

ORIGINAL RESEARCH

To compare the efficacy of oral furosemide-metolazone versus oral furosemide-spirolactone combination therapy in management of edema in nephrotic syndrome

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Abstract

Background & Method: The aim of the study is to compare the efficacy of oral furosemide- metolazone versus oral furosemide- spironolactone combination therapy in management of edema in nephrotic syndrome. All children of age group 6 months -14 years attending the out-patient department (OPD) and In-patient department (IPD) in pediatric department with complaint of generalized swelling and decreased urine output were admitted and diagnosed as case of nephrotic syndrome.

Result: Mean input and urinary output over 5 days in both group A and B patients. The mean urine output in patients of group B was higher than group A with values being statistically significant for day 5 (p-value 0.04). Thus concluding that Diuretic action of Group B (frusemide- metolazone) was better than group A (frusemide-spirolactone).

Conclusion: We conducted a study to compare the efficacy of frusemide- spironolactone and frusemide- metolazone combination in patients admitted in Pediatric department as a case of nephrotic syndrome having edema. Our study showed that group B had higher mean weight loss as compared to group A specially on days 4 and 5 of the diuretic therapy. Thus showing that frusemide metolazone combination had better diuretic action than frusemide spironolactone. On comparing the urine output we found that Group B had more urine output as compared to Group A particularly in days 4 and 5 of therapy.

Study Designed: Comparative Study

Keywords: efficacy, furosemide- metolazone, oral furosemide- spironolactone & nephrotic syndrome.

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Introduction

Nephrotic syndrome is defined as the presence of nephrotic range proteinuria, generalized edema, hyperlipidemia/ hypercholesterolemia, and hypoalbuminemia. Nephrotic range proteinuria in a 24 hour urine collection is defined as protein excretion of more than 40 mg/m²/hr to account for varying body sizes throughout childhood, which is 3+ to 4+ on urine dipstick protein examination. In both adults and children, a first-morning urine protein/creatinine ratio of 2-3 mg/mg or more indicates nephrotic-range proteinuria. Edema is

generalized and pitting type starting from face usually[1]. Hypercholesterolemia >200mg/dl, and hypoalbuminemia<2.5 mg/dl. Nephrotic syndrome has many causes, including primary kidney diseases such as minimal-change disease, focal segmental glomerulosclerosis, and membranous glomerulonephritis[2]. Nephrotic syndrome can also result from systemic diseases that affect other organs in addition to the kidneys, such as diabetes, amyloidosis, and lupus erythematosus[3]. Nephrotic syndrome may affect adults and children of both sexes and of any race. It may occur in typical form, or in

association with nephritic syndrome. The latter term connotes glomerular inflammation, with hematuria and impaired kidney function[4]. Estimates on the annual incidence of nephrotic syndrome range from 2-7 per100,000 children, and prevalence from 12-16 per 100,000. The glomerular capillaries are lined by a fenestrated endothelium that sits on the glomerular basement membrane, which in turn is covered by glomerular epithelium, or podocytes, which envelops the capillaries with cellular extensions called foot processes. In between the foot processes are the filtration slits. These three structures—the fenestrated endothelium, glomerular basement membrane, and glomerular epithelium—are the glomerular filtration barrier[5]. Filtration of plasma water and solutes is extracellular and occurs through the endothelial fenestrae and filtration slits. The importance of the podocytes and the filtration slits is shown by genetic diseases. In congenital nephrotic syndrome of the Finnish type, the gene for nephrin, a protein of the filtration slit, is mutated, leading to nephrotic syndrome in infancy. Similarly, podocin, a protein of the podocytes, may be abnormal in a number of children with steroid-resistant focal glomerulosclerosis[6].

Material & Method

All children of age group 6 months -14 years attending the out-patient department (OPD) and In-patient department (IPD) in pediatric department with complaint of generalized swelling and decreased urine

output were admitted and diagnosed as case of nephrotic syndrome by the following parameter:

1. Bedside urine protein 3+/4+ (significant nephrotic range proteinuria 40mg/m²/24 hour)
2. Hypoalbuminemia (serum albumin <2.5 g/dl)
3. Hyperlipidemia (serum cholesterol >200 mg/dl),

INCLUSION CRITERIA

1. Children diagnosed with nephrotic syndrome according to above mentioned Criteria and not achieving weight loss or diuresis after 2 days of treatment with oral furosemide therapy.
2. Age more than 6 month and less than 14 years.

EXCLUSION CRITERIA

1. Nephritic syndrome
2. Nephrotic syndrome patient caretakers who will refuse to give consent
3. The patients who will achieve weight loss or diuresis within 2 days of treatment with oral furosemide therapy.

