EFFECT OF INTRA-AORTIC INJECTION OF PROSTAGLANDIN E_2 ON RENAL FUNCTION IN ACUTE RENAL FAILURE FOLLOWING BLOOD TRANSFUSION

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KEW WORDS: heterologous blood transfusion; acute renal failure; prostaglandin E_2.

Despite the use of extracorporeal circulation methods mortality from acute renal failure (ARF) still remains high (40-60%) [9, 11, 13, 15]. Irrespective of the immediate cause of ARF, it is based on loss of kidney function, which causes accumulation of waste products in the body and may lead to death. The writers showed previously that intra-aortic injection of prostenon, the Soviet preparation of prostaglandin (PG) E_2, abolished ARF, developing as the result of the crush syndrome, and thereby led to revival of the experimental animals [7]. We know that one cause of clinical ARF is incorrect transfusion of incompatible blood or its components [5]. This paper describes the study of the effect of PGE_2 on renal function in ARF due to blood transfusion.

EXPERIMENTAL METHOD

Experiments were carried out on 20 mongrel female dogs weighing 15-20 kg, in which the ureters were exteriorized beforehand onto the anterior abdominal wall by the method of Tsitovich. ARF was induced by a method previously worked out in the laboratory: after blood loss (20-25 ml/kg body weight) heterologous blood was infused into the dogs (human blood, 25-30 ml/kg) [6]. The dogs thereafter developed blood transfusion shock, which was complicated by the development of ARF. In each series of experiments the 24-hourly and minute diuresis, glomerular filtration (by the endogenous creatinine clearance method) (the minute diuresis, against the background of which the glomerular filtration rate was studied over a period of time, is illustrated in Figs. 1 and 2), and the tubular reabsorption were determined in each series of experiments. To determine the renal plasma flow and maximal tubular secretion, 35% diodone was used; in each concrete case it was injected intravenously in one stage. The plasma diodone concentration during determination of the renal plasma flow did not exceed 5 mg %, but to ensure maximal tubular secretion, its plasma concentration exceeded 15-20 mg % [2]. Parameters of respiration and blood pressure (BP) were recorded on the continuously moving kymograph paper (14 cm/h; Fig. 3). The urea and creatinine concentrations in venous blood were determined by kits from Lachema (Czechoslovakia). The investigation was carried out the day before and the day of the experiment: in animals of the control group, 1 h after infusion of heterologous blood, in animals of the experimental group 40 min after the injection of PGE_2. Later the animals remained under observation daily until death, or in the experimental group, until complete recovery of renal function, which occurred by the 7th day. Prostenon, a Soviet preparation of PGE_2, synthesized in the Pure Substances Sector, Academy of Sciences of the Estonian SSR (Corresponding Member J. E. Lille) was used in the experiments. PGE_2 in a dose of 0.25 mg/kg, dissolved in 20-30 ml physiological saline, was injected 40-45 min after heterologous blood transfusion, in one stage in a jet with constant rate of 1 ml/min by means of the "Perfusor" apparatus (West Germany), through a catheter inserted into the temporal artery and along the aorta as far as the origin of the renal arteries. The results were subjected to statistical analysis by the Student–Fisher method. Mean values (M), mean standard error (m), standard deviation (σ), and Student's t were calculated, and using a table, the level of significance (P) was determined [8].

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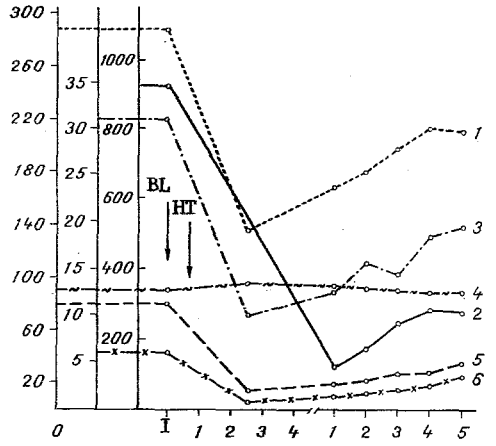

Fig. 1. Changes in renal function of animals of control group. Abscissa: I) initial values, first four numbers denote hours, next five numbers denote days. 1) Renal plasma flow (in ml/min/m^2); 2) 24-hourly diuresis (in ml); 3) maximal tubular secretion (in mg/min/m^2); 4) tubular reabsorption (in %); 5) glomerular filtration (in ml/min/m^2); 6) minute diuresis (in ml/min); BL) blood loss; HT) heterologous transfusion.

