Biochemical Analysis of End Stage Renal Disease Patients Following Regular Haemodialysis

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ABSTRACT

Dialysis is in empirical therapy of end-stage renal disease. Traditionally dialysis adequacy has been quantified referring to the Kinetics of urea but recent index of dialysis dose is the fractional clearance of urea expressed as Kt/v. Eighty end stage renal disease cases were enrolled in the study out of which 40 cases underwent two haemodialysis per week (Group A) and rest 40 cases three haemodialysis/week. Serum urea, Creatinine, Potassium registered a significant fall (P<0.001) along with improvement in systolic blood pressure and Haemoglobin concentration (P<0.05) in Group- B whereas Group A cases showed significant fall (P<0.001) in serum urea values only. Urea reduction ratio and Kt/v were found higher in Group B as compared to Group A (P<0.001) which was as per the recommendation of National Kidney Foundation Dialysis outcomes Quality Initiation (K/DOQI). ESRD cases undergoing HD twice a week is inadequate whereas three HD/week cases had better compliance and post dialysis clinical outcome.

Keywords: *Dialysis, End-stage renal disease, Dialysis dose, Kt/v, Urea Reduction Ratio (URR)*

INTRODUCTION

National kidney foundation Kidney disease outcome quality initiative (NKF-K/DOQI) classified chronic kidney disease (CKD) in to five different stages. The fifth stage is called ESRD where Glomerular filtration rate is less than 15ml per min per 1.73m^2 surface area[1]. End stage renal disease (ESRD) lead to temporary or permanent damage to the kidneys. When 90% or more of kidney function is lost, either kidney transplantation or dialysis is required to sustain life. An Indian population based study determined the crude and age – adjusted ESRD incidence rates at 151 & 232 per million population respectively[2]. It is estimated that about 55 thousands patients are on dialysis in India and the dialysis population is growing at a rate of 10 to 20% annually[3]. Nearly 400,000 persons in United States and 2 million worldwide are dependent on dialysis, of these approximately 90% in United States undergo Haemodialysis which is typically delivered three times a week[4]. Haemodialysis (HD) is preferred over peritoneal dialysis (PD) in ESRD and from the beginning of the dialysis era the issue of optimal dialysis dose and frequency has been the central topic in the delivery of dialysis treatment. Dialysis dosing has been informed by numerous observational studies[5,6] and a few carefully conducted randomized clinical trials[7,8]. Based on literature reports, the American guidelines were issued first (DOQI 1997:K-DOQI,2001) followed by European Based Practice Guideline (2002). The K- DOQI Guidelines recommend a minimum single pool Kt/v(urea) of 1.2 roughly corresponding to a minimum prescribed Urea Reduction Ratio (URR) of 65% for thrice weekly HD[9]. The European Based Practice Guidelines recommend higher values: double-pool Kt/ v (urea) of at least 1.2, single – pool Kt/v (urea) of at least 1.4[10]. Urea Reduction Ratio (URR) is defined as reduction in urea as a result of dialysis. The URR is one measure of how effectively a dialysis treatment removed the waste products from the body and is commonly expressed as a percent. According to National Kidney and Urologic Diseases Information Clearing house (NKUDIC) minimum values of URR should be 65%[1,11]. Other method that was used to measure the accuracy of dialysis dose is Kt/v. The minimum Kt/v should be 1.2[12]. K is defined as total dialyzer residual while t is the period of dialysis in minute. Meanwhile v is defined as urea's volume of HD patients. Two randomized controlled trials on dialysis adequacy were conducted one performed on HD i.e.; HEMO study and other on peritoneal dialysis (PD) i.e. the ADEMEX study. HEMO study conducted on 1846 patients completed on 2002, documented that the risk of death was the same in high and standard dose group. There was no increase in the health or survival rate of patients who had a higher dialysis dose[7]. However the solute removal can be dramatically augmented by increasing the frequency of haemodialysis sessions[13]. Several uncontrolled studies showed that there were significant improvement in patient - reported outcome and results of laboratory tests when patients were treated with more frequent haemodialysis[14]. The best available evidences at present indicate an uncertainty regarding the optimal dose of Haemodialysis. So the present studies are designed to compare the effectiveness of three HD per week with two HD per week in ESRD patients by evaluating the biochemical parameters. Patient's acceptance and

compliance is analysed by recording the clinical complications during HD twice in a week and thrice in a week.

