EXPERIMENTAL TREATMENT OF ACUTE RENAL FAILURE DUE TO THE CRUSH SYNDROME WITH PROSTAGLANDIN E_2

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KEY WORDS: crush syndrome; acute renal failure; prostaglandin E_2.

Acute renal failure (ARF) is one of the severest of pathological states. Suffice it to say that the mortality from ARF at present is 40% [4]. The reason for this is evidently that methods of treatment available and, in particular, methods involving the extracorporeal circulation, although satisfactorily removing from the blood those waste products which accumulate in it as a result of loss of renal function, do nothing to restore kidney function. Hence the fundamental importance of development of methods of treatment of ARF which would restore renal function.

ARF has a complex etiology and, in particular, it may arise in clinical practice as a result of transfusions of incompatible blood or of the crush syndrome. It has recently been shown that the neurohumoral system [2] plays an essential role in the pathogenesis of ARF [2], and also that prostaglandins (PG) in the kidney are physiological antagonists of ADH, ACTH, and catecholamines, interact with the kinin system and the renin-angiotensin-aldosterone system, and restore normal metabolism in the kidney [1]. These considerations served as the basis for the use of PGE_2 for the experimental treatment of ARF. The writers showed previously that injection of Soviet PGE_2 (prostenon) into the abdominal aorta of dogs with experimental ARF due to incompatible transfusion completely restores glomerular filtration and tubular reabsorption, and thus abolishes ARF [3].

EXPERIMENTAL METHOD

A crush syndrome was induced in 20 unanesthetized female dogs weighing 10-24 kg by crushing the soft tissues of the right hind limb with a metal press of special construction. The compressive force was 0.5 kg/cm^2, the area of compression of the soft tissues was 200 cm^2, and the duration of crushing was 4 h. The animals' ureters were exteriorized beforehand by Tsitovich's method.

Renal function was judged by the intensity of glomerular filtration (calculated on the basis of endogenous creatinine), tubular reabsorption, renal plasma flow and maximal tubular secretion relative to diodone, and the minute and 24-hourly diuresis. The tests were carried out on the day before the experiment, on the day of the experiment 1 h after decompression (in the experimental animals 40 min after PGE_2 infusion), and later in the control animals daily until death. Observations on the experimental dogs continued for 7 days.

Soviet PGE_2 (prostenon), synthesized in the Pure Substances Sector, Academy of Sciences of the Estonian SSR (Professor Yu. E. Lille) was used. Prostenon in a dose of 0.25 mg/kg, dissolved in 20 ml of physiological saline, was injected rapidly into the aorta through a polyvinyl chloride catheter, introduced into the femoral artery as far as the level of origin of the renal arteries from the aorta.

EXPERIMENTAL RESULTS

Crushing of the soft tissues of the limb was accompanied by a violent motor response of the animals and elevaton of the arterial pressure (BP) on average by 31.2 ± 5.2 mm Hg ($P <$

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0.01), which fell 1 h after decompression by 46.4 ± 0.9 mm Hg ($P < 0.01$) from its initial level. All animals developed ARF, as shown by a sudden and progressive reduction of glomerular filtration, the renal plasma flow, maximal tubular secretion, minute diuresis, and tubular reabsorption. All this was accompanied by oliguria or anuria. All the control animals died from progressive ARF: five dogs after 2 days, three after 3 days, and two after 4 days. Fundamentally different results were obtained in the experimental animals. Of 10 experimental dogs three died 2-3 h after decompression from acute cardiovascular failure. Glomerular filtration and minute diuresis in the surviving animals exceeded the initial values, tubular reabsorption was within normal limits and the remal plasma flow and maximal tubular secretion were completely restored. All these phenomena were accompanied by rapid recovery of the 24-hourly diuresis. Of seven dogs in which ARF was successfully abolished, one died on the 4th day from thromboembolism of the pulmonary artery and one on the 6th day from hemorrhage caused by erosion of the femoral artery due to wound suppuration.

All these data provide experimental confirmation of the value of PGE_2 (prostenon) for clinical treatment of patients with ARF.

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REACTIVITY OF MESENTERIC MICROVESSELS IN RATS WITH MESENTERIC SHOCK

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In the opinion of many authorities, a breakdown of circulatory mechanisms plays an essential role in the pathogenesis of shock of varied etiology [2, 3, 5]. In particular, disturbance of regulation of vascular tone is one cause of the appearance of resistance of hypotension in the late stages of development of shock. The nature of this resistance has not been finally settled. Resistance of hypotension to injection of exogenous adrenalin and of other vasopressor agents likewise is not understood. Some light on the relations of hemorrhagic shock and posthemorrhagic hypotension has been shed by the investigations of Matvienko [1], who showed that in the late stages of acute blood loss decreased reactivity of the mesenteric microvessels to adrenalin is observed.

The object of this investigation was to study changes in sensitivity of the mesenteric microvessels to adrenalin on a model of mesenteric shock.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male rats weighing 250 ± 10 g, anesthesized with pentobarbital in a dose of 3.5 mg/100 g. The microcirculation was observed by the method in [4]. Reactivity of the microvessels was estimated by determining threshold concentrations of adrenalin applied locally in a volume of 0.1 ml [6]. The minimal concentration of adrenalin, application of which caused distinct changes in the velocity of the blood flow or contraction of metarterioles was taken as the threshold. Mesenteric shock was produced through a mid-

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