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THOMSON REUTERS
International Journal of Medical Research and Pharmaceutical Sciences
Volume 5 (Issue 6): June 2018 ISSN: 2394-9414
DOI- 10.5281/zenodo.1293607 Impact Factor- 4.174

THE MOST SAFE AND EFFECTIVE ANTIHYPERTENSIVE THERAPY FOR REDUCTION OF PROTEINURIA AND HYPERTENSION IN CHILDREN'S NEPHROTIC SYNDROME

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Keywords:
Nephrotic syndrome-Proteinuria, Blood Pressure- Antihypertensive-Pediatric

Abstract

Introduction (Background):

Nephrotic syndrome (NS), also known as nephrosis, is defined by the presence of nephrotic – range proteinuria, hypertension, edema, hyperlipidemia, and hypoalbuminemia. Antihypertensive therapy should be given when hypertension is present and particularly if it persists, but caution should be exercised.

The Aim of study:

The aim of the present study is to investigate the effectiveness of various types of antihypertensive agents that prescribed for reduction of hypertension and proteinuria in children with nephrotic syndrome with fewer side effects.

Materials and Methods:

A total number of 150 patients with nephrotic syndrome will be included in this retrospective randomized study, with the various types of antihypertensive therapy of ACEIs, ARBs, Calcium channel blockers and beta-blockers as antiproteinuric in children patients, in addition to the regimen of therapy provided. The Age range will be from 2 years to 14 years. Proteinuria was assessed as protein/creatinine ratio. This study will be held for the period between 2015 and 2017 at pharmacy department, Children and Maternity hospital.

Results:

The significant differences were observed in mean systolic (SBP) and diastolic blood pressures (DBP) and proteinuria in children that were treated with amlodipine rather than any other type of antihypertensive therapy.

Conclusion:

We conclude that amlodipine provides effective BP control in children without significant adverse effects in children with nephrotic syndrome and can be used as monotherapy in most children.

Introduction

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Nephrotic syndrome (NS), also known as nephrosis, is defined by the presence of nephrotic – range proteinuria, hypertension, edema, hyperlipidemia, and hypoalbuminemia.

Nephrotic – range proteinuria in adults is characterized by protein excretion of 3.5g or more per day. However, because of great range of body sizes in children, The pediatric definition of nephrotic range proteinuria is more cumbersome. nephrotic range proteinuria in children is protein excretion of more than 40 mg/m^2 /h. [(1)]

Antihypertensive therapy should be given when hypertension is present and particularly if it persists, but caution should be exercised. In some patients, the hypertension will respond to diuretics. Angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) may also contribute to reducing proteinuria [(2)], Calcium channel blockers and beta-blockers may also be used.

Antihypertensive therapy should be given when hypertension is present and particularly if it persists, but caution should be exercised. In some patients, hypertension will respond to diuretics. Angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) may also contribute to reducing proteinuria, Calcium channel blockers and beta-blockers may also be used.

In humans, both hypertension and proteinuria determine the rate of progression of renal insufficiency[(3-5).] This was recently confirmed in the largest prospective study to date, that is, the Modification of Diet in Renal Disease (MDRD) study[(6-7).] The rate of decrease of glomerular filtration rate was highest in patients with proteinuria. Furthermore, in this particular group of patients antihypertensive treatment was most effective in inhibiting the loss of GFR. In the MDRD study, the achieved systolic blood pressure rather than the diastolic blood pressure correlated best with the extent of renal protection. Of note, renal function was best preserved in patients who achieved very low blood pressures: lowering of blood pressure from normal levels of 135/85 mm Hg to Â“belownormalÂ” levels of 125/75 mm Hg was associated with a preservation of renal function. As a consequence, patients with proteinuric renal diseases will need effective antihypertensive treatment.

The aim of the present study is to investigate the effectiveness of various types of antihypertensive agents that prescribed for reduction of hypertension and proteinuria in children with nephrotic syndrome with fewer side effects.

Materials and methods

A total number of 150 patients with nephrotic syndrome will be included in this retrospective randomized study, with the various types of antihypertensive therapy of ACEIs, ARBs, Calcium channel blockers and beta-blockers as antiproteinuric in children patients, in addition to the regimen of therapy provided. The Age range will be from 2 years to 14 years. Proteinuria was assessed as protein/creatinine ratio. This study will be held for the period between 2015 and 2017 at pharmacy department, Children and Maternity hospital.

