THE THERAPEUTIC ACTION OF HYPERTONIC SOLUTIONS DURING TRAUMATIC CEREBRAL EDEMA

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(Received May 19, 1955. Submitted by Active Member of the Academy of Medical Sciences USSR V. N. Shamov)

Of the therapeutic measures aimed at controlling cerebral edema, the greatest value is attached to methods of dehydration and esmotic therapy, i. e., therapy by means of hypertonic solutions of glucose, table salt, and some other substances; and although this type of therapy has existed since the days of N. I. Pirogov, however, there still is no single distinct method for the osmotic therapy of edema, so that the actions of clinicians in this direction are not always sufficiently well-founded. Even the mechanism of osmotic therapy is itself understood from somewhat empirical standpoints.

The problem of studying the action of hypertonic solutions on the brain and of discovering the mechanisms of this action was before us. The investigations were unique due to the fact that the observations were carried out under conditions of experimental traumatic cerebral edema.

We determined the action of hypertonic solutions not by the state of fluid pressure [2, 3, 10, 12-15], but by the reaction of the brain itself to the solutions introduced into it. For this purpose, cerebral oncometry, which allows the observation and registration of changes in the size of the brain, was the method used and the changes in the edema were judged by these changes.

The experimental method was essentially as follows. Under acute experimental conditions, an area 3 cm^2 was trephined in dogs under morphine-urethane anesthesia, the dura mater was dissected, and a brain oncometer was fastened in the opening. This consisted of a steel drum, with a rubber membrane stretched over its base, the upper portion of which was connected by means of a rubber tube to a water manometer which registered the variations of the brain on a chymograph.

With prolonged observation, the oncometric curve could be observed to rise, hour by hour, in connection with the gradual rise in intracranial pressure and the development of cerebral edema. The edema did not stop at the boundaries of the trephination but extended beyone it, moving over into the opposite cerebral hemispheres; consequently, the edema was of a diffuse, generalized nature. Microscopic analysis completely confirmed the diagnosis of cerebral edema.

The edema was provoked by operational trauma, anesthesia, the pressure of the water column of the registering manometer, and, finally, by prolonged immobilization of the dog with the vessels of the neck clamped.

One to two hours after onset of the edema, hypertonic solutions of glucose (40%) and table salt (15%) were tested. The solutions, 36 and 37° in temperature were administered into the femoral vein at a rate of 2 ml per minute in quantities which corresponded to the average therapeutic doses used in clinical practice (taking the weight of the animal into account).

In all, 140 observations were carried out on 86 dogs.

The intravenous administration of hypertonic glucose and table salt solutions was accompanied by a series of typical changes in the intracranial pressure and volume of the brain. By oncometric observations, three stages of change in intracranial pressure were found during the administration of hypertonic solutions into a vein (Fig. 1 and Table).

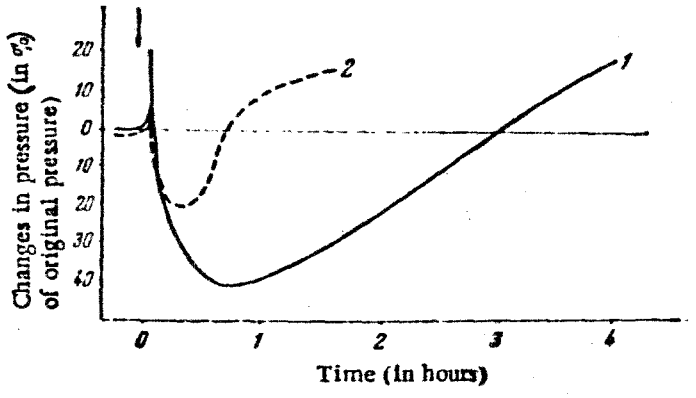

Fig. 1. Changes in intracranial pressure during intravenous administration (↓) of a 15% solution of table salt (1) and of a 40% solution of glucose (2).

The first (initial) stage was the shortest, from the moment the solution was injected into a vein until the intracranial pressure began to fall; the second stage (fall of intracranial pressure) took up the greatest portion of the oncometric curve – from the moment the pressure fell until it returned to the original level. This state is of greatest interest since the therapeutic efficacy of the administered solution can be judged by the extent and duration of the pressure decrease; the third stage (secondary action) occupied the final section of the oncometric curve and determined the period from the moment the intracranial pressure returned to the original state until the end of the observations.

Detailed study of the action of glucose and table salt solutions facilitated the determination of certain rules.

When glucose solution was administered, a brief rise in intracranial pressure was observed during the initial stage. At the same time, when table salt solution was administered, rising as well as falling pressure could be observed.

In the second stage, the difference between the actions of the hypertonic solutions is most pronounced. Thus, when glucose is administered, the intracranial pressure usually falls 20% on the average (in relation to the original pressure), while when table salt solution is administered, the fall in pressure reaches 39-40%. The pressure drop with glucose usually lasts 42 minutes; when table salt is administered, 3 hours. Thus, table salt solution is twice as effective as glucose solution and lasts 4 times as long.