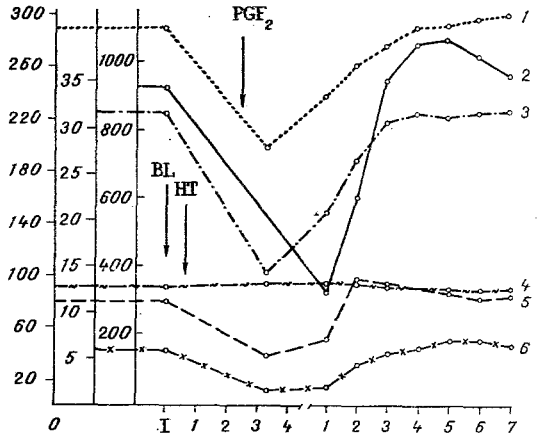

Fig. 2. Renal function in animals treated with PGE_2. Legend as for Fig. 1.

EXPERIMENTAL RESULTS

Of the 10 animals of the control group seven died at different times of progressively developing ARF: one dog after 2 days, two after 3 days, two after 4 days, and two after 5 days. The course of the disease was accompanied by disturbance of all kidney functions tested. On the 5th day, for instance, the minute diuresis was reduced by half (from 5.84 ± 0.96 to 2.90 ± 0.28 ml/min, $P > 0.05$), the 24-hourly diuresis by 3.4 times (from 915.00 ± 20.93 to 270.00 ± 90.00 ml/day, $P < 0.05$), glomerular filtration by 2.4 times (from 79.92 ± 3.29 to 33.61 ± 4.31 ml/min/m^2, $P < 0.05$), maximal tubular secretion by 1.6 times (from 31.11 ± 1.06 to 18.92 ± 0.89 mg/min/m^2 ($P < 0.05$), and renal plasma flow by almost 1.4 times (from 287.13 ± 7.27 to 210.35 ± 7.84 ml/min/m^2, $P < 0.05$). The urea concentration in the venous blood rose by more than 10.3 times (from 5.60 ± 0.70 to 57.80 ± 24.1 mmoles/liter, $P < 0.05$), and creatinine by 2.4 times (from 0.11 ± 0.01 to 0.27 ± 0.02 mmole/liter, $P < 0.05$). Tubular reabsorption rose in some animals, but fell in others; however, these changes were not statistically significant ($P > 0.05$; Fig. 1).

