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FLUID CONSUMPTION, ELECTROLYTE EXCRETION AND HEART REMODELING IN RATS WITH MYOCARDIAL INFARCT MAINTAINED ON REGULAR AND HIGH SODIUM INTAKE

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The purpose of the study was to determine effect of high sodium intake on fluid and electrolyte turnover and heart remodeling in the cardiac failure elicited by myocardial infarction (MI). The experiments were performed on four *groups* of Sprague Dawley rats maintained on food containing 0.45% NaCl and drinking either water (*groups 1, 2*) or 1% NaCl (*groups 3, 4*). *Groups 1* and *3* were *sham*-operated while in *groups 2* and *4* MI was produced by the coronary artery ligation. In each *group* food and fluid as well as sodium intake, urine (V_u), sodium ($U_{Na}V$), potassium (U_KV) and solutes ($U_{osm}V$) excretion were determined before and four weeks after the surgery. Size of the infarct, left ventricle (LV) weight and diameter of LV and right ventricle (RV) myocytes were determined during *post-mortem* examination. Before the surgery *groups 3* and *4* ingested significantly more fluid and sodium, had higher V_u , $U_{Na}V$, U_KV and $U_{osm}V$ than the respective *groups 1* and *2*. In *groups 2* and *4* MI resulted in significant decrease in V_u , $U_{Na}V$ and $U_{osm}V$ in comparison to the *pre-surgical* level. In *Group 4* MI resulted also in a significant decrease of food and sodium intake. The MI size did not differ in *groups 2* and *4* while diameter of LV myocytes was significantly greater in *groups 2* and *4* than in *groups 1* and *3*, and in *group 4* than in *group 2*. The study reveals that prolonged high sodium consumption increases fluid and electrolyte turnover both in the *sham* and in the MI rats and that the MI causes decrease in food and sodium intake in rats on high but not on regular sodium intake. In addition high sodium diet promotes development of greater *post-MI* hypertrophy of the LV myocytes.

Key words: *heart failure, sodium balance, heart hypertrophy*

INTRODUCTION

An extensive myocardial infarction dramatically changes hemodynamic conditions within the cardiovascular system. Reduced performance of the left ventricle (LV) causes disturbances in the systemic and pulmonary circulation and an imbalance in activity of the parasympathetic and sympathetic components of the autonomic nervous system. This is associated with an activation of the neurohormonal mechanisms involved in maintenance of the long-term tissues perfusion (1-8). At the same time persistent overloading of the active portion of the cardiac muscle results in structural remodeling of the heart (9). High sodium intake is one of the environmental factors that may influence these processes (2, 5, 10-12). However, thus far the effects of prolonged high sodium intake on water-electrolyte turnover and remodeling of the heart in the *post*-infarct cardiac failure have not been addressed and an integrated analysis of fluid and sodium intake and excretion has not been performed. The primary purpose of the present study was to compare fluid and electrolyte intake and excretion before and 4 weeks after myocardial infarction produced by ligation of the left coronary artery in the Sprague Dawley (SD) rats maintained either on water or on 1.0% NaCl as the sole drinking fluid. In addition, we have investigated whether the prolonged high sodium ingestion influences diameter of surviving myocytes of the left and right ventricle of the heart.

MATERIAL AND METHODS

Animals

The study was performed on Sprague Dawley (SD) male rats that were 11-12 weeks old at the start of the balance studies. The rats were maintained on 12h /12h light/dark cycle and fed *ad libitum* with a commercial rat diet containing 0.45% NaCl. At age of 10 -11 weeks the rats were divided at random into four groups. *Group 1 (sham-water)*, and *group 2 (infarct-water)* were maintained on water whereas *group 3 (sham-saline)* and *group 4 (infarct-saline)* received 1% NaCl as the sole drinking fluid during 2 weeks before and four weeks after the surgery. The experimental procedure was approved by the Ethical Committee on the Animal Research of the Warsaw Medical University.

