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Dialyzer Reuse and Its Logical Practice

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Summary :

Reuse of dialyzer has been an integral part of hemodialysis both in the developed and developing countries since its inception. We studied the reuse of hemodialyzer in 18 stable chronic hemodialysis patients who have been registered in the nephrology unit of Chittagong Medical College Hospital for maintenance hemodialysis. During the study period, 18 dialyzers were used for a total 108 sessions of dialysis. After each use, dialyzer membrane clearance was tested by measuring the fiber volume of blood compartment and the efficacy of the dialyzer was determined by measuring the urea reduction ratio (URR). The URR was maintained between 51 ± 7% at the first use and 50 ± 7% at the 6th use. Dialyzer volume was maintained between 65 ml and 52.7 ml at the 1st and at the 6th use, respectively. Total cost savings of 32% was achieved with the reuse of dialyzer in our center. In conclusion, we observed that dialyzer reuse is safe with maintaining its efficacy, as well as logical with economical benefits.

Introduction :

Now a days, dialyzer reuse has become a logical practice in almost all countries in the world except Japan, most of the Middle East countries and a few scattered countries in Europe and South America[1]. But controversial reports about its efficacy, safety and economic benefits were followed since the development of dialyzer reuse concept in 1964[2-4]. Some previous studies suggested that there are increased rates of infection with higher mortality and morbidity with dialyzer reuse[5]. However, recent studies suggested that reused dialyzer is safe and more beneficial than single use dialyzer due to less risk of hemodialysis and first use phenomenon, like leucopenia, complement activation, and anaphylactic reaction[6-8]. Despite some discouraging reports, the practice of reuse has been increasing throughout the world due to immunological tolerance besides its major economic benefits especially in the developing countries. Recently, Agoda et al[9] reported their preliminary evaluation of 20000 patients from the USRDS data showing an increase in the percentage of HD-units practicing reuse from 68% to 81 % during the period of 1989- 1996. They also noticed prescription of a higher dialysis dose, greater reuse of high-flux dialyzer and higher serum albumin levels in units practicing reuse. Although we have been practicing dialyzer reuse at our center for a while the efficacy of dialyzer and its exact economical advantage have not been evaluated earlier. In this study, we evaluated the dialyzer efficacy by measuring urea reduction ratio (URR), and the cost effectiveness of the dialyzer reuse procedure in 18 stable chronic hemodialysis patients.

Materials and Methods :

Eighteen end stage renal disease (ESRD) patients (15 males and 3 females) with mean age of 43.5 ± 11.1 yrs. on regular hemodialysis at our center were randomly selected to participate in this study. Informed consent was signed by each patient. Each patient underwent regular hemodialysis (8 hours/week) with the same dose of heparin, and with blood flow of 200-250 ml/min and acetate dialysate flow of 500 ml/min. We used 1.2 sq. m Hemophan dialyzer (Diacap, B-Braun, Germany) during the study period. After each use, the dialyzer was cleaned manually as follows. First dialyzer was cleaned with filtered water and hydrogen peroxide (6%), and then sterilized with 4% formaldehyde. The whole process of preparation of a dialyzer for reuse took about thirty minutes and included; initial check for any fiber breaks followed by measurement of fiber volume of blood compartment. The fiber bundle volume of dialyzer was measured by purging the filled blood compartment with air and measuring the volume of obtained fluid. The change in fiber volume was then followed after each use. Dialyzer was discarded if the membrane is ruptured or if the fiber bundle volume loss was more than 25% in one dialysis session. After all procedures the dialyzer were labeled and stored for the next use. Each dialyzer was cross-checked by the nurse for correct labeling before initiation of dialysis. Rinsing of dialyzer was as usual before connecting the patients.

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Blood samples were drawn from the arterial side (at the initiation) and from the venous side (at the end), and processed for urea and creatinine estimation by a standard laboratory method. Data of each use were recorded in a pre-structured sheet. Urea reduction ratio (URR) was calculated by the formula; (l- post HD urea/ pre HD urea level) and expressed in percentage to represent the efficacy of dialysis. During the study period, if there were any adverse events such as, access problem, allergic reaction, infection or any other medical illness were recorded.

Statistics :

All data were reported as mean ± SD. Paired t test was used to analyze the data and statistical significance was considered when P value was <0.05.

Results :

The demographic and the clinical characteristics of the dialysis patients are shown in Table 1. Out of 18 patients 15 were males and 3 were females, having dialysis duration of 6 - 40 months.

Table-I

Patient demographic and clinical characteristics

Parameters	Values
Age in years	43.5 ± 11.1
Male/Female ratio	5:1
Dialysis duration in months	6-40
CRF Causes:	
Chronic glomerulonephritis	8(44%)
Diabetic nephropathy	5(28%)
Others	5(28%).

Initial dialyzer volume was 65.0 ± 0 ml and after 6th use it was reduced to 52.7 ± 2.9 ml which showed the mean dialyzer volume reduction was 18.9%. Heparin was used with maximum dose of 8,000 U/session. However, no episode of bleeding or prolonged post--hemodialysis hemostasis was noted. The mean urea reduction ratio (URR) was 51 ± 7% at the first use and 50 ± 7% at the 6th use of dialyzer (Fig. 1). Percentage of URR after each use of dialyzer was shown in Fig.-2 and there was a correlation between the percentage of dialyzer volume reduction and the percentage of URR (P<0.05; Fig. 3). Baseline hemoglobin of 8.0 ± 1.2% increased to 8.3 ± 1.1% at the end of the study. No significant episode of infection, allergic reaction or access problem were noted. No labeling error happened during the study and reuse processing was easily done by the dialysis unit staff. Cost of the dialyzer and other consumables including

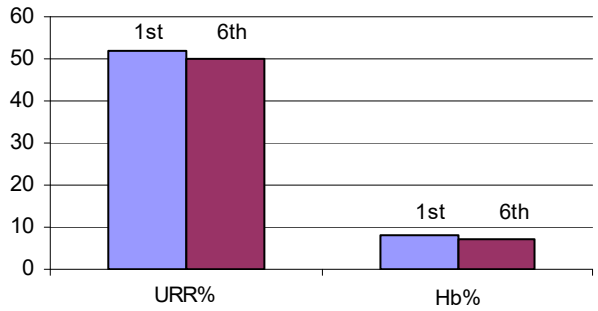

Fig-1 : *Percentage of urea reduction ratio (URR) and Hemoglobulin (Hb) changes in the 1st and 6th use*

cleaning and sterilization materials, and excluding reuse machine computer system and HD-personnel was 95,400 Bangladeshi taka (approx US.$ 1645) for total 6 sessions of dialysis in 18 patients. Whereas, without dialyzer reuse the projected cost would have been 140,400 Bangladeshi taka (approx. US.$ 2430). Thus, yielding a saving of 2500 taka (32%) for only 6 session dialysis i.e., yearly saving of 43,334 taka (approx. US $ 747) per patient. Dialysis expenses for 6 session dialysis in a patient with and without dialyzer reuse is shown in Table-II. This calculation was done on the basis of local market price of the dialysis items without adding any percentage of profit.

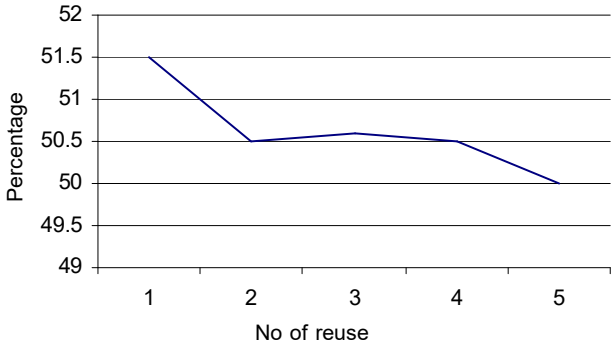

Fig.-2 : *Changes in URR (%) after each use of dialyzer*

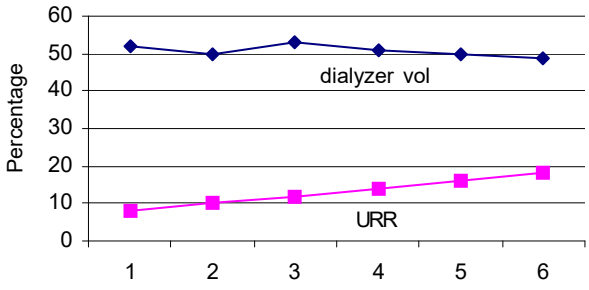

Fig.-3 : *Correlation between dialyzer volume decrease and urea reduction ratio (%)*

Table-II

Dialysis expenses in 6 sessions with and without dialyzer reuse

	Single use dialyzer			Reuse dialyzer	
	Dialyzer	Others	Dialyzer	Others	Reprocessing cost
1st use	Tk. 650	Tk. 650	Tk. 650	Tk. 650	
2nd use	Tk. 650	Tk. 650		Tk. 650	Tk. 150
3rduse	Tk.650	Tk.650		Tk.650	Tk.150
4th use	Tk. 650	Tk. 650		Tk. 650	Tk. 150
5th use	Tk. 650	Tk. 650		Tk. 650	Tk. 150
6 use	Tk.650	Tk.650		Tk.650	Tk.150
Total	3900/=	3900/=	650/=	3900/=	Tk.750
Grand Tk. total	7800			Tk. 5300	

Discussion :

The results of this study showed that dialyzer reuse does not affect its clearance capacity, as the URR was maintained well all through the reuse period and the dialyzer clearance capacity was directly related to the dialyzer volume reduction. In our study, we used the recommended cell volume of more than 80% to achieve the optimum solute clearance. Sometimes, repeated failure to reach a target number of reuse has been observed because of loss of fiber bundle volume, usually resulting from clotting in the fibres[10]. Heparin requirement was increased in our patients but despite this increment, we did not notice any episodes of bleeding and the mean hemoglobin level has improved from base line. We measured the clearance of small solutes i.e., urea which was well maintained all through the study, as evidenced by other studies[11,12].

The reuse process itself was not an extra burden on our staff, as HD-nurses learnt the reuse processing by a week and were able to perform the processing between the shifts.

Our study did not show any short-term adverse effects like febrile episodes or infections on patient's morbidity with dialyzer reuse. Infection has been reported in higher frequency in some centers practicing reuse. This has been attributed to microbial contamination of water and/ or when dialyzers were reused more than 20 times[13,14]. Although increased morbidity and mortality have been described in dialyzer reuse previously, which were largely associated with the type of germicide, infection outbreak, type of dialysis facility (hospital based or clinic based), and type of dialyzer (low-flux or high-flux)[5,15]. While hepatitis C infection among HD-patients is a growing concern, and the role of dialyzer reprocessing in this process has been questioned, studies have shown that reuse when performed by the conventional cleaning and sterilization procedures, is not a cause of hepatitis C transmission.

The current trend of steady increase in dialyzer reuse practice especially in the developing countries has been motivated by its economical advantage. This resulted to the trend for better dialysis using high-flux dialyzers and cost containment practices at the same time[9]. In our study, we saved 32% of our expenditure for 6 session dialysis in each patient, which was significant enough that the overall saving would have been 43,334 taka per patient per year. Our HD-unit being small (20 patients), we could handle the reuse procedures without need for extra nursing staff. For most medical practices, especially in case of chronic maintenance procedures, economic considerations are weighed against safety and effectiveness for patients. As no country is so rich that it can afford to squander its health care resources unnecessarily.

We conclude that dialyzer reuse in our patients did not affect the efficacy of the dialyzers in the clearance of urea upto 6 times and we can reuse more with considerable saving of cost if the fiber bundle volume does not reduce more than 25%. However, a large and multi-center study would be needed to address the safety and efficacy of dialyzer reuse in HD patients in our country.

