Effects of Hypertonic Mannitol on Renal Function in Open Heart Surgery

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SUMMARY

An extracorporeal bypass was performed in mongrel dogs for 2 hours with or without hypertonic mannitol infusions. In animals given mannitol, the plasma osmolality was elevated maximally to 344±7.1 mOsm/L and the urine volume was maintained well during bypass. A hypertonic mannitol solution was effective in maintaining the C_{PAH} during and after bypass, but was not effective in minimizing the reduction in Ccr. When the mean arterial pressure during bypass was kept at 60 mmHg, the carbon filling rates in glomeruli showed the favorable effects of mannitol upon renal function, but no effects were observed at a mean arterial pressure of 80 mmHg.

In 11 patients who had undergone a bypass lasting more than 2 hrs with mannitol infusions, the plasma osmolality reflected the serum mannitol level and reached 320±11.0 mOsm/L at 150 min of bypass. The mean urine volume was 5.0±3.3 ml/min/M^2 during the bypass, which was about 7 times as great as before the bypass. The Ccr increased during the first 30 min of the bypass, but it fell to about one half of the initial value after 90 min of the bypass. It was concluded that a hypertonic mannitol solution is effective in maintaining the RPF and urine volume during and after the bypass and that it also preserved the glomerular perfusion even at a low arterial pressure.

Additional Indexing Words:

Acute renal failure — Ischemic renal dysfunction — Renogram
Osmotic diuresis — Glomerular carbon filling rate

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ACUTE renal failure after open-heart surgery is a rare (1–3% of incidence)[1),2)] but often lethal complication, with a mortality rate of 80–90%. Many investigators have pointed out that extracorporeal bypass procedures, such as non-pulsatile flow,[3)] low flow rate,[4)] long timed perfusion,[5)] denaturation of plasma protein,[6)] excess hemolysis and acidosis[7)] may be factors in renal failure. During extracorporeal circulation (ECC), both the renal plasma flow (RPF) and glomerular filtration rate (GFR) have been shown to decrease markedly, even in conditions of high flow rate[8)] and high arterial pressure.[9)] The reduction in RPF and GFR are characteristic manifestations of ischemic renal damage, which may be induced by an elevation of renal vascular resistance due to a drop in arterial pressure,[10)] a non-pulsatile flow rate[11)] and a renal reflex.[12)]

A number of procedures[13)–15)] have been employed to protect renal function during bypass surgery. In our Department of Thoracic Surgery, a hypertonic mannitol (20% D-mannitol) solution has been administered routinely during ECC in order to prevent ischemic renal dysfunction, with a good success rate. Hypertonic mannitol is a strong osmotic diuretic. In 1961, Barry et al[16)] reported that it prevents postoperative renal insufficiency after abdominal aneurysmectomy. Similarly, Porter et al[17)] administered hypertonic mannitol successfully to minimize hemolysis during ECC. This report is concerned with clinical and experimental investigations on effects of hypertonic mannitol upon renal function during and after ECC.

Experimental Investigation Methods

Twenty-six mongrel dogs, weighing 8 to 20 Kg, were anesthetized intravenously with sodium thiopental. An endotracheal tube was inserted and connected to a volume-limited respirator. After median sternotomy, the usual ECC circuit with a bubble oxygenator and roller pump was set. The venous blood drawn from the right ventricle was oxygenated and infused into the right femoral artery. The main pulmonary artery was clamped. A vent cannula was inserted into the left ventricle to prevent the lung congestion caused by blood inflow from bronchial arteries and the blood was drawn into the oxygenator. The arterial pressure was monitored through a catheter in the thoracic aorta. A lower median laparotomy was performed and a thin catheter was inserted into each ureter to collect urine. The abdominal wall was then closed. The bypass circuit was primed with a mixture of freshly drawn heparinized homologous blood, Ringer's lactate solution and either a 20% D-mannitol solution or a 10% maltose solution, adjusted to a hemodilution rate of 25%. Chlorpromazine hydrochloride (1 mg/Kg) was adminis-

tered to the animal before ECC and the same dose was added to the bypass circuit 1 hour after the onset of ECC. Heparin was injected intravenously at an initial dose of 3 mg/Kg, followed by 1 mg/Kg/hr. During ECC the arterial blood pH was kept between 7.4 and 7.5, and esophageal temperature was at 37°C. Fifty mg of creatinine and 80 mg of para-amino hippurate were added initially to the priming fluids. This was followed by 2 mg of creatinine and 5 mg of para-amino hippurate every 30 min.