Surgery

The myocardial infarct was produced by ligation of the left coronary artery. The surgery was performed under chloral hydrate anesthesia (300 mg/kg). The thoracic cavity was opened between the 4th and the 5th intercostal space while the lungs were ventilated by frequent air puffs administered manually by means of a small rubber balloon connected with the rat's nose by means of the plastic tube. The heart was exteriorized and the left coronary artery was ligated with a 7-0 prolene suture (Ethicon). The heart was placed back in the thoracic cavity, the wound was closed with a 4.0 surgical suture (Ethicon) and the rat started to breathe spontaneously. After surgery the rats were given antibiotic (Augmentin, Polfa) and placed in their home cages. Similar procedure was applied during the *sham* surgery, except that the pericardium was only touched

with the needle but the coronary artery was not ligated. In each rat the size of the infarct was evaluated during the *post mortem* examination. The method of maintenance of respiration by means of the balloon is faster, less traumatic for the animal and equally effective than the methods requiring application of the respiratory pump. The rate of survival of the rats subjected to the myocardial infarct was equal to 55%. The rats were dying during the course of the surgery or during the first 24 hours after the surgery.

Experimental protocol

Four days before the surgery the *sham-water* (n=9), *infarct-water* (n=9) *sham-saline* (n=9) and *infarct-saline* (n=8) groups were placed in the metabolism cages (Tecniplast). After two days of adaptation to the new environment control measurements of 24h food and fluid intake and 24h urinary excretion of sodium, potassium and solutes were performed. The same procedure was repeated 4 weeks after the surgery.

Determination of fluid and electrolyte turnover

Sham-water, *infarct-water*, *sham-saline* and *sham-infarct* rats were always placed to the metabolism cages in parallel experimental trails. Urine was collected under paraffin to avoid evaporation. At the end of each collecting period its volume was measured and sodium (U_{Na}) and potassium (U_K) concentrations were determined by means of a flame photometry (FLM3 Flame Photometer Radiometer). Urine osmolality (U_{osm}) was measured by means of an osmometer (Knauer Microosmometer). Daily excretion of sodium, potassium and solutes was calculated by multiplying U_{Na} , U_K and U_{osm} by 24h urine excretion, and expressed per 100g of body weight. Daily sodium intake (Na_m) was calculated by adding sodium ingested in the food and in the drinking fluid.

Measurements of heart weight and infarct size

At the end of the experiments the rats were sacrificed by an overdose of the anesthetic and the heart was removed for histological examination and morphometric measurements. Immediately after excision of the heart from the thorax, the blood was removed from the chambers by gentle washing with saline and the heart was dried with tissue. After separation of the ventricles from the atria the wall of the left ventricle (LV) including the septum, was separated from the right ventricle wall (RV) and weighed. Subsequently the LV was cut along the longitudinal axis and placed flat on a transparent paper. The dimensions of the infarct were determined by means of planimetry. To this end, the circumference of the infarct and of the whole ventricle on the internal and external surfaces were outlined on graph paper, and the results of the two measurements were averaged. The size of the infarct is presented throughout the study as the ratio of the averaged surface of the infarct to the averaged surface of the whole ventricle and expressed as a percentage of the LV surface. The rats in which the infarct size was smaller than 25% of the LV surface were excluded from the statistical analysis because it was found in preliminary experiments that in the rat the infarct occupying less than 25% of the LV wall does not cause significant changes in the renal excretory functions.

Histology and morphometry

Histological inspection of the hearts and morphometric measurements were performed in each rat subjected to the balance studies. Left and right ventricles were placed in 10% formaldehyd solution. Fixed tissue blocks from both ventricles were paraffin-embedded and sectioned at 4 μ m. In case of the infarcted rats tissue blocks encompassing the entire LV circumference were excised from each heart, fixed in 10% formalin, paraffin-embedded and sectioned, as described. The slices

from the LV were processed for hematoxylin and eosin staining for routine morphologic examination. To evaluate fibrosis in the postinfarct scar the 4 μm -thick paraffin-sections were deparaffinized, rehydrated and stained for 1h with 0.1% Sirius Red (a collagen specific dye) in saturated aqueous picric acid (13). This was followed by rapid dehydration for 2 x 1min in 100% ethanol. To determine the collagen volume fraction within the postinfarctal scar the morphometry was performed using computer-based semi-automated image-analysis system AnalySIS (Zeiss) coupled to CCD camera (PAL, 768x576 fps). The whole area of the scar was analyzed under white light at x 200 objective magnification. For each optical field color level threshold was set for stained collagen. The summarized surface of all detected objects (positive for collagen staining) was expressed as a fraction of the total area within each field. Measurements of diameter of myocytes were performed on slices prepared according to the procedure described above, in the white optical field, at x 400 objective magnification using the AnalySIS system. In each case only perpendicular sections of the myocytes were approved for diameter evaluation. In each rat 20 myocytes were selected for diameter measurements and the mean values of these measurements were subjected to statistical analysis. In case of slices taken from the hearts of the control group measurements were performed on randomly chosen optical fields. In the myocardium from the infarcted rats the diameter of myocytes in the infarct-free wall located at the distance of at least 2 mm from the infarct scar was determined.