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Original Articles

Peritoneal Permeability of Bangladeshi Patients and its Relation with Serum Albumin and Dialysate Protein Loss

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Summary :

Objective : Peritoneal membrane transport characteristics have a significant impact on dialysis clearance. Indian study has a different pattern of membrane transport characteristics, contrary to the findings in other authors in Canada. We determined the peritoneal permeability pattern in Bangladeshi patients and, we also examined the relationship between serum albumin level and dialysate protein loss to peritoneal transport status.

Methods : We studied 29 end stage renal failure (ESRD) patients, from June to December, 2000, in Dhaka Medical college Hospital, who were on peritoneal dialysis for a duration less than 3 months. Patients with suspected peritonitis were excluded. Standard 4 hour peritoneal equilibration test (PET) was done and patients were grouped into conventional four classes according to permeability status. We recorded serum albumin and estimated dialysate 24 hour protein loss in each patient to find out relationship with PET results.

Results : There were 21 men and 8 women. Mean age was 51±10.27 (SD) years. Causes of ESRD were diabetic nephropathy in 12, Chronic Glomerulonephritis in 10, Hypertensive Nephrosclerosis in 4 and other causes in remaining 3 cases. Among the 29 patients, there were 9 (31%) high (H), 11 (38%) high average (HA), 7 (24%) low average (LA), and 2 (7%) low transporters (L) and mean serum albumin levels were 28.81, 32.34,35.71 and 43.50 g/L (P<0.001) and calculated 24 hours dialysate protein loss were 16.30, 8.27, 8.71 and 5.6 gram (P<0.001) respectively. Serum albumin level showed a significant inverse correlation with the 4 hour D/P creatinine ratio (r= -579; p=<0.001). D/P creatinine ratio also revealed a good correlation with 24 hour dialysate protein loss (r=0.722; p=<0.001).

Conclusion : Majority of the Bangladeshi patients were HA and H transporters. Our study also observed that increased peritoneal permeability was associated with increased peritoneal protein loss and also with hypoalbuminemia Membrane permeability pattern of our patients differ from those reported by Indian and Canadian authors. Further study with large number of patients may uncover the factors causing the differences.

Introduction :

Continuous Ambulatory Peritoneal Dialysis (CAPD) is one of the modality of choice for treatment of End-stage Renal Disease (ESRD). In patients with peritoneal dialysis (PD), higher peritoneal membrane transport is associated with worse patient outcome[1,2,3]. Similarly, low serum albumin after the initiation of PD is associated with high peritoneal membrane transport[1,3,4] and decreased patient survival. The patients peritoneal permeability characteristics are classified by the standard 4-hours Peritoneal Equilibration Test (PET)[5]. The therapy is individualized according to the PET result for each patient.

Indian study has demonstrated a different pattern of membrane transport characteristics contrary to the findings in other authors in Canada [6.7]. We studied peritoneal permeability pattern in Bangladeshi patients and we also have analyzed the relationship between serum albumin level and dialysate protein loss, to peritoneal transport status, since these parameters have not been analyzed for Bangladeshi peritoneal dialysis population to date.

Methods :

We studied 29 end stage renal failure (ESRD) patients from June to December, 2000, in Dhaka Medical College Hospital, who were on peritoneal dialysis for duration less than 3 months. Patients with history of and/or having peritonitis were excluded from the study.

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Age, aetiology, serum albumin, total protein and serum cholesterol levels were noted at the beginning of PET test. Detail history was taken and physical examination done to exclude evidence of peritonitis. 2.5% Baxter CAPD fluid was instilled and kept in peritoneal cavity overnight for duration of 10-hours, then the fluid drained away, measured and sample taken for analysis. Thereafter a fresh 2.5% CAPD fluid instilled again and samples were colleted from effluent at 0, 2 and end of 4 hour; Simultaneously blood samples were collected and analyzed. In this way PET test were done according to standard method described by Twardowski et al.[5] 1987 and based on the results the patients were divided into four groups : High (H), High-Average (HA), Low Average (LA) and Low (L). We analyzed the correlation between serum albumin and 24 hours dialysate protein loss. We also compared between membrane transport pattern and - serum albumin level and membrane transport pattern with 24 hours dialysate protein loss.

Statistical analysis were done using SPSS package. Pearson's Correlation Test, Paired T Test and Student's T Test were done wherever applicable.

Results :

The study group consisted of 29 patients (21 males and 8 females) : Mean age was 51± 10.27 (SD) years. Causes of ESRD were Diabetic Nephropathy in 12, Chronic Glomerulonephritis in 10, Hypertensive Nephrosclerosis in 4 and other causes in remaining 3 cases. Out of 29, 9 (31%) patients were classified as High (H), 11 (38%) as High Average (HA), 7 (24%) as Low Average (LA) and 2 (8%) as Low (L) transporter (Table-1)and mean serum albumin levels were 28.81 ± 4.85, 32.34 ± 5.33, 35.71 ± 5.84 and 43.50 ± 2.54 gm/L respectively (Table-2). The H and HA peritoneal membrane groups had significantly diabetic patients compared with L and LA group (P=0.01) (Table-1). Our study showed significant inverse correlation between peritoneal membrane permeability and serum albumin (r=-57, p<0.001) (Fig-1). 24 hour dialysate protein loss were 16.30, 8.27, 8.73 and 5.6 gm/d in H, HA, LA and L group respectively. The dialysate protein loss also revealed good correlation with membrane permeability pattern (r=0.67, P<0.001) (Fig-2). Serum albumin level showed a significant correlation with the 4 hour Dialysate to plasma (D/P) creatinine ratio (r=0.58; P<0.001). D/P creatinine ratio also revealed a good correlation with 24 hour dialysate protein loss (r=0.722; P<0.001)

Table - I

Clinical Variables of PD Patients According to Peritoneal Transport Type.

Group	No. of Patients	% of patients	Age SD	Sex (M/F)	Diabetics %
Low	2	7	54 ±14	2/0	0%
Low Average	7	24	54 ± 8	5/2	14.29%
High Average	11	38	50 ± 8	8/3	54.55%
High	9	31	48 ± 13	6/3	55.55%

Table - II

Distribution of laboratory parameters according to peritoneal transport

Group	Albumin Mean (SD)	Protein Loss Mean (SD)
Low	43.5 ± 2.5 gm/L	5.6 ± 0 gm/d
Low Average	35.4 ± 5.8 gm/L	8.7 ± 2 gm/d
High Average	32.3± 5.3 gm/L	8.3 ± 2 gm/d
High	28.8 ± 4.8 gm/L	16.3 ± 4 gm/d

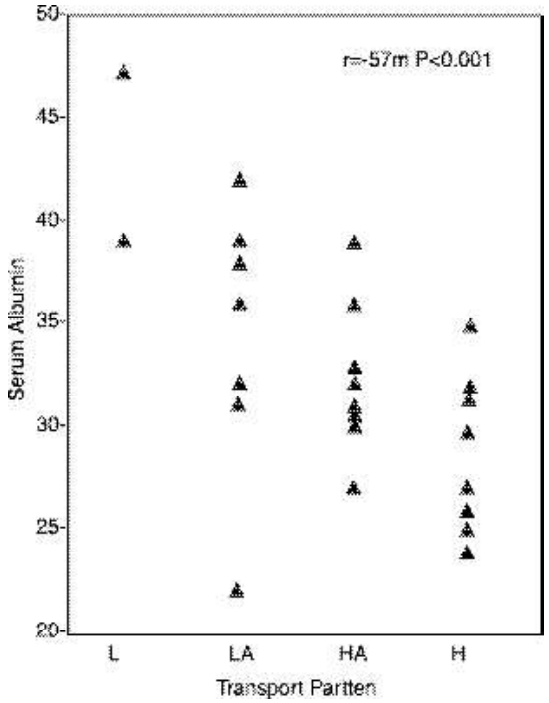

Fig-2 : *Correlation between transport pattern and serum albumin*

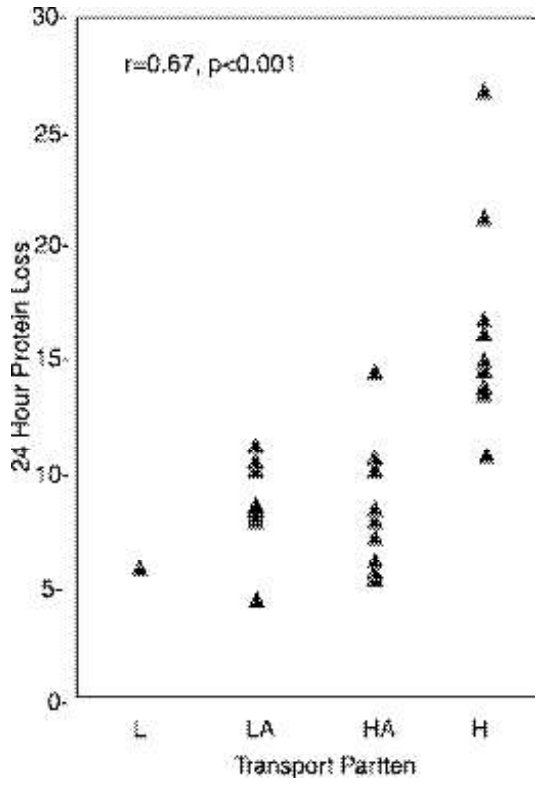

Fig-3 : *Correlation between transport pattern and 24 hour dialysate protein loss*

Discussion :

PET test can be used to tailor PD prescription. Patients with higher transport characteristics are more likely to have adequate Kt/V values, but may have problems with ultrafiltration that requires shorter dwell times than provided by typical continuous ambulatory PD. Patients with lower transport characteristics usually do not have problems with ultrafiltration but may require higher dose prescriptions to achieve adequate Kt/V values, especially as residual renal function is lost[6]. The systems by which PET groupings were originally defined should identify the two subsets of patients on either side of average e.g. H and L, who may require these special considerations when writing a PD prescription. In the current study majority of the patient fall in average group (62%) whereas only 38% fall in extreme group. This results contrast with those reported by Indian authors[7] where extreme group predominate. However our findings are consistent with those reported by other authors[8].

Protein and caloric malnutrition is highly prevalent in CAPD patients and has been shown to be associated with increased morbidity and mortality[9,10]. Multiple factors can lead to malnutrition in dialysis patients including anorexia, decreased nutritional intake, and increased catabolism. Peritoneal protein loss is an additional factor for PD patients. In the present study we reviewed 24 hour dialysate protein loss and D/P status according to peritoneal transport pattern.

It was previously established that albumin loss was higher in H transport group[11,12]. Our study revealed similar relationship. Multiple studies have reported that peritoneal protein loss is greater with an increased peritoneal permeability[13,14,15.] Our study agrees with the previous studies. Our study showed good correlation between protein loss and transport type. However, K.C. Prokah et al[7] did not find such correlation in their patients. Further study with large sample is needed to explain the fact making the difference.

Diabetic patients have a high permeable membrane[16]. Our study is consistent with the report. Diabetes was found in none of the low transporter whereas majority of the high transporter were diabetic.

Conclusion :

We conclude that there is likely to be an ethnic variation in peritoneal permeability, which differs from country to country. Majority of the patients in our study

were high and high average transporters. Our study also observed that increased peritoneal permeability was associated with increased peritoneal protein loss and also with decreased serum albumin level. Diabetic patient revealed higher peritoneal permeability type. Membrane permeability pattern of our patients differ from those reported by Indian and Canadian authors. Further study with large number of patients may uncover the factors causing the differences.

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Doppler Ultrasonographic Measurement of Intrarenal Resistive Index Compared to Diuretic Radionuclide Renography : Noninvasive Method For Evaluating Different Grades of Obstruction In The Urinary Tract.

