

# HYPERTONIC LACTATED RINGER'S SOLUTION IN EXPERIMENTAL VASOGENIC BRAIN EDEMA IN RABBITS: EFFECT ON BLOOD PRESSURE, ELECTROLYTES, BLOOD UREA NITROGEN, TOTAL PROTEIN CONCENTRATION, PLASMA OSMOLALITY, AND CEREBRAL WATER CONTENT

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## ABSTRACT

Hypertonic solutions play an important role in the treatment of tissue edema. Following the induction of experimental vasogenic brain edema by occlusion of the common carotid arteries in eight rabbits, the effect of hypertonic lactated Ringer's solution (subjects), vs. isotonic lactated Ringer's solution (control), was studied on blood pressure, electrolyte (sodium, potassium, and calcium) concentrations, blood urea nitrogen, total protein concentration, plasma osmolality, urine volume, and cerebral water content.

Significant differences were seen in calcium concentration ( $11.54 \pm 1.2$  vs.  $13.16 \pm 1.18$ ;  $P \sim 0.05$ ), final urine volume ( $17.5 \pm 3.53$  vs.  $5.25 \pm 2.06$ ;  $P < 0.05$ ), systolic blood pressure ( $105.2 \pm 12.9$  vs.  $122.9 \pm 5.81$ ;  $P < 0.05$ ), diastolic blood pressure ( $60 \pm 15.2$  vs.  $79.1 \pm 6.8$ ;  $P < 0.05$ ), and mean arterial pressures ( $74.9 \pm 14.2$  vs.  $93.7 \pm 6.2$ ;  $P < 0.05$ ) between study and control groups. The results also indicate that no significant differences existed in sodium and potassium concentrations, blood urea nitrogen, total protein concentration, plasma osmolality, and tissue brain water content between the two groups.

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## INTRODUCTION

Brain edema (BE) is one of the most complicated situations that must be monitored precisely in intensive care units. BE increases the brain fluid volume and intracranial pressure (ICP), and as a consequence, may disturb the Starling forces<sup>1</sup> and compromise cerebral functions. Starling forces normally regulate the fluid balance in the micro-environment of the brain. BE increases the systemic blood

pressure (SBP)<sup>2</sup> and ICP<sup>3</sup>. However, it is important to control SBP in order to minimize the expansion of tissue edema. Hypertonic solutions have been used to reduce the ICP via controlling brain cell volume<sup>4</sup>. It has been reported that hypertonic solutions have significant effects on decreasing the brain water content due to an increased osmotic gradient across the blood brain barrier.<sup>5-7</sup> Among the electrolytes, sodium is the major one that creates plasma osmolality, and in BE sodium may increase both in brain

## Effect of Hypertonic Lactated Ringer's on Brain Edema

tissue<sup>8</sup> and in plasma<sup>2</sup>. On the other hand, metabolic acidosis<sup>9</sup> produced in BE may also affect the reabsorption of potassium from renal tubules, and therefore the plasma potassium concentration may be elevated. In this study the effect of hypertonic lactated Ringer's solution (HTLRS) vs. isotonic lactated Ringer's solution was investigated on SBP, sodium, potassium, and calcium concentrations, plasma osmolality, blood urea nitrogen (BUN), total protein concentration, and brain water content in experimental animals with vasogenic brain edema.

### MATERIAL AND METHODS

Two groups (case and control) of male *Lepouse americanus* rabbits weighing 1.3-1.8 kg were used in the study (4 animals in each group). The induction was performed with 0.5 - 1.5 ml of 5% thiopental sodium injected into the ear vein and anesthetization was continued with ether in oxygen. The left and right femoral arteries were isolated, and a heparinized cannula was inserted into each artery for continuous monitoring of SBP with a transducer (HSE - Druck - Koppler, type 551A, Hugo Sachs Elektronik, Germany) and to withdraw blood samples for analysis. In order to obtain vasogenic BE, the common carotid arteries were exposed and occluded completely for 15 minutes with # 280 umbilical cotton tape (Ethicon; Scotland). The tapes were released after 15 minutes in order to restore blood flow to the brain. Experimental animals were injected with 4 ml/kg HTLRS (calculated osmolality = 631 mosmol / kg) as follows: half of the total required volume was administered in two minutes, and 15 minutes after the first injection, the other half was administered slowly during a period of 15 minutes. The control animals were injected with isotonic lactated Ringer's solution with the same procedures. A brain tissue biopsy was obtained 30 minutes after the final injection for determination of brain water content with a specific gravity method which is described elsewhere.<sup>10</sup> Blood samples were taken before occlusion of the common carotid arteries, and 30 minutes after the final injection for analysis. Sodium, potassium, and calcium concentrations were determined with a KONE electrolyte analyzer (Espoo, Finland). Total protein concentrations, BUN, and glucose concentrations were measured by routine colorimetric methods. Bladders of the animals were also isolated at the beginning of the experiment, and all urine was removed simultaneously with each blood sample withdrawn. The last available volume of urine (30 minutes after the final injection) in the bladder was measured in both groups as a final urine volume (FUV). Plasma osmolality was calculated by the following equation<sup>11</sup>:

$$\text{Osmolality} = 2.0 \times [\text{sodium}] + [\text{glucose}]/1.8 + \text{BUN}/2.8$$

Mean arterial pressure (MAP) was calculated by the following equation:

$$\text{MAP} = [2 \times \text{diastolic pressure} + \text{systolic pressure}] / 3$$

### Statistical analysis

Results are reported as mean  $\pm$  SD. The two groups were statistically compared using Student's t-test. Statistical P-values of less than 0.05 were considered as significant.