Statistical analysis

All values presented in the text and Figures are means \pm standard errors. The data were analyzed by means of Statistica software (release 5). The overall analysis of significance was performed using three-way ANOVA with two levels of rats (*sham* vs *infarct*) x two levels of experimental designs (*water* drinking vs *saline* drinking rats) and two levels of measurements (before and after surgery) (14). Two-way ANOVA was applied to isolate significant differences between the control and the postsurgery measurements in MI and *sham* rats drinking either water or saline. Detailed comparisons to isolate significant differences between the *pre*- and *post*-surgery measurements, and between the *sham* and the *infarcted* rats, and water and saline drinking rats was performed using the Tukey test. The homogeneity of variance was tested and square root transformation was applied, whenever necessary. The results were considered significant if P was less than 0.05.

RESULTS

General characteristics. Before the surgery body weight of the *infarct-water*, *sham-water*, *infarct-saline* and *sham-saline* rats was similar in all groups, being equal to: 320 ± 9 g, 336 ± 9 g, 320 ± 10 g, and 337 ± 5 g, respectively. Four weeks after the surgery body weight increased significantly in all groups [F(1,31) = 60.5; P < 0.0001]. The increase in body weight in the *infarcted* rats was significantly smaller than in the *sham* rats [F(1,31) = 5.81; P < 0.02], however no significant differences were found between the *infarct-water* and the *infarct-saline* groups.

Post mortem examination of infarct size The infarct size in the rats maintained on saline was equal to $38.2 \pm 2.4\%$ (range 27.6% - 45.5%) of the LV wall and did not differ from that found in the rats maintained on water ($36.7 \pm 2.5\%$; range 31.5 - 48.5%) of the LV wall. The LV weight expressed in g/100g of body weight

in the *infarct-water* (0.23 ± 0.01), *sham-water* (0.22 ± 0.01), *infarct-saline* (0.26 ± 0.02) and *sham-saline* (0.24 ± 0.01) groups did not differ significantly.

Histology and morphometric measurements. A macroscopic evaluation of the infarct size was confirmed by histological examination. Significant differences were found in diameter of myocytes between the *sham-operated* and the *infarcted* rats [$F(1,31) = 889.4$; $P < 0.0001$], water-drinking and saline-drinking rats [$F(1,31) = 15.5$; $P < 0.0004$], and LV and RV myocytes [$F(1,31) = 825.1$; $P < 0.0001$]. Detailed analysis revealed that the differences were caused by significant changes in diameter of myocytes of the LV and RV of the infarcted rats. In the *sham-water* rats the average diameter of the LV myocytes amounted to $17.0 \pm 0.01 \mu\text{m}$. In the *infarct-water* rats diameter of LV myocytes was significantly greater and amounted to $26.2 \pm 0.01 \mu\text{m}$ (*sham vs infarct* $P < 0.0001$) (*Fig. 1*). The average diameter of the RV myocytes in the *sham-water* and *infarct-water* rats did not differ and amounted to $16.7 \pm 0.01 \mu\text{m}$ and to $17.6 \pm 0.01 \mu\text{m}$, respectively. In the *infarct-water* rats diameter of the RV myocytes was significantly smaller than the diameter of LV myocytes ($P < 0.0001$). In the *sham-saline* rats diameter of the LV myocytes was equal to 17.6 ± 0.01 and did not differ from that found in the *sham-water* rats. In the *infarct-saline* rats the average diameter of the LV myocytes increased to $27.2 \pm 0.01 \mu\text{m}$ and was significantly greater than in the *sham-saline* ($P < 0.0001$) and in the *infarct-water* rats ($P < 0.05$) (*Fig. 1*). In the *sham-saline* rats the average diameter of RV ($17.3 \pm 0.01 \mu\text{m}$) and LV myocytes did not differ. In the *infarct-saline* rats the diameter of the RV myocytes amounted to $18.1 \pm 0.01 \mu\text{m}$ and was significantly smaller from the average diameter of the LV myocytes in the *infarct-saline* rats ($P < 0.0001$). No significant differences were found in the total collagen concentration in the infarct scar of rats maintained on water (0.29 ± 0.03) and in those drinking saline (0.33 ± 0.03).