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Abstract :

Urinary tract obstruction may be defined clinically as restriction to the flow of urine that gives rise to irreversible renal parenchymal damage. Distinction of the obstructed from the nonobstructed dilated renal collecting system is a difficult problem. To overcome this, 24 patients with unilateral collecting system dilatations, either complete or partial obstruction, were studied with diuretic radionuclide renography. Intrarenal resistive index (RI), before and after hydration, were correlated with the results of diuretic renography with the aim, a) to assess the induced flow changes in renal haemodynamics and b) whether such flow changes contributes useful clinical information regarding obstruction. Five normal volunteers were also undergone for intrarenal RI before and after hydration. Mean RI in normal subjects was (0.58 ± 0.01) and no significant difference was found between the two kidneys. Renography showed normal transit in 20.8% of patients (mean RI: 0.59 ± 6.01), slow transit of tracer through excretory phase in 29.2% of patients (mean RI: 0.66 ± 0.02) and with no evidence of excretion in 50% of patients (mean RI: 0.72 ± 0.02). Relative renal function in the affected kidney was < 42 %. The mean RI in obstructed kidneys was elevated (> 0.70) and was higher than the mean RI in normal contralateral kidney (RI: < 0.60). Combined evaluation of diuretic renography and intrarenal RI are important tools in the assessment of urinary tract obstruction.

Introduction :

Recent advances have increased the value of radionuclide scintigraphy by an intervention that stresses an organ to assess its function. Stress of this kind may permit observation of dysfunction that may not appear under basal condition. Test of any organ's functional reserve have a direct diagnostic, prognostic and therapeutic significance[1].

Introduction of diuretic renogram is an important milestone in renal Nuclear Medicine. It is the only study to evaluate the renal function and urodynamics in a single test[2]. This noninvasive test is based on a high endogenous rate of urine flow stimulated by administration of diuretics and interpretation of the test is based on the rate of the washout of radiopharmaceuticals from the collecting system in the upper urinary tract - instead of a measurement of intrapelvic pressure. When a dilated collecting system is being imaged, additional evaluation of the intrarenal Resistive Index (RI) with a Doppler ultrasound may help to distinguish obstructed from nonobstructed dilatation, which may be of particular benefit in patients with conditions that usually predispose them to collecting system dilatation[3,4,5].

Due to partial obstruction by small stones or by narrowing of ureter by chronic inflammation of the urinary tract, passage of some urine through ureter is observed, but hydrostatic pressure proximal to obstruction is elevated[6]. Following ureteral obstruction, tubular concentrating ability is lost, followed by a reduced ability to excrete uric acid. GFR falls as a result of a drop in the transglomerular pressure gradient and renal blood flow decreases threrafter. Pressure within the nephron gradually rises and long standing obstruction leads to tubular atrophy and interstial fibrosis[7, 8,9]. So, obstruction must be identified and treated rapidly because. obstruction can cause irreversible renal parenchymal damage[6-9].

Diuresis augmented renography is an excellent method, as 20 - 30 % of the glomerular filtrate may be delivered in the urine, causing under acute condition, urine output to be as great as 25 times normal for a period of at least a few minute[10,11]. Furosemide (0.5 - 1 mg/kg) has been selected for its potent and rapid inhibition of chloride pump in the ascending limb of loop of Henle that results in effective diuresis[12-18].

The response of the glomerulus to the diuretics makes it possible to separate structural obstruction of the

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collecting system from dilatation without obstructions[1, 2,7,12- 17]. The results are evaluated either subjectively or with the help of various derived parameters, such as half time of the wash out after the peak or peak to final ratio[12-17]. Transit time indices, such as peak time wash out slope and excretory indexes are extensively used in renal Nuclear Medicine, because they provide a noninvasive quantitative physiological measurements obtained as a simple adjunct to imaging[12 – 15]. In 1982, a multicenter study showed the utility of the tubular transit time in evaluating obstruction. In patients with an unobstructed dilated collecting system, rapid washout of tracer from the pelvis and ureter has been demonestrated [12.] This is reflected by a sharp complete change in the shape of time activity curve. With widespread use of diuretic renography, a third group of patients was identified characterized by incomplete / or slow tracer washout, which is usually considered to be consistent with partial or low grade obstruction[12].

Doppler sonography has been reported to be a useful noninvasive technique for the diagnosis of renal obstruction[3-5, 19-22]. A mean RI of more than 0.7 and a difference of more than 0.06 to 0.08 between the average values of the patient's two kidneys have been considered diagnostic of obstruction[19]. Recent studies have suggest that the diagnostic accuracy of Doppler ultrasonography in assessing renal obstruction may improve after administration of loop diuretics[3].

Materials and Methods :

Twenty-four patients with unilateral renal pelvi-calyceal dilatation were selected for the study. Patients were selected from the referred cases for routine ultrasound studies for suspected renal colic. Five normal control subjects were also included in the study group.

Patients with single kidney were excluded from the study because increased RI may be due to a variety of pathologic conditions unrelated to renal obstruction. Detailed evaluation was done including clinical onset of pain, other manifestations, and drug history. All investigations regarding urinary system were assessed.

Doppler sonography has been performed using a standardized protocol of the HP Image Point HX with a 3.5 MHz curvilinear transducer with software for RI calculation. After an examination of the renal morphology, three Doppler spectrum were obtained from interlobar vessels in different regions of the kidney under guidance of colour Doppler technique and average RI of each kidney were measured for further evaluation. Furthermore, the differences between the average RI of each kidney was calculated, in both group of cases (patients with renal colic and normal subjects). After the basal measurement, patients were hydrated with 10ml of fluid /kg of body weight for 30 minute, so that the urine flows during the test is 1-4 ml/min[15.] Then serial RI measurements were obtained for each kidneys of each group of cases at the 30th minute of the basal study and then every 15 min interval for about an additional 90 min.

Diuretic renography was performed on SIEMENS Orbiter-75 gamma camera with a low energy all purpose collimator. 185 MBq of 99m Tc DTPA was injected intravenously under camera for dynamic study, pre-selected for 35 minutes. 40 mg of furosemide was injected at 20th min of the study followed by an additional 15 min data collection Computer generated time-activity curves of each kidney were obtained, which includes relative renal function, and the response to diuretics, outflow efficiency and measurement of transit times.

Results :

Isotope renogram shows normal progression of tracer through all phases in both kidneys in all normal volunteers.

RI changes before and after hydration in normal volunteers was within normal limits (0.58±0.01). No significant difference was found between two kidneys. RI value after hydration shows significant decrease at 90 to 120 min of hydration (0.57 ± 0.02), shown in Fig.1. In patients with dilated collecting system diuretic renography shows normal transit time in 5 patients (20.8%), slow transit in 7 patients (29.2%) and no transit in 12 (50%) of patients, in ipsilateral kidneys (Table. I). All the contralateral kidneys shows normal transit of tracer through the excretory phase.

Table-I

Findings of Diuretic Renogram in patients with suspected urinary obstruction.

Excretory feature of kidneys	Transit time	Impression	No.
Normal transit of tracer through excretory phase	t ½ < 10 minutes	Non obstructed	5
Slow transit of tracer through excretory phase	t ½ 10 - 20 minutes	Indeterminate (Intermediate)	7
No excretion of tracer through excretory phase	t ½ > 20 minutes	Obstructed	12

Table-II

Doppler Sonographic analysis before hydration and diuresis.

Non obstructed		Indeterminate	Obstructed
RI	0.59± 0.01 (p>0.05)	0.66± 0.02	0.72± 0.02 (p<0.01)
4 RI	0.07	0.16	0.22

Relative renal function in normal cases were (Contralateral - 50-56% : Ipsilateral - 44-50 %), in cases of slow transit of tracer (Contralateral 57-59% Ipsilateral 41-43%) and in obstructed kidney shows < 30 % of relative renal function in the pathologic kidney.

Patients were categorized according to gray scale ultrasound findings as

* marked hydronephrosis : severe pelvicalyceal dilatation with cortical thinning.
* moderate hydronephrosis : dilatation of pelvicalyceal system but no cortical thinning
* mild hydronephrosis : minimal amount of urine producing slight distension.

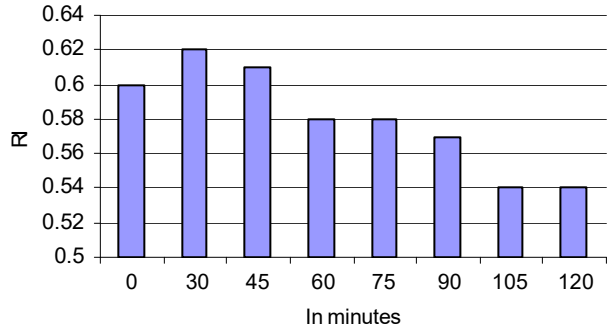
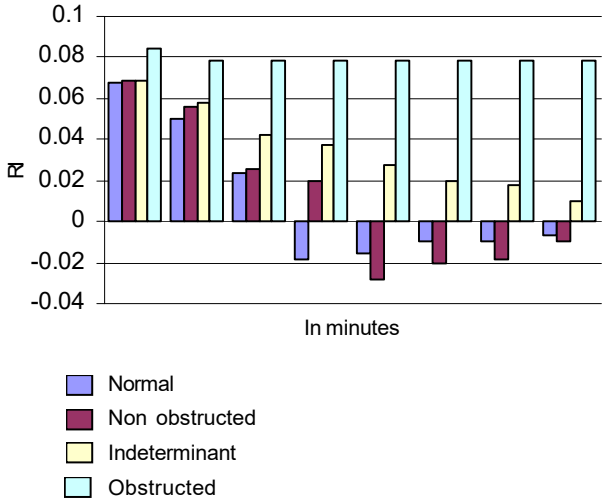


Fig- 1 : *Time changes in RI before and after hydration and furosemide administration in normal kidneys.*

In Doppler ultrasonography, RI were found normal in all the 5 patients with normal renogram. RI increased with left to right RI difference more than 0.6 in all the rest patients (Table-II). Comparison of contralateral kidneys and the kidneys with obstructive feature with difference between RI measurement before and after hydration & furosemide administration are shown in Fig. 2.



Discussion :

In this study, we investigated the effect of diuretics in suspected unilateral renal tract obstruction and also the effect of diuretics and hydration on the RI in both

normal and pathological kidneys. In addition we tried to correlate the changes in RI with the renographic findings for grading the different stages of obstruction.

Collecting system dilatation is the most common sonographic sign in cases of urinary obstruction but in only 4 - 11.8 % of cases can an organic cause of obstruction be found[22]. Almost 5% of patient with renal failure suffer from urinary obstruction[19]. The obstructing lesion may lie within the lumen or in the wall of urinary tract or outside the wall and overall frequency is the same in men and women[23]. Obstruction affecting the upper tract results in immediate rise in ureteric basal pressure and increase in peristaltic activity. In the earliest stage of acute obstruction pelvic pressure, normally ranges from 4-10 cm of H_2O, may reach as high as 50-60 cm of H_2O[14]. Raised proximal tubular pressure causes an initial reflex rise in renal blood flow as a result of vasoconstriction[14,19].This produces an elevated RI (>0.7) or asymmetry between the ipsilateral and contra lateral RI (0.06 - 0.08 or more)[19].

In our study, 99m TC DTPA renogram has been used as the reference method to assess obstruction. In most studies, diagnostic accuracy of diuretic renography exceeds 85 %[24-26]. Neither severe hydronephrosis nor any severe renal parenchymal impairment were observed in the patients of this study. In this series, both in normal subjects and in the patients, diuretic renography were performed within 48 hours after the Doppler sonography. Our results are in keeping with physiologic investigations proving decreased renal vascular resistance in response to hydration[27]. We considered the contralateral kidney of the patients with suspected obstruction as normal for ease of interpretation of the study. However, the changes of renal haemodynamics in the contralateral kidney could not be ruled out. And as we mentioned earlier, we could not find any haemodynamic changes in the contralateral kidney in our series of patients. In the normal subjects, baseline RI, diuretic renography as well as RI after hydration and furesemide administration, all were within normal limit (Table 1 & Fig. 1).