The dogs were divided into 4 groups according to the dosage of mannitol:

Group 1 (5 dogs): 10 ml/Kg of mannitol in the priming solution and a drip infusion of mannitol (10 ml per total circulating blood volume (dl) per hour) during ECC.

Group 2 (8 dogs): 5 ml/Kg of mannitol and 10% maltose solution, respectively, in the priming solution and a drip infusion of both solutions (each 5 ml per total circulating blood volume (dl) per hour) during ECC.

Group 3 (8 dogs): 10 ml/Kg of 10% maltose solution in the priming solution and a drip infusion of maltose (10 ml per total circulating blood volume (dl) per hour) during ECC.

Group 4 (5 dogs): hourly administration of furosemide (2 mg/Kg) during and after ECC under the same conditions as Group 3.

After 2 hours of ECC with a mean arterial pressure of 80 mmHg (at a flow rate of 80–100 ml/Kg/min), the systemic circulation was returned to the animal's heart and was maintained for 2 hours. The blood and urine were sampled every 30 min throughout the experiment. In 5 animals from each group, both kidneys were perfused with 300 ml of warm (37°C) Ringer's lactate solution through catheters in both renal arteries after completion of the experiment, followed by perfusion with 200 ml of a 5% suspension of carbon particles in warm Ringer's lactate solution at 100 cmH_2O pressure to investigate the glomerular carbon filling rate.[18] Histological sections were stained with hematoxylin and eosin. In the 3 other dogs in Groups 2 and 3, an I^{131}-labeled Hippuran renogram was recorded before, during and 2 hours after ECC. All values in this report are shown as mean values$\pm$SD and the statistical differences were assessed with Student's t-test.

Results

Serum mannitol and plasma osmolality

The serum mannitol level in Group 1 was more than twice as high as in Group 2, and the urinary excretion of mannitol was high and continuous in these 2 groups. The plasma osmolality corresponded to the dose levels of mannitol and the highest value was found in Group 1 (maximum 345 mOsm/

