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THE REACTION OF RAT KIDNEY TO ACUTE STRESS SOLUTION OF SODIUM CHLORIDE IN NORMAL AND OCCASIONAL ABUSE OF THYROID STATUS

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Abstract

Objective: To study the effectiveness of osmoregulation of renal function in rats with occasional violation of thyroid status in the acute intragastric load of sodium chloride solutions.

Materials and Methods: The study was carried out on white male rats, thyroxine was administered once intraperitoneally, 50 mg/100 g body weight. Kidney function was studied in conditions induced diuresis after intragastric administration of stress testing water or 0.3%, 0.8%, 2% and 3% sodium chloride solution in a volume of 5% of body weight.

Results: It was found that thyroxin causes a decrease in creatinine clearance and increased renal excretion of endogenous nitrates and nitrites. In control solutions, increasing concentrations of sodium chloride cause progressive increase in glomerular filtration rate values and excretion of osmotically active substances. Discovered a more complex dependence of the values of diuresis and the concentration of NaCl. Minimum performance diuresis recorded using a solution of 0.8% NaCl, and the maximum - in load and aqueous 3% solution of NaCl.

Conclusions: 1. The kidneys of rats administered once T4 retain the ability excretion of excessive amounts of liquid and OAB, protecting the internal tissues and organs from hypoosmia and hyperosmotic stress. 2. A single dose of T4 rats can induce switching mechanisms of renal volume regulation and osmoregulation in the phylogenetically ancient tubular type of regulation of fluid excretion by the kidneys and the OAB. 3. For short abuse thyroid status changes in GFR and tubular transport OAB are reversible.

Abbreviations: T4 - thyroxine, TH - thyroid hormones, OAS - osmotically active substances; GFR - glomerular filtration rate; RFR - renal functional reserve, GF - glomerular filtrate

Introduction

Reactions rat kidney for a single and continuous exogenous T4 shown in creatinine clearance and creatinine concentration index, as well as to increase the discharge of nitrates and kidney protein (1). Thyroid Hormones (TH) have an effect on tubular reabsorption of sodium (2, 3), and sodium-dependent transport (2), mineral (4, 5) and organic substances (6, 7) in the tubular epithelium. TH closely involved in the regulation of humoral intrarenal autoregulation systems, including renin-angiotensin system (8, 9) and nitric oxide synthase (10, 11). TH directly stimulate secretion of atrial natriuretic peptide (12) for background suppression product arginine vasopressin (13). Prolonged for hyperthyroidism can lead to distinct structural violations of the nephron (14). However, the pathophysiological mechanisms of renal dysfunction in hyperthyroidism require deeper analysis.

The aim was to study the effectiveness of osmoregulation of renal function in rats with occasional violation of thyroid status in acute intragastric load of sodium chloride solutions.

Materials and Methods

The studies were conducted during the winter season. In experiment 3-month selected male rats weighing 95-115 g (n = 100). 3 days prior to the introduction of thyroxine hyponatric animals were switched to a diet. As stress tests using water or sodium chloride, whose concentration was 0.3%, 0.8%, 2% and 3%. Intra-gastric load water or saline in a volume of 5% by weight was carried out 24 hours after a single intra-gastric administration of thyroxine to 50 g/100 g bw. Urine was collected in individual metabolic cages for 2 hours after administration of liquid loading. From experimental animals derived by decapitation under light ether anesthesia. Heparin stabilized blood was centrifuged at 3000 rpm / min for 20 minutes and collected the blood plasma for further analysis. In the resulting plasma and urine concentrations of creatinine were determined photometrically in reaction with picric acid in an SF-46 (Russia). The concentration of nitrite and nitrate photometric method using the Griess reagent (15) in our modification (1). The amount of osmolality of blood and urine were determined by freezing point depression osmometer 3D3 (USA). Indicators and the kidneys were calculated guided previously published formulas (16).

