The effect of desmopressin on reducing blood loss in cardiac surgery: a meta-analysis of double-blind, placebo-controlled trials  
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Authors' objectives
To examine the effectiveness of desmopressin (DDAVP) as a prophylactic haemostatic agent in cardiac surgery by meta-analysis.

Searching
MEDLINE was searched from 1986 to November 1993, but no search strategy was given.

Study selection
Study designs of evaluations included in the review
Double-blinded placebo-controlled randomised trials were included.

Specific interventions included in the review
The vasopressin analogue DDAVP administered at a dose of 0.3 microg/kg. Two studies specified a maximum of 20 microg and the drug was usually infused over 15 minutes (range: 10 - 30 minutes) in 50 mL physiologic saline (range: 25 - 100 mL).

Participants included in the review
Adult patients undergoing cardiac surgery involving cardiopulmonary bypass. The actual operative procedure varied between trials and included coronary artery bypass grafting (CABG) and complex valve replacement surgery. The mean age (plus or minus the standard deviation) of the patients in the included trials ranged from 55 (+/-13) to 63 (+/-16), and overall, just under half were women (279 out of 579 patients).

Outcomes assessed in the review
Blood loss in mL. Intra-operative blood loss was measured after drug administration while the chest was open. Post-operative blood loss was measured after the chest was closed and at defined times thereafter, usually up to 24 hours. The need for transfused blood was also assessed.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
All randomised controlled trials (RCTs) included are double-blinded. No further validity assessment was carried out. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction. Where data on blood loss per square metre of body surface area were presented, authors were contacted to obtain blood loss in ml.

Methods of synthesis
How were the studies combined?
Meta-analysis: the ratio of blood loss in the treated, compared to the placebo, group was used as a measure of effect. A confidence interval (CI) was computed by log transforming the ratio in order to use a normal approximation. An overall effect estimate was then obtained by calculating a sum of all the study estimates, with individual studies weighted by the inverse squared standard error of their effect estimates. The CI for the overall effect estimate was then obtained by a normal approximation.

To examine the effect of DDAVP in patients with excessive bleeding, data on blood loss in the treated and untreated groups were correlated. A similar correlation was carried out to examine this effect using data on transfusion requirements.

How were differences between studies investigated?
Data on patients with excessive bleeding was analysed separately. Variation between studies in terms of blood loss is described briefly. No other statistical test of heterogeneity was carried out.

Results of the review
Seventeen RCTs including a total of 1,171 patients were included; of these, 579 were treated with desmopressin and 592 with a placebo.

The meta-analysis showed that DDAVP significantly reduced peri-operative blood loss by 9% (ratio 0.91; 95% CI: 0.87, 0.97). Statistical significance was reached in only 3 of 17 trials and individual study blood losses showed a substantial variation between studies. The overall ratio of transfusion requirements for DDAVP to placebo was 1.0 (95% CI: 0.9, 1.1). To examine the effectiveness of DDAVP in patients with excessive bleeding, the correlation between blood loss reduction in DDAVP- and placebo-treated groups was calculated. This showed a significant inverse correlation between blood loss in the DDAVP-treated group and the placebo group (r=-0.72, P=0.008, n=12 studies). A similar correlation was observed between blood transfusion requirements in DDAVP- and placebo-treated groups (r=-0.73, P=0.02, n=9 studies).

For studies with 24 hour post-operative blood loss measurement, DDAVP only reduced blood loss significantly in trials where the blood loss was more than 1100 ml per 24h in the post-operative period. The overall effect size in these studies was 0.66 (95% CI: 0.56, 0.77), which represents a reduction in blood loss of 34% in treated patients.

Insufficient data were available for analyses of transfusion requirements.

Authors’ conclusions
DDAVP significantly reduces blood loss, but only in cardiac operations where there is excessive blood loss. Further trials of DDAVP in cardiac patients at high bleeding risk are needed.

CRD commentary
The review appears to be methodologically sound. Although there is no formal test of heterogeneity, the heterogeneity among studies in blood loss was identified and dealt with adequately by separate analysis of an appropriate subgroup. A wider search strategy may have identified other trials, and potentially improved the precision of the overall estimates of the effectiveness of DDAVP.

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