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Original Article

Biochemistry Section

Achieving the Urea Reduction Ratio (URR) as a Predictor of the Adequacy and the NKF-K/DOQI Target for Calcium, Phosphorus and Ca × P Product in ESRD Patients Who Undergo Haemodialysis

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ABSTRACT

Introduction: Among patients with end-stage renal disease (ESRD) who are treated with haemodialysis (HD), the solute clearance during dialysis is a determinant of the mortality. Also, elevated serum calcium (Ca), phosphorus (P) or the Ca × P product is associated with cardiovascular calcification and mortality in these patients. Our study was aimed at assessing the targets to be achieved, which were laid down by the NKF-K/DOQI guidelines for the urea reduction ratio (URR), serum calcium (Ca), phosphorus (P) and the Ca × P product in ESRD patients who underwent haemodialysis.

Methods: We retrospectively analyzed the pre-dialysis and post-dialysis blood samples of 35 patients who were on chronic haemodialysis. For the adequacy of the dialysis, the urea reduction ratio (URR) was calculated by ($predialysis_{urea}$ – $postdialysis_{urea}$) divided by $predialysis_{urea}$ and it was expressed in %. Calcium and phosphorus were measured from the fasting blood samples and the Ca × P product was calculated.

Results: The mean urea reduction rate (URR) was 66.4% (adequate URR is >65%). The Student's t-test (paired) was done on the results of the pre-dialysis and post-dialysis serum urea, creatinine and the uric acid levels. There was a significant ($p<0.001$) reduction in these parameters, thus suggesting the adequacy of the dialysis. The levels of the mean serum calcium, phosphorus and the Ca × P product were 8.59 ± 0.78 mg/dL, 5.82 ± 0.98 mg/dL and 49.88 ± 8.42 mg^2/dL^2 respectively. There was no achievement of the target phosphorus levels but the target levels of calcium and the Ca × P product were achieved.

Conclusion: The NKF-K/DOQI target of the mean urea reduction rate (URR) was achieved, thus suggesting the adequacy of the dialysis. The NKF-K/DOQI target for mean phosphorus was not achieved, thus suggesting the inadequacy of the oral phosphate binders, poor compliance or no proper dietary phosphorus reduction.

Key Words: Calcium × phosphate (Ca × P) product, End stage renal disease (ESRD), Haemodialysis (HD), Hyperphosphataemia, National Kidney Foundation – Kidney Disease Outcome Quality Initiative (NKF-K/DOQI), Phosphate binders, urea reduction ratio (URR)

INTRODUCTION

Numerous outcome studies have demonstrated a correlation between the delivered dose of the haemodialysis and the patient mortality and morbidity [1-7]. The evidence from them has demonstrated that the mortality among the ESRD patients was lower when sufficient haemodialysis treatments were provided. Because there is a poor correlation between the dialysis care team's clinical assessment of the haemodialysis adequacy and the patients' clinical outcomes, an unnecessary risk is placed on the patient, unless rigorous methods of evaluation are used. The clinical signs and symptoms alone are not the reliable indicators of the haemodialysis adequacy [8].

Urea is a substance that is most often monitored in the clinical practice as a surrogate for the measurement of the clearance of small solutes in general. The reasons for this are that urea is a small, readily dialyzed solute that is the bulk catabolite of the dietary protein, that it constitutes 90% of the waste nitrogen that is accumulated in body water between the haemodialysis treatments, that it is easily measured in blood, and that the fractional clearance of urea in body water correlates with the patient outcomes such as mortality and morbidity.

Of the three methods (Urea Kinetic Modelling, Kt/V and URR) that the NKF- K/DOQI considered as appropriate for measuring the delivered dose of haemodialysis, the URR is the simplest to execute, which is the parameter which is most commonly used to express the dialysis dose [9] and the resultant popularity of the URR [10]. The URR has been shown to be a statistically significant predictor of mortality for the ESRD patients. It was recommended that Kt/V should be reported in terms of equilibrated Kt/V (eKt/V) [11] or single-pool Kt/V (spKt/V) [12].

The K-DOQI guidelines recommend that the adequacy of the dialysis dose should be measured routinely, typically on a monthly basis, by using either $spKt/V_{urea}$ or the Urea reduction ratio (URR). The minimum recommended target adequacy levels are either $spKt/V_{urea}$ of 1.2 or URR of 65% per dialysis session, which is delivered 3 times a week [13].

NKF-K/DOQI recommends serum concentrations of corrected calcium in the range from 8.4 to 9.5 mg/dL and serum phosphorus

concentrations between 3.5 and 5.5 mg/dl. The serum Ca × P product concentration should be <55 mg^2/dL^2 and the serum iPTH concentrations should range from 150 to 300 pg/mL in patients who suffer from chronic kidney disease (CKD) stage 5 (ESRD) [14]. However, several studies still report a high prevalence of hyperphosphataemia [15,16]; only 5.5% of the patients achieved all of the target levels of the K/DOQI, thus indicating that the proportion of the patients who achieved the K/DOQI recommendations was very low and that they may require new approaches for the management of bone and mineral abnormalities [16].