Results of the study

It is established that the amount of urine output depends on the type of load used and under the influence of exogenous thyroxine does not change significantly (Table 1). Thus, the maximum values of the volume of urine in the control and experimental groups of animals found with the introduction of water and 3% sodium chloride solution. At the same time, the minimum amount of urine parameters recorded using 0.8% saline. Table 2 presents the dynamics of creatinine clearance is influenced by the water and salt stress. The results show that in the water load, 24 hours after a single administration of thyroxine noted a significant decrease in creatinine clearance. In this group of animals as compared to control, water stress and strain of 0.3%, 0.8% and 2% solutions of sodium chloride does not have a significant effect on the amount of creatinine clearance. However, the use of 3% NaCl solution, accompanied by an increase in creatinine clearance up to a level close to the reference values. In the control group of rats administered with 0.8% solution of NaCl, in comparison with those in group water load euthyroid animals registered a significant increase in creatinine clearance. In control animals the indicator reaches a maximum when administered 2% saline. Table 3 shows the values of the endogenous renal excretion of nitrites and nitrates - chemically stable metabolite of nitric oxide molecule. These results indicate that administration of thyroxine accompanied by increased renal excretion of these substances with water load in comparison with the control group. At the same time, load conditions 0.8% active sodium index was higher in the intact rat (2 times) and 3%

load solution did not have significant differences between groups, although higher than the same parameter set in the aquatic load for 10 times control and 4.5 fold in rats receiving thyroxine. Analysis of the renal excretion of osmotically active substances (OAS) (Table 4) showed a direct correlation of this indicator on the value of osmolality of the stress test. Not found significant changes in kidney allocation OAB under the influence of thyroxine. Table 5 presents the standardized per 1 ml of glomerular filtrate (CF) excretion of OAB. Found that the active component in the group of rats treated with thyroxine, than the same parameter in control animals in the water load, and when used as a liquid load of 0.3%, 0.8% and 2% solution of sodium chloride. In addition, using 3% sodium chloride solution no significant differences between OAS excretion standardized groups of control rats and animals against thyroid status. Table 6 shows the results of measuring the blood plasma osmolality. Found that in comparison with the data of the water load, the use of liquid as a loading of 0.3%, 0.8% and 2% solution of sodium chloride does not lead to a significant increase in the osmolality of the extracellular fluid in the control group rats and animal disorders of thyroid status. A moderate increase in plasma osmolality in both groups of rats recorded only under the influence of 3% saline solution.

Discussion

Studies have shown that the dynamics of the value of diuresis in the series used loads of salt has no clear-cut differences between the experimental group and the control animals. However, attention fact distinct reduction rate of urine influenced 0.8% sodium chloride solution as compared with the other salt solutions. It should be noted that the progressive decrease in magnitude of diuresis influenced sodium chloride solutions in concentrations ranging from 0.05 to 0.5% of 0.5% of body weight was observed in several studies in the earlier tests of renal function in humans (17). In our opinion, the effect can be detected be of practical interest, since similar concentrations of sodium chloride are used in medicine to make up the massive blood loss. In this case, the early recovery of renal function in surgical patients and patients with multiple injuries in the postoperative period is essential. Based on the above research results, it can be assumed that the use of only the salt solution close to physiological extracellular fluid does not fully correspond tasks. We believe this may be due to the fact that the iso-osmotic sodium chloride solution, firstly, insufficiently effective for the stimulation of the glomerular filtration rate (GFR), and secondly, it can lead to oliguria.

Discussing the dynamics of change in creatinine clearance value (a marker of GFR) in series of studies conducted, note that in normal GFR values may vary significantly influenced shifts system constants water-salt (16) and reversible changes in the energy metabolism proximal

nefrostitah (16, 18). In this regard, discusses the diagnostic value of detection of renal functional reserve (RPF) - the ability of the kidneys to increase the value of GFR (19). However, distinct structural damage to the renal parenchyma of rats in experimental hyperthyroidism are registered only in the long course of Experimental Pathology (20). An analysis of the physiological mechanisms that control the inclusion of the RPF, is an important area of research. Thus, the inclusion of the RFR in dogs induced by intravenous injection of 2% sodium chloride, but not isoosmotic solution against the background reduce RAS activity - the renin-angiotensin system (21). A number of publications expressed the view that some of the features of the body's response to oral and intravenous routes of administration of sodium chloride solutions (22). However, the results of a direct comparison of effects of the intravenous infusion and oral consumption of salt solutions in general have not revealed the principal differences (23).

