

Title: CARDIOVASCULAR REACTIONS DUE TO HISTAMINE RELEASE DURING BONE-CEMENT IMPLANTATION FOR TOTAL HIP JOINT REPLACEMENT

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Cardiovascular reactions, occurring soon after the implantation of acrylic bone cement into the femur are common in patients with total hip replacement. Hypotension and arrhythmias are the most frequently observed symptoms. Elderly patients with fractures of the femoral neck constitute a special group of risk. In some patients these reactions can be fatal (1). Mechanism suggested to explain these reactions are embolism of air, polymer or fat, reaction to the heat and toxic or vasodilating effects of the acrylic monomer. Hypotension and arrhythmias are often observed in patients with anaphylactoid reactions caused by histamine release. We therefore performed an investigation if application of bone cement into the femur causes histamine release and if cardiovascular reactions due to the application of bone cement can be prevented by combined premedication with H₁- + H₂-antagonists.

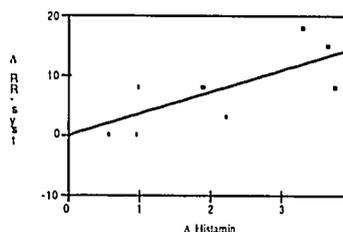
METHODS. *Part I:* After institutional approval 40 patients, submitted for elective surgical hip replacement were anesthetized by general or epidural anesthesia. Blood loss < 20 % was substituted by the administration of crystalloid fluid, while a blood loss > 20 % was followed by the administration of whole blood. Patients were continuously monitored by ECG. Blood pressure was recorded noninvasively every minute (DINAMAP). Blood samples were taken just before the application of the bone cement into the femur, and two, five and ten minutes later. Blood samples were immediately cooled in melting ice. Plasma was prepared and plasma histamine was determined fluorometrically (3).

Part II: After institutional approval 20 emergency patients with fractures of the femoral neck planned to receive a total hip replacement were randomly assigned to receive either 4 mg clemastine + 400 mg cimetidine intravenously 15 - 20 min prior to the application of the bone cement into the femur or placebo. All patients were anesthetized by general anesthesia. ECG and blood pressure were monitored as described above. Changes in systolic blood pressure and therapeutic interventions following the application of the bone cement were documented.

Statistics: Statistical analysis of the data was performed using the student-t-test on a level of significance of $p < 0.05$.

RESULTS. *Part I:* In 11 of the 40 patients (27.5 %) plasma histamine increased to > 1 ng/ml. In eight of these patients the maximum histamine release could be observed between the 5th and the 10th min. There was a direct correlation between the histamine level and the decrease in the systolic blood pressure (Figure). In a few patients we also observed

a decrease in the systolic blood pressure which was independent of the histamine release. These blood pressure falls only occurred during the first four minutes.



Part II: Emergency patients were significantly older than in group I (elective). In the placebo group blood pressure dropped significantly deeper than in elective patients and in patients treated with H₁- + H₂-antagonists (Table). In the placebo group seven of the 10 patients required therapeutic interventions, while in the verum group only one therapeutic intervention was necessary ($p < 0.05$).

	elective	emergency control	H ₁ - + H ₂ -antagonists
N	40	10	10
age (y) (x±SD)	73.7±5.2*	84.9±7.9	78.5±9.2
RRsys decrease	13.8±11.7	41.5±8.0	8.5±3.3§
RRdia decrease	8.4± 7.2	23.5±8.2	4.5±6.4§
HR increase	5.1± 5.2	9.6±11.9	4.6±3.0
therap. interventions		7	1&

* $p < 0.05$ vs emergency ; § $p < 0.01$ vs control; & $p < 0.05$ vs control

DISCUSSION: We have demonstrated that the implantation of acrylic bone cement into the femur may increase plasma histamine > 1 ng/ml. In patients with preexisting cardiac diseases or/and hypovolemia even moderate histamine release (plasma histamine level < 10 ng/ml (2)) may cause serious, sometimes deleterious cardiovascular complications. In these patients the prophylactic administration of H₁- + H₂-antagonists significantly reduced the hypotensive response due to the application of bone cement into the femur.

REFERENCES:

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