In the group of patients under study, the baseline RI and renography were normal in all contralateral kidneys and in 5 patients in the ipsilateral kidney, supporting no obstruction. In 12 patients with obstruction in urinary tract, the average RI was 0.72 and the difference between the kidneys were 0.22 and in indeterminate cases, the average RI was 0.66 with the difference of 0.16, which fulfill the diagnostic criteria reported in the literature as diagnostic of obstruction[3 - 5, 19 - 22]. In patients with primary suspicion of indeterminate studies, the basal RI and the RI difference were higher than those with non-obstructed kidneys, but obviously lower than the pure obstructive cases.

Therefore the unilateral elevated RI suggest the presence of obstruction even when the hydronephrosis is mild and also suggest obstruction suspected on clinical ground even if there is no hydronephrosis. On the other hand, a normal RI in the setting of the hydronephrosis suggest that dilatation of the collecting system is not due to obstruction. One of the difficulties of RI is that they may not detect either acute or partial obstruction.

Conclusions :

Diuretic augmented renogram is an excellent method to rule out the, obstructive uropathy. But in case of long standing obstruction, response of the kidney to diuretics is reduced. Doppler sonography seems promising noninvasive diagnostic tools for assessing the presence or absence of obstruction to urinary flow. So, combination of diuretic renography and Doppler sonography in dilated pelvi-calyceal system will be a great help to differentiate different grades and duration of obstruction.

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Outcome of Children of Acute Renal Failure with Seizure - In a Teaching Hospital

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Summary :

This study was conducted to evaluate the aetiology, outcome and risk factors of seizure in children with Acute Renal Failure. It was conducted in Dept. of Paediatric Nephrology Dhaka Shishu (children) Hospital from January' 97 to December 98. In this study 35 children with convulsion positive ARF were compared with similar number of convulsion negative ARF children. Among the 35 convulsion positive children age ranged from 4 days to 144 mo. Vs 5 days to 144 mo. in convulsion negative group. In convulsion positive group majority 12(34.28%) were with haemolytic uremic syndrome, 10(28.57%) with septicemia, 6(17.14%) with post diarrhoeal ARF and others. but in convulsion negative group majority were post diarrhoeal 11(31.42%), followed by AGN 6(17.14%), HUS 5(14.28%) septicemia 4(11.42%), obstructive uropathy 4(11.42%) and others. Severe hyponatremia was found in 23 (65.71%) convulsion positive children Vs 5 (14.28%) in convulsion negative children. Hypoglycemia was found in 12 (34.28%) convulsion positive children Vs none on the other hand. Pyogenic meningitis found in 5 (14.28%) convulsion positive children Vs none on the other hand. Thirteen (37.14%) convulsion positive children were septicemic Vs, 5(14.28%) in convulsion negative group. Blood urea and serum creatinine levels were high in both groups (27.22± 13mmol/l Vs 28.05 ± 16mmol/l) & (371±219umol/l Vs 413±266μmol/L) respectively. Majority of children of both groups had metabolic acidosis. Leucocytosis found in 31(88.57%) convulsion positive children Vs 26 (74.28%) in convulsion negative children. Among the convulsion positive group 16 (45.71%) children died, 19 (54.28%) children improved with normal renal function, 2(5.71%) of them with pyogenic meningitis developed hydrocephalus on follow up and rest with normal CNS function. In convulsion negative group 32 (91.42%) children improved with normal renal function and CNS function and only 3(8.57%) died. Outcome of neonatal age group is worst in both groups 3 (60%) Vs 1(100%) and those who survived developed neurological sequelae (hydrocephalus). In convulsion positive group majority of ARF children were between 1 mo-12 mo age group 16 (45.71%) Vs 11 (31.42%). Out of 16 infant 8 (50%) died compared with none on the other hand. Between 13 mo to 60 mo group out of 11 (31.42%) of convulsion positive group 5 (45.45%) died whereas in convulsion negative children out of 15 (42.85%) only 1 (6.66%) died. Children older than 5 yeas all patients in convulsion positive group improved with normal renal and neurological function. So metabolic abnormalities, septicemia and CNS infection are the major cause of seizure in this study. Outcome is fatal in neonatal age group and poor in infant

Introduction :

Acute renal failure is characterized by increase in the blood concentration of creatinine and nitrogenous waste product and by the inability of the kidney to appropriately regulate fluid and electrolyte homeostasis[1].

Gastroenteritis is the number one cause of acute renal failure in Bangladesh[2]. Haemorrhage, shock, pyrexia, glomerulonephritis, ureter calculus disease are other major causes[3].

So, metabolic abnormalities are very common in renal failure. It is well known to us that dyselectrolytemia is one of the important cause of CNS manifestation. Sodium values <120 mmol/L results weakness, values <100 mmol/L causes bulbar or pseudo bulbar palsy; and values between 90 and 105 mmol/L causes severe signs and symptoms of neurological impairment[4].

The brain is totally dependent on blood glucose and very low level of plasma glucose <20 or 30 mg/dl causes severe CNS dysfunction and these symptoms are known as neuroglycopenia[4].

Alteration in consciousness including seizure) delirium and coma are known to occur in shigellosis[5] in our clinical practice. We have seen many of the ARF patient presented with seizure. Several studies have

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been done related to etiopathogenesis of seizure in ARF associated with hemolytic uremic syndrome. However there are lots of patients of ARF of different etiology presenting with seizure. Therefore this study was designed to find out the risk factors and outcome of ARF children presented with seizure. This study also attempted to find out the exact etiology of seizure in such children and we particularly focused on the importance of metabolic abnormalities in ARF

Patients and Methods :

A total of 35 ARF children with documented seizure were compared with 35 ARF children without seizure in this study. This study was conducted in the department of pediatric nephrology, Dhaka Shishu Hospital, Sher-e-Bangla Nagar Dhaka-1207 during the period of January 1997 to December 1998. ARF patients with history of seizure during the current illness or having a documented seizure in hospital during treatment were selected. Patients those who had history of seizure disorder like cerebral palsy, epilepsy, genetic disorders, and congenital malformations were excluded from this study. Thorough history was taken at first, and then clinical and neurological examinations of each patient were done on an appropriate questionnaire.

Biochemical and other necessary investigations were done to find out the cause. Patients were managed conservatively and by IPD where there were indications. Out come was assessed by observing clinical and biochemical parameters and neurodevelopmental status. Patients out come were classified as improved and discharged against medical advice and were on follow up or died in the treatment center.

Data were entered on to a computer database using SPSS programme, data analysis were performed by T test unpaired.

Results :

Among the 35 convulsions positive children age ranged from 4 days to 144 mo. (mean age 24±37 mo; 21M:14F) Vs 5 days to 144 mo. (mean age 43±41mo.; 22M:13F) in convulsion negative group. Hyponatremia was found in majority of convulsion positive children mean S. Na^+ 117.92±18.38mmol/L Vs 127.50±l1.84 mmol/L in convulsion negative group (P<0.001). Hypoglycemia was found in 12(34.28%) convulsion positive children Vs none on the other hand (mean glucose level 4.13±1.6mmol/dl Vs 6.09±79mmol/dl) (P<0.001). Pyogenic meningitis found in 5(14.28%) convulsion positive children Vs none on the other hand. Thirteen (37.14%) convulsion positive children were septicemic Vs 5(14.28) in convulsion negative group. Seven (20%) convulsion positive children were hypertensive compared with 19(54.28%) in convulsion negative children (mean systolic and diastolic BP 78±37/46±37mmHg Vs 107±29/69±28 mmHg). Blood urea and serum creatinine levels were high in both groups (mean blood urea 27.22±13mmol/L Vs 28.05±16mmol/L and S. Creatimn 371±219μmol/L Vs 413±266umol/L). Significant number of children of both groups had metabolic acidosis (S. $HC0_3$ 11±4mg/dl Vs 11.1±7mmolg/dl). Leucocytosis found in 31(88.57%) convulsion positive children Vs 26(74.28%) convulsion negative children (mean WBC count 21,207±16,816/cumm Vs 14700±4856/cumm). Mean duration of hospital stay in convulsion positive group 12±10 days Vs 19±14 days in convulsion negative group. Among the convulsion positive group 19(54.28%°) children improved with normal RFT, 2 of the pyogenic meningitis developed hydrocephalus and rest with normal CNS function and 16(45.71%) died. In convulsion negative group 32(91.42%) children improved with normal RFT and CNS function and 3(8.57%) died. Outcome of neonatal age group is worse in both groups 3(60%) Vs 1(100%) and those who survived developed neurological sequelae. Majority of ARF children were between 1 mo. - 12 mo. age group 16 (45.71%) Vs 11(31.42%): Out of 16 convulsion positive infant) 8(50%) died compared with none on the other hand. Between 13 mo. to 60 mo. group out of 11(31.42%) of convulsion positive group 5(45.45%) died whereas in convulsion negative children out of 15(42.85%) only 1(6.66%) died. Among children older than 5 years all patients in convulsion positive group improved with normal renal and neurological function. Diarrhoeal diseases was found in 6(17.14%) convulsion positive children Vs 11(31.42%) in convulsion negative group. Hemolytic uremic syndrome was highest in convulsion positive group 12(34.28%) Vs 5(14.28%) in convulsion negative group. Among the convulsion positive group 6(17.14%) patient were, unconscious and finally died, 11(31.42%) children were drowsy and irritable and among them 3(8.57%) died. Among the rest 16(45.71%) of well conscious children 9 (25.71%) died.

On the other hand in convulsion negative group only 1(2.85%) patient was unconscious and died, 5(14.28%) patient were irritable and 1(2.85%) died and among the rest 29(82.85%) well conscious patient only one (2.85%) died.

Table - I
Outcome in relation to Age

	Convulsion Positive ARF (n=35)		Convulsion Negative ARF (n=35)	
Age	Improved	Death	Improved	Death
0 - 28 days	2(5.71%)	3(8.57%)	-	1(2.85%)
1 mo - 12 mo	8(22.85%)	8(22.85%)	11(31.42%)	-
13mo - 60 mo	6(17.14%)	5(14.28%)	14(40%)	1(2.85%)
61 mo - 120 mo	1 (2.85%)	-	6(17.14%)	1 (2.85%)
121 mo-144 mo	2(5.71%)	-	1(2.85%)	-
Total	19 (54.28%)	16 (45.71%)	32 (91.42%)	3(8.57%)

Table –II
Etiology of ARF and outcome

Convulsion Positive			Convulsion Negative		
Diagnosis	Improved	Death	Diagnosis	Improved	Death
HUS n=12(34.28%)	7(20%)	5(14.28%)	HUS n=5(14.28%)	4(11.42%)	1(2.85%)
Septicemia n=10(28.57%)	6(17.14%)	4(11.42%)	Septicemia n=4(11.42%)	11(31,42%)	-
ARF following acute watery diarrhea n = 6(17.14%)	2(5.71%)	4(11.42%)	ARF following watery diarrhea n=11(31.42%)	4(11.42%)	-
ARF following Viral hepatitis n=1(2.85%)	1(2.85%)	-	ARF following AGN n=6(17.14%)	16(17.14%)	-
ARF following severe perinatal asphyxia n=2(5.71%)	1(2.85%)	1(2.85%)	ARF due to obstructive uropathy n=4(11.42%)	4(11.42%)	-
ARF due to Salmonella nephritis n=1(2.85%)	1(2.85%)	-	ARF due to salmonella nephritis n=1.(2.85%)	1(2.85%)	-
ARF due to post surgical complication after operation of Wilms tumour n=2 (5.71%)	1(2.85%)	1(2.85%)	ARF due to post surgical complication after anorectal operation n=1(2.85%)	1(2.85%)	-
			Nephrotic Synd. With septicemia N=1(2.85%)	-	1(2.85%)
			Bronchopneumonia With heart failure N=1(2.85%)	1(2.85%)	
			ARF due to Nephroblastoma n=1(2.85%)	-	1(2.85%)

Table- III
Comparison of risk factors of seizure in ARF children.

