

Effect of Saline and Saline Deprivation on Adrenal Regeneration Hypertension

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Abstract

Chronic increased ingestion of sodium chloride speeds up the rate of hypertension development caused by unilateral adrenalectomy and contralateral adrenal enucleation. Also, sodium retention is possibly a factor in the pathogenesis of adrenal Regeneration Hypertension (ARH). The present studies were undertaken to test the hypothesis that acute deprivation of excessive sodium intake leads to decreased sodium retention during the initiating period of ARH and thus alleviates or delays the onset of the disease. Sixty female weanling rats were adrenalectomized on the right side and adrenal enucleated on the left side, and were divided into five groups of 12 animals per group. Group 1 was given 1% NaCl to drink, group 2 was allowed tap water for 24 hours and then placed on saline, group 3 was allowed tap water for 48 hours and then placed on saline, group 4 drank water for 72 hours and then was given saline, group 5 was given tap water. The rats were individually housed and body weights and blood pressures taken at 3, 5, and 7 weeks post surgery. They were sacrificed at 7 weeks and weights taken of the hearts and kidneys. At 7 weeks the mean systolic blood pressure in mm Hg was as follows for the successive groups as given above: 190, 163, 134, 165, 140. The percentage hypertensive (>149 mm Hg) in each successive group was: 84, 75, 20, 66, 27. Such results indicate that continuous drinking of saline results in the severest form of hypertension in the greatest number of animals. Drinking only water, results in a drop in the incidence of hypertension but the animals that became hypertensive had extremely high blood pressures. Reducing the intake of salt during the first three days reduced the incidence and severity of hypertension but did not prevent its development in about 50% of the animals. Therefore, acute removal of excessive saline does not stop, but does alleviate somewhat, the early pathogenic processes in the development of adrenal regeneration hypertension. (Aided by a grant from the Eagles' Max Baer Heart Fund).

Introduction

Adrenal Regeneration Hypertension (ARH) is produced in young rats by unilateral adrenalectomy, contralateral adrenal enucleation and feeding 1% NaCl as drinking fluid (1). Studies by Skelton (3) indicate that unilateral kidney removal and elevated sodium intake are essential to the development of ARH. However, Hall et al. (4) reported that most rats on a normal stock diet ultimately develop hypertension, after appropriate operative procedures, even if tap or distilled water is used as the drinking fluid. The importance of sodium in aggravating or inducing hypertension is generally accepted. So, when Gaunt et al. (2) reported that sodium retention occurs after adrenal enucleation the logical conjecture was made that such a phenomenon could be important in the etiology of adrenal-regeneration hypertension. Since NA retention expands the extracellular fluid volume and increases the work load on the cardiovascular and excretory systems, it was deemed advisable to study the effects of acutely reducing this load by depriving the rats of saline immediately after operative procedures and at a time when the animals were undergoing severe traumatic stress as well as changes in water and electrolyte balance.

Thus, a series of experiments were conducted on rats deprived of saline for 24, 48, and 72 hours immediately after operation in hopes that such procedures would prevent or alleviate initial pathogenic processes brought about by excessive sodium retention. Results of these experiments are reported here.

Methods and Materials

Sixty female Charles River rats, 23 ± 1 day old, were used to study the effects of salt deprivation on the development of Adrenal Regeneration Hypertension. Using ether anesthesia, five groups of animals (12 per group) underwent right adrenonephrectomy and left adrenal enucleation. The enucleations were performed by making a small incision in the adrenal capsule and extruding the contents with forceps. Purina laboratory chow was given *ad libitum* and the rats were individually housed immediately post surgery. Group 1 was given 1% sodium chloride as drinking fluid continuously. Group 2 was allowed tap water for 24 hours and then placed on 1% saline. Group 3 was allowed tap water for 48 hours and then placed on 1% saline. Group 4 was allowed tap water for 72 hours and then placed on 1% saline. Group 5 remained on tap water throughout the experiment.

The arterial blood pressures were determined by the tail-cuff plethysmographic method in the unanesthetized rats at 3, 5, and 7 weeks following surgery. Blood pressures at or above 150 mm HG were considered hypertensive. After completion of blood pressure determinations at 7 weeks, the rats were sacrificed. The heart and kidney were removed, stored in formaldehyde, trimmed and weighed at a later date. Student's t-test was employed in arriving at statistically significant differences between paired means.

Results

The effect of salt deprivation on systolic arterial blood pressure and incidence of hypertension is shown in Table 1. Rats on continuous saline developed severe hypertension by the end of the five week period and this condition persisted until termination of the experiment at seven weeks. At this point, eighty-five percent of these animals were hypertensive.

Animals that were on tap water for twenty-four hours and then placed on 1% saline also exhibited marked hypertension at the end of five weeks with the mean being 187 mm Hg. Interestingly, at the end of seven weeks, their systolic arterial pressure had dropped to a mean of 163 but most (75%) of them were still hypertensive.

Rats maintained on tap water for 48 hours and then switched to 1% saline drinking fluid were mainly normotensive throughout the experiment with only 20 percent reaching the hypertensive level. At the end of the five week period, the blood pressures were spread over a large range with the mean being 137 mm Hg. At the end of seven weeks, a somewhat narrower range of values had developed with the mean being 134. One animal in this group died between the 5th and 7th week with a blood pressure of over 250 mm Hg.

