ELECTROPHYSIOLOGICAL INVESTIGATION OF THE EFFECTS OF CHEMICAL SUBSTANCES IN THE URINE ON RENAL RECEPTORS

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UDC 612.467.3 :612.461].014.421.7

Injection of solutions of various substances contained in the urine, isotonic with the blood, in near-physiological doses, produces two types of afferent impulse activity in the renal nerves: fast activity, with individual oscillations 1-2 msec in duration and 30-40 μV in amplitude, and slow activity, in which the complex component of the wave is about 20 msec in duration and up to 20 μV in amplitude. Substances dilating the renal blood vessels (urea, sodium phosphate, sulfate, and bicarbonate) increase the renal blood flow, and stimulate the fast impulse activity in 80-90% of the experiments and the slow activity in 20-30% of the experiments. Substances having no effect on the renal vessels (glucose, protein, creatinine, sodium chloride) do not alter the renal blood flow and do not change the fast impulse activity in 90-100% of the cases.

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In previous electrophysiological studies of the renal receptors the activity of vascular receptors in the kidneys was investigated in connection with changes in the tone of the renal vessels and the level of the general blood pressure [11, 12]. Predominance of fast impulses (1-2 msec), not synchronized with the pulse rhythm and reflecting the renal blood volume, was observed. Besides the fast impulse activity, a slow impulse activity was also recorded in the renal nerves, the complex component of its wave having a duration of 20-50 msec. This type of impulse activity was observed in particular after injection of biologically active substances such as adrenalin, histamine, and acetylcholine into the renal vessels [12]. A later investigation [14] showed that injection of large doses of substances normally present in the urine ("urinary substances") into the renal artery leads to the appearance of groups of spikes, not synchronized with the pulse, ranging from 20-80 μV in amplitude.

In the present investigation the effect of substances contained in the urine was studied in near-physiological doses on the activity of the renal receptors. Its object was to study the connection between the function of the renal receptors and vascular processes taking place in the kidney. Accordingly, besides recording afferent impulses in the renal nerves, the renal blood flow was also measured.

EXPERIMENTAL METHOD

Experiments were carried out on 74 cats under deep thiopental or hexobarbital anesthesia (70-80 mg/kg body weight). One of the two branches of the renal artery was divided and the "urinary substances" were injected into its central end by means of a syringe in concentrations close to isotonic with the blood. Substances dilating the renal vessels which were used included urea (1.8% solution), sodium sulfate (1.42% solution), disodium hydrogen phosphate (1.06% solution), and sodium bicarbonate (1.26% solution). Substances not affecting the renal vessels included glucose (5.5% solution), protein (3.5% solution of gelatin in Ringer's solution*), creatinine (3.75% solution), and sodium chloride (0.9% solution). The concentration of these substances was determined by a cryoscopic method. Depression of the freezing point of a solution is directly proportional to the concentration of molecules and ions in the solution. Depression of the freezing point of mammalian blood is 0.56-0.62°. Depression of a unimolecular aqueous solution of any nonelectrolyte is 1.85°. Consequently, a 0.3 M solution of a nonelectrolyte is isotonic relative to blood, and a 0.15 M solution of an electrolyte splitting up into two ions, or a 0.1 M solution of an electrolyte splitting up

* The threshold concentration for gelatinization of Ringer's solution.

Laboratory of General Physiology of Reception, I. P. Pavlov Institute of Physiology, Academy of Sciences of the USSR, Leningrad. (Presented by Academician V. N. Chernigovskii). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 67, No. 4, pp. 3-7, April, 1969. Original article submitted January 15, 1968.