MATERIALS AND METHODS

This study was conducted in the department of Biochemistry, IMS & Sum Hospital, Bhubaneswar. Eighty End Stage Renal Disease (ESRD) patients receiving regular haemodialysis in the dialysis unit of Nephrology department of IMS & Sum Hospital were enrolled in the study. Depending on the Clinical condition, feasibility, logistics cost and patient's own acceptance, these patients were categorised into 2 groups i.e., Group A and Group B.

Group A: Received 2 times HD/ week

Total 40 ESRD Patients

Group B: Received 3 times HD/ week

Total 40 ESRD Patients

Patients in extremes of age, receiving immune suppressive therapy were excluded from this study. None of the patients were receiving peritoneal dialysis. Blood urea, Creatinine, Sodium, Potassium and Haemoglobin levels were evaluated in both the study groups, before and after 4 hours dialysis. Urea Reduction Ratio (URR) and Kt/v were calculated to assess the adequacy of haemodialysis in Group A and Group B.

Serum Urea[15], Creatinine[16] level were estimated by Cobas Integra 400$^+$ Auto analyser. Serum Sodium and Potassium levels were analysed by Ecolyte Electrolyte Analyser by using an ion selective electrode technology[17]. Urea Reduction Ratio (URR) is calculated by using the formula:

- Urea Reduction Ratio (URR) $=\frac{\text{U pre}-\text{U post}}{\text{U pre}}$ X 100%

Where, U pre- is the pre-dialysis urea level

U- post- is the post-dialysis Urea Level

Kt/v another important measure of dialysis adequacy. It is a mathematical formula where K (clearance) is multiplied by t (time) divided by v (volume)

K= Clarence- the amount of urea dialyzer can remove (litres/minute)

T= time- the duration of treatment (minutes)

V= volume- the amount of body fluid (litres)

All the results were expressed as mean ± SD. Statistical analysis was done using SPSS software (19: version). A comparison of paired data from the two groups of subjects was done using T test (t), a p value of <0.05 was considered indicative of a statistically significant difference.

RESULTS

Both the study groups (Group A and Group B) are age and sex matched (Table 1). Baseline characteristics i.e., BMI, body weight, Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) of both the groups showed no significant differences (Table I). Group A patients registered a significant fall in the serum urea level (P<0.001) and serum K^+ levels (P<0.05) following 2 times haemodialysis per week. Serum Creatinine and SBP were found decreased with increase in Haemoglobin Concentration, Serum sodium and Diastolic Blood Pressure values but these findings were not statistically significant (Table II). Following 3 HD/week (Table II) there was significant decrease in serum urea as well as creatinine (P<0.001). Haemoglobin value was found increased (P<0.05) with a fall in systolic blood pressure. Potassium value was decreased significantly (p<0.05) but no significant change is registered in serum sodium values following 3 HD/week. Urea Reduction Ratio (URR) and Kt/v value were found higher in Group B patients as compared to Group A (Table III) which was highly significant (P<0.001) pointing towards the more effectiveness of three Haemodialysis/week as compared to 2HD/week.

Dyspnoea, post dialysis rise in blood pressure, chest discomfort and transient hypotension were documented more frequently in Group A patients whereas nausea and vomiting was complained more in Group B patients (Fig. 1) suggesting better patient compliance in 3 HD/week.