TABLE 1. *The effects of salt deprivation on the systolic arterial blood pressures during development of adrenal regeneration hypertension.*

salt deprivation hours	3 weeks blood pressure mm/Hg	5 weeks blood pressure mm/Hg	7 weeks blood pressure mm/Hg	percent hypertensive
none	148 $\pm$ 8.1+	189 $\pm$ 7.7	190 $\pm$ 9.7	84
cont saline	(12)	(12)	(12)	
24	150 $\pm$ 5.1	187 $\pm$ 5.7	163 $\pm$ 6.2*	75
	(12)	(12)	(12)	
48	144 $\pm$ 7.2	137 $\pm$ 16.7*	134 $\pm$ 5.7*	20
	(11)	(11)	(10)	
72	151 $\pm$ 8.7	171 $\pm$ 9.1	165 $\pm$ 10.1	66
	(12)	(12)	(12)	
cont water	134 $\pm$ 8.1	166 $\pm$ 13	140 $\pm$ 4.1*	27
	(11)	(11)	(11)	

+ Entries are mean value $\pm$ standard error and number of cases.

* Denotes significant difference ($P < .05$) between the continuous saline controls and the deprived animals.

Hypertensive equals a systolic blood pressure >149 mm/Hg.

Rats maintained on tap water for 72 hours then switched to 1% saline drinking fluid exhibited hypertension at the end of both 5 and 7 weeks with the mean being 171 and 165 respectively. Here again, a slight fall in the pressures is noted between the 5th and 7th week, but it is not as pronounced as in group 2 (24 hour salt deprivation). In the 72 hour experiment, 66% of the animals were hypertensive at the end of 7 weeks.

The animals on continuous water exhibited the recurring odd characteristic of a drop in blood pressure between the 5th and 7th weeks. At the end of five weeks, the animals exhibited blood pressure rises of varying degrees; most remained normotensive, while a few of the animals developed severe hypertension. The mean at 5 weeks was 166. At seven weeks the mean was 140 with only 27% of the animals exhibiting hypertension.

The effects of salt deprivation on kidney, heart, and body weight are shown in Table 2. The body weights showed only one significant change, this being in group 2 (24 hour salt deprivation). The animals in this group exhibited a greater mean body weight than the control animals on continuous saline. This change is probably unimportant and the reason for the increase is unknown.

The kidney weights of the animals ingesting saline continuously and those deprived of saline for 24 and 72 hours, all showed marked increases over those given water continuously. The animals that were given saline after 48 hours (group 3) exhibited normal kidney weights and this correlated with their low blood pressures. Also, the mean kidney weight of animals given water continuously (group 5) was significantly lower than for saline fed controls. The heart weights showed the same pattern of change as the kidney weights. That is, those animals exhibiting hypertension had large hearts and kidneys, whereas those that were normotensive had smaller organ weights.

TABLE 2. *The effects of salt deprivation on the body weights, kidney, and heart weights at seven weeks after adrenal enucleation and unilateral nephrectomy.*

salt deprivation hours	kidney weights mg	heart weights mg	body weights g
none cont saline	2113.2 $\pm$ 95.0	846.5 $\pm$ 39.3	226 $\pm$ 13.2
24	2137.1 $\pm$ 69.3	886.4 $\pm$ 24.1	261 $\pm$ 7.5*
48	1691.4 $\pm$ 83.6*	685.4 $\pm$ 35.4*	225 $\pm$ 9.2
72	2034.8 $\pm$ 135.8	771.7 $\pm$ 45.0	230 $\pm$ 10.8
cont water	1492.9 $\pm$ 74.3*	710.0 $\pm$ 27.1*	246 $\pm$ 8.2

Entries are mean value $\pm$ standard error. Number of cases given in Table 1.

* Denotes significant difference ($P < .05$) between the continuous saline controls and the deprived animals.

Discussion

The results reported here confirm those of Hall et al. (4) who reported that adrenal-regeneration hypertension can be induced in sensitive animals without a high salt intake being imposed and that the hypertensive condition is aggravated by NaCl excess. Increased sodium chloride intake does not appear to be prerequisite for the pathogenic process to occur but extra sodium loads and accompanying body fluid expansion no doubt contribute to the severity and increase in incidence of the disease.

The report of sodium retention occurring soon after adrenal enucleation, and the suggestion that such retention may be a contributing factor in the early pathogenesis of adrenal regeneration hypertension (2) prompted us to test the hypothesis that acute deprivation of saline for 1 to 3 days immediately post-operatively might relieve the fluid and NaCl load placed on the cardiovascular system and kidneys and thus delay or alleviate the development of the hypertensive state. The results, while not striking, do indicate that short periods of salt deprivation immediately following operative procedures are helpful in reducing the severity and incidence of adrenal regeneration hypertension but do not prevent it from developing in about 50% of the animals. Again, such findings are consistent with those of others (4) who reported that replacement of saline drinking fluid with water at 2, 4, or 6 days post-operatively resulted in a mild form of hypertension development characterized by mean pressures approximating 152 mm Hg. Such values are in the same range as ours for rats deprived of saline for up to 72 hours.

In our studies group 2 (48 hour salt deprivation) deviated considerably from the expected and from the other salt deprivation groups. The mean blood pressure here was in the normotensive range but 2 rats of 10 were mildly hypertensive. Such findings by others are not uncommon. For instance, Rapp (5) reported a spontaneous decline in systolic arterial blood pressure in adrenal-regeneration hypertensive rats between 4 and 6 weeks post-operatively, and Hall et al. (4) reported unusually low blood pressures in one of his experimental groups and remissions of high pressure in sick animals. In our experiments, the seemingly aberrant group consisted of healthy rats and we have

no explanation as to why their blood pressures were lower than in the other groups deprived of salt for short periods of time.

Literature Cited

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