## RESULTS

The experimental data for sodium, potassium, and calcium concentrations, BUN, total protein concentration, brain water content, plasma osmolality, systolic and diastolic pressures, and MAP are shown in Tables I (before occlusion of common carotid arteries) and II (30 minutes after the final injection).

**Table I. Parameters measured in the two groups before occlusion of common carotid arteries.**

Parameter	Case	Control	P
Sodium (mEq/L)	141 $\pm$ 4.16	143.25 $\pm$ 1.7	N.S.*
Potassium (mEq/L)	3.02 $\pm$ 0.4	2.65 $\pm$ 0.25	N.S.
Calcium (mEq/L)	12.39 $\pm$ 1.27	12.21 $\pm$ 0.95	N.S.
BUN (mg/dL)	14.92 $\pm$ 0.5	14.55 $\pm$ 1.12	N.S.
Total protein (g/dL)	6.94 $\pm$ 0.23	7.21 $\pm$ 0.45	N.S.
Osmolality (mosm/kg)	302.2 $\pm$ 5.11	303.7 $\pm$ 7.51	N.S.
Systolic pressure (mmHg)	111.5 $\pm$ 19.6	117 $\pm$ 6.63	N.S.
Diastolic pressure (mmHg)	65.8 $\pm$ 20.9	79.25 $\pm$ 8.7	N.S.
MAP (mmHg)	81 $\pm$ 20.3	91.7 $\pm$ 7.5	N.S.

\*N.S. = not significant

**Table II. Studied parameters (30 minutes after the final injection) in two groups of brain edema animals treated with HTLRS (case) and isotonic lactated Ringer's solution (control)**

Parameter	Case	Control	P
Sodium (mEq/L)	143 $\pm$ 5.29	142.25 $\pm$ 0.5	N.S.*
Potassium (mEq/L)	3.4 $\pm$ 0.37	3.12 $\pm$ 0.37	N.S.
Calcium (mEq/L)	11.54 $\pm$ 1.2	13.16 $\pm$ 1.18	P<0.05
BUN (mg/dL)	14.95 $\pm$ 0.99	14.25 $\pm$ 0.77	N.S.
Total protein (g/dL)	6.28 $\pm$ 0.4	6.3 $\pm$ 0.64	N.S.
Osmolality (mosm/kg)	317.4 $\pm$ 5.9	310.66 $\pm$ 4.45	N.S.
FUV (ml)	17.5 $\pm$ 3.53	5.25 $\pm$ 2.06	P<0.05
Brain water content (%)	87.08 $\pm$ 6.2	86.53 $\pm$ 7.5	N.S.
Systolic pressure (mmHg)	105.2 $\pm$ 12.9	122.9 $\pm$ 5.81	P<0.05
Diastolic pressure (mmHg)	60 $\pm$ 15.2	79.1 $\pm$ 6.8	P<0.05
MAP (mmHg)	74.9 $\pm$ 14.2	93.7 $\pm$ 6.2	P<0.05

\*N.S. = not significant

## DISCUSSION

There has recently been an increased interest in the use of hypertonic solutions for the treatment of BE in order to



decrease brain water content<sup>12</sup> and manage the SBP. Brain water content and SBP are not the only factors which are affected by hypertonic solutions. The effect of these solutions on other parameters such as sodium have been investigated by others with different experimental designs<sup>5,7</sup>. In our study, there was no significant difference in sodium and potassium 30 minutes after the final injection between the two groups. It has been reported that sodium concentrations in brain tissue increase in BE,<sup>8,13</sup> while in our previous study on vasogenic BE, plasma sodium increase was not statistically significant.<sup>2</sup> The reason may be related to the produced hypertension in BE which is caused by the reabsorption of sodium in renal tubules. The increase in glucose concentrations in BE<sup>3</sup> makes this substance appear in the urine, and due to the co-transport of water with glucose, the sodium concentration will increase in the interstitial space around the tubules. This phenomenon makes sodium move from the peritubular space into the tubular lumen, and finally appear in the urine with glucose. It seems that this mechanism will control sodium and potassium concentrations in both groups. On the other hand, the significant difference in calcium concentrations between the two groups is also related to sodium excretion. The reabsorption of calcium is proportionate to sodium reabsorption, and in HTLRS-treated animals, because of the high concentration of sodium in plasma, the excretion of sodium was more than the control group. Therefore due to an increase in calcium excretion, its plasma concentration would also be decreased. It has been reported that hypertonic solutions markedly increase SBP in experimental animals.<sup>14</sup> In this study, systolic pressure, diastolic pressure and MAP in the HTLRS-treated group were significantly lower than the control group. HTLRS injection into the systemic circulation creates a hyperosmolar state with subsequent water transport from the interstitial space to the intravascular space.

This phenomenon increases the SBP and glomerular filtration rate. As a result, there is a large volume of urine which decreases extracellular volume and SBP. There was no significant difference in brain water content among both groups, hence HTLRS had no effect on the degree of water accumulation in the animals' brain. It seems that 15 minutes of occlusion of the common carotid arteries causes serious damage to the microenvironment barrier and impairs osmosis regulation<sup>7</sup>.

Finally, in our experimental model, calcium concentration, systolic and diastolic pressures, and MAP are decreased while no changes occurred in brain water content, plasma osmolality, sodium and potassium concentrations, BUN, and total protein concentration. As a conclusion, the results of this study suggest that HTLRS may be a candidate for decreasing SBP in brain edema victims.

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