Finally, in the third stage, a rise in intracranial pressure is observed whose extent appears to be approximatel the same (16-17%) whether glucose or table salt is administered.

The nature of the described fluctuations of the stages in intracranial pressure is complex and the decipherme of these fluctuations, undoubtedly, is of value in understanding the mechanism by which hypertonic solutions act on cerebral tissue.

Study of the oncometric curves of the initial stages show that the variations in intracranial pressure during this stage are determined by the action of hypertonic solution on the vessel wall and its receptors. The following facts support this proposition: a) the speed with which the intracranial pressure reacts b) the existence of a

distinct relationship between the rate at which the solution is administered into a vein and the amplitude of the variations in intracranial pressure (the slower the solution is administered, the less obvious are the variations in pressure; as the solution is administered more rapidly, the pressure fluctuations increase) c) the parallel between changes in arterial and intracranial pressure. Thus, when a pressor reaction of the arterial pressure begins (at the moment the solution is administered), a similar reaction is observed in the intracranial pressure. On the other hand when a depressor reaction of the vessels occurs, a decrease in intracranial pressure is observed also.

Thus, the explanation of the initial changes in intracranial pressure at the moment hypertonic solutions are administered should be sought in the initial changes of the arterial pressure which are of a neuro-reflex nature.

The explanation of the action of hypertonic solutions at the stage of decreasing intracranial pressure is much more difficult.

It is customary to consider that the intravenous administration of hypertonic solutions as a method of combatting cerebral edema creates the conditions necessary for the removal of stagnant edematous fluid from the brain tissues, the introduction of this fluid into the bloodstream and the further elimination of it with the urine. But is the supposition that the edematous brain can be freed from water mechanically sufficiently founded ?

As is known, a hypertonic solution consisting of, generally, less than 1% of the entire blood volume is administered to the patient. When such a small quantity of the solution is administered, can any appreciable osmotic effect be expected ? It is difficult to imagine this.

The same considerations arise when studying the action of hypotonic solutions also. It would seem that when water is injected, the blood could be expected to become thicker due to the transfer of liquid from the blood into the tissues. However, when hypotonic solution is administered, a dilution of the blood is usually observed, as is the case when hypertonic solution [8] is administered.

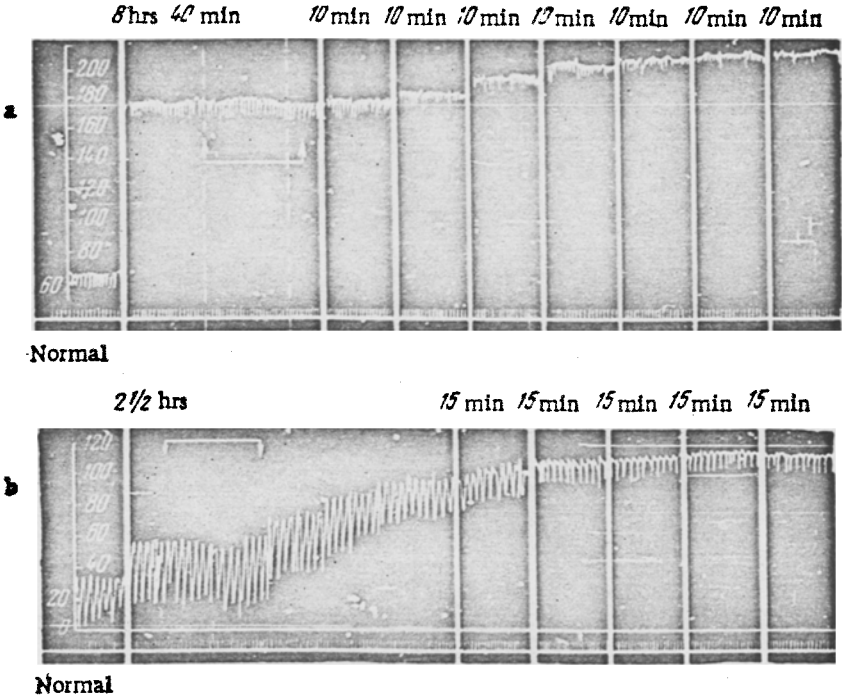

Fig. 2. Rise in intracranial pressure (in mm of water column) during intravenous administration of hot (42°) 15% table salt solution (a) and physiological solution at the same temperature (b).

Therefore, the therapeutic effect of osmotic therapy can only be explained completely within the laws of osmotic equilibrium.

Changes in Intracranial Pressure Influenced by Intravenous Administration of a 15% Solution of Table Salt and a 40% Solution of Glucose (By Stages)

Solution	Initial stage			Stage of decreasing pressure			Stage of secondary action	
	characteristics of the reaction	duration of the reaction	extent of the pressure changes (in %)	onset time of maximum decrease in pressure	duration of reaction	extent of maximum decrease in pressure (%)	time of onset of stage of secondary action	extent of pressure rise in the course of an hour (in %)
15% table salt	Pressor or depressor	3 min 3 sec	20	40 min	3 hrs	39	3 hrs 3 min	17
40% glucose	Pressor	2 " 48 "	6	22 "	42 "	20	45 min	16

Our investigations of the action of solutions of various temperatures on the brain confirmed the data [4, 11] regarding the significance of the temperature of the administered solution. Thus, the intravenous administration of solution which had been heated to 42 or 43°, caused a rise in intracranial pressure, regardless whether hyper- or hypotonic solution was administered (Fig. 2a). The administration of these same solutions when cooled (10° and lower) was accompanied by a lowering of intracranial pressure. Even the injection of physiological salt solutions, which had been heated to 43° involves a distinct rise in intracranial pressure (Fig. 2b).

