THE USE OF HYPERTONIC UREA SOLUTIONS IN HYPOTHERMIA

AN EXPERIMENTAL STUDY*

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HYPERTONIC urea solutions are used primarily for the reduction of brain volume and intracranial pressure, while hypothermia is used basically to reduce cerebral metabolism to allow temporary circulatory arrest. It is not unreasonable, therefore, to use these two techniques concomitantly, and in order to do this to the best advantage, detailed knowledge is required about the effects of hypothermia upon the use of hypertonic urea solutions. This paper presents a study of hypertonic urea given intravenously to dogs at various body temperatures from 38°C to 23°C.

METHODS AND MATERIALS

Male mongrel dogs weighing about 15 kg. were used as the experimental animals. They were anesthetized for the experiment with a mechanically regulated intravenous infusion of pentobarbital which provided a steady level of anesthesia. Hypothermia was produced by shaving the dogs, covering them with cloths soaked in iced alcohol and blowing cold air on them. Thorazine was used to control shivering. During the experiments, recordings were made of arterial blood pressure, superior longitudinal sinus pressure, the electrocardiogram and the electroencephalogram. Either the intracranial pressure was recorded throughout the experiment or serial samples of cerebrospinal fluid were taken for chemical analysis, depending upon the experiment. Chemical analyses on serum and cerebrospinal fluid for Na, K, Cl, protein and total osmotic pressure were made by standard methods. The solution of urea used was approximately a 30 per cent solution of sterile, lyophilized urea in 5 or 10 per cent dextrose. The urinary bladder was catheterized for measurement of urinary flow.

Before injection of urea, samples of arterial blood and cerebrospinal fluid were taken, urinary flow was measured and the collection bottle was changed. The solution of urea, in the amount of 1½ gm. urea per kg. of body weight, was then injected intravenously in one single rapid injection, the midpoint of injection taken as T-O. Observations were recorded for 5 to 6 hours with samples of blood, urine and cerebrospinal fluid taken at appropriate intervals during this time. Temperatures were recorded from thermistors in the rectum, the esophagus, the region of the kidney

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and, in some cases, the forelimb. When the animals were studied at other than normal body temperature, they were allowed to equilibrate at the experimental temperatures for an hour before the injection of urea was made.

In considering the results of the disappearance of urea from the blood, the original level of blood-urea nitrogen was subtracted from the observed levels and these values, plotted against time on semilogarithmic paper, gave a straight line after about 15 min. (Fig. 1). The slope of this line was considered a measure of the rate of elimination of urea, and the time for the concentration of urea to fall by one half, called the blood-urea half-time, was used to compare the results at one tempera-

**Fig. 1.** Disappearance of urea from the blood stream of dog following an intravenous injection of 1.5 gm urea per kg. of body weight in a 30 per cent solution.

ture with those at another. The same treatment was applied to the fall of the osmotic pressure, here called the osmotic pressure half-time.

The results of all experiments at any one temperature have been averaged and the mean has been taken for comparison. Changes in intracranial pressure were recorded as the percentage change from the original intracranial pressure recorded.

**RESULTS**

Forty-one experiments were carried out at temperatures ranging from 38°C. to 23°C. These have been grouped according to temperature as follows: 36°–38°C., 34°C., 30°–32°C., 26°–28°C., 23°–25°C. and the mean value for each group was used in considering the results. The pertinent data are summarized in Table 1.

**Blood-Serum Composition.** The blood-urea concentration rose to a maxi-