Convulsion Positive group		Convulsion Negative group	
Risk Factors	Mean Value	Mean Value	P. Value
Serum Sodium (mmol/L)	117.92±18.38	127.50±11.84	<0.001
Blood Glucose (mg/dl)	4.13±1.6	6.051±0.79	<0.001
Blood Urea (mmol/L)	27.22±13	28.05±16	NS
Serum Creatinine (mol/L)	371±219	413±266	NS
Leucocyte Count (per cumm)	21207±16816	14700+4856	<0.001
Serum Bicarbonate (mmol/dl)	11±4	11±7	NS
Mean systolic & diastolic BP (mmHg)	78±37 / 46±37	107±29 / 69±28	NS
Serum Potassium (mEq/L)	4.05±2.2	4.02±1.4	NS

* NS = Not Significant

Table-IV
Comparison of outcome in relation to risk factors

Risk factors	Convulsion improved	Positive (n=15) Death	Convulsion Improved	Negative(n=35) Death
Uraemia	19(54.28%)	16(45.71%)	32(91.42%)	3(8.57%)
Hyponatremia	10(28.57%)	13(37.14%)	1(2.85%)	-
Hypoglycemia	6(17.14%)	6(17.14%)	-	-
Metabolic acidosis	24(68.57%)	11(31.42%)	15(42.85%)	3(8.57%)
Hypertension	7(20%)	2(5.71%)	17(48.57%)	2(5.71%)
Septicemia	8(22.85%)	5(14.28%)	4(11.43%)	1(2.85%)
Leucocytosis	23(65.71%)	14(40%)	25(71.43%)	1(2.85%)
Hypernatremia	3(8.57%)	1(2.85%)	-	-
Meningitis	3(8.57%)	2(5.71%)	-	-
Hyperkalemia	8(22.85%)	5(14.28%)	6(17.14%)	2(5.71%)
Hypokalemia	14(40%)	9(25.71%)	2(5.71%)	-
Hypotension	9(25.71%)	5(14.28%)	2(5.71%)	-

Discussion :

Factors associated with seizure includes higher body temperature, uraemia, severe metabolic acidosis, hyponatremia, septicemia, hypertension, CNS infection[5].

Why seizures are apparently more common in ARF is not certain. In this study the high prevalence of hyponatremia, which is thought to lower the seizure thresh hold in children[6,7], may have acted in concert with fever to precipitate seizure. The mean serum Na^+ value in our patient with seizure were 117.92±18.38, considerably lower than found in previous studies[8]. Previous studies have found mild hyponatremia (130-134 mmol/l) in one third to one half of patients with shigellosis and seizure[8] but have not identified hyponatremia as a risk factor for the development of seizure[9].

Other additional metabolic abnormalities i.e. elevated serum creatinine and lower serum bicarbonate level

were common. Patients with seizure had higher serum potassium concentration. This high potassium concentration have not been etiologically linked to the development of seizure[8]. Majority of septicemic child in convulsion positive group died. Although seizures are known to increase the peripheral leucocytes count but they are not thought to increase the proportion of immature leucocytes. The increase in leucocytes in patients with seizure in this study may reflect a more severe underlying disease, a finding consistent with their higher body temperature[5].

The shorter duration of illness in patients with seizure is consistent with previous findings that seizures tends to occur early in the course of illness[7,8]. However majority of convulsion positive ARF patient referred late to hospital and succumbed within a short period. Twenty five percent of convulsion positive children were hypotensive as diarrhoeal diseases were common in this group and septicemia may be the underlying cause. In convulsion negative group majority were normotensive and 6(17.74%) were with acute gomerulonephritis. Mean blood pressure was higher in convulsion negative group.

Hemolytic uremic syndrome is higher in convulsion positive group, which is consistent with previous findings that seizures are more common in HUS induced by shigellosis and outcome is fatal in case of late referral[5].

In this study 5(14.28%) patients had meningitis. So direct infection of the CNS was also a major cause of altered consciousness or seizures in patients with ARF.

Cerebral edema may occur in patients of ARF with seizure[7,8,9] but in this study brain imaging were not performed in all patients, so we are not sure about that.

In our study unconscious patients were 3 times more likely to die than conscious patient. This study suggests that seizure in ARF occur in an age group known to be of increased risk of seizure from fever or metabolic alteration. The fever could be controlled by antipyretics. Treatment of hyponatremia is also problematic, as the capability to measure electrolytes is often not available at medical facilities in poor countries and adequate treatment for this complication is still difficult.

Hypoglycemia could presumably be prevented by continuous feeding, but profound anorexia is one of the hall mark of ARF due to uraemia. Early antimicrobial treatment in septicemia, shigellosis, and meningitis has been shown to markedly reduce the rate of complication like seizure in ARF patient.

So from this study we can come to a conclusion that metabolic abnormalities, septicemia, hypoglycemia and CNS infections are the major cause of seizure in ARF patient. Outcome is worse in neonatal age group. Septicemia still is an important cause of mortality in ARF patient. HUS with CNS manifestations develop long term sequlae and increase mortality as they are referred late with DIC.

So management of ARF if started before developing complication, prognosis will be good. Prompt attention to fever reduction and metabolic alterations may help to reduce these potentially lethal complication, but often this is not easy to accomplish in the poor countries where diarrhoeal diseases are more common and responsible for majority of cases of ARF.

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Review Article

Management of Rapidly Progressive Glomerulonephritis

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Rapidly progressive glomerulonephritis (RPGN) remains a catastrophic illness with significant mortality and long term morbidity[1] and its incidence seems to be increasing[2]. Despite the severity of renal injury in RPGN, it is one form of nephritis in which treatment has had profound effects on outcome. Over the last 20 years there has been much debate as to the ideal management of RPGN, with several well conducted studies and a plethora of uncontrolled and anecdotal reports, based on markedly heterogeneous populations of patients, using a variety of interventions.

Two treatment modalities that lead to dramatic improvement of RPGN both in renal functions and many of the histological changes are pulse methyl prednisolone and plasmapheresis . Plasmapheresis removes free antibody, circulating immune complexes and mediators of inflammation such as fibrinogen and complement. But plasmapheresis is extremely expensive, time consuming and there are some serious complications.

RPGN is a clinical syndrome that results in a rapid loss of glomerular filtration rate (GFR) of at least 50% over a short period (a few days to 3 months). RPGN is classified pathologicaly into 3 categories. 1) Anti GBM antibody disease (including Goodpastures syndrome) with variable incidence of app.15-20% in Europe[3] and rare in developing countries with reported incidence of 0.97% in India[4]. 2) Immune complex disease caused by a miscellaneous set of conditions including SLE, infective endocarditis, postinfectious glomerulonephritis. This group is rare cause of RPGN in developed countries but common in developing countries[2,3]. 3) Pauci-immune disease (>50% of cases), usually ANCA positive. This group includes Wegener's granulomatosis, microscopic polyangiitis or systemic or renal limited vasculitis.

The diagnosis and treatment of RPGN is a medical emergency. The only predictor of renal survival is the serum creatinine value at the time of diagnosis. Therefore, it is imperative to have a high index of suspicion and to establish the diagnosis quickly and institute treatment as soon as possible. Serologic studies including, complements, ANF, anti ds-DNA, viral markers,anti GBM antibody and ANCA with ELISA sub-typing now permit early and easy identification of renal vasculitis[5]. Renal biopsy for both light microscopy and immunofluresence is crucial in the evaluation of a patient in RPGN both for diagnostic confirmation and prognostic information gained based on the degree of glomerular sclerosis and interstitial fibrosis. Also, renal biopsy helps to exclude other diseases that mimic crescentic GN like, thrombotic microangiopathes, SLE, scleroderma renal crisis, acute tubular ncerosis, acute interstitial nephritis etc[6].

Specific Management :

A) Anti GBM - antibody associated disease.

The immediate aim is to control pulmonary hemorrhage and glomerular inflammation as swiftly as possible. Also, it may be necessary to treat underlying infection and to support renal and pulmonary function[7]. The approach to treatment is determined by the level of renal function at presentation. a) If the serum creatinine is only moderately elevated (<2 mg% dl) then the combination of glucocorticoids and cyclophosphamide alone may be used. Addition of plasma exchange is probably not helpful. b) For non oliguric patients with serum creatinine values between 2 mg to 6 mg/dl, plasma exchange in addition to immunosuppressive regimens are generally used. c) If serum creatinine >6 mg/dl and particulary if patient is oligoanuric, it is unlikely that, useful renal function will be recoverable despite triple therapy with steroids,, cytotoxic agents and plasma exchanges[8].

The standard regimen for treating Goodpasture syndrome is outlined in table I. It consists of daily whole volume (4L for adults) plasma exchanges for albumin combined with 60 mg. of prednisolone daily and 100 to 150 mg of cyclophosphamide per day orally depending on weight. In patients older than 55 years of age cyclophosphamide is given 100 mg/day. Plasma exchanges are performed for 14 days or until clinical evidence of continuing disease activity has

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subsided. Cyclophosphamide is discontinued after 8 to 12 weeks provided that, anti GBM antibody titres are no longer detectable. The prednisolone is also reduced rapidly and stopped after 8-12 weeks[7].

Supportive treatment for renal failure, respiratory failure anaemia and intercurrent infection should continue. Cigarette smoking must be stopped because it is an important cause of pulmonary hemorrhage and resumption of smoking can precipitate relapse[7]. Patient should be monitored meticulously for the effects of treatment and complications. Assessment of disease activity is made by monitoring anti GBM antibody titre daily for first 2 weeks and 3 times weekly thereafter are continued[7].

Table-I

Regimen for Good pastures syndrome

Plasma Exchange	Corticosteroids Daily 4-L exchange for albumin for 14 days. Prednisolone : 60 mglday for 1 week; thereafter 45, 30, 25, 20, 15, 10 and 5 mg for 1 week each.
Cytotoxic drugs	cyclophosphamide : 100 - 150 mg/day given for 8-12 weeks; 100 mg/day in patients over 55 years of age.

B) RPGN associated with immune complex deposit.

Crescentic Nephritis in infection

Exocapillary proliferation with extensive crescent formation has been found in <1% of cases of acute post streptococcal glomerulonephritis (PSGN). In Natal, South Africa, PSGN is the commonest cause of crescentic glomerulonephritis. Development of RPGN in acute PSGN is an indication of renal biopsy and may need dialysis. It has been suggested that, cresentic GN of post streptococcal origin has a better prognosis than others but this contention was not substantiated by the work of Bhuyan et al[9] and they showed that, the extent of crescents and the proportion of glomeruli affected mainly determines the outcome rather than the etiology of nephritis. With persistent oligoanuria longer than 7 days it may be worthwhile to try an I.V methylprednisolone bolus of 0.5 gm/day for 3 days[4].

Chronic infections particularly infective endocarditis, ventriculoatrial shunt infection and deep seated visceral abscesses may cause crescentic GN with rapidly deteriorating renal function. The priority in these patients is to treat the underlinig infection with appropriate antibiotics and if necessary, by surgical intervention. There are case reports in which renal function has not improved with apparent control of infection, but in which immunotherapy (including plasma exchange) has been followed by recovery[2]. Recommendations for immunosuppressive therapy in this setting are based on ancedotal case reports. Use of such therapy should be tempered by the possible risk of exacerbation of the underlying infectious process as well as other side effects.

Crescentic Nephritis in SLE

Proliferative glomerulonephritis of lupus are often associated with crescent formations. They require more intensive therapy to preserve renal function. Initial therapy consists of I.V Methylprednisolone (10mg/Kg) for 3 days followed by oral prednisolone (0.5 to 1 mg/kg/day) in a single morning dose. Cyclophosphamide can be given orally (1.5 to 2 mg/kg/day) for 2 to 3 months followed by azathioprine (2 mg/kg/day) for 12-14 months. Alternatively intermittent IM high dose cyclophosphamide (fixed schedule) plus oral steroid may be given[10].

