CENTRAL CHOLINERGIC MECHANISM FOR CONTROL OF URINE VOLUME AND ELECTROLYTE EXCRETION

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Summary : 1. Studies were conducted on urine volume and electrolyte excretion chiefly of Na and K in anaesthetized hydrated dogs.

2. Central injection of acetylcholine caused a dose dependent antidiuretic response but without any change in excretion of urinary Sodium (UNa) and Potassium (UK).

3. After central atropinization, antidiuretic response to acetylcholine was partially blocked without any effect on electrolyte excretion.

4. Intracerebroventricularly (I.C.V.) administered acetylcholine after vagotomy and spinalectomy, each done separately and together also elicited an antidiuretic response. There was no effect on electrolyte excretion.

5. It is thus suggested that acetylcholine may be acting on central cholinergic receptors concerned with A.D.H. release.

Key words: acetylcholine   atropinization   antidiuresis
cholinergic receptors

INTRODUCTION

Besides changes in systemic blood pressure and glomerular filtration rate, other mechanisms controlling urine volume (UV) and electrolyte excretion are renin, aldosterone and antidiuretic hormone (A.D.H.). Fisher *et al.* (7) showed that essential lesion in the experimentally produced diabetes insipidus is the interruption of supraoticophypophyseal tract and considerable synthesis of acetylcholine can be demonstrated in the supra optic nuclei (6). Feldberg (5) has reported that the fibres impinging on the supraoptic nuclei are cholinergic. Thus there is evidence regarding the presence of large amounts of acetylcholine and cholinergic fibres in supraoptic nucleus which in turn controls the secretion of A.D.H. The effects of centrally administered acetylcholine *per se* on urine volume and urinary excretion of sodium and potassium are ill defined. The present investigation was undertaken to study the effects of centrally administered acetylcholine on urine volume and urinary sodium and potassium excretion.

MATERIALS AND METHODS

Experiments were performed on mogrel dogs of either sex weighing between 10-15 *kg*. They were anaesthetized by pentobarbitone (30 *mg/kg*) in normal saline given intravenously.

Femoral vein was cannulated and saline infusion was given continuously throughout the experiement at the rate of 10-12 drops/min.   For the collection of urine both ureters were cannulated and connected to a graduated cylinder.   Urine samples were obtained after every 10 minutes and the volume of each sample was recorded.

Carotid artery was cannulated and blood pressure was recorded by means of mercury manometer on smoked kymograph paper.   Trachea was also cannulated and   connected to respiratory pump for artificial respiration.   Intra-cerebro ventricular (I.C.V.) cannula was implanted by the technique described by Bhargava *et al.* (1) I.C.V. injections were made in a fixed volume of 0.5 *ml.*   Vagotomy and spinalectomy were performed in some of the animals.

Electrolyte excretion in urine was measured by flame photometer and rate of   excretion (mEq/L) was calculated in each urine sample.

RESULTS

In the initial control experiments the dogs were infused intravenously with normal saline at the rate of 10-12 drops/min for 4 hours.   After initial fluctuations urine volume stabilized within half an hour and remained unchanged throughout the observation period.   There was no change in Urine Sodium (UNa) and Urine Potassium (UK) excretion.

Acetylcholine was administered intracerebroventricularly in different doses (1,5,10,20,50, 100 μg).   All the doses of acetylcholine caused a decrease in urine volume and the   effect was dose dependent.   The maximal effect was observed within 20 minutes after its   administration and the same magnitude persisted for 30 minutes.   Urine volume returned to normal after 2 hours. There was, however, no change in UNa and UK excretion   (Table I).   Higher doses (50,100 μg) caused   only   a   slight and   transient rise of   5-10   mm   Hg   in BP   which   lasted for 10 to 15 minutes.

