The Effect of Adding Albumin 20% to Mannitol-Furosemide Combination in Adolescent ICU Patients with Acute Renal Failure

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ABSTRACT

Introduction: Acute renal failure is one of the major problems of patients admitted to the ICU, for which several treatments have been suggested, such as adequate hydration and administration of diuretics. This study aimed to evaluate the effect of adding albumin to mannitol-Lasix composition in adolescent ICU patients with acute renal failure. Methods: This study is a double-blind clinical trial that was performed on 100 adolescent patients in the ICU of Bahonar Hospital in Kerman, Iran from March 2013 to March 2015. Patients with acute renal failure. Patients were randomly divided into two groups. In group A, the combination of mannitol-Lasix-albumin and group B, only mannitol-Lasix was administered as an infusion for up to 48 hours. Variables such as Central venous pressure (CVP), Peripheral edema, PaO2/Fio2, Urine volume, Nitrogen Urea Blood (BUN), creatinine (Cr) before and at the end of the infusion were evaluated and compared. Results: Before the intervention, the demographic findings and the variables were the same in both groups. But after 48 hours in group A with a significant increase in urinary goiter, the rate of edema and CVP compared to group B was reduced and oxygenation of patients was increased, while the amount of BUN and creatinine in the two groups was not significantly different. Conclusion: It seems that the addition of albumin to the mannitol-lazyx combination in adolescents with acute renal failure increases diuresis and oxygenation and reduces peripheral edema, but has little effect on renal function.

Key Words: *Aliguria, Acute renal failure, Ferrosomide, Mannitol, Albumin.*

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INTRODUCTION

Oliguria means a decrease in the urinary output below 3.0 h / kg/cc. According to studies [1], more than 18% of patients admitted to the ICU suffer from it even with healthy kidneys [2].

prevalence of acute renal failure (ARF) is about 2.5-10% in patients admitted to the ICU[3,4] and the subsequent mortality rate has been reported to be between 30-90% [5-7].

Even a slight increase in serum creatinine levels after surgery can be associated with an increased mortality rate [8].

Also, most patients with ARF who require dialysis remain dependent on it and leading to significant long-term morbidity and mortality [9].

The diagnosis of ARF is based on a decrease in glomerular filtration rate (GFR), which is based on an increase in serum creatinine, and the reduction of urine output. On the other hand, patients who admitted to the ICU are also prone to generalized edema due to increased central venous

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pressure due to the effects of mechanical ventilation, decreased lymphatic flow due to immobility, sodium retention due to the effects of secondary hyperaldosteronism or internal renal vasomotor activity or ARF [10].

The treatment of choice in adolescent ARF ICU patients is adequate hydration and the use of diuretics, to increase the clearance of water and salt [11]. Hypoalbuminemia is one of the most important reasons that lead to resistance to the diuretics which interferes with the secretion of furosemide into the lumen of the tubule. Mannitol, on the other hand, is another diuretic that is thought to have renoprotective benefits in patients with oliguria. However, disagreement about the best medication regimen for oliguria and ARF in the ICU adolescent patients has led to efforts are being made to find the best treatment [12].

Based on the results of randomized clinical trial (RCT) studies, little evidence has yet been found of the effectiveness of albumin addition in the oliguria treatment regimen, and the results of the study are inconsistent [13]. It has been shown that adding albumin to furosemide does not increase diuresis compared to administration of furosemide alone, while another study reported that the combination of furosemide and albumin was most effective than furosemide in increasing water and sodium diuresis in a short time [14-17]. Also, in the literature review, no studies were found to investigate the effects of adding albumin to the combination of furosemide and mannitol in adolescent ICU patients with ARF & oliguria. This clinical trial study aimed to investigate the effects of adding albumin 20% to furosemide -mannitol combination on edema and urine volume and renal function in adolescent patients with ARF who admitted to the ICU.

MATERIALS AND METHODS:

This study is a double-blind randomized clinical trial that was performed on adolescent patients admitted to the ICU of Shahid Bahonar Hospital in Kerman, Iran from March 2015 to March 2016 with ARF & oliguria.

