTT, Factor VIII:C, plasma fibrinogen, fibrinogen-fibrin split products (FSP), and D-dimer (a lytic product of cross-linked fibrin) were determined prior to skin incision and 2 hrs after protamine. Restricted forearm access prohibited measurement of bleeding time. Mass of blood drained via mediastinal tubes in the first 12 hrs after operation constituted blood loss. Mass of blood products administered in the first 12 hrs and first 5 days documented transfusion need. Two-tailed Student's t-test compared laboratory values at baseline and after operation (paired) and demographic variables among groups (unpaired). Two-way analysis of variance (ANOVA) with interaction term determined the independent contributions of aspirin and D to blood loss and transfusion requirement. $P<0.05$ determined significance.

RESULTS

Of 82 patients, 39 had received aspirin within 7 days of operation (18 group P; 21 group D) and 43 had not (20 group P, 23 group D). Groups P and D did not differ in age (63±11 yr overall), gender (55M/27F), weight (76±15 kg), CPB time (95±34 min), type of operation (68 ACB; 9 valve; 4 both; 1 ASD), or initial coagulation tests. 8 patients had a repeat sternotomy (3 group D; 5 group P). Hemodilution from CPB decreased platelet count 118,000/μL and fibrinogen 64 mg/dL (each $P<0.0001$). Coagulation parameters after operation did not differ between groups. ANOVA disclosed no effect of D alone, aspirin alone, or their interaction on 12 hr blood loss (**Table**), with 80% power to detect a true difference of ≥134 mL. Groups did not differ in blood transfused.

DISCUSSION

Follow-up studies[1-3] did not support the initial salutary effect[6] of D on bleeding after open heart surgery. While D improved the bleeding time in 10 volunteers[4] and 2 patients[7] taking aspirin, no data address its ability to counteract aspirin's effect after surgery. Yet D is often given then for a presumed hemostatic effect. With sufficient power, our data reveal no advantage of D with ($P=.91$) or without aspirin ($P=.46$). These data did not confirm the previously demonstrated increase in bleeding from aspirin therapy.[5] This difference might arise from surgical technique (patients in the current study bled less), time elapsed since last aspirin ingestion, or precision of blood loss measurement (±1g *v.* ±25 mL).

We do not recommend routine desmopressin administration to aspirin-taking patients undergoing CPB. However, aspirin-taking patients who bleed excessively after operation may benefit: these data do not evaluate the benefit of desmopressin in that context.

Table. Blood loss as mean±SD; (n)=number of patients

GROUP	(+) aspirin	(-) aspirin	Mean±SD
Placebo	542±257 (21)	478±232 (23)	509±243 (44)
Desmopressin	512±226 (18)	437±120 (20)	473±180 (38)
Mean±SD	528±240 (39)	459±188 (43)	492±216 (82)

REFERENCES

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WHAT DOSE OF TRANEXAMIC ACID IS OPTIMALLY HEMOSTATIC?

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Reluctance to administer blood products has renewed interest in the antifibrinolytic drugs tranexamic acid[1] (TA), ε-aminocaproic acid[2] and aprotinin.[3] Since the optimal dose of TA for hemostasis after cardiac surgery remains unknown, we investigated how TA dose affects bleeding in a double-blinded, dose-response model.

METHODS

With IRB approval, 65 patients for cardiac surgery gave informed consent to receive placebo (P) or one of 4 doses of TA randomly. Full-dose[4] (F) patients received 10 $mg \cdot kg^{-1}$ iv over 30 min beginning before skin incision, followed by 1 $mg \cdot kg^{-1} \cdot hr^{-1}$ for 10 hrs; Other patients received a half-dose (H, 5 $mg \cdot kg^{-1}$ followed by 0.5 $mg \cdot kg^{-1} \cdot hr^{-1}$), quarter-dose (Q, 2.5 $mg \cdot kg^{-1}$; .25 $mg \cdot kg^{-1} \cdot hr^{-1}$), or double-dose (D, 20 $mg \cdot kg^{-1}$; 2 $mg \cdot kg^{-1} \cdot hr^{-1}$). Moderate-dose fentanyl or sufentanil, with isoflurane as needed in 100% O_2, provided anesthesia. Beef-lung heparin, 400 $U \cdot kg^{-1}$ iv plus 5000 U in clear fluid pump prime, provided anticoagulation, with ACT <480 s determining the need for additional heparin. CPB utilized a non-occlusive roller pump and membrane oxygenator. Protamine neutralized heparin before (4 $mg \cdot kg^{-1}$ + 1mg / 200U extra heparin) and after (30% of 1st dose) infusion of remaining pump blood, with extra protamine to achieve ACT within 15s of baseline. Volume of blood drained via mediastinal tubes for the first 12 hrs determined blood loss. Prior to incision and 2 hr after surgery we measured aPTT, platelet count, plasma fibrinogen, plasminogen, and D-dimer titre (a marker of fibrinolysis). Daily visits sought evidence of myocardial infarction and stroke.

Analysis of variance and Tukey's HSD multiple comparison test compared demographic data, coagulation data, and blood loss data among groups, with blood loss data first undergoing logarithmic transformation. D-dimer titre comparison utilized χ^2 statistics.

RESULTS

The 5 groups did not differ in age (61±12 [SD] yr), height (68±5 in), weight (84±15 kg), gender (55M/10F), kind of surgery (50 CABG, 13 VALVE, 1 ASD, 1 CABG+AVR), number of re-operations (total 12, range 1-4), or initial coagulation profile. After operation, group affected plasminogen ($P=0.0012$: D<P;D<Q), D-dimer titre ($P=.006$, D,F,H < Q,P), and blood loss ($P=.017$, see figure). Group P bled more than group D (661 *v.* 368 mL, $P=.009$); other groups did not differ pairwise. None of the 65 patients suffered myocardial infarction or stroke after surgery.

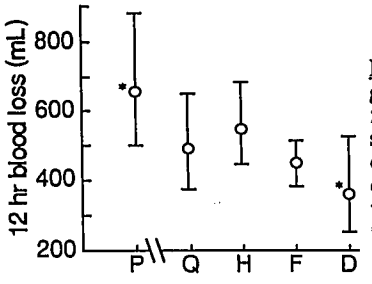

Figure: Blood loss by group. Horizontal axis from Q to D is a log-dose scale. Open circle is mean; error bars are 95% confidence intervals for back transformed data. *P=.009, groups P *v.* D

DISCUSSION

These data suggest that TA exerts a hemostatic effect by inhibiting plasminogen and limiting fibrinolysis. While they do not demonstrate progressive reduction in bleeding with increasing doses of TA, lack of sufficient statistical power is the most likely cause. Significance between the most extreme groups (P,D) supports this explanation. These data justify enrollment of additional patients and inclusion of a four-fold dose group. Like aprotinin,[3] very large doses of TA may provide better hemostatic effect.

References:

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