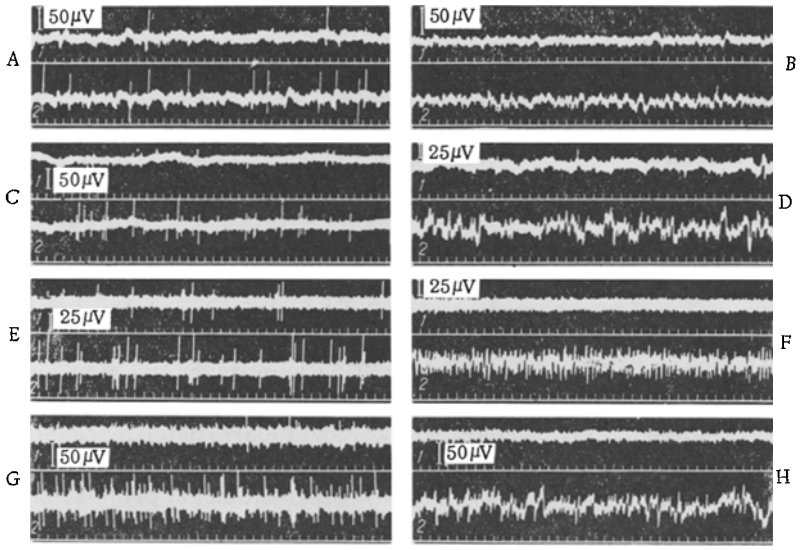

Fig. 1. Fast and slow afferent impulses in renal nerves after injection of isotonic solutions of urinary substances increasing the renal blood flow into the renal artery. AB) After injection of 0.05 ml of 1.8% urea solution into renal artery; CD) after injection of 0.025 ml of a 1.06% solution of disodium hydrogen phosphate; EF) after injection of 0.025 ml of a 1.42% solution of sodium sulfate; GH) after injection of 0.25 ml of a 1.2% solution sodium bicarbonate; 1) before; 2) 3-5 sec after injection. Time marker 0.02 sec.

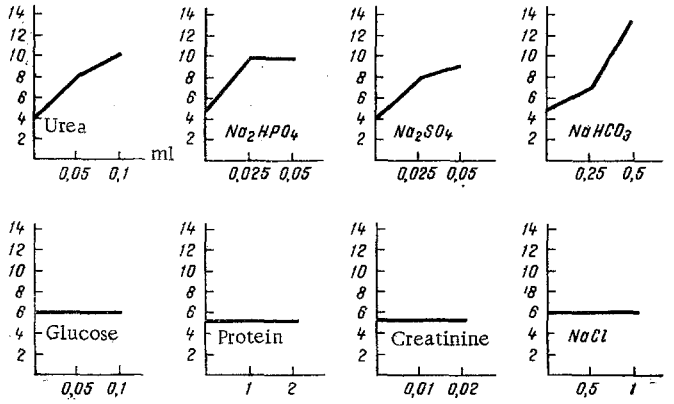

Fig. 2. Changes in the renal blood flow after injection of solutions of "urinary substances" isotonic with the blood into the renal artery. Abscissa, volume of solutions of substances injected (in ml); ordinate, number of drops of blood from branch of renal vein during 15 sec after each injection (recording made 3-5 sec after each injection, injection carried out in two stages). Results are mean values of several experiments (three experiments with sodium sulfate, four with sodium bicarbonate, five with urea, three with sodium phosphate, four with creatinine, three with protein, and five experiments with sodium chloride).

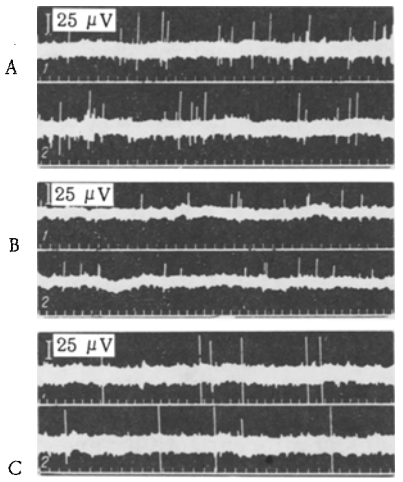

Fig. 3. Fast and slow impulses in renal nerves after injection of isotonic solutions of "urinary substances" not affecting the renal bloodflow into the renal artery. A) After injection of 0.1 ml of 5.5% glucose solution into renal artery; B) after injection of 1 ml of 3.5% gelatin solution; C) after injection of 0.02 ml of 3.7% creatinine solution; 1) before; 2) 3-5 sec after injection. Time marker 0.02 sec.

into three ions, and so on, is isotonic with blood. This argument is valid because the electrolytes under consideration are highly dissociated and also dilute. These substances were injected in the following dose (in ml): urea 0.05-0.1, sodium phosphate 0.025-0.05, sodium sulfate 0.025-0.05, sodium bicarbonate 0.25-0.5, glucose 0.05-0.1, protein 1-2, creatinine 0.01-0.02, and sodium chloride 0.5-1. The dose of substances to be injected was calculated (using glucose as the example) as follows. The volume of blood flowing through the renal vessels during moderately deep anesthesia and when the renal circulation was undisturbed was 3 ml/5 sec. If the blood glucose concentration is 100 mg%, i.e., 100 mg/100 ml blood (1 mg/1 ml blood), the quantity of glucose flowing through the renal vessels every 5 sec is 3 mg. One ml of glucose solution isotonic with blood (5.5% solution) contains 55 mg glucose. Injection of 3 mg glucose (0.05-0.06 ml of this solution) doubles the quantity of glucose flowing through the renal vessels in a period of 5 sec. However, bearing in mind that the renal circulation was reduced by approximately half after division of the branch of the renal artery, this injection increased the glucose content in the kidney in a period of 5 sec by approximately 4 times. The renal blood flow was determined by the direct method as the number of drops of blood flowing from a thin cannula (0.5 mm in diameter) introduced into one branch of the renal blood. The blood flow and afferent impulse activity were recorded separately from the various animals 3-5 sec after each injection of solution. Spikes were recorded for 5 sec and the blood flow for 15 sec after each injection.