The sample size was determined based on the study of Doungngern et al. 50 patients in each group and the significant level was considered less than 0.05.

Exclusion criteria: 10 >age > 19 years. Patients with a history of, severe proteinuria, renal diseases such as glomerulonephritis, ATN, etc., use of furosemide or mannitol in two last weeks, and albumin level lower than normal (3.5 g/dL), if urine volume was not measured correctly.

The first group of patients was treated with a combination of 100 ccs of mannitol 20 % and 400 mg of frusemide with a 1cc / kg / h infusion rate for 2 consecutive days. The second group of patients was treated with the same combination without albumin.

After recording the patient's demographic data, the variables such as Serum levels of albumin, blood urea nitrogen (BUN), creatinine, and urinary volume, central venous pressure (CVP), and FiO2 / PaO2 were measured before and after of treatment.

Finally, the recorded findings were analyzed by SPSS software version 20.

RESULTS:

As you can see in Table 1, the demographic findings were the same in both groups. Also, before the intervention, the urine volume, peripheral edema grade, CVP, Pao2/Fio2, BUN, and creatinine were not significantly different between the two groups (Table 2).

However, 48 hours after the intervention, the urinary output in group A (2.34±0.6 cc/kg/h) was significantly more than group B (1.82±0.48 cc/kg/h) (P-V=0.038). Also, the mean central venous pressure was in group A (11.57±2.88 mm hg), which was significantly lower than group B (13.58±3.99mm hg) (P-V=0.034). 48 hours after the intervention, the rate of peripheral edema in group A patients was significantly lower than group B (Table 3) and most patients had grade 1 and 2 edema, while patients in group B often had grade 2 and 3 edema.

Another finding of this study was a significant increase in oxygenation (Pao2/Fio2) in group A patients (188±40.54) compared to group B(150±39.02)(P-V=0.041).

As can be seen in Table 2, the levels of BUN and creatinine as two indicators of renal function before and after the intervention were not significantly different between the two groups.

Table 1: Demographic characteristics of patients in two groups

Variables		Group A N=50	Group B N=50	P-Value
Sex	Male	32(64%)	38(76%)	0.584
	Female	18(36%)	12(24%)	
Age (year)		11.7±6.18	12.2±6.43	0.095

Table 2: Comparison of the studied findings in the two groups before and after the intervention.

Variables	Time of measurement	Group A N=50	Group B N=50	p-value
Albumin level mg/dl	Pre-treatment	4.68±0.20	4.66±0.15	0.663
	Post-treatment	4.86±0.18	4.49±0.23	0.330
BUN mg/dl	Pre-treatment	53.47±14.19	50.40±14.94	0.201

	Post-treatment	54.4±5.95	51.2±4.1	0.291
Cr mg/dl	**Pre-treatment**	4.97±3.55	1.55±0.7	0.340
	Post-treatment	1.41±0.67	1.9±0.28	0.117
CVP mmhg	**Pre-treatment**	15.8±2.26	15.41±2.98	0.628
	Post-treatment	11.57±2.88	13.58±3.99	0.034
Pao2/fio2 ml/kg	**Pre-treatment**	146.13±36.72	142.56±38.59	0.95
	Post-treatment	188±40.54	150±39.02	0.041
Urine output cc/kg/h	**Pre-treatment**	1.56±0.45	1.66±0.43	0.989
	Post-treatment	2.34±0.6	1.82±0.48	0.038

Table 3: Comparison of edema in the two groups before and after the intervention.

Grade of peripheral edema	Time of measurement	Group A N=50	Group B N=50	p-value
1	**Pre-treatment**	6	7	0.95
	Post-treatment	28	13	0.01
2	**Pre-treatment**	28	25	0.89
	Post-treatment	17	25	0.04
3	**Pre-treatment**	10	10	0.99
	Post-treatment	3	6	0.04
4	**Pre-treatment**	6	8	0.31
	Post-treatment	2	6	0.03

DISCUSSION:

This study aimed to evaluate the effect of adding albumin to the furosemide-mannitol combination in adolescent patients with acute renal failure admitted to the ICU.

