

Effect Of Management On Serum Electrolytes, Urea And Creatinine In Children With Nephrotic Syndrome And Acute Glomerulonephritis

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Abstract

Primary nephrotic syndrome (NS) and acute glomerulonephritis (AGN) are known to cause varying degrees of renal insufficiency depending on the severity. Certain drugs and management strategies used in these two disorders also have profound effect on the serum electrolyte and urea profiles. This study determines the effect of management on the profile of serum electrolytes, urea and creatinine in children with NS and AGN.

A retrospective analysis of the biochemical profiles of children admitted with a diagnosis of NS and AGN between 1996 and 2004 was carried out. A total of 21 and 16 children with AGN and NS respectively met the study criteria. There was no significant difference in the serum sodium, potassium and urea in both groups during the study except at the 4th week. The prevalence of hypokalemia in both groups of children was low. The serum sodium and potassium were significantly low compared to those with AGN in the 4th week, while the serum urea and creatinine was higher in NS patients in the same period. There was also generally a low prevalence of hypokalemia throughout the study period. While the study may have confirmed the occurrence of electrolyte imbalance following the use of diuretics, it has also shown that the prevalence of such electrolyte imbalance in the first 4 weeks of treatment is rather low and insignificant despite using significant dose of the drug.

Keywords: Electrolyte; urea; acute glomerulonephritis; nephrotic syndrome; children.

Introduction

Primary nephrotic syndrome (NS) and acute glomerulonephritis (AGN) are known to cause varying degrees of renal impairment depending on the severity. ¹ Acute renal failure (ARF) remains an important component of AGN implying that certain levels of electrolyte and fluid derangement occur, but anecdotal observation have shown

that the pattern of severity of these derangements varies at presentation. While ARF is not an important component of NS at presentation, it could occur as a complication due to diminished renal perfusion resulting from contraction of intravascular volume. ² Both AGN and NS therefore affect serum electrolytes, urea and creatinine. ²⁻⁵

Certain drugs and management strategies employed in the management of these disorders also have profound effects on serum electrolyte and urea profiles of these patients⁶. Frusemide, thiazide, spironolactone, steroids and antihypertensives regularly used in the treatment of these 2 disorders are known to have profound effect on the serum electrolyte urea and creatinine. Frusemide may produce hypokalemia and hypochloremic alkalosis. The hypokalemia is as a result of increased excretion of potassium while the hypochloremia occurs due to the inhibition of active chloride reabsorption mechanism at the ascending limb of the loop of Henle. Thiazide also causes potassium depletion by increasing the rate of delivery of tubular fluid to the distal exchange sites. Spironolactone may cause hyperkalemia especially in patients with impaired renal function. They may cause hyperkalemia by reducing the excretion of potassium. Steroid causes sodium and water retention, while hyperkalemia can occur in patients receiving angiotensin converting enzyme inhibitors (ACEI) due to either medication induced renal failure or inhibition of aldosterone in patients with relatively normal function. The calcium channel blockers on the other hand are known to increase urinary sodium and potassium. However, the prevalence of the various possible biochemical complications is not known in the different group of patients. This study therefore aims to determine the effect of management on the profile of serum electrolytes, urea and creatinine in children with NS and AGN.

Materials and Methods

A retrospective analysis of the biochemical profiles of children admitted with a diagnosis of NS and AGN to the Children's ward of the University of Ilorin Teaching Hospital, Ilorin, Nigeria between 1996 and

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2004 was carried out. The inclusion criteria were newly diagnosed NS who required frusemide, thiazide and spironolactone for their treatment and had commenced steroid within four weeks after admission. The exclusion criteria for the NS patients included relapse of NS and children who had been commenced on steroids, diuretics or anti-hypertensives prior to admission. The inclusion criteria for the children with AGN included newly diagnosed AGN who required frusemide, thiazide, spironolactone and anti-hypertensives for their treatment during the four weeks under study. The exclusion criteria included children who had been commenced on frusemide, thiazide, spironolactone or anti hypertensives before admission.