Table I. The Results of the Animal Experiments

		Before ECC	During ECC				After ECC			
			30 min	60 min	90 min	120 min	30 min	60 min	90 min	120 min
Serum Mn (mg/ml)	G 1	0	10.8± 2.2	11.5± 1.8	12.4± 1.0	15.0± 3.2	15.9± 2.1	15.2± 2.2	13.2± 2.5	12.4± 1.7
	G 2	0	4.7± 0.8	5.4± 0.6	5.3± 0.6	5.6± 0.8	6.5± 1.2	6.1± 1.2	5.9± 1.0	5.4± 1.1
	G 3	—	—	—	—	—	—	—	—	—
	G 4	—	—	—	—	—	—	—	—	—
Plasma Osm (mOsm/L)	G 1	294 ± 6.1	325 ±10.5	330 ± 8.2	341 ± 6.6	344 ± 7.1	343 ± 7.2	344 ± 7.6	345 ± 7.2	345 ± 6.8
	G 2	290 ± 6.2	309 ± 4.8	313 ± 4.9	313 ± 4.4	320 ± 5.5	324 ± 6.2	323 ± 5.9	321 ± 4.8	322 ± 5.3
	G 3	282 ± 6.4	296 ± 5.3	297 ± 4.9	299 ± 5.0	304 ± 5.7	302 ± 3.6	300 ± 3.6	296 ± 4.8	299 ± 3.1
	G 4	292 ± 5.3	294 ± 4.0	295 ± 4.2	297 ± 3.9	299 ± 3.3	303 ± 4.5	304 ± 3.5	304 ± 3.3	304 ± 4.2
Urine Mn (mg/ml)	G 1	0	55.4±25.1	145.5± 74.0	140.4±51.8	116.7±43.2	187.3±108.3	220.8±78.6	220.9±75.5	206.5±49.4
	G 2	0	52.4±25.0	86.7± 22.7	76.0±32.4	87.2±30.6	125.8± 64.3	117.1±34.3	140.4±42.5	109.4±28.7
	G 3	—	—	—	—	—	—	—	—	—
	G 4	—	—	—	—	—	—	—	—	—
Urine Osm (mOsm/L)	G 1	948 ±94	452 ±45	401 ± 54	401 ±34	381 ±23	393 ± 19	389 ±24	387 ±18	398 ±22
	G 2	843 ±42	570 ±87	398 ± 57	362 ±37	369 ±22	359 ± 22	361 ±27	359 ±36	362 ±21
	G 3	943 ±81	585 ±91	381 ± 44	351 ±26	349 ±22	338 ± 19	334 ±25	331 ±15	343 ±24
	G 4	896 ±51	578 ±79	465 ±101	451 ±81	415 ±62	365 ± 43	365 ±37	364 ±39	381 ±41
Ccr ((ml/Kg/min)	G 1	3.4± 0.9	0.8± 0.3	1.0± 0.4	0.8± 0.2	0.8± 0.2	0.8± 0.3	1.0± 0.3	1.0± 0.3	1.1± 0.3
	G 2	3.7± 0.7	0.9± 0.2	1.1± 0.4	0.8± 0.3	0.8± 0.3	0.8± 0.3	1.0± 0.3	1.2± 0.4	1.4± 0.4
	G 3	3.7± 1.5	0.7± 0.2	0.3± 0.2	0.5± 0.3	0.5± 0.1	0.7± 0.2	0.8± 0.2	0.9± 0.2	1.0± 0.3
	G 4	3.5± 0.7	0.6± 0.3	0.6± 0.1	0.6± 0.1	0.6± 0.2	0.7± 0.2	0.8± 0.4	0.8± 0.4	0.8± 0.4

Mn = mannitol; Osm = osmolality; Ccr = creatinine clearance.

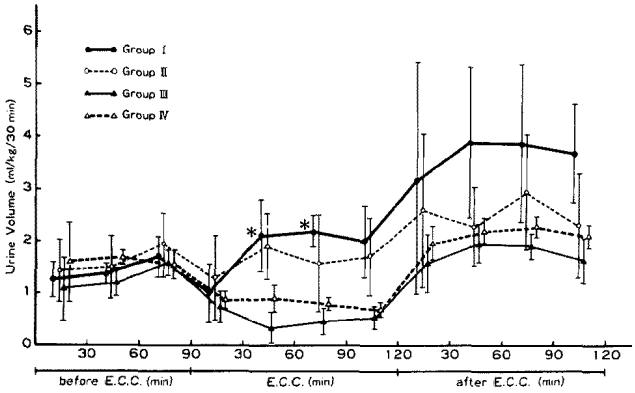

Fig. 1. Urine volume. The urine volume in Group 1 was significantly ($p<0.05$) greater than in Groups 3 and 4 during the second and third (30 min) segments of ECC.

L). The plasma osmolality was also higher in Group 2 (324 mOsm/L) than in Groups 3 (304 mOsm/L) and 4 (304 mOsm/L) (respectively $p<0.01$), both during and after ECC (Table I).

Urine volume

During the first 30 min of ECC, the urine volume was usually reduced in all 4 groups; the reduction was especially significant in Groups 3 and 4 (both $p<0.05$). Afterwards, the urine volume showed a steady recovery in Groups 1 and 2, but it remained low in Groups 3 and 4 during ECC. There were significant differences between Group 1 and Groups 3 and 4 in the second and third 30 min periods (respectively $p<0.05$). After cessation of ECC, the urine volume increased markedly in all groups (Fig. 1).

Creatinine clearance (Ccr)

With the onset of ECC, the Ccr decreased markedly in all groups. It fell to about 23% of values before ECC in Groups 1 and 2, and about 18% of the original values in Groups 3 and 4. The values remained low, and 120 min after cessation of ECC they remained at 32% of the initial value in Group 1, 38% in Group 2, 27% in Group 3, and 23% in Group 4. There were no statistical differences between groups (Table I).