Table 1: Baseline Characteristics of the study Participants

Parameters		Group-A 2 HD/week (n=40)	Group-B 3 HD/week (n=40)
Age (yrs)		55 ± 11.7	57 ± 9.8
Sex	Male	32	25
	Female	08	12
BMI (Kg/m^2)		22.7 ± 4.4	21.9 ± 3.78
SBP (mmHg)		149 ± 16	147 ± 24
DBP (mmHg)		80 ± 2	83 ± 12
Body weight (Kg)		60.2 ± 11.5	61.5 ± 11.5

Table 2: Comparison of Biochemical Blood Parameters before and after haemodialysis

Parameter	Group A		Group B	
	Baseline	After 2 HD/week	Baseline	After 3 HD/week
Hb (gm %)	7.8 ± 1.7	8.3 ± 1.6	8.2 ± 1.6	*9.1 ± 1.4
Urea (mg/dl)	136 ± 45	**72 ± 27	149 ± 46	50.74
Creatinine (mg/dl)	8.9 ± 3	7.6 ± 2.6	8.9 ± 3.1	**3.9 ± 3.2
Na^+ (mEq/lit)	131 ± 6.2	133 ± 5.4	134 ± 11.2	133 ± 5.2
K^+ (mEq/lit)	5.0 ± 1.0	*4.7 ± 0.6	5.2 ± 0.8	*4.7 ± 0.6
SBP (mmHg)	149 ± 16	144 ± 20	147 ± 24	*138 ± 11
DBP (mmHg)	80 ± 2	81 ± 11	83 ± 12	80 ± 7

*P<0.05- significant as compared to respective base line.
**P<0.001- highly significant.

Table 3: Effectiveness of Hemodialysis in different clinical setting

Groups	URR (%)	Kt/v
Group A	**44.6 ± 12.3	1.0 ± 0.2
Group B	**66.3 ± 4.89	2.03 ± 1.04