We emphasize that the study of adaptation to acute shifts system constants of water-salt homeostasis in healthy subjects showed the priority of NO-dependent mechanisms control the activity of the RAS in comparison with the role of prostaglandins (24). The balance of the activity of the intrarenal NO-synthases and the RAS is one of the basic factors controlling tubulo-glomerular feedback (25, 26). Thus, TH, have the ability to directly stimulate the intrarenal synthesis of prorenin (8, 27) and nitric oxide (28), inducing a deep structural and functional changes the filtration and tubular transport of substances in rats by prolonged administration of thyroxine (29). However, detailed interpretation index endogenous renal excretion of nitrites and nitrates, is difficult, because of the possible changes in the parameter shifts can be due to systemic products intrarenal and NO, and the state of tubular reabsorption physiologically important nitrite and nitrate anions. In addition to these factors, it should be noted that the experimental conditions associated with the use of sodium chloride solutions. This means that the liquid used for loads animals containing water, sodium cations and chloride anions. Meanwhile, the chlorine ions have the ability to compete with nitrite anions in relation to the specific anion-transporting system (30). Consequently, the growth rate of distinct dynamics excretion by the kidneys stable NO metabolites with increasing concentrations of NaCl can be caused also by the fact that increasing concentrations of chloride ions interfere with the processes of their tubular reabsorption.

Own results suggest that the group of control animals using saline solutions intensity increases renal excretion chemically stable nitric oxide - endogenous nitrites and nitrates in comparison with the water load. However, a linear relationship between the speakers sodium chloride concentration in the sample loading, the size of creatinine clearance and renal excretion

rates of nitrite and nitrate was observed. However, the highest possible rate of renal excretion of NO metabolites coincide with the highest possible performance of GFR - using 2% and 3% solutions of NaCl. In a water load in the group of animals exposed to single administration of T4 value renal excretion of NO metabolites is significantly higher than in controls. Image endogenous kidney excretion rate of nitrates and nitrites in the group of rats treated with T4 recorded only under the influence of 2% solution of NaCl. Meanwhile, in the group of animals load 2% NaCl did not lead to significant changes in GFR values. With occasional violations of thyroid status marked increase in GFR (including RPF) we see only under the influence of 3% solution of NaCl.

Stimulation of the salt solutions intrarenal NO production is important not only for the regulation of filtration processes, but also to control the tubular transport of sodium. The results of earlier histochemical studies have shown that the highest levels of expression of NO-synthase occur in the ascending limb of the loop of Henle and topologically identical to the location of sodium-potassium-2chlor transport system (31, 32, 33). Later it was shown that stimulation of NO production intrarenal provides enhanced renal excretion of sodium in excess of its entry into the body (34, 35). Results of the research show that in the control group of rats, a sharp increase in renal excretion of NO metabolites occurs only if a 3% solution of NaCl. Then, as in rats receiving T4 significant increase in excretion of NO metabolites detected at 2% solution of NaCl. Thus, the values of renal excretion osmotically active substances (OAS) - only one of the parameters studied, correlating with increasing NaCl concentration in the sample load, as in euthyroid rats and animals against a sporadic thyroid status. Also draws attention to a significant between-group difference in the mechanisms that control the gain of excretion by the kidneys OAB. In particular, the group of control animals increase excretion OAB occurs as increased GFR. Then, as in rats receiving T4 OAS increase renal excretion occurs mainly against steadily reduced GFR. Tracing the dynamics of the magnitude of excretion by the kidneys OAS, standardized to 1 ml glomerular filtrate (GF), it is permissible to assume that the control rats excretion of excessive amounts of OAB is both due to the growth of the filtration charge, and as a result reduce the tubular reabsorption of OAB. While both animals treated with T4 filtration none OAB may influence their rate of excretion by the kidneys but using 3% solution of NaCl. Complementing the views expressed integral indicator of the effectiveness of osmoregulation of renal function - the value of plasma osmolality studied groups of animals, we should note two important features. First, the number of loads of salt used is not revealed distinct differences in this parameter between the control rats and animals treated with T4. Second, except for the

results load 3% solution NaCl (solution osmolality value of 1050 mOsm / kg H₂O), osmoregulation renal function ensures a sufficiently stable level osmolality of the extracellular fluid.

Conclusions

1. The kidneys of rats administered once T4 retain the ability excretion of excessive amounts of liquid and OAB, protecting the internal tissues and organs from hypoosmia and hyperosmotic stress.
2. A single dose of T4 rats can induce switching mechanisms of renal volume regulation and osmoregulation in the phylogenetically ancient tubular type of regulation of fluid excretion by the kidneys and the OAB.
3. For short abuse thyroid status changes in GFR and tubular transport OAB are reversible.

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Table 1. Effect of a single administration of an amount of thyroxine in rats 50 g per 100 g bw on value diuresis - ml/ch/100 g bw (M ± m).