Para-amino hippurate clearance (C_{PAH})

During the first 30 min of ECC, the C_{PAH} usually decreased in all groups, reaching 34% of the value before ECC in Group 1, 51% in Group 2, 29% in Group 3, and 26% in Group 4. During the next 30 min, the C_{PAH} increased in Groups 1 and 2. However, it decreased further in Group 3 and remained low in Group 4. After 60 and 90 min of ECC, the C_{PAH} was significantly higher in Groups 1 and 2 than in Groups 3 and 4 ($p<0.05$). After cessation of ECC, the C_{PAH} increased in all groups and it recovered significantly in

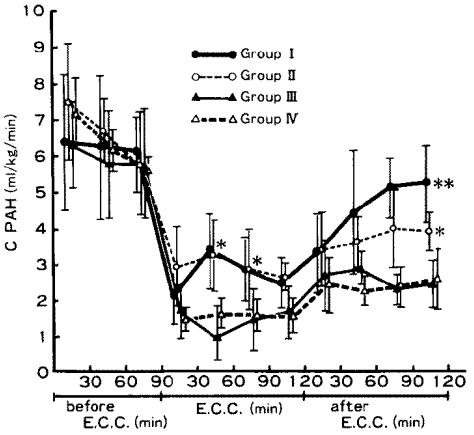

Fig. 2. Para-amino hippurate clearance (C_{PAH}). In the second and third (30 min) segments of ECC, the C_{PAH} in Groups 1 and 2 was higher than in Groups 3 and 4. After cessation of ECC, the recovery of C_{PAH} was most prominent in Group 1 and more significant in Group 2 than in Groups 3 and 4 (** $p<0.01$, * $p<0.05$, compared to Groups 3 and 4).

Groups 1 and 2 (86% and 69% of value before ECC respectively) after 2 hours. However, C_{PAH} remained significantly lower (43% and 46% respectively) in Groups 3 and 4 than in Groups 1 ($p<0.01$) and 2 ($p<0.05$) after cessation of ECC (Fig. 2).

Serum electrolytes and urinary excretion

In all groups, the serum sodium levels decreased and urinary excretion dropped markedly during ECC, to one fourth to one eighth of the initial values. After cessation of ECC, both serum and urinary sodium levels in-

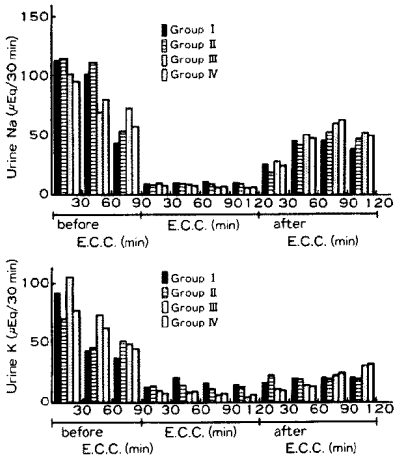

Fig. 3. Urinary excretion of sodium and potassium. During ECC, both sodium and potassium excretion dropped markedly in all 4 groups.

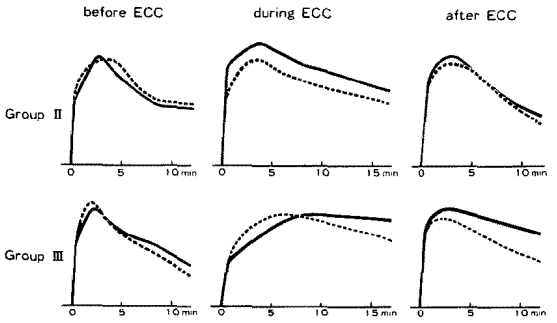

Fig. 4. Typical renograms from animal in Groups 2 and 3. The solid line reveals the left and the dotted line the right kidney. In Group 2: Before ECC, left kidney (L): Tmax 2'30'', Tl/2 9'00''. right kidney (R): Tmax 3'20'', Tl/2 9'00''. During ECC, L: Tmax 3'40'', Tl/2 not measured. R: Tmax 2'40'', Tl/2 not measured. After ECC, L: Tmax 2'00'', Tl/2 8'50''. R: Tmax 3'50'', Tl/2 7'20''. In Group 3: Before ECC, L: Tmax 2'00'', Tl/2 8'00''. R: Tmax 1'50'', Tl/2 6'00''. During ECC, L: Tmax 10'10'', Tl/2 not measured. R: Tmax 5'40'', Tl/2 not measured. After ECC, L: Tmax 2'30'', Tl/2 13'00''. R: Tmax 1'40'', Tl/2 11'10''.