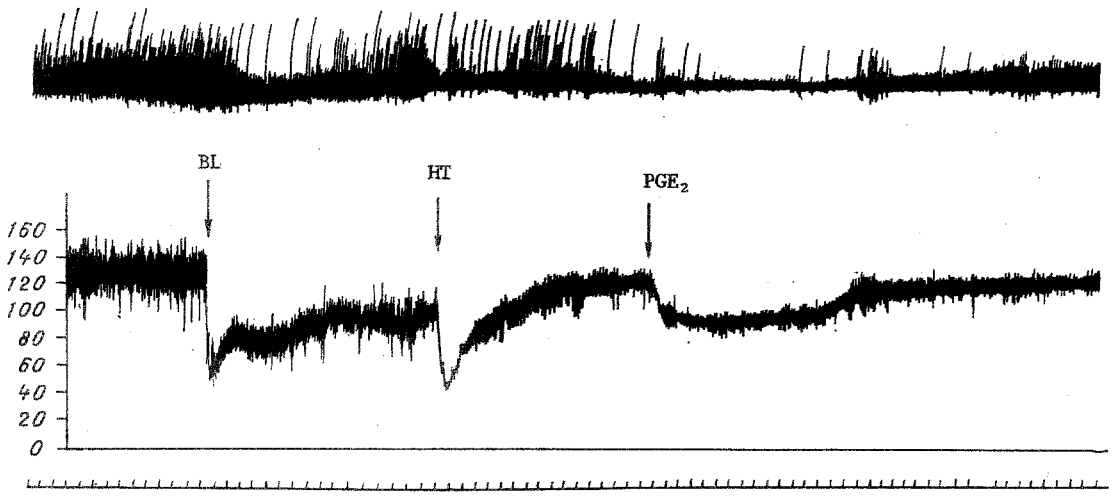

Fig. 3. Time course of BP and respiration in dogs after blood loss (BL), heterologous blood transfusion (HT), and injection of PGE_2. From top to bottom: respiration, BP (in mm Hg), zero line of BP, time marker (2 min). Arrow indicates beginning of procedure.

In the three surviving dogs of the control group the parameters of renal function on the 7th day were lower (renal plasma flow 232.30 ± 12.06 ml/min/m^2, $P > 0.05$, maximal tubular secretion 24.99 ± 2.00 mg/min/m^2, $P > 0.05$; glomerular filtration 47.01 ± 4.22 ml/min/m^2, $P < 0.05$; tubular reabsorption 86.44 ± 0.67%, $P > 0.05$; 24-hourly diuresis 883.33 ± 15.56 ml/day, $P > 0.05$; minute diuresis 4.80 ± 0.53 ml/min, $P > 0.05$), whereas the urea and creatinine concentrations were higher than initially (19.43 ± 0.84 and 0.24 ± 0.03 mmole/liter, respectively, $P < 0.05$).

Basically different data were obtained in animals of the experimental group. Intraaortic injection of PGE_2 was accompanied in these animals by a transient fall of BP (on average by 20 mm Hg), which returned spontaneously to its initial level after the infusion of PGE_2 ended (Fig. 3). Throughout the period of observation all the parameters studied returned to normal. For instance, the renal plasma flow, maximal tubular secretion, and glomerular filtration on the 7th day were within normal limits (300.90 ± 12.09 ml/min/m^2, 31.44 ± 1.00 mg/min/m^2, and 82.75 ± 3.69 ml/min/m^2, respectively, $P > 0.05$). Parameters of 24-hourly and minute diuresis, starting from the 5th day, were higher than initially (965.50 ± 25.26 ml/day and 6.56 ± 0.68 ml/min, $P > 0.05$; Fig. 2), whereas the urea and creatinine concentrations were within normal physiological limits (5.67 ± 0.61 and 0.12 ± 0.01 mmole/liter, respectively, $P > 0.05$).

We know that PG do not accumulate in the body but are fairly rapidly transformed in the organs and tissues. Nevertheless it has been established that even after administration of a single dose of PG their effect persists for quite a long time [1, 10, 12, 14].

The beneficial effect of PGE_2 on the course and outcome of experimental ARF due to blood transfusion is determined by its ability to modify the functions of neurohumoral renal factors involved in the regulation of kidney function. In ARF all extrarenal and renal factors regulating renal function are modified: the concentrations of adrenalin and noradrenalin in the kidneys are increased, and this is accompanied by increased function of the blood clotting and fibrinolysis system, all kinds of metabolism are disturbed, functions of the hypothalamo-hypophysial-adrenal system are modified ,the kallikrein-kinin system is activated, and the serum vasopressin level rises [3, 4].

PGE_2 released under the influence of catecholamines, of angiotensin II, and of vasopressin, is their physiological antagonist. This, as well as potentiation by PGE_2 of the vasodilator effect of components of the kallikrein-kinin system on vessels of the renal cortex and medulla, lead to an increase in the total blood flow through the kidney and to the redistribution. Thus PGE_2 blocks the most important pathogenetic factors of ARF.

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