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Miscellaneous

Blood Circulation in the Urethra During Hypovolemia – An Experimental Study

M. Talja, T. Schröder, A. Lehtola, P. Nuutinen, M. Ruutu and O. Alfthan

Second Department of Surgery/Urological Unit, Helsinki University Central Hospital, Helsinki, Finland

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Summary. The changes in urethral blood circulation caused by hypovolemia were studied in male piglets to simulate the hemodynamic changes during extracorporeal perfusion used in open-heart surgery. Changes caused by mild pancreatitis were studied which produced a similar reduction in urethral blood flow measured by microspheres comparable to a 34% hemorrhage of the circulating blood volume. According to this study the urethral mucosa is very sensitive to hemodynamic changes. It may be the case that catheter toxicity is more significant when the urethral blood flow is diminished.

Key words: Urethral stricture, Urethral catheter, Urethral blood flow, Hypovolemia, Pancreatitis.

Introduction

Urethral strictures induced by latex urinary catheters have been documented following open-heart surgery [5, 6, 12, 15, 19, 22, 23, 27]. These strictures are different from post-catheterization strictures, because they affect the whole urethra [19]. Latex urinary catheters have been shown to have toxic effects both in vivo and in vitro [7, 8, 20, 25]. Urethral strictures caused by latex catheters are rare except in patients who have undergone open-heart surgery [3, 18].

Our own suggestion [18, 19] later emphasised by Sutherland et al. [23] and by Abdel-Hakim et al. [1] was that decreased blood pressure during open-heart surgery influenced the development of postoperative strictures. The theory has been supported by Edwards et al. [3] who found strictures similar to those seen in open-heart surgery in patients with myocardial infarction and after major trauma.

The present study was undertaken to investigate urethral blood circulation during hypovolemia which simulated extracorporeal perfusion, and also in acute pancreatitis with minimal systemic hemodynamic changes.

Materials and Methods

19 male piglets weighing 13–18.5 kg were used. Each animal served as its own control. Animals were anesthetized with sodium pentobarbital (Mebumat 25 mg/kg), and were intubated and ventilated. Arterial gas analysis was made every 1–2 h. Normal saline 50 ml/kg was given as an infusion.

Continuous Hemorrhage was caused by cannulating the aorta through the left femoral artery. The tip of the catheter was kept just above the bifurcation of the iliac artery. The position was verified at the end of the experiment. The blood volume was reduced by continuous suction by approximately 35% over 5 h, when the total blood volume was calculated to be 8% of the body mass.

Pancreatitis was caused by injection 25 ml of autologous diluted bile into the common pancreatic duct with a pressure of 40 cm H_2O. Duodenotomy and laparotomy wounds were closed after the induction of pancreatitis.

Blood Circulation Measurements. A Swan-Ganz catheter was inserted into all animals and cardiac output was recorded by thermodilution using an Edwards computer. Cardiac output, blood pressure and heart rate were recorded before hemorrhage, hourly during the experiment and at completion.

Organ Blood Perfusion Measurements were performed as described by Rudolf and Heyman [17]. Microspheres were injected via a catheter inserted into the right carotid artery with its tip in the left ventricle. The correct intraventricular position was checked by pressure measurement. For the collection of a reference sample another catheter was inserted into the left femoral artery with its tip just above the iliac bifurcation. All catheters were heparinized.

Carbonized microspheres (NEN, New England Nuclear), 16.2 +/– 0.3 μm and 15.5 +/– 0.3 μm in diameter labelled with 113 Sn and 46 Sc respectively, were suspended in 10% dextran containing 0.1% Tween 80. Immediately before injection, the microspheres were evenly suspended by shaking for about 20 s in a vortex shaker. A volume of 0.9–1.1 ml were injected slowly over 10 s. Each injection contained $4–5 \times 10^6$ microspheres. After the injection, the catheter was flushed with 5 ml saline. A reference sample (5 ml/min) was taken simultaneously with the injection of the microspheres.