Our study was aimed at assessing the haemodialysis adequacy by URR measurement, the NKF-K/DOQI target in bone metabolism and the disease in CKD stage 5 (ESRD) for Calcium, Phosphorus and Ca × P.

MATERIALS AND METHODS

Setting

This study was conducted during April to September 2011. The individuals for the study were selected from the Haemodialysis Unit, Prathima Hospital, Karimnagar, Andhra Pradesh, India. The individuals are End Stage Renal Disease (ESRD) patients who were on chronic haemodialysis for >1year. A total of 35 individuals were studied. An informed consent was obtained from all the 35 individuals. All the 35 individuals were explained the nature of the study. This study was approved by the Institutional Ethical Committee (IEC).

Inclusion Criteria

Male and female patients between 20 to 60 years of age, who were suffering from End Stage Renal Disease (ESRD), who were on chronic haemodialysis treatment.

Patients who were on regular (3 times per week) haemodialysis sessions.

Exclusion Criteria

Patients who were not on phosphate binders.

METHODS

Haemodialysis was performed by using a Fresenius Medical Care (4008S) haemodialyzer machine, on ESRD patients with permanent arterioveinous fistulas. It was indicated in patients whose glomerular filtration rate (GFR) was below 15mL/min. The time duration for HD was 4 hours and it was performed thrice a week. HD was advised in all the ESRD patients.

Urea was measured by Berthelot's enzymatic method [17] by using a kit which was supplied by the Nicholas Piramal Diagnostics.

Calcium was measured by the Arsenazo III method [18] by using a kit which was supplied by Liquimax calcium, Avecon Healthcare, Pvt. Ltd.

Phosphorus was measured by the modified Metol method [19] by using a kit which was supplied by Excel diagnostics.

All the parameters were measured on an ERBA chem 7 semi-auto analyzer.

The urea reduction ratio (URR) as expressed in % was calculated by [1];

$$URR = 100 \times [1 - (C_t/C_0)]$$

in which C_t is the postdialysis BUN and C_0 is the predialysis BUN.

Serum calcium was adjusted for the albumin levels by using the conversion factor;

$$\text{Corrected Calcium (mg/dL)} = \text{Total Calcium(mg/dL)} + 0.0704 \times [34 - \text{albumin (g/L)}]$$ [20].

The Ca × P product in mg^2/dL^2 was calculated by multiplying the corrected calcium concentration by the phosphorus concentration, both in mg/dL [21].

RESULTS

The data was obtained from 35 patients. The serum parameters were urea, calcium and phosphate. The data analysis was done by using SPSS, version 17.

Parametric statistics like Mean, SD and the Student's t-test (paired) were applied for the continuous data.

Demographic Distribution

Most of the patients were from the district of Karimnagar.

Demographic Data

Age and Sex Distribution: The mean age (mean ± S.D.) of the study patients was 54.6 ± 8.6 years. Eighty percent were male patients.

Parametric Data

The Urea Reduction Ratio (mean ± S.D.) in 35 patients was 66.4 ± 15.6 %. The pre-dialysis urea (mean ± S.D.) level was 142.3 ± 46.5 and the post-dialysis urea (mean ± S.D.) level was 43.0 ± 18.9. The Student's t-test (paired) was done on pre-dialysis and post-dialysis serum urea, which showed significant ($p<0.001$) reduction.

The mean serum calcium (mean ± S.D.) level was 8.59 ± 0.78 mg/dL. 48.5% of the patients had serum calcium levels which were below the target levels. In 37.2% of the patients, the serum calcium levels were within the target levels. 14.3% of the patients had serum calcium levels which were above the target levels.

The mean serum phosphorus (mean ± S.D.) level was 5.82 ± 0.98 mg/dL. 34.3% of the patients had serum phosphorus levels which were within the target levels. 65.7% of the patients had serum phosphorus levels which were above the target levels.

The mean Ca × P product (mean ± S.D.) level was 49.88 ± 8.42 mg^2/dL^2. 68.6% of the patients had serum Ca × P product levels which were within the target levels. 31.4% of the patients had serum Ca × P product levels which were above the target levels.

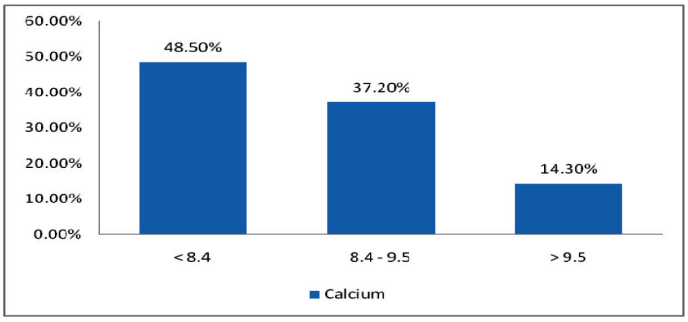
[Table/Fig-1] Shows the distribution of the ESRD patients as per the NKF-K/DOQI targets for Ca, P and Ca × P.