C) RPGN associated with paucimmune crescenting nephritis

The outcome of patients in this group has dramatically improved with oral cyclophosphamide and steroids. Even renal failure requiring dialysis is not a contraindication to treatment. Many patients are able to come off dialysis for an extended period of time. The goals of pharmacotherapy are to induce remission, reduce morbidity and prevent complication.

The preferred treatment starts with pulse methyl prednisolone therapy (Table (II) with a dose of 30 mg/kg (max. 3 g) given I. V. over 20 minutes on days 1, 3 and 5. Blood pressure measurements every 5 minutes during infusion and every hour for 6 hours are recorded because of risk of hypotension. 48 hours after the last dose of methyl prednisolone, oral prednisolone is began in a dose of 2 mg/kg/every other day. After 2 weeks prednisolone is given 1.75 mg/kg/every other day and continued for 1 month. Patient is assessed monthly and oral prednisolone is gradually tapered[11].

Patients with ANCA positive (80% of cases) are usually given cyclophosphamide. The dose is 2 mg/kg of ideal body weight orally every day. The target WBC count is 4,000 to 6,000 and a complete blood count is checked weekly for 2 months after initiation of therapy or after a dosage change. Patients are encouraged to take cyclophosmide in the morning and enough fluid intake and to empty their bladder frequently in the first 6 to 8 hours after ingestion. Cyclophosphamide is continued for one year after the latest remission[11].

The combination of steroids and cyclophosphamide has been the mainstay of treatment for both microscopic polyangiitis and Wegener's granulomatosis. This combination can induce remission in the majority of patients (70-85%). The CYCAZAREM (cyclophosphamide versus azathioprine for early remission phase of vasculitis) trial examined whether azathioprine was as effective as cyclophosphamide in maintaining remission and preventing relapses in ANAC-associated systemic vasculitides, but with fewer side effects. Given the equal efficacy of both treatments, and the known long-term safety profile of azathioprine compared with cyclophosphamide, this trial has clearly established the superiority of azathioprine over cyclophosphamide for preventing relapse after initial induction of remission in ANCA-associated disease[3].

Table -II

Procotol for Administering pulse Methylprednisolone, Oral Prednisolone, and Cyclo/phosphamide Therapy

Pulse Methylprednisolone

Volume repletion ascertained

No diuretics 3 hr before pulse or 24 hr after

30 mg/kg methylprednisolone given IV over 20 min every other day for 3 doses

Single dose not to exceed 3 g

Monitor blood pressure during and for 6 hr after infusion

Oral Prednisone

Given every other day

DOSE* (MG/KG)	DURATION OF THERAPY (MO)
2.0	0.5
1.75	1.0
1.50	3.0
1.25	6.0
1.00	6.0
0.75	6.0
0.50	6.0
0.25	6.0
0.125	12.0
0.0625	12.0

Cyclophosphamide Dose For ANCA- Positive Patients

2.0 mg/kg/day x 3 mo

1.5 mg/kg x 3 mo

1.0 mg/kg/day x 3 mo

0.5 mg/kg/day x 3 mo

Decrease dose 50% for creatinine clearance $\leq$ 10 ml/min

Hold dose if WBC $\leq$ 3500/mm^3 or platelets $\leq$ 100,000/mm^3

After WBC, platelet counts recover, restart after 0.5 mg/kg/dose reduction.

The role of plasmapheresis in pauci immune RPGN has been a subject of debate. The results of 3 well controlled studies (Hammersmith Hospital controlled trial, Canadian apheresis study group and trial by Frasa et al) clearly demonstrated a significant benefit of plasma exchange in dialysis dependent patients but not in those presenting prior to needing renal replacement therapy[12]. Ancedotal evidence supports an additional role for plasma exchange in patients with pulmonary hemorrhage[2,3].

Other New Methods of Treatment

Intravenous immunoglobulin-A number of studies have reported beneficial effects of intravenous immunoglobulin (IVIG) in patients with chronic grumbling vasculitis despite more conventional treatments or in patients with acute disease. A major concern over IVIG preparations has been the risk of acute renal failure, which may be increased in patients with pre-existing renal disease[3].

Mycophenolate (MMF) has been used to treat patients with a variety of immune-mediated nephritides, including lupus nephritis, other proliferative glomerulonephritis and ANCA-associated vasculitis. MMF could therefore have a place in the treatment of vasculitis in remission (although it is much more expensive that azathioprine and there is no data suggesting superior efficacy), or more importantly in patients with chronic active disease unresponsive to cyclophosphamide, or in whom further courses of cyclophosphamide would be inappropriate[3].

Deoxyspergualin (DSG). The mechanism of action of DSG is not entirely clear, but includes inhibition of IL1 synthesis and anti proliferative effects and decreases macrophage infiltration. It has proved effective in animal model of crescentic nephritis[11]. DSG may increasingly be used for resistant vasculitis, but the mode of administration and leukopenia are potential drawbacks.

Entirely new approaches. Lymphocyte depletion using monoclonal antibodies (for example CAMPATH IH-anti-CD52 pan lymphocyte antigen, or anti-CD4) has been reported in a handful of patients with relapsing or persistent disease[3]. Treatment of ANCA-associated vasculitis remains a challenge. Current treatments can be very successful in inducing remission, but with significant risk of infective complications in particular. Long-term treatment is necessary to maintain remission and prevent relapses, and here the balance

must be struck between disease suppression and treatment toxicity. The vasculitides are relatively rare, with an incidence of 20 new cases per million population per year[3], and are heterogeneous in their presentation; hence the importance of well conducted, multi-centre collaborative trials to identify promising new therapies, and to maximize the benefit of existing treatment regimens.

General management of Rapidly Progressive glomerulonephritis

Hypertension almost invariably accompanies acute renal failure caused by aggressive glomerulonephritis. Under this circumstance, hypertension is frequently a consequence of volume expansion is addition to other intrarenal mechanisms (e.g., decreased perfusion). Treatment of hypertension consists of control of volume expansion by fluid restriction, diuretic therapy (the dose adjusted to the level of renal insufficiency) and anti hypertensive medications. Any of the manifestations of uremia, if severe enough, prompt dialysis treatment is required which also improves oxygenation in patients with pulmonary edema and dyspnoea. Other indications include severe acidosis, hyperkalemia, uremic pericarditis, and uremic encephalopathy[6].

The approach to diagnosis and management of infection should be aggressive, with regular cultures of blood, sputum, urine, peritoneal dialysis fluid and other available material. Opportunistic infection particularly with nosocomial bacteria, cytomegalovirus, pneumocystis carinii and various fungui is common. The choice of antimicrobial will frequently be made on the basis of the likely clinical diagnosis because there is often delay or uncertainity in providing a precise etiology[13]. Maintenance of adequate nutrition is important and early tube enteral or parenteral feeding is indicated in many patients because recovery is often protracted and complicated by procatabolic events[13].

Immunosuppressive and cytotoxic drug treatment in all patients must be based strictly on histopathological criteria of activity. Experience in India showed use of aggressive immunosuppressive therapy led to loss of over 90% of patients from high chronicity index group due to infectious complications[4]. Many therapies used to treat RPGN have the potential to induce not only infections but also hemorrhages, sterility and malignancy. Patients at risk of side effects (elderly, infected, patients with peptic ulcer) is better treated by aggressive control of hypertension, renal failure rather than by immunosuppressive.

Long term monitoring to detect and prevent recurrence and to preserve residual renal function is essential. Relapse may occur in patients with SLE, ANCA positive syndromes, Henoch-schonlein purpura and other conditions. Anti GBM disease does not usually recur as long as the anti GBM titre has returned to baseline. Regular follow up of patients is of utmost importance to retain useful renal function.

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Article of Special Interest

Nephrotic Syndrome- Evidence Based Management

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Introduction:

Glomerulonephritis is one of leading cause of end stage renal failure (RSRF) throughout the world. It comprises 25-45% causes of ESRF in developing nations. This is because the treatment of primary glomerulonephritis is unsatisfactory. Although corticosteroid has long been used in patients with idiopathic nephrotic syndrome particularly minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS) and membranous nephropathy (MN), the response rate is variable. The treatment of IgA nephropathy (IgAN), diffuse and focal proliferative glomerulonephritis is not satisfactory[1].

Clinical Presentation:

The clinical presentation of glomerulonephritis is largely nephrotic syndrome, which comprises 80% of cases. In 10-15% cases, the patient is presented with acute nephritic illness. The other causes of presentations are, recurrent hematuria and or asymptomatic proteinuria. A small number of patients presented with chronic renal failure. The clinical presentation of nephrotic syndrome includes gradual onset of edema, raised or normal blood pressure,proteinuria in excess of 3.5gm in 24 hours. Patients with minimal change nephrotic syndrome, focal segmental glomerulosclerosis and membranous nephropathy are usually presented with these types of clinical symptoms.

Patients with acute nephritic illness usually have acute onset with puffiness of face, oliguria and hematuria. Blood pressure is usually raised and renal failure may be present at onset. The typical presentations are acute post-streptococcal glomerulonephritis (PSGN), some cases of IgA nephropathy and rapidly proliferative glomerulonephritis (RPGN).

Pathogenesis:

Pathogenesis of glomerulonephritis is thought to be immunological. There is interaction of antigen and antibody to form the immune complexes together with complement and coagulation factors have been involved in the pathogenesis of glomerulonephritis. Involvement of the resident glomerular cells with liberation of cytokines and growth factors are also found to be important in the pathogenesis of glomerulonephritis. Cytokines regulating the response have been characterized, involvement of additional molecules and leukocyte recruitment defined and mechanism based therapy identified. These advances are already bearing fruit in understanding mechanism of glomerular inflammation and may point to new therapies[2,3].

Diagnosis:

Diagnosis of glomerulonephritis is usually made by clinical presentation, routine and microscopic examination of urine. Renal function tests are checked in every patient and size of the kidney is measured through ultrasonography. Urinary protein excretion is done by estimating 24 hours urinary total protein and diagnosis is confirmated by renal biopsy. Specific diagnosis is made by complement (C3, C4), anti-nuclear factor (ANF), anti-dsDNA, Hepatitis B&C virus and antineutrophilic cytoplasmic antibodie (ANCA). Abnormalities of lipoprotein and low serum albumin are seen in patients with nephrotic syndrome.

Histological diagnosis:

In adults, histological diagnosis is usually minimal change disease, membranous glomerulonephritis, focal segmental glomerulosclerosis (FSGS), diffuse and focal proliferative glomerulonephritis, membranoproliferative glomerulonephritis (MPGN), IgA nephropathy and heredofamililial glomerulonephritis (Alport's syndrom). In a recent series, Rashid et al, 2001[4] found, minimal change disease 23 (6%), membranous glomerulonephritis 88 (23%), focal segmental glomerulosclerosis 22 (5%), diffuse and focal proliferative glomerulonephritis 77 (22%), membranoproliferative glomerulonephritis 62 (16%),

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mesangial proliferative glomerulonephritis 112 (29%) among 386 cases of glomerulonephritis [abstract in WCN,][4].

Management:

Management of glomerulonephritis is dependent on clinical presentation, degree of proteinuria, renal failure at presentation and above all histological diagnosis. Symptomatic treatment is necessary in almost all the cases, restriction of fluid and salt intake is also very important. Edema should be appropriately treated with loop diuretics and hypertension by ACE inhibitors if renal function is normal or mildly deteriorated. Proteinuria should be treated with ACE inhibitors even in the absence of hypertension if specific treatment is not available. Similarly, hypercholesterolaemia and hypertriglyceridemia should also be treated if there is no specific treatment for the primary disease.