The first injection containing microspheres labelled with 113 Sn (270 +/– 41 μCi) was given before the experiment and the second injection containing microspheres labelled with 46 Sc (82 +/– 14 μCi) 5–6 h after starting the experiment. The animals were killed by ex-

Table 1. Hemodynamic changes in hypovolemia ($n = 11$, mean ± SEM)

	Start value	5 h value	Significance
Cardiac output (l/min)	2.18 ± 0.12	1.42 ± 0.09	$p < 0.01$
Systolic blood pressure (mmHg)	146 ± 5.8	109 ± 5.8	$p < 0.01$
Heart rate (beat/min)	117 ± 4.0	136 ± 7.9	ns.

Table 2. Tissue blood flow changes in hypovolemia ($n = 5$, mean ± SEM, ml/100 g/min)

	Start value	5 h value	Significance
Urethra	17.8 ± 4.8	4.5 ± 2.4	$p < 0.05$
Corpora cavernosa	6.0 ± 1.5	1.3 ± 0.07	$p < 0.05$
Left kidney	290 ± 29	122 ± 14	$p < 0.05$
Right kidney	297 ± 33	123 ± 13	

Table 3. Hemodynamic changes in acute pancreatitis ($n = 8$, mean ± SEM)

	Start value	6 h value	Significance
Cardiac output (l/min)	2.4 ± 0.23	2.1 ± 0.016	$p < 0.05$
Systolic blood pressure (mmHg)	148 ± 5.5	135 ± 5.6	ns.
Heart rate (beat/min)	111 ± 4.0	109 ± 5.0	ns.

sanguination. The urethral mucosa together with the submucosa, corpus cavernosum and both kidneys were taken and specimens from them were placed in plastic tubes. The tubes were weighed and the activity in them was registered in an automatic gamma counter (Wallac).

The blood flow was then calculated for each isotope using a computerized program.

In the statistical calculations, the Wilcoxon signed Rank Sum test was used to study the hemodynamic and local tissue flow changes.

Results

Continuous Hemorrhage. The exsanguinated blood volume was 34 +/− 1.9% (27 +/− 1.5 ml/kg) of the total blood volume. The total volume of saline infused was 52 +/− 4 ml/kg. Cardiac output decreased from 2.18 +/− 0.12 l/min to 1.42 +/− 0.09 l/min ($p < 0.01$, $n = 11$). The decrease in blood pressure was also significant ($p < 0.01$), from 146 +/− 5.8 mmHg to 109 +/− 8.6 mmHg. The heart rate increased from 117 +/− 4.0 beats/min to 136 +/− 7.9 beats/min (ns. Table 1).

The blood flow in the urethral mucosa decreased from 17.8 +/− 4.8 ml/100 g/min to 4.5 +/− 2.4 ml/100 g/min and the change was significant ($p < 0.05$, $n = 5$). The variation between the individual animals was great: decreases between 46 and 93% were seen. In the most hypovolemic animals with severe tachycardia and lowering of the blood pressure, the reduction in the mucosal blood flow was not as great as in the animals with a better hemodynamic condition. In the corpora cavernosa the change was also significant ($p < 0.05$). The blood flow to the kidneys was symmetric and the reduction was significant ($p < 0.05$, Table 2).

Table 4. Tissue blood flow changes in acute pancreatitis ($n = 8$, mean ± SEM, ml/100 g/min)

	Start value	5 h value	Significance
Urethra	11.3 ± 1.6	3.09 ± 1.0	$p < 0.05$
Corpora cavernosa	2.54 ± 0.39	0.88 ± 0.17	$p < 0.05$
Left kidney	274 ± 30	186 ± 22	$p < 0.05$
Right kidney	285 ± 31	190 ± 21	

Pancreatitis. All animals had intraperitoneal exudate and odematous pancreatitis was seen at autopsy. The condition was confirmed by histological sections.

The cardiac output values decreased from 2.4 +/− 0.23 l/min to 2.1 +/− 0.016 l/min ($p < 0.05$, $n = 8$). Blood pressure and pulse were unchanged (Table 3). In spite of these less remarkable circulatory changes, the changes in the mucosal blood perfusion of the urethra were similar to those in the hypovolemic group (Table 4): the reduction was from 11.3 +/− 1.6 ml/100 g/min to 3.09 +/− 1.0 ml/100 g/min ($p < 0.05$). The variation was considerable. The change in the cavernous blood flow was from 2.54 +/− 0.39 ml/100 g/min to 0.88 +/− 0.17 ml/100 g/min ($p < 0.05$). The kidney flow was symmetric and the reduction was significant ($p < 0.05$).