Children (above 6 months to 14 years) with nephrotic syndrome admitted in our department fulfilling inclusion criterion.

Results

The Table 1: describes about the mean Age of the patients enrolled for the study with the minimum age being 1 year and maximum age being 14 years and the mean age was 5.6 years.

Table : 1

Descriptive Statistics					
	N	Min	Max	Mean	SD
AGE (in years)	60	1.00	14.00	5.61	3.09

The patients were divided into 2 groups with 30 patients in each group. The number of males in Group A and B were 20 and 16 while the number of females being 10 and 14 respectively. The p value for this was insignificant(0.292).

Table : 2

	Group A		Group B		P value
	Male	Female	Male	Female	
N	20	10	16	14	0.292
%	66.7 %	33.3 %	53.3 %	46.7 %	

The table below mentions the mean age (in years) of both the groups A and B. The mean Age of group A and B being 5.57 years and 5.65 years respectively.

Table 3

	GROUP						p-value
	Group A		Group B		Total		
	Mean	SD	Mean	SD	Mean	SD	
AGE (in years)	5.57	2.81	5.65	3.40	5.61	3.09	0.918

Applied unpaired t test for significance. The table below shows the number of New Cases and Relapse cases in both group A and B. Both the groups had almost equal number of new cases and relapse cases. The p value(0.56) was not significant.

Table: 4

cases	GROUP					
	Group A		Group B		Total	
	N	%	N	%	N	%
New case	7	23.3%	9	30.0%	16	26.7%
Relapse	23	76.7%	21	70.0%	44	73.3%

p-value=0.559 The table below describes about the weight loss following the diuretic therapy for 5 days in both the groups. It shows that weight loss at day 4 and 5 was significantly higher in group B as compared to group A (the p-values being 0.17 and 0.05 for day 4 and 5 respectively). Thus it showed that efficacy of frusemidemetolazone combination (group B) was more than frusemide spironolactone combination (group A).

Table 5

	GROUP						p-value
	Group A		Group B		Total		
	Mean	SD	Mean	SD	Mean	SD	
WEIGHT in kgs. at DAY 1	20.18	6.02	20.03	7.11	19.61	6.54	0.619
WEIGHT in kgs. at DAY 2	19.71	5.88	19.13	7.21	18.92	6.53	0.806
WEIGHT in kgs. at DAY 3	19.30	5.90	18.35	6.81	18.32	6.32	0.976
WEIGHT in kgs. at DAY 4	17.77	5.77	16.08	6.60	17.42	6.15	0.171
WEIGHT in kgs. at DAY 5	17.42	5.58	15.64	6.49	17.03	6.01	0.051

Applied unpaired t test for significance. The table below describes about mean input and urinary output over 5 days in both group A and B patients. The mean urine output in patients of group B was higher than group A with values being statistically significant for day 5 (p-value 0.04). Thus concluding that Diuretic action of Group B(frusemide- metolazone) was better than group A (frusemide- spironolactone).

Discussion

The various descriptive characteristics of both Group A and B in Table were compared. The number of males and females in both the groups were similar[7]. The mean Age of group A and B were 5.57 and 5.65 years for both group A and B respectively. The number of new cases and Relapse Cases were almost same in both the groups. Similar results were seen in other comparative studies like Garin et al(1987), Arnold et al(1984). Results shows weight loss following diuretic therapy in both the groups. It showed that group B had higher mean weight loss as compared to group A specially on days 4 and 5 of the diuretic therapy[8&9]. Thus showing that frusemidemetolazone combination had better diuretic action than frusemide spironolactone. Similarly ghose et al(1981) showed frusemide -metolazone combination better, Paton et al(1977) also showed that metolazone higher efficacy than other thiazide diuretics. Sica et al (1996) showed that combination diuretic therapy was better than use of

single diuretic in refractory edema states due to sequential nephron blockage[10].Input /output charting for both the groups. Group B had more urine output as compared to Group A particularly in days 4 and 5 of therapy[11]. Marone et al(1985) showed that addition of metolazone to frusemide increased the urine output in patients with refractory edemastates. Oimomi et al(1990) also showed that combination diuretic therapy has better diuretic action as compared to single diuretic

Conclusion

We conducted a study to compare the efficacy of frusemide spironolactone and frusemide-metolazone combination in patients admitted in Pediatric department as a case of nephrotic syndrome having edema. Our study showed that group B had higher mean weight loss as compared to group A specially on days 4 and 5 of the diuretic therapy. Thus showing that frusemide metolazone combination had better diuretic action than frusemide spironolactone. On comparing the urine output we found that Group B had more urine output as compared to Group A particularly in days 4 and 5 of therapy.

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