creased gradually and approached the levels before ECC. The serum potassium level fell gradually throughout the experiment in all groups, finally dropping to 2.8 mEq/L in Group 1. Urinary potassium excretion decreased markedly during ECC in all groups. Although more potassium was excreted in Groups 1 and 2 (with mannitol) than in Groups 3 and 4 (without mannitol) during ECC, there were no statistically significant differences in serum and urinary potassium levels (Fig. 3).

Renograms

Renograms were recorded in Groups 2 and 3. During ECC, Tmax and $T^1/_2$ in Group 3 were markedly prolonged in contrast with Group 2. After ECC, Tmax return to normal in both groups but $T^1/_2$ still showed a marked prolongation in Group 3 (Fig. 4).

Glomerular carbon filling rates and histological findings

The percentages glomeruli filled with carbon out of up to 50 glomeruli in the upper and lower poles of the kidney were $77\pm15.9\%$ in Group 1, $79\pm8.7\%$ in Group 2, $70\pm15.6\%$ in Group 3, and $66\pm14.6\%$ in Group 4. There were no significant differences between groups.

Glomerular degeneration, degeneration and swelling of tubules and interstitial edema were not observed commonly in any group. In Group 3, though, cylinder formation was observed in the proximal tubules.

Clinical Investigation Methods

Eleven patients who underwent open heart surgery with ECC for longer than 2 hours were selected for the study (Table II). The average perfusion time was 2 hours and 42 min and the longest (in Case 8) was 4 hours and 39 min. In these patients, ECC was performed routinely with a bubble oxy-

Table II. Eleven Patients Who Underwent Open Heart Surgery with ECC for Longer than 2 Hours

Case	Age	Sex	Diagnois	Bypass Time	
1.	29	male	MR	130 min	alive
2.	11	male	VSD	193 min	alive
3.	36	female	AI	230 min	died
4.	29	female	AI	158 min	alive
5.	51	male	AI	137 min	alive
6.	47	female	angina	154 min	alive
7.	5	male	TAPVC	127 min	alive
8.	51	male	angina	279 min	alive
9.	13	female	Fallot	123 min	alive
10.	9	female	Fallot	126 min	alive
11.	42	male	MR	131 min	alive

MR=mitral regurgitation; VSD=ventricular septal defect; AI=aortic insufficiency; angina =angina pectoris; TAPVC=total anomalous pulmonary venous connection; Fallot=tetralogy of Fallot.

Table III. The Results

	Before ECC	During ECC			
		30 min	60 min	90 min	120 min
Hematocrit (%)	44 ± 2.8	26 ± 2.5	26 ± 2.8	25 ± 3.1	25 ± 3.5
Plasma Osm (mOsm/L)	278 ± 7.5	303 ± 8.3	305 ± 8.8	313 ± 11.7	313 ± 9.9
Urine Osm (mOsm/L)	546 ±194.6	423 ± 76.6	362 ± 44.6	360 ± 46.7	379 ± 50.5
Serum Mannitol (*mg/dl*)	0	6.9± 0.97	7.5± 0.97	8.5± 1.65	9.1± 1.16
Urine Mannitol (*mg/M²/min*)	0	0.7± 0.31	1.8± 0.98	1.7± 1.19	2.4± 1.25
Urine Vol (*ml/M²/30 min*)	0.7± 0.49	3.0± 1.72	6.4± 3.60	5.2± 3.74	5.2± 2.71
Ccr (*ml/M²/min*)	75 ± 23.9	108 ± 49.0	60 ± 34.3	31 ± 19.7	38 ± 25.8
Urine Na (*μEq/M²/min*)	39 ± 30.5	183 ±213.8	443 ±399.6	293 ±265.6	316 ±366.6
Urine K (*μEq/M²/min*)	24 ± 11.9	73 ± 45.4	72 ± 44.0	66 ± 24.7	80 ± 49.2