Fluid turnover. The rats maintained on saline ingested significantly greater amount of fluid than those maintained on water [$F(1,31) = 68.9$; $P < 0.0001$]. Detailed analysis revealed that the *sham-saline* and the *infarct-saline* rats consumed significantly more fluid than their water drinking counterparts both during the control (*pre-surgical*) period and four weeks after the surgery (*Fig. 2*). Significant difference was also found between fluid intake during the control and the *post-infarct* period [$F(1,31) = 7.31$; $P < 0.01$], however the detailed analysis did not show significant differences between pairs of any of the essential measurements, either in the saline drinking or in the water drinking rats (*Fig. 2*).

Urine excretion was significantly higher in saline drinking than in water drinking rats [$F(1,31) = 63.84$; $P < 0.0001$]. In the saline drinking rats urine excretion was significantly higher both before and after the surgery (*Fig. 2*). Significant difference was also found between the control and the *post-surgical* periods [$F(1,31) = 6.16$; $P < 0.01$] and the data obtained in the *sham-operated* and the *infarcted* rats significantly interacted [$F(1,31) = 7.21$; $P < 0.01$]. Detailed analysis revealed that the significance was caused by a significant *post-infarct*

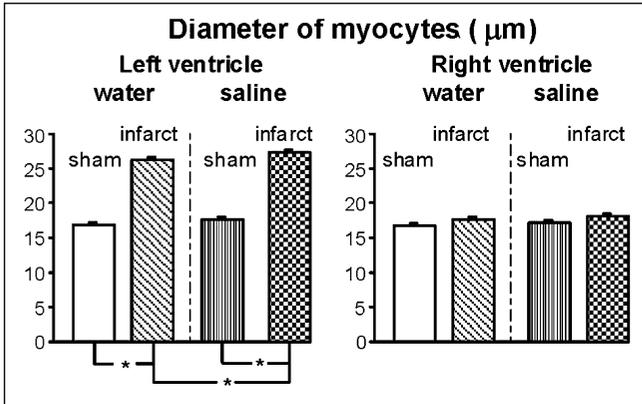


Fig. 1. Diameter of myocytes in the wall of the left and right ventricle of the heart. The asterisks indicate significant difference between the corresponding columns. Empty column: *sham-water* rats, diagonally dashed column: *infarct-water* rats, vertically dashed columns: *sham-saline* rats, squared dashed columns - *infarct-saline* rats. Other explanations in text.

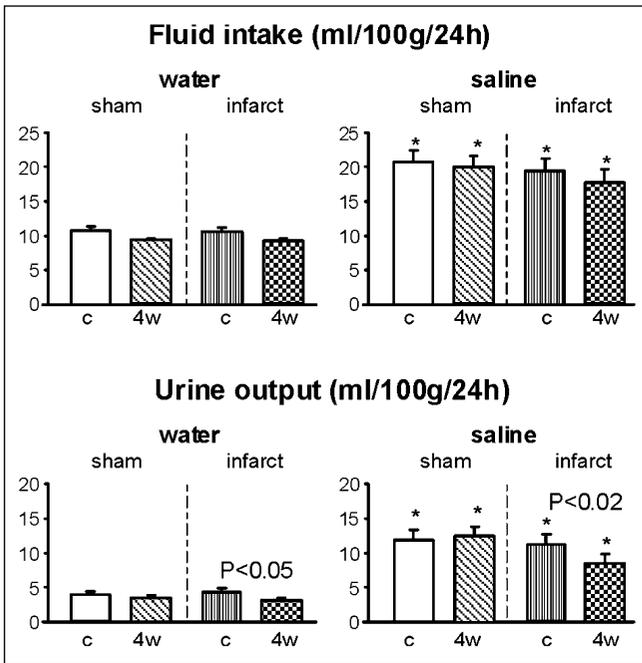


Fig. 2. Twenty-four hour fluid intake and urine output expressed per 100 g of body weight, in the *sham-operated* and the *infarcted* rats drinking either water or saline, c - control before surgery, 4w - four weeks after the *infarct* or the *sham-operation*. * significant difference between the *saline-drinking group* and the corresponding *water-drinking group* at the level of $P < 0.0001$. For other explanations see Fig. 1.

decrease in urine output in the *infarct-water* ($P < 0.05$) and the *infarct-saline* groups ($P < 0.02$), whereas in the other groups urine excretion was not significantly affected (Fig.2).