The results of the present study showed that although adolescent patients with acute renal failure had the same condition in the ICU before the intervention, after two days of receiving two different diuretic compounds, there were significant differences between the two groups. With better diuresis, we saw a significant reduction in peripheral edema, central venous pressure, and an increase in the ratio of pao2 / fio2. But the serum creatinine, BUN, glomerular filtration rate (GFR) were not significantly different between the two groups.

Previous studies have compared the effect of adding albumin to furosemide or mannitol on the amount of diuresis produced by these two drugs, most of which have not found a definitive answer about the positive effect of albumin

In a study by Doungngern et al., The addition of 25% albumin to furosemide did not affect the rate of diuresis in ICU patients with a normal level of albumin [13]. Also, the results of the study by Chalasani et al. showed that the addition of albumin to furosemide in hypoalbuminemia patients who admitted to ICU did not improve diuresis in them [9]. The results of these two studies, contrary to our results, did not show the positive effect of adding albumin to furosemide to increase its diuretic effect.

Dharmaraj et al showed that co-administration of albumin with Lasix produced more urinary output compare to Lasix alone in patients with nephrotic syndrome. This shows the positive effect of albumin on the amount of diuresis obtained from furosemide, which is also the result of our study [14].

As a result, the Young and Ghafari studies also showed a positive effect of albumin on the establishment of furosemide diuresis [15].

Hsu CW et al. showed that the addition of albumin or FFP to furosemide could increase diuresis in ICU patients Which is consistent with our results [16].

But what is common to almost all previous studies is that in none of them the addition of albumin has no negative effect on diuresis and, except two studies in most other studies, has a positive diuresis effect [17-21].

However, even considering the hypothesis that one of the main mechanisms of resistance to diuretics is hypoalbuminemia, it seems that the administration of additional albumin to diuretics in patients with acute renal failure is Logical [22].

The following points can be noted about why the administration of albumin with diuretics is effective or not in increasing the rate of diuresis, including the method of administration is one of the most important factors in the effect of albumin on the development of diuresis [23].

For example, in the study by Doungngern et al., Albumin and lasix were given as a six-hour infusion, while in most studies that reported albumin as positive, albumin and lasix were given as a bolus or short-term infusion [13].

Other effective factors are the dose of Lasix and its combination with other diuretics [24]. For example, in our study, the combination of Lasix (100 mg) with Mannitol 20% (100 ccs) was used at a rate of 1cc/kg/h for 48 hours

was too effective in increasing the urine volume of adolescent patients with acute renal failure.

In a meta-analysis performed by Kitsios GD et al., The addition of albumin to lasix for 8 hours could increase urinary excretion and urinary sodium excretion, but after 24 hours the difference was not significant. However, in our study, a 48-hour infusion of mannitol-lasix and albumin had a significant effect on urinary output.

One of the most important factors in the effect of diuretics on the volume of urine output of patients is GFR which has caused differences in the results of studies. As Hsu CW et al. Showed, the addition of albumin to Lasix in patients with GFR more than 20 ml/min causes a significant increase in diuresis, while in cases of GFR less than 20ml/min, no positive effect of adding albumin to Lasix was observed.

Age of the patient and the underlying cause of renal failure can affect the effect of albumin and lasix on diuresis, so that in children, especially in nephrotic syndrome have a significant effect. In our study, patients were also in adolescent age and albumin was significantly effective in increasing mannitol-Lasix diuresis. However, in other studies performed in adults, the addition of albumin had a positive effect on increasing the urine volume.

In our study, mannitol was used as an osmotic diuretic that is filtered into the glomerulus but is not reabsorbed from the tubules. In theory, mannitol has a nephron protective effect as a result of this study, in combination with albumin and furosemide, it may have positive effects in patients with acute renal failure [25].

CONCLUSION:

The results of our study showed that infusion of mannitol-furosemide-albumin combination (1cc/kg/h) for 48 hours in adolescent ICU patients with acute renal failure It can reduce edema and improve oxygenation in patients by increasing the amount of diuresis, but this method did not affect BUN & serum creatinine levels.

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