Osm=osmolality; Urine Vol=urine volume; Ccr=creatinine clearance.

genator and roller pump, and the flow rate was maintained at 2.4 L/min/M² and the temperature at 30°C. Selective coronary perfusion with blood was adopted in 3 patients for myocardial protection during ECC, (Cases 3, 4, and 5). In 8 other patients, topical cooling with an icc slush of Ringer's lactate solution and intermittent coronary perfusion by aortic declamping were performed. The 20% D-mannitol solution was added to the priming fluid and was infused into the bypass circuit by the same methods as in the experimental animals in Group 2.

Results

One patient (Case 3) died of low cardiac output syndrome. She had received usual cardiopulmonary bypass for 230 min and, after a short time interval, received an assisted partial bypass without mannitol infusion for 190 min.

In all patients, the plasma osmolality reflected the serum mannitol level and increased progressively with bypass time. It reached 320 mOsm/L after 150 min of the bypass procedure, and it was 329 mOsm/L after 180 min of bypass in 3 patients. Postoperatively, the plasma osmolality and serum mannitol level decreased with good urinary excretion, and reached 293 mOsm/L and 1.1 mg/dl, respectively, 17 hours after bypass (Table III). The mean urine volume was 5.0±3.3 ml/min/M² during bypass, which was about 7 times as great as the value before bypass. After bypass, the administration of

from 11 Patients

	After ECC				
150 min	1 hr	4 hrs	7 hrs	10 hrs	17 hrs
24 ± 4.9	39 ± 0.7	39 ± 3.6	37 ± 3.4	37 ± 1.6	37 ± 2.3
320 ± 11.0	305 ± 20.7	306 ± 8.6	303 ± 3.1	302 ± 14.0	293 ± 17.7
365 ± 31.4	353 ± 44.8	456 ±116.5	472 ±143.4	562 ±222.3	605 ±244.6
9.5± 0.29	8.0± 1.34	6.1± 1.06	3.7± 1.88	2.3± 1.91	1.1± 1.29
2.5± 1.48	3.5± 0.84	2.1± 0.70	0.9± 0.41	0.6± 0.21	0.3± 0.17
5.9± 3.47	10.3± 2.75	4.1± 0.61	1.9± 0.61	1.3± 0.42	0.9± 0.36
41 ± 14.3	45 ± 17.9	37 ± 18.4	38 ± 23.8	50 ± 36.7	57 ± 32.7
413 ±357.8	1,135 ±736.2	239 ±227.0	169 ±175.4	65 ± 53.0	78 ± 67.1
93 ± 27.5	136 ± 63.7	60 ± 26.0	68 ± 47.3	77 ± 48.4	96 ± 43.7

fluid was restricted to elevate hematocrit, and the urine volume decreased gradually. No other diuretics were generally used.

The blood urea nitrogen (BUN) did not change before, during, and after bypass. However, the urine urea nitrogen (UUN) dropped abruptly with the beginning of the bypass from 537 mg/dl to 297 mg/dl. It fell to 41 mg/dl after 150 min of bypass, and returned to the level before bypass within 17 hours of the end of the procedure. The endogenous creatinine clearance (Ccr) decreased during bypass, except during the first 30 min. It did not recover well, reaching only 57 ml/min (76% of the value before bypass) at 17 hours after the bypass procedure. The Ccr in 24 hours' urine was 94.8±30.2 ml/min before the operation, 69.2±36.6 ml/min on the first, 90.8±39.8 ml/min on the second, and 96.7±37.5 ml/min on the third postoperative day. Both serum sodium and potassium levels decreased slightly during the bypass, but returned to normal. The urinary excretion of electrolytes was always much greater during and after the bypass than that before the bypass procedure.

