Equipotency of Hypertonic Solutions of Mannitol and Sodium Chloride in Eliciting Thirst in the Dog*

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Received January 24, 1974

Summary. The dogs were infused intravenously with either 3.6% NaCl or 20% mannitol solutions. Both infusions stimulated the animals to drink water when similar osmotic loads were introduced and exactly the same degree of cellular dehydration achieved. The amounts of water drunk at thirst threshold did not differ significantly.

The results are discussed with relation to the hypothesis of osmometric control of water intake.

Key words: Thirst Threshold — Hypertonic Saline — Hypertonic Mannitol.

According to a currently accepted view the cellular dehydration brought about by an increase in the effective osmotic pressure of a tissue fluid is a primary stimulus to thirst and ADH release [19,22].

Recently, the osmometric theory of body water control has been criticized and a new hypothesis proposed, that the hypertonic NaCl load as well as other hypertonic solutions exert their dipsogenic and antidiuretic effects through the sodium receptors system localized near the 3rd cerebral ventricle and stimulated specifically by an increase in Na concentration [1,8,16,17].

There is accumulating evidence on the existence of hypothalamic specific osmosensitive units in different species [6,9—11,13,20,21]. Some of these units were identified as neuroendocrine cells of the hypothalamo-hypophysial antidiuretic system, the others located near the supraoptic nucleus were proposed to be osmoreceptors of Verney [21]. Unfortunately, it was impossible with the techniques available to find out whether they are involved in initiation of thirst.

The purpose of the present study was to compare the effectiveness of the hypertonic solutions of mannitol and sodium chloride given intravenously in eliciting drinking by measuring the threshold osmotic load.

* A preliminary account of some of this study has been reported at the Symposium on Thirst organized by the Union des Sociétés Suisses de Biologie Expirimentale, Lugano, October 1973.
The degree of cellular dehydration achieved at the thirst threshold was also calculated using a quantitative osmometric analysis of thirst proposed by Wolf [22]. Both mannitol and sodium chloride poorly penetrate through cell membranes [3,7] and are equally excluded by the blood-brain barrier. Thus, they are supposed to be equipotent in causing brain dehydration. As the blood-cerebrospinal fluid barrier is permeable for Na⁺, intravenous infusions of mannitol and NaCl should not produce the same increase in sodium concentration in the cerebrospinal fluid. According to the osmometric theory of water intake equal osmotic loads of mannitol and NaCl should be equally effective in eliciting drinking. On the other hand, NaCl load should be more effective in causing thirst if sodium receptors were exclusively involved in regulation of water intake. Two of the previous reports, in which the influence of NaCl and various saccharides confined to the extracellular space on water intake was examined give contradictory data [12,16].

Material and Methods

Experiments were performed on four mongrel, male dogs weighing 12—17 kg. The animals were kept fasting for 18 hrs preceding the experiment, but they had free access to water. At the beginning of the experiment an indwelling catheter was introduced into the urinary bladder through the urethra. Another catheter for blood sampling and infusing tested substances was placed in the cephalic or saphenous vein. Thirty minutes later a blood sample was taken to measure plasma osmolarity. The bladder was emptied by air flushing. A hypertonic solution of either 3.6% NaCl (1128 mOsm/l) or 200% mannitol (1105 mOsm/l) was subsequently infused intravenously at a constant rate of 5.0 ml/min. The infusion was stopped at the moment when the dog started to drink water, which was easily available throughout the whole experiment. It was assumed that at this point the osmotic load was sufficient to activate thirst mechanism. The amount of water ingested within following 10 min was measured. Urine collected during the infusion was sampled to measure its osmolarity. The magnitude of a threshold osmotic load causing drinking was calculated by subtracting number of mOsm excreted during an infusion from the number of mOsm infused. The degree of threshold cellular dehydration was calculated from osmometric equations as given by Wolf [22], but the values of plasma osmolarity (mOsm/l) and osmotic load (mOsm) were substituted for values of plasma sodium concentration and sodium load.

Extracellular fluid volume was measured using sodium thiocyanate. Total body water was calculated as the percentage of body weight. Twenty four experiments with mannitol and 27 experiments with NaCl infusion were performed. Means (X ± SE) are given throughout the paper and in Table 1.

Results

Both hypertonic solutions of mannitol and NaCl infused intravenously stimulated the dogs to drink water. The results assessing the reactivity of the thirst mechanism to 3.6% NaCl and 200% mannitol are presented in the table. It is evident that the animals started to drink when similar osmotic load was given and exactly the same degree of cellular dehydration