Specific treatment:

Specific treatment with prednisolone and prednisolone with cytotxic drugs are available in patients with minimal change disease, focal segmental glomerulosclerosis and indiopathic membranous glomerulonephritis. IgA nephropathy with heavy proteinuria and normal renal function can also be treated with long term steroid therapy. Patients with membranoproliferative glomerulonephritis with hepatitis B or C can be treated with appropriate antiviral therapy.

Minimal change disease:

In children: Eighty percent of patients respond to initial corticosteroid therapy (prednisone). One widely used regimen administers prednisone, 60mg/m^2/day for 4 to 6 weeks, followed by 40mg/m^2/day every other day for another 4 to 6 weeks and then discontinuation. In case of relapse, prednisone should be given at a dose of 60mg/m2/day till protein is nil for 3 days and then 40 mg/m^2 alternate day for another 4 to 6 weeks. In case of relapse for the second time, same regimen as in 1st relapse can be repeated. In third relapse cyclophosphamide is the drug of choice, which should be given at a dose of 1.5 to 2mg/kg/day for 2 to 3 months. Dosage should be monitored by frequent CBCs assuming a WBC count>4000/mL.

In corticosteroid nonresponders (<5% in children), frequent relapse's and corticosteroid-dependent patients, prolong remission may be obtainable with oral cyclosporine 6mg/kg/day till remission. Then reduce the dose 1 mg/kg every month to a maintenance dose of 2-3 mg/kg for about one year[5].

Other drugs: Levamisole, an antihelminthic drug has been used to successfully treat children with MCNS. In one study, 30 children with frequently relapsing nephrotic syndrome were treated with oral levamisole, 2.5 mg/kg body weight twice a week for 10 months and in 16 children, corticosterioid dose could be reduced significantly without relapse while the drug was ineffective in the remaining 14 children.

In adults: There are two widely accepted regimes for the use of prednisone in the treatment of MCNS in adults.

A. Administer prednisone 1.5 to 2 mg/kg /day per orally for 8 to 12 weeks, then gradually taper the dose 5mg two weekly and continue for 6 months.

B. Prednisolone 2mg/kg on alternate day for 2 months followed by tapering off 5-10 mg two weekly and continue for 6 months to 1 year.

In frequently relapsing and steroid dependent nephrotic patients, cyclophosphamide is the drug of choice, which should be given at a dose of 1.5 to 2 mg/kg/day for 2 to 3 months. Another alternative is oral cyclosporine 5mg/kg/day, which is usually continued for 1 year.

Focal segmental glomerulosclerosis:

Patients with focal segmental glomerulosclerosis should be treated with prednisolone 0.5 to 2 mg/kg/day for 6 months. This dose should be continued at least for three months before declaring that, the disease is not FSGS. The dose of prednisolone should be reduced to 0.5mg/kg/day when proteinuria is nil but after three months. In patients not responding to steroid therapy, additional cytotoxic drugs don't make any difference in the respnse rate or prevention of renal failure. However addition of cyclosporine 6mg/kg/day in children and 5mg/kg/day in adults showed variable response. Cyclosporine should be continued at least for one year. Treatment with tacrolimus, MMF and plasmapheresis seems to be encouraging[6].

The prognosis of FSGS is variable. Those patients response to prednisolone, 10 year survival is around 90%, where as in non-responders 5 year survival is 50-60% and 10 year survival is 25-40%. Patients presented with nephrotic syndrome leaving untreated, 5 year survival is approximately 50-90% and 10 year survival is 30-50%. Patients presented with non nephrotic proteinuria, 10 year survival is 85-90%. The

prognostic indicators are; initial creatinine level, degree of proteinuria, presence of hypertension and interstitial scarring on renal biopsy.

Membranous glomerulonephritis:

Asymptomatic patients with nonnephrotic range of proteinuria should not be treated. Patients who have edema can be controlled with diuretics or asymptomatic patients with proteinuria should be followed, because ³ 30% will have a partial or complete remission within 3 to 4 year.

Two recommendations have been widely accepted for the treatment of patients with symptomatic NS and for those most at risk of progressive renal disease and those with an elevated serum creatinine.

Recommendation 1:

Methyl prednisolone 1 g/day slowly intrvenously for 3 days followed by oral prednisone 0.5mg/kg/day for 27 days followed by chlorumbucil 0.2 mg/kg/day for 30 days. Repeat for another 2 cycles. Dosage should be monitored by frequent CBCs assuming a WBC count > 4000/mL.

Recommendation 2:

Prednisone 2mg/kg alternate day for 2 month and then gradually taper the dose & continue for 6 months.Cyclophasphamide is added at a dose of 1.5 to 2 mg/kg/day for 3 to 6 months. Dosage should be maintained by frequent CBC, WBC > 4000/mL.

Prognosis of membranous nephropathy is dependent on several factors. Patients with older age, male sex, heavy proteinuria (>10gm/day), presence of hypertension, hypercholesterolemia, renal failure at onset, advanced changes on renal biopsy predict worst prognosis of membranous nephropathy. Where as patients with younger age, female sex, non-nephrotic proteinuria, persistent normal renal function for 3 years, absence of tubulointerstitial changes in renal biopsy, absence of glomerular scarring has favorable prognosis[7].

IgA Nephropathy:

Treatment of IgA nephropathy is controversial. Prednisone may be given in patients with proteinuria > 3gm/day with normal renal fucntion. However prednisone is not effective if renal function is impaired and fish oil is prescribed in those circumstances. ACE in hibitor may be given for patients having proteinuria 1 to 3 gm/day. Prognosis of IgA nephropathy is usually good unless there is heavy proteinuria of nephrotic range, presence of hypertension and impaired renal function at presentation. Histological evidence of glomerular sclerosis, tubulointerstitial atrophy, fibrosis and scarring also predict bad prognosis of IgA nephropathy[8].

Membranoproliferative glomerulonephritis:

Treatment of membranoproliferative glomerulonephritis is symptomatic unless there is evidence of association with hepatitis virus B or C. In those circumstances where there is direct link of hepatitis B or C virus, appropriate therapy for the virus is usually given. The symptomatic treatment includes use of diuretics, treatment of hypertension, fluid and salt restriction and treatment of hyperlipidemia.

In other glomerulonephritis, specific treatment is also not available. Other glomerulonephritis Treatment of Focal and diffuse proliferative glomerulonephritis and mesangial proliferative glomerulonephritis are also symptomatic[9].

General measure:

Diet, restriction of fluid and salt is important in the general management of patients with nephrotic syndrome.

Edema is treated with loop direct and the dose is increased according to response of the drug.

Hypertension is treated with appropriate antihypertensive drugs and special emphasis is given to ACE and ARB group of drugs.

Hyper lipidaema, should also treated with antilipidaemic drugs.

Conclusion:

The prognosis of nephrotic syndrome is dependent on type of histological diagnosis degree of proteinuria, presence of hypertension and renal function at presentation.

Male sex, older age groups, family history, type of HLA, may also important in predicting long term prognosis of the disease.

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Abstract form Current Literature

Selected Abstract from 10th Annual Convention and International CME

2nd and 3rd December 2003

Impact of Na+ Profiled Dialysis on Control of Blood Pressure on MHD Population

DR. NIATUZZAMAN

A prospective case-control study is conducted upon 38 patients on MHD receiving about 12 hour HD/week for nine months (observation three months and Na+ proffiling six months). Nausea and vomiting; chest pain; hypotension and hypertension, headache are recorded during and in interdialytic period. Patients are on anti-hypertensive drugs in single or incombination without no gross alteration in drug groups both during observation and intervention (Na+profiling) period. Five important parameters are considered for statistical analysis-(Pre-MAP; Post-MAP, Pre-weight; Post-weight; Kt/v) before and after intervention (Nat+profiling). Objective complaints are reduced significantly. Nausea and vomiting (42.5 vs 31.57%) chest pain (35% vs 23.68%); Hypotension (27.5% vs 18.42%); Hypertension (22.5% vs 13.15) and Headache (60%vs 39.47%) (p-value <0.001). This results are further strengthened, by reduction of anti-hypertensive drug regimen-combination-double (57.5% vs 19.44%) and triple (7.5% vs 0%) (p-value <0.001). Profiled dialysis was inter-individualised and regession analysis shows-significant linear correlation with post-MAP; pre- and post-weight and inverse correlation with kt/v (p-value in all cases is <0.001). Correlation with pre-MAP is not significant (p-value <0.05) suggesting other factor also regulates interdialytic blood pressure. Conclusion: Na+ profiled heamodialysis is helpful in MHD but with inter-individual dose regulation considering the individual's pre- and post dialytic biochemical profile. It exerts positive impact on interdialytic blood pressure regulation but other variables like-sympathetic over-activity; vasoactive hormones etc. also been implicated. However, this study is on short duration and small population based; so large scale study on longer duration is needed for further evaluation.

ABV: Pre-MAP- Pre-dialysis mean arterial pressure
Post-weight- Post dialysis weight.

Effects of ACE Inhibitor on Proteinuria and Renal Function in Patients with Type2 Diabetes With or Without Renal Failure

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Diabetic Nephropathy (DN) is the leading cause of ESRD throughout the world. Greatest importance is focused on proteinuria and hypertension in addition to control of diabetes in declining of renal function. Few clinical trials have studied the effects of ACE Inhibitors (ACEIs) on type2 diabetic patients with overt proteinuria. We have studied the effects of ACEI on proteinuria and renal function in type2 diabetic patients with overt proteinuria with or without hypertension and/or renal failure.

This randomized, controlled, prospective study was carried out on eighty diagnosed type2 diabetic patients with overt proteinuria with or without hypertension and/or renal failure to see the efficacy of ACEI, lisinopril in reducing proteinuria and preserving renal function as compared to calcium channel blocker, amlodipine. Forty one were assigned to "ACEI group" who got lisinopril at a maximum tolerated dose. Thirty nine were assigned to "control group" who received amlodipine in a dosage sufficient to control BP below target level. Patients were followed three monthly for a mean period of one year for BP, s. creatinine, creatinine clearance rate (Ccr.) & 24hrs UTP.

BP was equally controlled without any significant difference between groups. There was significant reduction in UTP from 3.24±3.0 G/24hr to 1.55±1.35 G/24hr in ACEI group, whereas in control, group, reduction was from 2.52±2.1 to 1.69±1.64 G/24hr only. S.creatinine rose from 130.5±43.4 to 168.1±59.4mmo1/L in ACEI group and from 145.1±54.3 to 188.4±71.9 in control group. Decline in Ccr was from 58.4±20.4 to 44.4±15.8 in ACEI group and from 54.3±25.0 to 46.3±26.9 in control group.

Neither the rate of rise of s.creatinine nor the decline in Ccr. showed any statistically significant difference in between the two groups. This declining renal function was not affected by baseline renal function status.

In the present study, although there was significant reduction of proteinuria by ACEI there was no improvement in renal function. S.creatinine increased & Ccr decline significantly from base-line value to each quarterly time-point throughout the one year study period (all values p<0.001) in both groups.

It is concluded that ACE inhibitor causes significant reduction in proteinuria but no improvement in renal function as compared to calcium channel blocker in this particular group of type2 diabetic patients with overt proteinuria with or without hypertension and/or mild renal failure.

Effect of Calcium Carbonate and Oral calcitriol on PTH in MHD patients

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Secondary hyperparathyroidism is common in MHD patients. Accumulated evidence suggests that PTH is a major uremic toxin. Oral calcitriol and calcium carbonate therapy can effectively reduce elevated PTH level. A total no. of 45 MHD patients (male 24 female-21) of different duration (6 months to 60 months) were studied in the department of nephrology and INM, BSMMU Dhaka to see to effect of oral calcitriol and calcium carbonate on PTH. Subjects were divided into 3 groups according to duration of haemodialysis.