Nephrotic syndrome was diagnosed in the presence of anasarca, massive proteinuria >2gms/24hours, hypoproteinemia- serum protein <2g/dl and hypercholesterolemia >5.2 mmol/l, while AGN was diagnosed by the presence of haematuria, hypertension, proteinuria and azotaemia.

All the patients received the appropriate management for the acute stage of illness. The serum sodium, potassium, urea and creatinine estimation at admission, then within the first, second and fourth week of admission were retrieved. The NS patients that received steroid and diuretics (frusemide, hydrochlorothiazide and spironolactone) were harvested. Similarly, AGN patients that received antihypertensives (nifedipine and captopril) and diuretics (frusemide, hydrochlorothiazide, and spironolactone) were also harvested.

The mean and standard deviations of the biochemical profiles at the four different periods under study were computed and comparison made among the 2 disease groups using a student t test. Comparison between mean serum electrolytes, urea and creatinine during the 4 different periods for each disease was carried out using the analysis of variance (ANOVA).

Definition of terms; Normal range for serum sodium is 138-145 mmol/l (<138-hyponatramia, >145-hypernatraemia). Normal range for serum potassium is 3.4-4.7 mmol/l (<3.4 mmol/l-hypokalemia, >4.7 mmol/l-hyperkalemia). Normal range for serum urea 1.8-6.4mmol/l (azotaemia >6.4mmol/l). Normal range for serum creatinine in child is 27-62mmol/l, in adolescent 44-8mmol/l. Values of serum creatinine > maximum range for age group is ARF.⁷

Results

A total of 21 and 16 children with AGN and NS respectively met the study criteria. Children with AGN

comprised 17 males and 4 females giving rise to a male: female ratio of 4.3:1 while those with NS comprised 10 males and 6 females giving rise to a male: female ratio of 1.7:1. The age range of children with AGN was 2.5-15 years with a mean (SD) of 7.2±4.6 years while that of children with NS was 3-17 years with a mean (SD) of 9.3±4.1 years.

Serum Sodium: The mean serum sodium at admission, 1st, 2nd and 4th week among the children with AGN were 136±5, 134±5, 130±5 and 138±6 mmol/l respectively while that among the children with NS were 137±5, 134±8, 131±7 and 127±2 mmol/l respectively (Table 5). Hyponatremia at admission, 1st, 2nd and 4th week occurred in 5/21 (24%), 8/15 (54%), 7/7 (100%), 1/4 (25%) of children with AGN, while it occurred in 4/16(25%), 5/13(38%), 6/7 (86%), 4/4 (100%) of children with NS. Hypernatraemia did not occur among the 2 groups at any of the period under study (Tables 1-4).

Serum Potassium: The mean serum potassium at admission, 1st, 2nd and 4th week among children with AGN were 4.6±0.9, 4.2±1, 4.0±1.1, 4.3±0.7 mmol/l respectively, while that among children with NS was 3.7±0.9, 3.9±0.9, 3.7±0.6, 3.7±1.3 mmol/l respectively (Table 5). Hypokalemia at admission, 1st, 2nd and 4th week occurred in 0/21,1/15 (7%), 1/7 (14%), 0/4 of children with AGN, while it occurred 2/16 (13%), 2/13 (15%), 1/7 (14%), 1/4 (25%) of children with NS. Hyperkalemia at admission, 1st, 2nd and 4th week occurred in 4/21 (19%), 3/15 (20%), 2/7 (28%) and 0/4 children with AGN while it occurred in 1/16 (6%), 2/13 (15%), 0/7, 1/4-(25%) children with NS (Tables

Table 1: Serum electrolytes, urea and creatinine at admission

Clinical profiles	AGN n=21	NS N=17	P-value
Serum sodium	136±5	137±54(25%)	>0.05
Hyponatraemia	5(24%)		>0.05
Serum Potassium	4.6±0.9	3.7±0.9	<0.05
Hyperkalemia	4(19%)	1(6%)	>0.05
Hypokalemia	0	2(13%)	>0.05
Serum Urea	9±5	6.5±2.6	<0.05
Azotaemia	13(65%)	8(50%)	>0.05
Serum Creatinine	158±150	158±247	>0.05
Elevated Scr	11(73%)	9(60%)	>0.05