Discussion

With the exception of nephrotoxic substances,[19] the most important cause of acute renal failure after open heart surgery may be renal ischemia, manifested by reductions in RPF and GFR. Hypertonic mannitol is a strong osmotic diuretic which has been shown to increase the RPF and GFR without a significant increase in the blood volume.[20] Microscopic examinations of the kidney demonstrated that the administration of mannitol during ECC resulted in good preservation of the proximal tubular epithelium[21] and prevented the formation of casts.[18),22] On the other hand, Etheredge et al[23] described a reduction in GFR during ECC in spite of the administration of mannitol.

In our clinical study, a hypertonic mannitol solution was used prophylactically to prevent renal ischemia. Our dosage was much greater than those of Schuster[24] and Etheredge.[23] The plasma osmolality in our series reached 313±9.9 mOsm/L at 120 min of bypass and 320±11.0 mOsm/L at 150 min of bypass, while it was only 280–290 mOsm/L in the report of Etheredge. The experimental study also showed significant increases in plasma osmolality and urine volume in the groups given mannitol during bypass procedures.

In clinical cases, the creatinine clearance (an index of GFR), increased during the first 30 min of bypass. However, it declined to very low values at 17 hours after the bypass. Furthermore, Ccr in total daily urine did not recover until the third postoperative day. On the other hand, the Ccr in

animals dropped markedly throughout the experimental procedures. It was not affected by administration of mannitol or furosemide and was accompanied by a significant reduction in the urinary excretion of electrolytes. This reduction in electrolyte excretion may be caused by a reduction in GFR without a concurrent increase in urine volume.

The para-amino hippurate clearance (an index of RPF), showed a favorable effect of mannitol during and after bypass in animals. The time to peak (Tmax) in renograms, reflecting the renal blood supply and functional integrity of tubular cells was prolonged in Group 3 (without mannitol) as compared with Group 2 (with mannitol). As mentioned by Stahl et al[19] and Lilien et al,[26] we have shown that a hypertonic mannitol solution maintains a high RPF during the bypass. In our preliminary experiments, performed in the same manner as these studies but with the mean arterial pressure of 60 mmHg during bypass, the glomerular carbon filling rate was 69.6± 13.4% in animals corresponding to Group 1, 68.3±12.7% in Group 2, 41.0± 14.1% in Group 3, and 36.0±9.5% in Group 4. The carbon filling rate was significantly higher in animals with mannitol than without mannitol ($p < 0.05$). When the arterial pressure was kept at 80 mmHg during bypass, there were no significant differences in the carbon filling rate between animals with and without mannitol. This suggests that mannitol is effective in maintaining the glomerular perfusion, even at a low arterial pressure.[18]

A hypertonic mannitol solution can be filtered into the renal tubules, even at low arterial pressure and hypovolemia, and it withdraws water into the renal tubules.[21] This strong osmotic diuresis is thought to be beneficial in flushing out the accumulated debris in the renal tubules. This debris, a reflection of decreased glomerular perfusion may contain nephrotoxins, waste products and cast-forming elements whose continued presence might lead to acute tubular necrosis.[24]

It is conceivable that the indiscriminate use of a hypertonic mannitol solution may cause a severe electrolyte derangement[19] or osmotic nephrosis.[23] In this study, though, histological examination revealed no degeneration and no swelling of tubules in animals which were given mannitol at twice the clinical dose.

Some investigators have reported deleterious effects[27] of hyperosmolality upon cardiac function. However, there was no difficulty in maintaining good hemodynamics during and after bypass in our experimental and clinical materials. Moreover, we have used a hypertonic coronary perfusate with mannitol (380–400 mOsm/L) for myocardial protection[28] during ischemic cardiac arrest.

One must exercise caution in administering mannitol to patients suffer-

ing from renal insufficiency. When sufficient urinary outflow is not obtained with a mannitol infusion, the circulating blood volume may increase, inducing both cardiac and renal insufficiency. Although Yoboah et al[2] reported that there was no evidence to suggest that a hypertonic mannitol solution can influence the development of renal failure, it is necessary to examine the diuretic effects of mannitol in such patients before cardiac surgery.

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