**P<0.001- highly significant.

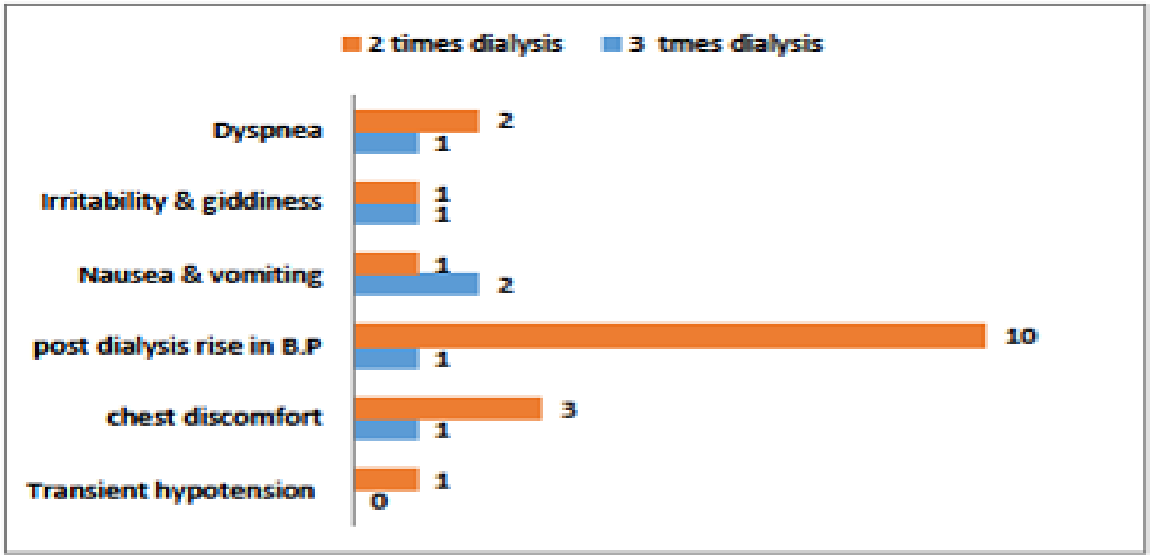

Fig. 1: Patient Compliance

DISCUSSION

The uraemia syndrome results from accumulation of solutes in the body water that are normally eliminated by the Kidneys and have concentration dependent toxicity. Dialysis being an empirical therapy of End-Stage Renal Disease (ESRD), is based on the rationale that the uremic syndrome is dependent on the concentration of toxic solutes accumulating in renal failure. During the early years of haemodialysis treatment, the definition of adequate dialysis was based on the two essential goals of dialysis i.e., eradication of signs and symptoms of uraemia and rehabilitation. Optimum dialysis is defined as that dose of dialysis above which no further improvement in the morbidity and mortality associated with dialysis can be expected[18]. Dialysis adequacy is a concept that moves ahead of simple clearance calculations from the laboratory data, but includes both laboratory evaluations (i.e., solute removal indices, biochemical nutritional parameters and anaemia status) and an evaluation of the patients clinical status i.e., blood pressure control, dialysis related symptoms, appetite, over-hydration signs and quality of life. Urea has been traditionally chosen as a solute marker for dialysis quantification for the following reasons:- its blood concentration is increased during uraemia, being low molecular weight (60 Da) it can rapidly diffuse between compartments and a simple single pool model is adequate for most applications, it crosses dialysis membrane easily, its concentration is easy to measure in the blood and in the dialysate, being the end product of protein metabolism, urea Kinetics can be correlated with dietary protein[19]. Urea Reduction Ratio (URR) and Kt/v urea are the two commonly accepted measures of haemodialysis dose[20,21,22].

Our results extend those that have been shown in previous observational studies and clinical

trials comparing conventional and 2 HD per week. Few studies documented that three HD/week should be recommended instead of 2 HD/week to improve the clinical outcome in chronic Kidney Diseases[23] and dialysis is inadequate in ESRD patients having HD twice a week[24]. Adequacy can be increased by increasing the frequency of dialysis. In another retrospective study, spKt/v was shown to be independently associated with patient survival[25]. In this study serum potassium levels fell significantly after 3 HD/week. The removal of potassium by haemodialysis is largely determined by the potassium concentration gradient between the plasma and the dialysate[26]. Measures that acutely shift potassium from the extracellular to the intracellular fluid compartment will reduce this gradient and attenuate potassium removal by the subsequent dialysis treatment[27]. Our study documented URR of 44.6% with a Kt/v of 1 with 2 HD/week which were below the recommended level by the National Kidney Foundation Dialysis Outcomes Quality Initiation (K/DOQI) but ESRD patients undergoing 3 HD/week registered Kt/v of 2.03 with a URR value of 66% that corresponds to K/DOQI recommendations, suggesting 3 HD/week as the optimum dose of HD. The benefits of frequents haemodialysis may result from improved control of other metabolic by-products i.e., phosphate or other retained uremic solutes, more physiologic removal of solutes, or improved control of extracellular fluid load. In the present study Clinical findings during 3 HD Haemodialysis/week showed that only few cases had dyspnoea, chest discomforts, irritability, giddiness and post dialysis rise in blood pressure whereas during 2 HD/week all these complaints were more evident. Lower haemoglobin levels may be due to difficulty to produce erythropoietin during HD treatment. Previous studies showed that anaemia was associated with left ventricular enlargement[28]. So, it is important for the HD patients to achieve the haemoglobin target i.e., Hb 10gm/dl (Foley at al 2000) which can be obtained with 3 HD/week in ESRD.

CONCLUSION

As compared to 2 HD/week, conventional haemodialysis of 3 HD/week was associated with favourable changes in biochemical markers of Kidney function i.e., serum urea, creatinine, URR and Kt/v (urea). There was an improvement in systolic blood pressure, Hb value with better patient compliance during 3 haemodialysis/week revealing that ESRD patients undergoing HD twice a week is inadequate and are at increased risk of mortality & morbidity. Patients with conventional 3 HD/ a week are more likely to have better clinical outcome and quality of life.

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