Discussion

Cardiopulmonary bypass causes marked systemic hemodynamic changes. At the beginning of the extracorporeal perfusion the mean arterial pressure falls to 40–60 mmHg with pump flow values of the preoperative level. Pulsatile and pulse-less methods are used. The blood pressure elevates during the perfusion as a result of peripheral vasoconstriction.

The sudden fall in blood pressure causes the redistribution of the circulating blood. This vasoregulation is mediated by the baroreflex system [21], cathecolamines [13], the pituitary gland [2] and temperature regulation [26]. As a result, peripheral vasoconstriction is seen in the skin and mucous membranes. In the present study hypovolemia and acute pancreatitis were used as models to study the changes in blood flow in the urethral mucosa in two different situations. In the hemorrhage situation there was a significant fall in the cardiac output, but the cardiac output remained normal in the animals with pancreatitis.

The hemodynamic changes in the hemorrhage are well known. During the continuous hemorrhage, the arterial pressure first falls slowly but then decreases dramatically upon additional blood loss. This biphasic response can be explained by an initial compensatory response, followed by loss of compensation during extreme blood loss. Thus as the compensatory reserve becomes exhausted, the arterial pressure falls more rapidly in response to a hemorrhagic insult [10]. This is caused by "accumulation of metabolites" [13] which overcomes the sympathetic vasoconstriction causing relaxation in earlier exhausted small arteries, arterioles and precapillary sphincters and thereafter increasing the capillary pressure and leading to a leakage of fluid out of the vessels to the interstitium. In addition to hemorrhage, this reduces the circulatory blood volume and this phase of shock is irreversible.

A failure in the compensation mechanism to hypovolemia was seen in some animals. The infused saline (mean 52 ml) did not compensate the lost intravascular colume. Moss [14] calculated in a situation with 36% blood loss that the replacement ratio is 5 : 1 when balanced electrolyte solution is used. In the present experiment the ratio was only about 2:1. The reduction of urethral blood flow was 80–90% in the animals with hemorrhage and good compensation to hypovolemia, but in the animals with severe hypotension and high heart rate this compensation was lost and in these animals the reduction of the urethral blood circulation was less prominent. This explains the considerable variation seen among the individual animals.

Hemorrhagic pancreatitis has been shown tho cause shock-like hemodynamic changes. The intravascular fluid escapes to the peripancreatic and intraperitoneal spaces, and the circulating pancreatic enzymes and vasoactive agents have been explained to cause generalized diffuse vascular injury, allowing the plasma volume to escape and causing hemoconcentration [4, 24]. These effects are seen during the first hour after the induction of the pancreatitis [11].

The pancreatitis induced in the present study was not hemorrhagic and hence the hemodynamic changes were not considerable. The cardiac output remained nearly normal throughout the study, but there was a significant decrease in the urethral mucosal flow. This result indicates that the urethra is vulnerable to hemodynamic changes and that the urethral blood flow can decrease significantly, even though the cardiac output is still normal.

Pentobarbital as anesthetics causes increase in sympathetic tone [9]. There are also reports with no effects on the mesenterial blood flow [16]. In the present study the animals were anesthetized at least 1.5 h before the microsphere injection so that the effect of pentobarbital was unchanged during the experiment and had, in our pilot studies, only minimal hemodynamic effects.

In the present experiment the hypovolemia caused by hemorrhage or acute pancreatitis reduced significantly the urethral blood circulation. It was found also that the decrease in the urethral blood flow was discovered before any change in the cardiac output was demonstrated.

Therefore it seems obvious that toxic substances dissolving from catheters will damage an urethral mucosa much easier and heavier in cases with diminished urethral blood flow.

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Dr. M. Talja
Rautakankareenkatu 1
SF-15950 Lahti
Finland