Table 2: Serum electrolytes, urea and creatinine in the first week

Clinical profiles	AGN n=15	NS n=15	P-value
Serum sodium	134±5	134±8	>0.05
Hyponatraemia	8(54%)	5(38%)	>0.05
Serum Potassium	4.2±1.0	3.9±0.9	>0.05
Hyperkalemia	3(20%)	2(15%)	>0.05
Hypokalemia	1(7%)	2(15%)	>0.05
Serum Urea	8.8±4.4	7.9±4.0	>0.05
Azotaemia	11(73%)	8(62%)	>0.05
Serum Creatinine	95±38	184±282	<0.05
Elevated Scr	5(63%)	9(75%)	>0.05

Table 3: Serum electrolytes, urea and creatinine in the second week

Clinical profiles	AGN N=7	NS N=7	P-value
Serum sodium	130±5.0	131±7.0	>0.05
Hyponatraemia	7(100%)	6(86%)	>0.05
Serum Potassium	4.1±1.1	3.7±0.6	>0.05
Hyperkalemia	2(28%)	0	>0.05
Hypokalemia	1(14%)	1(14%)	>0.05
Serum Urea	10.0±7.0	8.4±6.5	>0.05
Azotaemia	3(43%)	2(28%)	>0.05
Serum Creatinine	132±126	156±220	>0.05
Elevated Scr.	3(60%)	3(43%)	>0.05

1-4).

Serum Urea: The mean serum urea at admission, 1st, 2nd and 4th week among children with AGN were 9.3±5.1, 8.8±4.4, 10.2±7 and 5.5±3.3mmol/l respectively while that among children with NS were 6.5±2.6, 7.9±4.0, 8.4±6.5, 14.3±9.6mmol/l respectively (Table 5). Azotaemia at admission, 1st, 2nd and 4th week occurred in 13/20 (65%), 11/15 (73%), 3/7 (43%) and 1/4 ((25%) children with AGN while it occurred in 8/16 (50%), 8/13 (62%), 2/7 (28%) and 3/4 (75%) of children with NS (Tables 1-4).

Serum creatinine: The mean serum creatinine at admission, 1st, 2nd and 4th week among children with AGN were 158±150, 95±38, 131±126 and 77±49mmol/l respectively while that among children with NS were 158±247, 184±282, 158±220 and 635±759mmol/l respectively (Tables 5). Increased serum creatinine occurred at admission, 1st, 2nd and 4th week in 11/15 (73%), 5/8 (63%), 3/5

Table 4: Serum electrolytes, urea and creatinine in the fourth week

Clinical profiles	AGN N=4	NS N=4	P-value
Serum sodium	138±6.0	127±2	<0.05
Hyponatraemia	1(25%)	4(100%)	>0.05
Serum Potassium	4.3±0.7	3.7±1.3	<0.05
Hyperkalemia	0	1(25%)	>0.05
Hypokalemia	0	1(25%)	>0.05
Serum Urea	5.5±3.3	14±10	<0.05
Azotaemia	1(25%)	3(75%)	>0.05
Serum Creatinine	77±49	635±759	<0.05
Elevated Scr.	1(33%)	2(100%)	>0.05

Table 5: Mean serum electrolytes, urea and creatinine over the four weeks of study

Clinical profiles	Disease	Admission	1 st week	2 nd week	4 th week	P-value
Serum sodium	AGN	136±5	134±5	130±5	138±6	>0.05
	NS	137±5	134±8	131±7	127±2	>0.05
Serum Potassium	AGN	4.6±0.9	4.2±1.0	4.1±1.1	4.3±0.7	>0.05
	NS	3.7 ±	3.9±0.9	3.7±0.6	3.7±1.3	>0.05
Serum Urea	AGN	9.0±5.0	8.8±4.4	10.0±7.0	5.5±3.3	>0.05
	NS	6.5±2.6	7.9±4.0	8.4±6.5	14.0±10.0	<0.05
Serum Creatinine	AGN	158±150	95±38	132±126	77±49	>0.05
	NS	158±247	184±	156±220	635±	<0.05

(60%), 1/3 (33%) child with AGN while it occurred in 9/15 (60%), 9/12 (75%), 3/7 (43%), and 2/2 (100%) of children with NS (Tables 1-4).