Means and standard deviations of study variables were calculated for the three groups pre and post treatment. Numbers and percentages were calculated for qualitative variables. Chi-square test was used to test for differences in initial characteristics of the three groups. Paired t-test was used to test for differences between pre and post means for each group. Also, the mean difference between post and pre-values was calculated and the ANOVA test was used to test for differences between the three groups concerning the mean difference. A bar chart was used to display differences among the three groups.

Results of statistical analysis

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Table (1): Comparison between initial characteristics of the three groups

Initial characteristics	**Values**	**Groups**						Chi-square	p-value
		Captopril(n=13)		Amlodipin(n=43)		Enalapril(n=44)			
		No.	%	No.	%	No.	%		
Gender	Female	0	0.0	18	41.9	9	20.5	18.00	0.0001*
	male	13	100.0	25	58.1	35	79.5	9.97	0.01*
Age(years)	1-5	0	0.0	0	0.0	11	25.0	22.00	0.0001*
	6-10	7	53.8	25	58.1	18	40.9	9.88	0.01*
	11-15	6	46.2	18	41.9	15	34.1	6.00	0.05*
Diagnosis	Acute nephrotic syndrome	3	23.1	0	0.0	6	13.6	6.00	0.05*
	Chronic renal failure	0	0.0	6	14.0	0	0.0	12.00	0.0001*
	End stage renal dialysis	0	0.0	24	55.8	12	27.3	24.00	0.0001*
	Lupus nephritis	0	0.0	6	14.0	3	6.8	6.00	0.05*
	Nephrotic syndrome	10	76.9	7	16.3	18	40.9	5.54	0.06
	Renal impairment	0	0.0	0	0.0	5	11.4	10.00	0.01*

*significant

There is a significant difference between initial characteristics of the three groups. Percent of females is high in Amlodipin group while percent of males is high in Captopril group. Percent of age group 1-5 is high in Enalapril group. Percent of Chronic renal failure and End stage renal dialysis is high in Amlodipin group.

Table (2): Comparison between mean differences (between pre and post means) of study variables in the three groups

Study variables	**Groups**						F-value	p-value
	Captopril		Amlodipin		Enalapril			
	Mean difference	SD	Mean difference	SD	Mean difference	SD		
Serum urea (mmol/l)	1.85	2.36	-10.45	16.23	-1.86	2.88	9.808	.0001*
Serum albumin (g/l)	0.73	4.55	-5.67	3.24	-0.51	3.81	27.381	.0001*
Serum creatinine (umol/L)	9.28	15.86	-37.00	69.74	-20.81	80.61	2.204	.116
Systolic blood pressure	-8.31	5.99	-27.91	18.25	-10.30	19.96	12.356	.0001*
Diastolic blood pressure	-1.69	24.78	-14.16	18.22	-18.32	24.08	2.912	.059
Proteinuria	-0.03	0.25	-0.19	0.41	-0.02	0.02	4.139	.019*

*significant Note: Mean difference =Post mean-Pre-mean

There is a highly significant difference between mean difference of Serum urea of the three groups (p-value=0.0001). The mean difference is the highest in the Amlodipin group (mean=-10.45) indicating that the decrease in serum urea was the highest in this group. There is a highly significant difference between mean difference of Serum albumin of the three groups (p-value=0.0001).The mean difference is the highest in the Amlodipin group (mean=-5.67) indicating that the decrease in Serum albumin was the highest in this group. There is a highly significant difference between mean difference of Systolic blood pressure of the three groups (p-value=0.0001). The mean difference is the highest in the Amlodipin group (mean=-27.91) indicating that the decrease in Systolic blood pressure was the highest in this group. There is a significant difference between mean

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difference of Proteinuria of the three groups. The mean difference is the highest in the Amlodipin group (mean=-0.19) indicating that the decrease in Proteinuria was the highest in this group.