Sodium turnover. Total sodium intake (in food and water) in the infarcted and in the *sham-operated* rats maintained on saline was significantly greater than in the corresponding groups maintained on water [$F(1,31) = 194.17$; $P < 0.00001$] (Fig. 3). Significant difference was also found between the control periods and the *post-surgical* periods [$F(1,31) = 9.84$; $P < 0.004$]. Detailed analysis revealed that the latter significance was caused by a significant decrease in sodium intake

for the combined data from the *infarct-saline* and the *sham-saline* groups [$F(1,15) = P < 0.03$], but there was no significant decrease in each of these groups separately. Neither significant differences were found in any of the water drinking groups.

Excretion of sodium was significantly greater in the groups drinking saline than in those drinking water [$F(1,31) = 155.1$; $P < 0.00001$] (Fig. 3). Significant difference in sodium excretion was also found between the control and the *post-surgical* periods [$F(1,31) = 30.73$; $P < 0.0001$]. The data obtained in the *sham-operated* and the *infarcted* rats significantly interacted with time of measurement [$F(1,31) = 12.90$; $P < 0.001$]. Detailed analysis revealed significant decrease in $U_{Na}V$ during the *post-infarct* period both in the *infarct-water* ($P < 0.01$) and in the *infarct-saline* rats ($P < 0.0001$, Fig. 3). No significant changes in $U_{Na}V$ were found in the *sham-water* and the *sham-saline* groups.

Other parameters. Potassium excretion was significantly greater in the saline drinking rats than in the water drinking rats [$F(1,31) = 16,21$; $P < 0.0003$]. Detailed analysis revealed that both the *sham-operated* and the *infarcted* rats maintained on saline manifested greater U_KV than water drinking rats, however there were no significant differences in excretion of potassium between the *infarct-water* and the *sham-water* and between the *infarct-saline* and the *sham-saline* groups (before surgery: *sham-water*: 0.76 ± 0.04 mmol/100g/24h, *infarct water*: 0.73 ± 0.09 mmol/100g/24h; *sham-saline*: 1.07 ± 0.06 mmol/100g/24h,

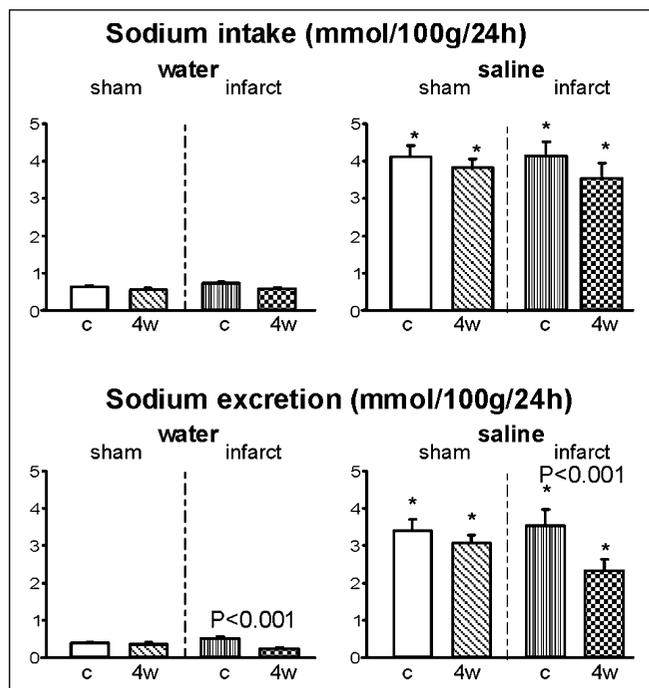


Fig. 3. Twenty-four hour sodium intake and urinary sodium excretion expressed per 100 g of body weight, in the *sham-operated* and the *infarcted* rats drinking either water or saline, c - control, 4w - four weeks after the *infarct* or the *sham-operation*. * significant difference between the saline-drinking group and the corresponding water-drinking group at the level of $P < 0.0001$. For other explanations see Fig. 1.

infarct-saline: 1.11 ± 0.15 mmol/100g/24h; after surgery: *sham-water* 0.77 ± 0.06 mmol/100g/24h, *infarct-water*: 0.71 ± 0.09 mmol/100g/24h, *sham-saline*: 1.11 ± 0.06 mmol/100g/24h, *infarct-saline*: 1.02 ± 0.14 mmol/100g/24h).