The data presented here indicate the undoubted significance of the temperature of the solution.

We studied the significance of the method of administering the solution also. As was indicated, intravenous administration of the solution leads to lowered intracranial pressure. However, administration of the same solution into an artery produced the opposite effect and is accompanied by increased pressure (Fig. 3).

Consequently, the various methods of administering the solution determine the difference in the reaction of the brain to this administration. From this point, the conclusion becomes obvious that the action of hypertonic solutions on the brain cannot be explained by a single osmotic law. The matter lies not only in the concentration of the solutions, but also in the conditions of administering them to the organism, since a solution is above all an irritant which, in one way or another, touches the vessel wall and its receptors; specifically, the osmoreceptors described by K. M. Bykov [3] which react to the least fluctuation in the osmotic pressure of the internal medium.

However, when the stimulants acting internally on the nervous system are under discussion, those stimulants should also be kept in mind which I. P. Pavlov [7] called automatic, considering these to include the changes in the blood and fluid which act directly on the nerve centers.

It is known that the administration of hypertonic solutions into the blood depresses the liquid-forming function of the vessel connections of the brain, which leads to a decrease in the fluid content of the cranial space, lowering the intracranial pressure. This inhibition of fluid-formation is especially noticeable when table salt [6, 9] is introduced, thus pointing to the greater prolongation of the action of salt compared with glucose.

When hypertonic solution is injected into a vein, the brain loses up to 5% of its moisture. This phenomenon of desiccation is usually explained by the process of osmosis. Actually, osmotic effects are widely represented in nature and we, of course, do not deny the role and significance of osmosis in physiological functions. However, in the live organism, osmosis does not occur as a physicochemical phenomenon independent of neural mechanisms, but as a process which is directly regulated by the nervous system. The speed with which osmotic balance is reestablished as described above can only be explained by the participation of neural mechanisms.

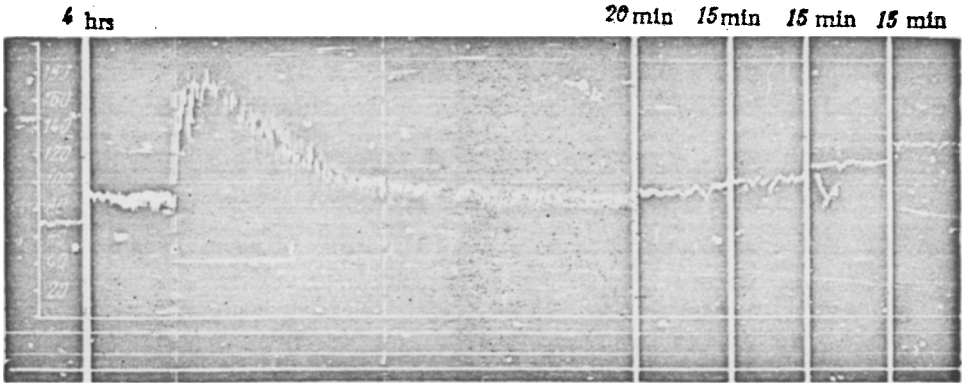

Fig. 3. Rise in intracranial pressure during arterial administration of a 15% solution of table salt. Period of solution administration delimited by arrows. Curves (top to bottom): intracranial pressure, null line, time mark (6 seconds).

The role of the reflex in increasing the permeability of the vessels of the brain when hypertonic solutions are administered into a vein was established earlier [1]. One can believe that this same mechanism which increases the permeability is the basis of increasing osmosis through the vessel membrane. The membrane factor (permeability) is one of the mechanisms which contribute to the changes in the force and direction of osmotic phenomena produced by the administration of hypertonic solution.

Three aspects of the action of hypertonic solutions on the brain can therefore be discussed: a) the action on the vessels of the brain and on their contractility; b) the effect on fluid formation; c) the action on vessel permeability and the osmotic processes. But both the vasomotor reflex and the capillary plexus reflex and the changes in permeability are all neurogenic factors, a fact which is not taken into consideration in the classical theory of osmotherapy.

The above lets certain practical conclusions be drawn; namely, solutions intended therapeutically should be administered at a temperature of not more than 38°; the use of solutions at a higher temperature can cause a rise in intracranial pressure and, consequently, can harm the patient instead of helping him; the intracranial administration of small quantities of distilled water is safe and can produce a rise in intracranial pressure which lets this method be recommended in the clinic when there is lowered intracranial pressure.

The effort to base the effect of hypertonic solutions on the nervous system and through it on the physicochemical processes in the organism can help point the way to active reflex influences on the brain during traumatic states.

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