Discussion

In this study, the effect of the various therapeutic managements employed on serum electrolyte, urea and creatinine were examined. The study also examined the magnitude of the various biochemical side effects amongst the patient studied over 4 weeks. The choice of initial 4 weeks of treatment in newly diagnosed patients with the 2 disorders came about because that was the time when significant amount of the drugs are employed in order to get maximum effect and quick recovery. This would not occur at follow up when some of the patient may not require

some of the drugs like diuretics and anti-hypertensives and even steroids which are only administered for limited period of time. Furthermore most patients with AGN are out of the acute phase at follow-up and may not need prolonged therapy.

Our finding indicated that there was no significant change in the mean serum sodium over 4 weeks in both the AGN and NS patients despite the commencement of steroid between the 2nd and 4th week in the NS patients. There was however a significant difference between the serum sodium in both groups in the 4th week with the NS group recording a lower mean serum sodium. This might be the resultant effect of steroids in these patients. Hyponatraemia was indeed a concern in an appreciable number of individual patient. Its prevalence was higher in the 2nd week in the 2 groups. This is likely the aftermath of the diuretic therapy especially frusemide and thiazide. Increased urinary excretion of sodium and water through the inhibition of sodium reabsorption in the cortical portion of the ascending limb of the loop of Henle and the first part of the distal convoluted tubule occurs following the administration of thiazides.⁸ Nifedipine also has a natriuretic effect which may have contributed to the occurrence of hyponatraemia especially in the AGN patient some of whom received it.⁹ It is important to note that hyponatraemia occurred unappreciably at admission when frusemide was commonly introduced. The hyponatraemia in the 2nd week could also have been as a result of the dilutional effect of the fluid shift from the interstitial space to the intravascular compartment. Hypernatraemia did not occur in both groups. The status of the extracellular fluid volume in the patient is not known been a retrospective study, hence whether the hyponatraemia recorded was with normal, reduced or increased ECF is difficult to enunciate. There was however no clinical symptom associated with hyponatraemia observed in them. Patients with hyponatraemia could convulse, develop lethargy and weakness.

The serum potassium also quite unexpectedly remained stable in both groups of patients throughout the 4 weeks despite been on frusemide and thiazide. It is likely that their combination with spironolactone could have contributed to this. However, as was the case with serum sodium, there was a significant difference between the mean serum potassium in both groups with the NS group having lower mean serum potassium even though it was still within normal limit (Table 5). An overview of individual patients indicated too that hypokalemia prevalence was higher in the 2nd week, though that prevalence was still low. There was also no symptom recorded. This justifies the rational use of frusemide if it is required in children

with severe oedema rather than subject them to this morbidity for a long time due to the fear of attendant hypokalemia from its use. Our finding showed that its combination with spironolactone is capable of drastically reducing this potential side effect. Hyperkalemia was recorded in very few patients in both groups though slightly more in AGN patients throughout the study period. The use of captopril to treat hypertension in the latter may have contributed to its occurrence. This is due to either captopril induced renal failure or inhibition of aldosterone.¹⁰

The serum creatinine was on the decline in the AGN patient over the 4 weeks. This was the contrast in NS where the serum creatinine remained high over the 4 weeks. The finding in AGN was in agreement with finding by other workers.¹¹ The occurrence of ARF (increased creatinine) was higher in AGN than NS. Similarly the serum urea was high in both groups over the 4 weeks period, though there was decline by the 4th week in the AGN patients. This cannot be completely relied upon because the dehydration effect of the diuretics could have contributed to that.

In conclusion, the prevalence of hyponatraemia was appreciable throughout the 4 weeks while that of hypokalemia was very low in both groups of patients. Both serum sodium and potassium were significantly low in the NS patients compared to AGN in the 4th week, while the serum urea and creatinine remained high in the same period in the NS patients compared to AGN. While the study may have confirmed the occurrence of electrolyte imbalance following the use of diuretics, it has also shown that the prevalence of such electrolyte imbalance in the first 4 weeks of treatment is rather low and insignificant despite using significant dose of the drug.

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