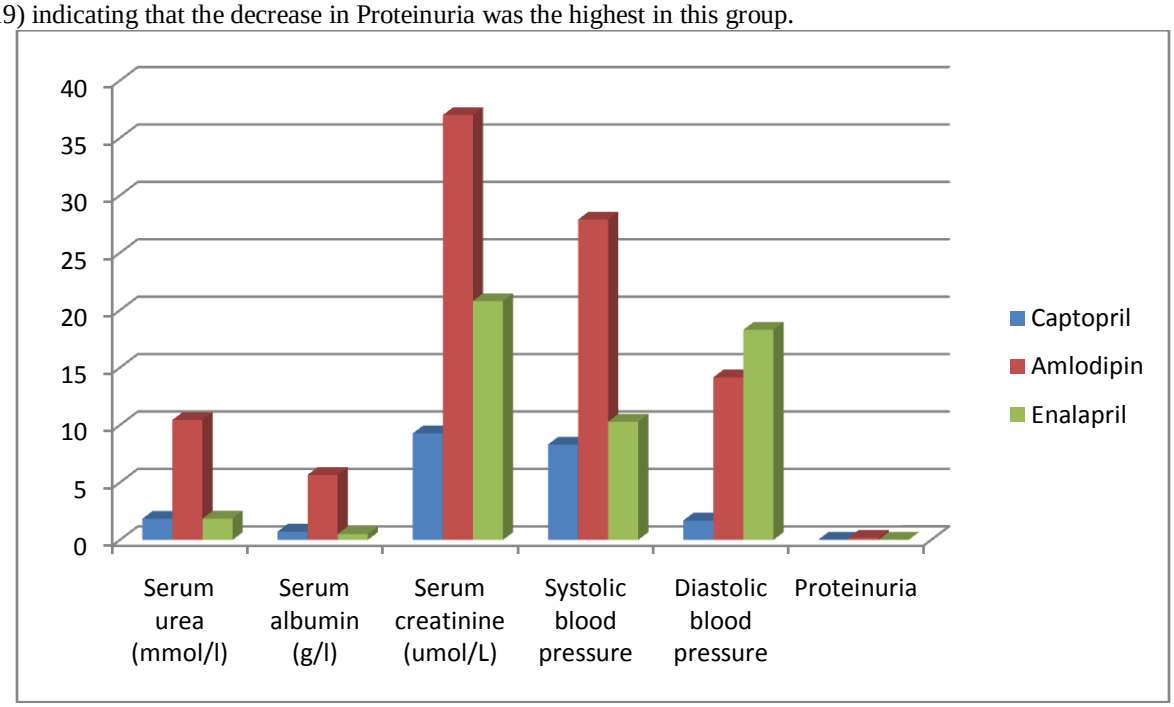

Figure (1): Comparison between mean differences (between pre and post means) of study variables in the three groups

Figure (1) shows the superiority of Amlodipin in decreasing all study variables especially urea, and systolic blood pressure.

Table (3): Comparison between pre and post means of study variables in each of the three groups

Study variables	**Groups**											
	Captopril				Amlodipin				Enalapril			
	Pre Mean	Post Mean	t-value	p-value	Pre Mean	Post Mean	t-value	p-value	Pre Mean	Post Mean	t-value	p-value
Serum urea (mmol/l)	6.7	8.5	2.8	0.01*	21.0	10.5	4.2	0.0001*	13.2	11.3	4.2	0.0001*
Serum albumin (g/l)	23.5	24.2	0.5	0.5	28.2	22.5	11.4	0.0001*	26.2	25.7	0.8	0.3
Serum creatinine (umol/L)	48.5	57.8	2.1	0.06	236.7	199.7	3.4	0.001*	226.5	205.7	1.7	0.09
Systolic blood pressure	120.3	112.0	4.9	0.0001*	147.1	119.2	10	0.0001*	132.0	121.7	3.4	0.001*
Diastolic blood pressure	70.4	68.7	0.2	0.8	95.8	81.6	5	0.0001*	88.8	70.5	5	0.0001*
Proteinuria	0.19	0.15	0.54	0.59	0.36	0.17	3	0.004*	0.12	0.10	5.5	0.0001*

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*significant

Although the three groups showed a significant difference between pre and post means in some variables, the Amlodipin showed the highest significant decrease in the means of all the study variables with p-value<0. 005.The Captopril group showed a significant difference in only urea and systolic blood pressure while the Enalapril group showed a significant difference in only four variables. Only the Amlodipin group showed a very high significant decrease in all the study variables.