TABLE I :   Effects of central (I.C.V.) administration of acetylcholine on urine volume and electrolyte excretion

Dose	Urine volume ml ±SE	UNa mEq/L ±SE	UK mEq/L ±SE
Control	2.5±.35	130±3.57	76±3.92
1 μg	2.1±.13**	122±4.87*	86±3.94*
5 μg	1.8±.27***	123±4.90*	84±4.49*
10 μg	1.7±.22***	137±3.45*	64±4.26*
20 μg	1.5±.31****	139±4.17*	70±3.22*
50 μg	1.2±.28****	120±3.57*	68±4.49*
100 μg	0.8±.25****	138±4.19*	85±3.74*

* P > .05	*** P < .01
** P < .05	**** P < .001

Central atropinization (1 *mg* I.C.V.) caused partial blockade of the effect of acetylcholine on urine volume in all doses.   Urinary excretion of Na, K and BP however remained unaffected with all the doses of acetylcholine given subsequently (Table II).

TABLE II :   Effects of central (I.C.V.) administration of acetylcholine on urine volume and electrolyte excretion after central atropinization.

Dose	Urine volume ml ±SE	UNa mEq/L ±SE	UK mEq/L ±SE
Control	2.7±.40	126±5.80	75±3.70
1 µg	2.4±.30*	132±6.10*	70±4.21*
5 µg	2.3±.29**	138±4.82*	80±4.40*
10 µg	2.1±.30**	136±4.10*	65±3.68*
20 µg	1.9±.10***	134±3.42*	82±3.82*
50 µg	1.7±.28***	140±5.9*	68±3.57*
100 µg	1.4±.24****	120±5.4*	84±3.94*

* P>.05   *** P<.01
** P<.05   **** P<.001

Acetylcholine given centrally after vagotomy again elicited a dose dependent antidiuretic response but without any change in UNa and UK excretion.   Similar response was observed after vagotomy coupled with spinalectomy.

DISCUSSION

There is evidence that both cholinergic and adrenergic neurones occur within central nervous system.   Many parts of brain and spinal cord contain acetylcholine, choline-acetylase and cholinestrase.   There are many cholinoceptive receptors on the cells which are stimulated or inhibited by the application of acetylcholine through microelectrode (11).   Fang *et al*. (4) have shown that stimulation of hypothalamus results, in mild to moderate antidiuretic effect.   This response was obtained not only by stimulation of supraoptic and paraventricular region but also by other areas of hypothalaumus.

That the antidiuretic response is due to liberation of acetylcholine has been confirmed by Pickford (9) who suggested that the pathway for antidiuretic response involves a synapse at the supraoptic nucleus at which acetylcholine acts as a transmitter of afferent nerve impulses.

Gerschenfeld *et al*. (8) have also reported that terminal portion of hypothalmohypophyseal tract contains both neurosecretory material and synaptic vesicles and that these synaptic vesicles release acetylcholine which in turn triggers the neurosecretion from the same axon.   Pickford (9) showed that acetylcholine acts on supraoptic nucleus to cause ADH release.

Our results suggests that acetylcholine given centrally acts on central cholinergic receptors present in supraoptic nucleus causing ADH release, which in turn affects the urine volume.   This

has also been reported by Bhargava *et al.* (2). Acetylcholine given centrally after vagotomy and spinalectomy done separately and together again caused a dose dependent antidiuretic repsonse without any effect on electrolyte excretion suggesting that the antidiuretic response is caused through the liberation of some neurotransmitter, presumably ADH.

The possibility that cholinergic receptors present in brain to cause ADH release is further supported by the fact that central atropinization only partially blocked the oliguria produced by acetylcholine because it has been known that the anticholinergic agents, atropine, ethylbenzatropine inhibit ADH release transiently (10). Atropine failed in completely blocking the effect of acetylcholine, because besides cholinergic receptors there are also adrenergic receptors present in supraoptic nucleus which have a dual function in the control of ADH release (3) since α-adrenoreceptors are responsible for the release of ADH whereas the β-adrenoreceptors inhibit the ADH release (2).

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