Group-1 (6 months to 18 months, N = 12), Group-2 (19 months to 36 months N = 20), Group-3 (37 months 60 months, N = 13) mean age of the patients were 40.24 ± 8.94 yrs. Total duration of study was 36 months initial 4 months was washout period remaining 32 months was study period. During this study period all the subjects received calcium carbonate 500 mg thrice daily with meal and oral calcitriol 0.25 mg once daily. S PTH (midregion), S. Calcium, SAlkaline phosphatase, S. Inorganic phosphate, SAlbumin, S Total protein were measured at the end of wash out period and at 5th and at 9th months of study period.

Elevated S. PTH (mid region) level, hypocalcaemia, hyperphosphataemia, increased alkaline phosphatase level was observed at beginning of study period. At the end of study period decreased PTH level, inorganic phosphate level, alkaline phosphatase level and increased S. calcium level was observed in all the subjects of 3 groups.

Median S.PTH (mid region) at beginning of study vs end of study was; In group-1 : 544. 19 pmol/L, vs 206, 31 pmol/L, In group-2 476-82 pmol/L vs 196.12pmol/L, In group-3 : 440. 68pmol/L vs 128.02 pmol/L

Mean±SD S. celeium level at begining of study vs end of study was; In grou 1 1.85+0.32 mmol/L vs 2.37 0.10mmol/L, P<0.01, In group-2 1.94 ± 0.30 mmol/L vs 2.43 ± 0. 10mmol/L, P<0.01, In group-3 : 1.96 ± 0.27 mmol/L vs 236 ± 0.16 mmol/L P <0.05.

Mean ± SD inorganic phosphate level at beginning of study vs end of study In group-1 : 2.60 ± 0.61mmol/L vs 1.80± 0.27 mmol/L P< 0.001, In group-2 : 2.71 ± 0.49 mmol/L vs 1.82 ± 0.27 mmol/L p< 0.001, In group-3 : 2.48 ± 0.67 mmol vs 1.74 ± 0.40 mmol/L P<0.06

Mean ± SD salkaline phosphatase : level at begening of study vs end of study was In group -1 315 ± 150.64 U/L vs 214.92 ± 86.68 U/L P<0.05, In group -2 : 305.34 ± 155.02 U/L vs 221.75 ± 96.16 U/L P < 0.05, In group -3 : 302.85 ± 94.54 U/L vs 220.69 ± 76.48 U/L p < 0.05.

It is concluded that elevated S. PTH, alkaline phosphatase, inorganic phosphate and hypocalcaemia was observed in MHD patients and oral calcitriol and calcium carbonate can reduce S. PTH level, S. alkaline phosphatase level, S. inorganic phosphate level and increase S. calcium level.

Experimental Nephropathy Induced by Staphylococcus Aureus Antigens

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Purpose : Much evidence suggests that, IgA nephropathy (IgAN) is an infectious associated GN although exact pathogenesis is unknown. We hypothesized that S.aureus, a common normal and pathogenic flora plays an important role in the pathogenesis of IgA nephropathy. Recently we have reported glomerulonephritis occurred during methicillin

resistant S. aureus infection, that have showed polyclonal elevation of serum IgA and IgG levels with IgA, IgG and C3 deposition in the glomeruli. In this study we have showed, induction of IgA -type glomerulonephritis in Balb/c mice by using antigens derived from S.aureus.

Method : Balb/cmice (Th2 dominant type) and C57BL/6 (Thl dominant type) were immunized with antigens derived from S.aureus with Freund's incomplete adjuvants biweekly for 4 months.

Results : Mesangial proliferative glomerulonephritis with IgA and IgG depositions were found in all Balbfc, not in C57BL/6 mice. In Balb/c mice, S.aureus antigens were detected in glomeruli using affinity-purified human anti-S.aureus antibodies, however there was no staining in C57BL/6 mice. In Western blot analysis, the band which was differently recognized by Balb/c and C57BL/6 anti-serum was 30-35 kDa.

Conclusion : S.aureus antigens, especially 30-35 kDa protein and genetic background of the hosts may play important roles in the pathogenesis of IgA nephropathy.

Serum Parathormone Level and Its Correlation with Different Biochemical Parameters in Children with Chronic Renal Failure

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Objective : A prospective study was conducted to estimate the level of serum intact parathormone and its correlation with different biochemical parameters with chronic renal failure in children. Setting: Paediatric Nephrology Unit, Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

Subjects and Methods : Study was conducted in 64 children (44 with chronic renal failure and 20 age and sex matched controls). Serum intact parathormone (PTH), creatinine clearance (Ccr), serum creatinine, urea, 'serum calcium; inorganic phosphate and alkaline phosphatase were estimated for both groups. Serum intact parathormone was estimated by Inmiulite analyzer. Serum creatinine, urea, calcium, inorganic phosphate and alkaline phosphatase were estimated in blood by standard technique.

Results: 44 (male 30, female 14) chronic renal failure children were divided into four groups according to their Ccr, mild CRF with mean Ccr 59.17±18.53 ml/min/1.73 m2, n=6; moderate CRF with mean Ccr 34.98±7.75 ml/min/1.73 M2, n=7; severe CRF with mean Ccr 17.71±5.40 ml/min/1.73 M2, n=15; End-stage renal disease with mean Ccr 6.46±1.71 ml/min/1.73 m2, n=16). Mean serum intact PTH value were in mild 48.50±4.76, moderate 67.29±7.91, severe 82.42±9.67 and end-stage renal failure 130.66±58.74 pg/ml, and control 16.52±9.35 pg/ml respectively . Mean serum intact PTH of CRF (93.00±46.42 pg/ml) was negatively correlated with mean Ccr (22.02±18.53 ml/min/1.73 n2) ($r = -0.564$, $P<0.001$) and mean serum calcium (7.30±1.02 mg/dl) ($r = -0.50$, $P<0.001$), and positively correlated with mean inorganic phosphate (5.76± 1.1 mg/dl) ($r = +0.345$, $P<0.05$) and mean alkaline phosphatase (355.14±185.53 U/L) ($r = +0.469$, $P<0.001$) respectively.

Conclusion : It is concluded that progressively increased PTH level may occur even early in the course of chronic renal failure and hypocalcaemia is an initiating factor for the development of hyperparathyroidism.

Continuous Ambulatory Peritoneal Dialysis, A Novel Mode of Treatment in End Stage Renal Failure Patients: Yet to be Popularized In Bangladesh

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Continuous Ambulatory Peritoneal dialysis (CAPD) is a well-accepted mode of renal replacement therapy (RRT) worldwide. But the method is yet to be popularized in Bangladesh. In order to evaluate the applicability of CAPD in Bangladesh we report the clinical outcome of the patients treated in this method. Between January 1997 to October 2003, 94 patients were managed by CAPD in this country. 12 patients discontinued or died due to unrelated cause before initiation of regular exchange and were excluded. Therefore, we studied 82 patients (mean age 58±16 (range 7-85] years; 50 male, 32 female.) Primary etiology were diabetic nephropathy in 43(52.43%) glomerulonephritis in 15(18.29%), hypertension in 11(13.41 %), heridofamilial disease in 2(2.43%), renal

cell carcinoma in one, Chronic pyelonephritis in two (2.43%), in 3 were other causes and causes in 5 patients were unknown. Indications of CAPD were cardiovascular instability in 44(53.6%), long distance from hemodialysis center in 20(24.39%), vascular access problem in 7(8.53%) and others in 11(13.41%). Most of the patients used Baxter PD fluid, Y-set with 2.bag system and daily 3 exchanges of 2 litre bag were practiced. Total duration of follow up was 1256 patient months; mean 15.32±17.96(range 1-77 months) and, technique survival was 94%. Major complications were peritonitis (one episode [ep] per 14.26% patient-month) exit site infection (one ep per 43 patient-month), catheter block (one ep per 34 patient month and were cleared in all cases with heparin wash except two), and leakage in 2 cases and hernia in two. Mean hemoglobin was 9.25±1.78 gm/dl, creatinine 584±153 mmol/l, urea 15.32±7.44 mmol/l, serum albumin was 30.24±5.74 gm/1 and serum potassium was 3.12±1.4 mmol/l. At the time of reporting, of 82 patients 20 pts. were continuing with this model of treatment, 14 discontinued and 38 died. Of the 12, 2 patients discontinued due to leakage and hernia, 4 patients due to peritonitis and were transferred to hemodialysis, 4 patients discontinued due to financial reason and 3 underwent kidney transplantation while renal function improved in 2 cases. 5 of the 38 death occurred due to septicemia resulting from peritonitis. The causes of remaining 33 mortalities were unrelated to CAPD. Though most of the patients were elderly, diabetic, debilitated yet our results lead to conclusion that CAPD may be the well-accepted mode of RRT in this country.

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Notes & News

INTERNATIONAL NEWS

International Society of Nephrology

MEMBERSHIP

The ISN provides an international forum for the exchange of knowledge, best clinical practice, and research. Since it was founded in 1960, the society has constantly made major contributions to the worldwide advancement of educational, science, and patients care in nephrology.

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European diabetic nephropathy study group (EDNSG) will be held May 7 and 8, 2004, in Bergamo, Italy. All abstracts on any topic relating to diabetic nephropathy research should be submitted by e-mail (to the address below) with the abstract as an attachment in a rich text format (RTF) or as a world file. Abstracts should be written with the following headings : Objective, Design, Setting, Patients, Main Outcome Measurements Results, and conclusion. The length of the abstract should notexceed on side of an A4 paper. With margins of 2.5 cm, and a font size no smaller than Times 12. Abstracts submitted by fax should also be sent by mail (5 sets) by January 10, 2004 to Dr. Roberto Trevisan, Secretary of EDNSG, U.O. Diabetologia, Ospedail Riuniti di Bergamo, Largo, Barozzi 1, 24128 Bergamo, Italy, Fax : +39 35 266889; E-mail : roby.trevisan@tin.it or retrevisan@ospedaliriuniti.bergamol.it

The 3rd International Course on Critical Care Nephrology will be held June 2-5, 2004, at the Congress Center Ente Fiera, Vieenza, Italy. For further information, contact : Web site : http://www.vicenzanephrocourses.com or http://www.efrologiavicenza.it

The 12th International Congress on Nutritional held Metabolism in Renal Disease will be June 19-22, 2004, in Venice/Padua, Italy. The chairpersons for the congress are Giuseppe Bucciante and Gian-franco Guarnieri. For further information, contact : the scientific secretariat, Annamaria Bernardi at E-mail : annamariabernardi@libero.ie. Or the Organizing Secretariat, Meet and Work. Piazza del Sole e della pace, 5, 35031 Abano Terme (Padova), Italy. Telephone : + 39 049 8601818; Fax : + 39 049 8602389; E-mail : meet@meetandwork.com ; congress web site : http://www.nutrition. Metabolism-004.it

The ISN 2004 Conference on Prevention of progression of Renal Disease will be held June 29 – July 1, 2004, at the Hong Kong convention and exhibition Center in Hong Kong. The Hong Kong Society of Nephrology is the host organizer for this meeting in conjunction with the ISN. This is the first ISN thematic conference held in Asia on the prevention of progression of renal disease. It will explore, in a multidisciplinary approach, the latest basic and clinical aspects on chronic renal failure and the prevention of its progression. It will also discuss the economic consequences of chronic renal failure and its global health care. A global consensus will be presented, and a way forward to help counter ohonic renal diseae worldwide will evolve. An outstanding international cast of speakers has been assembled to prevent the topics like health economics, diabetic nephropathy, glomerulonephritis, basic research, genetics, drugs and herbs, bypertension and cardiovascular diseases, renal screening programs, and blueprints for prevention. For further information, contact : Conference Secretariat, c/o International Conference Consultants, Ltd., Units 501-3, 5/F, Far East Consortium Building, 121 Des Voeux Road Central Hong Kong. Telephone : (852) 2559 9973; Fax : (852) 2547 9528; E-mail : infor@isn2004hkconference.org;l website : http://www.iwn2004hkconference.org.