Table (4): Comparison between normal ranges of urea, albumin and creatinine pre and post treatment in each of the three groups

Study variables	**Groups**																	
	Captopril(n=13)						Amlodipin(n=43)						Enalapril(n=44)					
	Normal pre treatment		Normal post treatment		CS	p	Normal pre treatment		Normal post treatment		CS	p	Normal pre treatment		Normal post treatment		CS	p
	No.	%	No.	%			No.	%	No.	%			No.	%	No.	%		
Serum urea (mmol/l)	9	69.2	9	69.2	0	1	24	55.8	24	55.8	0	1	17	38.6	30	68.2	3.6	0.06
Serum albumin (g/l)	0	0.0	0	0.0	0	1	7	16.3	0	0.0	7	0.008*	11	25.0	10	22.7	0.05	0.8
Serum creatinine (umol/L)	9	69.2	6	46.2	0.6	0.4	19	44.2	16	37.2	0.2	0.6	6	13.6	7	15.9	0.08	0.7

*significant Note:CS=Chi-square

For the three groups, there was no significant difference between percent of patients with normal ranges of urea, albumin and creatinine pre and post treatment except that the Amlodipin group showed a significant decrease in percent of patients with normal albumin (percent decreased from 16.3% to 0% with p-value=0.008).

Conclusions

There is a highly significant difference between mean difference of Serum urea, Serum albumin, Systolic blood pressure and Proteinuria of the three groups (p-value=0.0001) where the mean difference is the highest in the Amlodipin group indicating the superiority of Amlodipin over other treatments for decreasing urea, and systolic blood pressure. Also, only the Amlodipin group showed a very high significant decrease in all the study variables indicating that Amlodipin is recommended over other treatments in decreasing systolic and diastolic blood pressure as well as Proteinuria. Amlodipine provides effective blood pressure control without significant adverse effects in children with nephrotic syndrome and can be used as monotherapy in most children. The only drawback observed in the present study was that Amlodipine decreased the percent of patients with normal albumin level.

References

1. *Hogg RJ , Portman RJ , Milliner D , lemley KV , Eddy A,ingelfinger J , Evaluation and management of proteinuria and nephrotic syndrome in children : Recommendations from a pediatric nephrology panel established at the National Kidney foundation conference on proteinuria , albuminuria risk , assessment , detection , and elimination (PARADE). Pediatrics , Jun 2000;105 (6) : 1242-9 (Medline).*

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2. *Brewster uc ,perazella MA. The rennin angiotensin – aldosterone system and the kidney : effects on kidney disease . Am J Med 2004 ; 116 :263-72 .*
3. *P.C. BRAZY, W.W. STEAD, J.F. FITZWILLIAMProgression of renal insufficiency: Role of blood pressure Kidney Int, 35 (1989), pp. 670-674*
4. *P.S. WILLIAMS, G. FASS, J.M. BONERenal pathology and proteinuria determine progression in untreated mild/moderate chronic renal failure Q J Med, 67 (1988), pp. 343-354*
5. *A. ALVESTRAND, A. GUTIERREZ, H. BUCHT, J. BERGSTRÃ–MReduction of blood pressure retards the progression of chronic renal failure in manNephrol Dial Transplant, 3 (1988), pp. 624-631*
6. *S. KLAHR, A.S. LEVEY, G.J. BECK, A.W. CAGGIULA, L. HUNSICKER, J.W. KUSEK, G. STRIKER, FOR THE MODIFICATION OF DIET IN RENAL DISEASE STUDY GROUPThe effects of dietary protein restriction and blood-pressure control on the progression of chronic renal diseaseNEngl J Med, 330 (1994), pp. 877-884*
7. *J.C. PETERSON, S. ADLER, J.M. BURKART, T. GREENE, L.A. HEBERT, G. LAWRENCE, L.G. HUNSICKER, A.J. KING, S. KLAHR, S.G. MASSRY, J.L. SEIFTERBlood pressure control, proteinuria, and the progression of renal disease. The modification of diet in renal disease studyAnn Intern Med, 123 (1995), pp. 754-762.*