Groups	Type of load				
	Water	0.3% aq NaCl	0.8% aq NaCl	2% aq NaCl	3% aq NaCl
Control n = 10	2,1 ± 0,2	1,8 ± 0,2	1,1 ± 0,1	1,5 ± 0,1	2,5 ± 0,1
Introduction of thyroxine n = 10	1,9 ± 0,2	1,3 ± 0,1 p < 0,05	0,8 ± 0,1	1,7 ± 0,2	2,4 ± 0,2

p-confidence index differences between the groups of rats treated with thyroxine and control animals.

n-number of observations.

Table 2. Effect of a single administration of an amount of thyroxine in rats 50 g per 100 g bw rats on value creatinine clearance - l / min ($M \pm m$).

Groups	Type of load				
	Water	0.3% aq NaCl	0.8% aq NaCl	2% aq NaCl	3% aq NaCl
Control n = 10	528 ± 27	552 ± 20	680 ± 24	943 ± 40	970 ± 27
Introduction of thyroxine n = 10	387 ± 23 p <0,05	375 ± 31 p <0,05	455 ± 34 p <0,01	384 ± 28 p <0,01	885 ± 39 -

p-confidence index differences between the groups of rats treated with thyroxine and control animals.

n-number of observations.

Table 3. Effect of a single administration of an amount of thyroxine in rats 50 g per 100 g bw value on excretion of nitrites and nitrates - mkmol/ch/100 g bw ($M \pm m$).

Groups	Type of load				
	Water	0.3% aq NaCl	0.8% aq NaCl	2% aq NaCl	3% aq NaCl
Control n = 10	0,021 ± 0,008	0,054 ± 0,010	0,092 ± 0,009	0,079 ± 0,0013	0,203 ± 0,027
Introduction of thyroxine n = 10	0,042 ± 0,007 p <0,01	0,058 ± 0,012	0,041 ± 0,012 p <0,01	0,144 ± 0,021 p <0,01	0,188 ± 0,019

p-confidence index differences between the groups of rats treated with thyroxine and control animals.

n-number of observations.

Table 4. Effect of a single administration of an amount of thyroxine in rats 50 g per 100 g bw the value of excretion OAS - mosmol/ch/100 g bw ($M \pm m$).

Groups	Type of load				
	Water	0.3% aq NaCl	0.8% aq NaCl	2% aq NaCl	3% aq NaCl
Control n = 10	0,21 ± 0,04	0,28 ± 0,02	0,41 ± 0,03	1,19 ± 0,17	1,94 ± 0,09
Hyperthyroidism n = 10	0,22 ± 0,03	0,23 ± 0,05	0,44 ± 0,04	1,21 ± 0,12	1,85 ± 0,014

p-confidence index differences between the groups of rats treated with thyroxine and control animals.

n-number of observations.

Table 5. Effect of a single administration of an amount of thyroxine in rats 50 g per 100 g bw the value standardized excretion OAS - mOsm / ml SF ($M \pm m$).

Groups	Type of load				
	Water	0.3% aq NaCl	0.8% aq NaCl	2% aq NaCl	3% aq NaCl
Control n = 10	(6,4 ± 0,2) x 10 ⁻³	(8,4 ± 0,3) x 10 ⁻³	(9,7 ± 0,1) x 10 ⁻³	(20,6 ± 0,8) x 10 ⁻³	(33,1 ± 0,9) x 10 ⁻³
Introduction of thyroxine n = 10	(8,1 ± 0,2) x 10 ⁻³ p <0,05	(10,6 ± 0,3) x 10 ⁻³ p <0,05	(14,5 ± 0,3) x 10 ⁻³ p <0,01	(51,3 ± 1,5) x 10 ⁻³ p <0,01	(34,5 ± 1,2) x 10 ⁻³

p-confidence index differences between the groups of rats treated with thyroxine and control animals.

n-number of observations.

Table 6. Effect of a single administration of an amount of thyroxine in rats 50 g per 100 g bw the value of blood plasma osmolality - mOsm / kg H₂O (M ± m).

Groups	Type of load				
	Water	0.3% aq NaCl	0.8% aq NaCl	2% aq NaCl	3% aq NaCl
Control n = 10	300 ± 1	298 ± 2	295 ± 2	306 ± 2	315 ± 2
Introduction of thyroxine n = 10	298 ± 2	297 ± 2	298 ± 2	305 ± 2	312 ± 2

p-confidence index differences between the groups of rats treated with thyroxine and control animals.

n-number of observations.