Afferent impulses were detected from the peripheral ends of divided nerves of the renal plexus by means of silver electrodes, amplified, and recorded with a cathode-ray oscilloscope. The frequency characteristic curve of the amplifier was a straight line in the range from 10-1500 Hz.

EXPERIMENTAL RESULTS AND DISCUSSION

Injection of solutions of urea, sodium phosphate, sodium sulfate, and sodium bicarbonate into the renal vessels in near-physiological concentrations caused an increase in afferent spike activity in 80-90% of the experiments, as shown by the appearance of fast waves 1-2 msec in duration and 30-40 μV in amplitude. The frequency of the spikes was increased by between 2 and 30 times. During administration of these substances in about 20-30% of cases slow impulses also appeared in the renal nerves in the form of grouped discharges in which each component wave was about 20-50 msec in duration and up to 20-30 μV in amplitude (Fig. 1).

Fast and slow waves were recorded during the action of these substances either separately in different nerves (Fig. 1) or simultaneously in one nerve trunk. The fast impulse activity in the original experimental conditions was recorded in the form of a background activity, while the slow impulses in the renal nerves were as a rule absent before injection of the chemical compounds. After injection of these substances, a stronger than background fast impulse activity persisted for 1-4 min, and then gradually weakened and returned to its original level. After 2-stage injection of solutions of urea, or sodium phosphate, bicarbonate, or sulfate, the renal blood flow recorded for 15 sec after each injection as a rule increased (Fig. 2). These changes lasted for 2-3 min. The results obtained correspond to the findings previously reported in the literature concerning the dilator action of urea and sodium sulfates and carbonates on the renal vessels [18, 19, 24, 27, 33-35].

Injection of substances having no effect on the renal circulation (solutions of glucose, protein, creatinine, or sodium chloride) into the renal blood vessels in 90-100% of the experiments had no effect on the frequency of the fast waves (Fig. 3). Injection of solutions of glucose, protein, creatinine, or sodium chloride into the renal artery likewise did not affect the renal blood flow (Fig. 2), in agreement with published data [30, 37].

A number of workers have attributed the fast waves to responses of mechanoreceptors to moderately strong stimulation, and the slow impulses, produced by activity of free endings and of group C fibers, to responses of receptors to strong stimulation, nociceptive in character [16, 17, 25, 26, 36]. In their opinion, special afferent systems for pain participate in the latter case. However, it has been shown that the slow impulses are not only generated by nociceptive stimuli but they are also well defined in response to chemical stimuli and unlike the fast activity, they rarely arise in response to mechanical stimuli [1-5, 8, 10-15, 20-23, 28, 29, 31, 32, 38].

Activity of the slow type appears in the gastro-intestinal branches of the nerve and in the vagus nerve in response to mechanical and clinical stimuli which cannot be regarded as nociceptive, because the intensity fluctuates within physiological and normal limits [6-8]. It has been shown [1-5] that slow activity in the intestinal nerves inceases in response to mechanical, but in particular, to chemical stimulation of various types. An increase in strength of the slow activity, in the absence of any significant changes in the fast activity, was recorded in the afferent nerves of the heart after application of chemical stimuli to its surface [9]. The present experiments showed that immediately after injection of solutions of "urinary substances" isotonic with blood in near-physiological doses into the renal vessels, two types of afferent activity are generated in the renal nerves: fast activity, in which the duration of each wave is 1-2 msec and its amplitude about 30-40 μV, and slow activity in which the duration of the composite wave is 50 msec and its amplitude up to 20 μV. These impulses arise in response to injection of substances increasing the renal blood flow and dilating the renal vessels (urea, sodium phosphate, sulfate, and bicarbonate). Substances not affecting the renal blood flow or the renal vessels (glucose, sodium chloride, protein, creatinine) do not modify the fast activity. Consequently, the fast activity largely reflects vascular changes in the kidneys (the possibility of a direct action of these substances on the vascular receptors likewise cannot be ruled out).

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