Excretion of solutes was significantly greater in the rats maintained on saline than in those maintained on water [$F(1,31) = 142,09$; $P < 0.00001$]. Both the *sham-operated* and the *infarcted* rats maintained on saline manifested greater excretion of solutes than water drinking rats (Fig. 4). Significant difference in solute excretion was also found between the control and the *post-surgical* periods [$F(1,31) = 9.58$; $P < 0.004$]. The data obtained in the *sham-operated* and the *infarcted* rats significantly interacted with the time of measurement [$F(1,31) = 5.94$; $P < 0.02$]. Detailed analysis disclosed that both in the *infarct-water* and in the *infarct-saline* groups $U_{osm}V$ was significantly reduced during the fourth *post-infarct* week in comparison to the corresponding *pre-operative* periods (in both cases $P < 0.05$; Fig. 4). In the *sham-water* and the *sham-saline* groups $U_{osm}V$ did not change significantly after the surgery.

Food intake. No significant differences were found between the saline drinking and the water drinking rats. However, the data obtained in the *sham-operated* and the *infarcted* rats significantly interacted with the time of measurement [$F(1,31) = 6,71$; $P < 0.01$]. Detailed analysis revealed significant decrease in food intake during the fourth *post-infarct* week in the *infarct-saline* rats (Fig. 4). During the *post-infarct* period the *infarct-saline* rats manifested also significantly lower food ingestion than the *sham-saline* rats (Fig. 4).

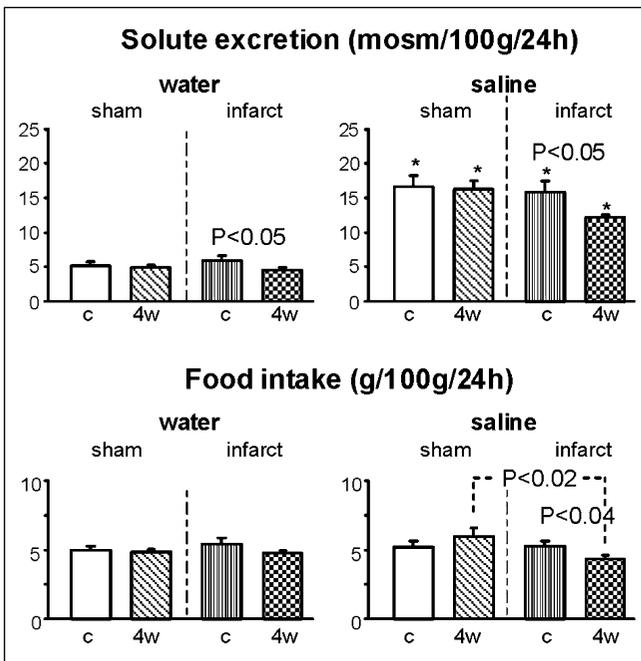


Fig. 4. Twenty-four hour solute excretion and food intake, expressed per 100 g of body weight, in the *sham-operated* and the *infarcted* rats drinking either water or saline, c - control, 4w - four weeks after the infarct or sham-surgery. * significant difference between the *saline*-drinking group and the corresponding *water*-drinking group at the level of $P < 0.0001$. For other explanations see Fig. 1.

DISCUSSION

The main findings of the present study may be summarised as follows: 1) prolonged elevated intake of sodium in drinking fluid increases sodium and fluid intake and renal sodium and fluid excretion but does not elicit hypertrophy of cardiac myocytes in the walls of the left and right ventricle, 2) the myocardial infarct causes reduction in urinary sodium and solute excretion both in the rats maintained on regular and on elevated sodium intake, 3) the myocardial infarct results in significant increase in diameter of the surviving cardiomyocytes of the LV, which is significantly greater in the infarcted rats drinking saline than in those drinking water.

The results obtained in our study clearly indicate that the *sham-saline* rats manifest an apparent osmotic diuresis and natriuresis. Fluid and sodium intake and excretion during an enhanced sodium loading is regulated by a combination of several factors, such as an enhanced activation of the sympathetic system, and an enhanced release of vasopressin, natriuretic peptides and ouabaine-like Na^+ , K^+ ATP-ase inhibitor (15). During prolonged sodium loading excessive retention of sodium and fluid occurs due to activation of the sympathetic system, that dominates over the natriuretic action of the other mechanisms (15). In the present study consumption of 1 % NaCl as the sole drinking fluid did not influence the diameter of cardiomyocytes in the *sham-operated* rats. Previously, Lal et al., (10) and Yuan and Leenen (12) reported an increase in LV weight in rats maintained on high sodium diet (food containing 8% NaCl). However, in the latter studies sodium load was approximately twice as high as in our experimental design and could activate some mechanisms that were not involved in our experiments.

