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EDITORIAL

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The Effect of Biliary Drenage on Uremic State

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Introduction

End stage renal disease(ESRD) patients have high mortality and morbidity rates. This is a serious public health problem. Therefore, new methods of treatment in ESRD patients continue to be investigated [1]. Regular follow-up and treatment that will minimize the uremia findings mortality rates in hemodialysis (HD) patients compared to previous years. However, in the normal population and high mortality rate for other patient groups HD it is necessary to carry out comprehensive studies to improve the results. ESRD, metabolic, cardiovascular and hematologic complex pathologies involving complications is a syndrome to character. Oxygen radicals and/or antioxidant systems inadequacy also contributes to the pathogenesis of ESRD.

Antioxidant capacity decreased in ESRD patients due to decreased glomerular filtration rates [2,3]. Failure to meet dialysis requirements, especially in patients with heart failure, burns, septic shock, and fistula problems and who cannot perform peritoneal dialysis can lead to hypervolemia and hyperpotasemia-related deaths. In this study, the effects of bile drainage on hyperpotasemia and tissue oxidative stress were investigated in rabbits with acute renal failure (ARF) without hemodialysis.

Methods

Study procedures

Ethical approval was obtained before the study (Adana veterinary research and control institute; Ethical committee). Sixteen mature Chincilla male rabbits weighing 1600 to 1850 grams were used, all rabbits were obtained from the same center, and they were housed in a temperature- and humidity-controlled room under a constant 12-hour light/dark cycle. Animals had free access to water, but their food consumption was restricted 12 hours before the surgery.

The rabbits were randomly divided into 2 groups, each including 8 rabbits.

Acute renal failure model and biliary drainage

General anesthesia was provided by 60 mg/kg of ketamine hydrochloride (Ketalar/Eczacibasi, Istanbul, Turkey) and 10 mg/kg xylazine hydrochloride (Rompun/Bayer, Leverkusen, Germany). A midline incision was made from the xiphoid process to the pelvic region after skin antisepsis with povidone iodine.

In the control group (group-1) (n=8), both kidneys were connected to renal artery and renal vein. Then bilateral nephrectomy was performed.

In the study group (group-2) (n=8), the choledoc was suspended in the middle. Then the proximal segment was ligated. A 0.6 mm diameter plastic stent was placed in the part of the common bile duct near the bile duct. Then the stent was removed from the anterior abdominal wall. The bile exits the stent. Bilateral nephrectomy applied to the control group was performed.

Intracardiac blood samples were taken at 0^{th} and 12^{th} hours under the anesthesia of each animal in each group. Bile specimen was taken from the stent point at the same time in the study group. Group-1 and group-2 euthanasia was administered to subjects at 12^{th} hour. Laparotomy was performed and liver and lung tissue samples were taken.

Biochemical studies were performed on blood and bile specimens taken. GSH (Glutathion) and TBARS (thiobarbituric acid reactive substances) levels in tissue samples were evaluated.

The Measurement of GSH: We the method proposed by Beutler et al. [4] to measure the hepatic glutathione (GSH). Dithionitrobenzoic acid (DTNB) was used as the substrate, and the amount of GSH was determined. GSH of the liver as non protein was measured at 412 nm. The results were expressed as µmol/mg protein.

The Measurement of TBARS: TBARS assay was determined by using colorimetric method with changes in absorbance read at 532 nm (Optizen 3220 UV) against standards (0.5-25 nmol ml-1 1,1,3,3-tetraethoxypropane). TBARS was calculated using the formula as nmol/mg protein [5,6].

Statistical Analysis

The statistical analysis of data was performed with SPSS 20.0 (IBM, Hong Kong) package program. Student t-test was used for normal dispersion data and Mann-Whitney U test for abnormal dispersion data. The limit of statistical significance was set at $p<0.05$.

Results

Biochemical levels

In 0th hour, there was no difference between the blood biochemical values of the group-1 and group-2 ($p>0.05$).

In the 12th hour, potassium level was lower in group-2 than in group-1 ($p=0.031$). Urea and creatinine levels were higher in bile duct samples in group-2 at 12th hour compared to 0th hour (<0.05). There was no statistical difference between the other values ($p>0.05$) (Table-1).

Glutathione (GSH) levels in tissue samples

GSH levels were higher in group-2 than in group-1 in tissue samples at the 12th hour. The statistical difference was $p=0.012$ in liver tissue and $p<0.001$ in lung tissue samples (Table-1).

TBARS levels in tissue samples

TBARS levels were lower in group-2 than in group-1 in tissue samples at the 12th hour. The statistical difference was $p>0.05$ in liver tissue and $p=0.028$ in lung tissue samples (Table-1).

Discussion

Hyperpotasemia and hypervolemia take an important place in the emergency trials of ESRD patients. Serious problems arise if a quick and correct approach is not taken in this case. In a study conducted by Sachetti et al. [7] the most frequent causes of patients receiving emergency HD are hypervolemia and hyperkalemia.

In the study; the low serum potassium levels of group-2 may be related with the high biliary excretion of potassium out of the body at the 12th hour. The high levels of GSH and low levels of TBARS in group-2 may be related with the positive effect of bile excression on uremic state and oxidative stress [8,9]. This positive effect may be related with the preservation of anuric rabbits from hypervolemic state via the bile excression out of body.

Particularly hyperpotasemia or hypervolemia and emergency dialysis may be necessary, and in cases of burn, heart failure, septic shock patients who cannot be dialyzed due to any reason, taking bile out of the body may be life saving. This procedure may be achieved with a minimally invasive nasobilier stent application. This stent can be removed easily when the patient's clinical condition improves.

This study suggests that in patients with hypotension requiring dialysis, excess fluid in the body and potassium may be expelled from the body by drainage of bile. This application suggests that hemodialysis or peritoneal dialysis may prevent severe hemodynamic disorders that may result in excessive body fluid removal from the body 24 hours instead of 3-4 hours. Bile excression may support the renal replacement treatments in hypercalemic and hypervolemic subjects of renal failure and further researches are needed for this study.

Limitation of study

1. Bile drainage cannot be performed with nasobilier due to the small size of the subjects taking it out through the stent.
2. The study was terminated at 12 hours because it was difficult to treat all the metabolic changes that occurred in the subjects.

Table 1: Biochemical. GSH and TBARS values of the group-1 and group-2

	0th hour			12th hour			Group-2 Bile		
	Group1 Blood	Group2 Blood	p	Group1 Blood	Group2 Blood	p	0th hour	12th hour	P
Sodium mmol/lt	139.5	141.5	>0.05	140.5	143.2	>0.05	154.4	151.1	>0.05
Potassium mmol/l	3.3	3.3	>0.05	5.5	4.2	**<0.05**	4.8	5.0	>0.05
Phosporus mg/dl	6.1	6.3	>0.05	6.5	7.25	>0.05	1.3	1.6	>0.05
Urea mg/dl	40.8	48.5	>0.05	125.6	132.3	>0.05	**42.1**	**133**	**<0.05**
Creatinine mg/dl	1.1	1.2	>0.05	4.7	5.0	>0.05	**1.0**	**4.9**	**<0.05**
Uric acide mg/dl	0.11	0.13	>0.05	0.16	0.15	>0.05	0.2	0.19	>0.05

	GSH µmol/mg			TBARS nmol/mg		
	Group-1	Group-2	P	Group-1	Group-2	P
Liver	0.003151	0.008882	**0.012**	1.2893	1.0425	>0.05
Lung	0.000543	0.015738	**0.001**	1.1213	1.0013	**0.028**

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