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TITLE: THE EFFECT OF MANNITOL ON RENAL FUNCTION DURING CORONARY ARTERY BYPASS

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Introduction. The incidence of renal failure post-operatively in patients who have undergone cardiopulmonary bypass (CABG) ranges from 2 to 13.5%. Mannitol (M) is commonly administered in order to help prevent acute renal failure in this setting. The purpose of this study was to determine the effect of M on both glomerular filtration rate (GFR) as estimated by inulin clearance and effective renal plasma flow rate (ERPF) as estimated by para-amino hippurate (PAH) clearance in patients undergoing CABG who were free of renal dysfunction preoperatively and who had an ejection fraction of >40%.

Methods. Eight patients scheduled for elective CABG were studied in a randomized, double blind fashion. 4 patients (3F, 1M; Age 60.5 ± 8.2 yrs) received M as an initial bolus of 12.5 grams and then at a rate of 12.5 grams/hr as a continuous infusion throughout the bypass procedure. An additional 4 patients (3M, 1F; Age 63.3 ± 15.8 yrs) received an equal volume as normal saline (S) administered in the same manner.

Boluses of PAH (8 mg/kg) and inulin (25 mg/kg) were administered 2 hrs before surgery followed by continuous infusions of each adjusted to attain final serum concentrations of .15 mg/ml inulin and .015 mg/ml PAH. Blood samples were collected and analyzed for plasma renin activity (PRA), aldosterone (aldo), atrial natriuretic peptide (ANP), PAH and inulin. Timed urine collections were analyzed for sodium, PAH and inulin.

Changes in GFR, ERPF, PRA, aldo, ANP, urine flow rate, and sodium excretion rate were compared both within and between groups utilizing standard statistical methodology. Significance was defined as a p value of < 0.05.

Results. Mean bypass duration and bypass arterial pressure were similar in each group (106 ± 36 min/ 61 ± 9 mmHg (M); 115 ± 29 min/ 64 ± 3 mmHg (S)). Other results are summarized in the table below. Significant differences in PRA, ANP, GFR, and ERPF occurred within each group. Only ANP was significantly different between groups.

Discussion. GFR and ERPF decline significantly during CABG, a decline which is not altered by M infusion. As would be expected, PRA was stimulated as renal blood flow was reduced during CABG. Elevation of ANP occurring in the placebo group may be related to differences in central pressures during and immediately following CABG.

| PRE/BYPASS/POST | | |
|---------------------------|--|--|
| | (M) | (S) |
| GFR (ml/min) | $69 \pm 46 / 25 \pm 11^* / 45 \pm 12$ | $79 \pm 4.2 / 41 \pm 16^* / 53 \pm 20$ |
| ERPF (ml/min) | $275 \pm 284 / 170 \pm 164^* / 253 \pm 70$ | $429 \pm 385 / 264 \pm 44 / 297 \pm 192$ |
| Max PRA (ng/ml/hr) | $1.8 \pm 1.5 / 3 \pm 2.1^* / 2.7 \pm 1.9$ | $.7 \pm .4 / 2.9 \pm 2^* / 2.7 \pm 1.5$ |
| Max ALDO (ng/dl) | $13.6 \pm 3.5 / 18.2 \pm 4.6 / 12.3 \pm 5$ | $9.3 \pm 1.7 / 9.5 \pm 1.8 / 12.3 \pm 5.2$ |
| Mean ANP (fmole/ml) | $28.4 \pm 17.9 / 21.9 \pm 20.1 / 12.6 \pm 5.3$ | $21.2 \pm 4.6 / 45.8^* \pm 12.6^{**} / 39^* \pm 14.2^{**}$ |
| Max Urine Rate (ml/min) | 5.9 ± 4.6 | 10.2 ± 1.9 |
| Max Na Exc Rate (meq/min) | $.5 \pm .5$ | $.6 \pm .1$ |

* Intragroup difference p < .05

** Intergroup difference p < .05

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Title: DIRECT ASSESSMENT OF MYOCARDIAL RETROGRADE CARDIOPLEGIA DISTRIBUTION DURING CARDIAC SURGERY

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Retrograde cardioplegia has gained popularity in coronary and non-coronary cardiac operations. Regional myocardial cardioplegia distribution from retrograde delivery has been described in animal models. Studies in such models with radio-labeled microspheres or contrast echocardiographic techniques have shown that cardioplegia does not typically perfuse the septum when delivered from the coronary sinus.^{1,2} The regional distribution of retrograde cardioplegia in humans, however, has not been directly characterized. We tested the hypothesis that cardioplegia distributed from the coronary sinus is delivered to all myocardial regions in humans and delivery can be assessed on-line with contrast echocardiography. We also evaluated the transmural distribution of retrograde cardioplegia by comparing the ratio of endocardial to epicardial perfusion by means of contrast echocardiography.

Methods: Institutional approval and individual informed consent was obtained to assess regional myocardial cardioplegia distribution via retrograde delivery during cardiac surgery using transesophageal contrast echocardiography in six patients. Sonicated Renografin-76 microbubbles were prepared by a method previously described³ and injected into the coronary sinus cardioplegia cannula during the infusion of cardioplegia solution. Cardioplegia flow rate was adjusted to produce a coronary sinus perfusion pressure of 40 to 50 mmHg. Regional myocardial cardioplegia distribution was noted at the time of contrast injection as continuous two-dimensional transesophageal echo images of the left ventricular short axis were recorded on videotape for off-line evaluation. The distribution of cardioplegia was determined by three independent observers based on regional myocardial contrast enhancement patterns. The relative transmural distribution of cardioplegia delivered to the endo- and epicardium was estimated off-line with quantitative contrast ultrasound. An ultrasound video acquisition program was used to measure regional contrast pixel intensity in the septum and free wall.

Average Peak Pixel Intensity by Region after Delivery of Retrograde Cardioplegia

Endocardial to Epicardial Flow Ratio

SEPTUM

$1.23 \pm 0.24^*$

FREE WALL

$1.47 \pm 0.29^*$

*P < 0.05

Conclusion: We conclude that in these six patients, cardioplegia perfused the entire myocardium (including the septal region) following retrograde delivery, and that the endocardium received more cardioplegia than did the epicardium.

1. J Thorac Cardiovasc Surg 98:1066-1076, 1989
2. Anesthesiology 73:A567, 1990
3. J Am Coll Cardiol 3:6-13, 1984