In accordance with previous studies (1, 3, 4) we have found significant reduction in urine, sodium and osmolytes excretion during the *post*-infarct period in the *infarct-water* rats. Significant reduction in urine, sodium potassium and osmolytes excretion was also found in the *infarct-saline* rats. However, in spite of our expectations prolonged sodium overloading in the *infarcted* rats did not result in significantly greater retention of fluid and sodium in the saline drinking than in the water drinking rats. Apparently, physical factors related to an osmotic diuresis as well as an increased secretion of natriuretic peptides and Na^+ , K^+ ATP-ase inhibitor oppose to some extent unfavorable effects of sodium overloading. Voluntary decrease in sodium intake which was observed after 4 weeks of saline consumption (both in *sham* and the *infarcted* rats) may reflect a decrease of sodium appetite and could reduce to some extent sodium overloading during the experiments. The mechanisms responsible for increased retention of sodium in the *infarct-saline* and the *infarct-water* rats were probably the same and involved activation of the sympathetic system and renin-angiotensin-system (1-4, 6-8) although an engagement of the sympathetic system might have been greater in the *infarct-saline* rats, because of the stimulatory effect of elevated sodium intake on this system (15). Significant inhibition of food intake in the *infarct-saline* rats

appears to be an interesting finding. In the *infarct-water* rats inhibition of food intake did not reach a level of significance. In our previous study (16) we have found that the renin transgenic rats TGR mRen2(27), which manifest chronically enhanced activation of the renin-angiotensin system (17), consume greater amount of food than the SD rats of their parent Hannover strain. Therefore it is rather unlikely that the inhibition of food intake found in the infarcted rats drinking saline could be caused by an activation of the renin-angiotensin system. The myocardial infarct increases also production of the proinflammatory cytokines such as IL-1 β , TNF- α and IL-6 (18, 19) which are known to inhibit food intake (20), it may be therefore hypothesized that the cytokines together with an altered ionic milieu caused by an elevated sodium intake could promote inhibition of food consumption during the *post-infarct* state in the *infarct-saline* group.

Dimensions of the infarct and the concentration of collagen in the fibrous scar did not differ in the *infarct-water* and the *infarct-saline* rats, which indicates that the same deficit of the contractile portion of the cardiac muscle was present in both groups. The morphometric measurements revealed that the myocardial infarct produced very significant increase in diameter of the surviving cardiomyocytes in the left ventricular wall of both groups of the infarcted rats. It is worth of noting that in spite of presence of the *post-infarct* scar which evidently caused thinning of the ventricular wall (the effect observed also by us during the *post-mortem* inspection), there was no significant difference in the LV weight between the infarcted and the *sham-operated* rats. Probably hypertrophy of the surviving cardiomyocytes significantly contributed to compensation of the LV weight. The increase in diameter of cardiomyocytes could result from an increased work load on the surviving LV myocytes. However, the influence of some endocrine or paracrine factors and especially involvement of aldosterone should be also taken into account especially that the recent study of Casal et al. (21) has provided evidence for enhanced synthesis of aldosterone in the cardiac myocytes of the left ventricle after the myocardial infarct. Interestingly, in our study diameter of LV cardiomyocytes was greater in the *infarct-saline* than in the *infarct-water* rats, which suggests that even in absence of apparent differences in sodium excretion between the both groups, the prolonged sodium loading was able to promote hypertrophy of the myocytes in the infarcted heart. In this context recent studies provide evidence that high salt diet activates a local renin-angiotensin system in the heart (22), and that angiotensin II is one of the important factors stimulating hypertrophy of the heart (23-24).

In summary, our study reveals, that enhanced sodium intake significantly influences sodium and fluid intake and excretion. In rats on regular sodium diet the myocardial infarct of the left ventricular wall causes hypertrophy of surviving myocytes in this ventricle, and decreases diuresis and retention of sodium and solute. Combination of elevated salt intake and cardiac infarct causes similar retention of fluid and sodium to that observed on regular sodium diet, however it promotes greater overgrowth of the cardiomyocytes of the left ventricle.

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