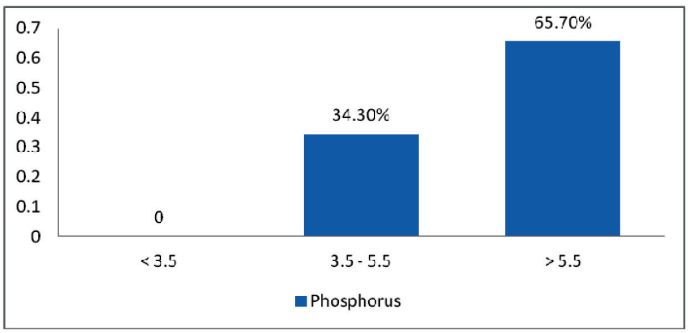
DISCUSSION

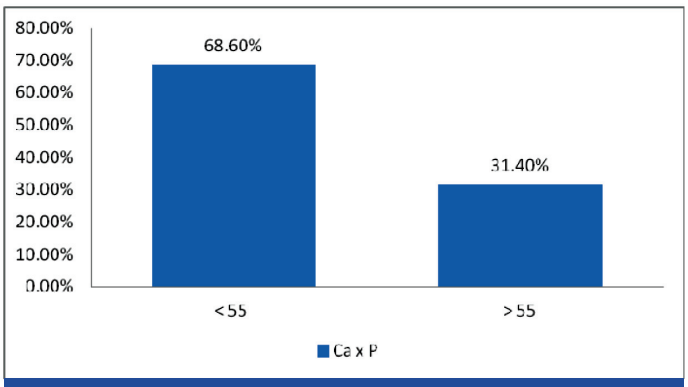
In this current study, we determined that the NKF-K/DOQI target for URR was achieved whereas for Ca, P and Ca × P, it was not completely achieved.

The median URR increased from 58.9% to 69.5% from 1990 to 1997, respectively [22]. From 1993 to 1997, the mean URR increased from 62.7% to 68.0% [23]. The percentage of the patients who received a URR value of ≥65% increased from 43% in 1993 to 72% in 1997. In this study, there was a significant ($p<0.001$) reduction in the pre-dialysis and post-dialysis serum urea levels. The mean urea reduction ratio (URR) was 66.4 % (the adequate URR was >65%), thus suggesting an adequate dialysis. One study reported a URR of 72% [24]. Another study reported URRs of 67.1% and 66.3 % [25].

This present study showed that the mean serum calcium (mean ± S.D.) was 8.59 ± 0.78 mg/dL and that it was within the target levels







[Table/Fig-1]: Proportion (%) of patients achieving K/DOQI target levels for calcium (8.4–9.5 mg/dL), phosphorus (3.5–5.5 mg/dL) and Ca × P (<55 mg^2/dL^2).

(8.4 to 9.5 mg/dL). 48.5% of the patients had serum calcium levels which were below the target levels. 37.2% of the patients had serum calcium levels which were within the target levels. 14.3% of the patients had serum calcium levels which were above the target levels. Similar studies showed that 43% [26] and 59% [21] of the patients had serum calcium levels which were above the target levels.

Despite substantial improvements over the last decade in the management of dialysis patients, little progress has been achieved in the control of the serum phosphorus levels. In 1988, Lowrie and Lew [27] analyzed data from 12000 haemodialysis patients and found that their mean serum phosphorus level was 6.2 mg/dL. Twelve years later, Block et al. [15] showed that hyperphosphataemia remained a relevant clinical problem. In our study, the mean serum phosphorus level was 5.82 ± 0.98 mg/dL and it was above the target levels (3.5 to 5.5 mg/dL). 65.7% of the patients had a phosphorus level which was greater than 5.5 mg/dL. Similar studies showed that 34% [26] and 49% [21] of the patients had serum phosphorus levels which were above the target levels.

The available evidence is limited, but convincing, that the primary outcome (increased death rate) and the secondary outcome (extra-skeletal calcification) were related to the Ca-P product. If this product exceeded 55, there would be an increased risk for the development of calcification and possibly, an increased risk for a lower patient survival. The DOPPS study [16] demonstrated that the percentage of patients who were within the K/DOQI guideline range remained surprisingly low, with 56.5% of the patients having a Ca × P level of <55 mg^2/dL^2. Our results showed slightly better results for the Ca × P control. The mean Ca × P level was 49.88 ± 8.42 (<55 mg^2/dL^2), with 68.6% of the patients having a Ca × P level of <55 mg^2/dL^2, thus proving again, that difficulties still existed in achieving the recommended levels of Ca × P. Other studies showed that 67% [26] and 56% [21] of the patients had serum Ca × P levels which were within the target levels.

CONCLUSION

The NKF-K/DOQI target for URR was achieved, thus suggesting that adequate dialysis dosing was possible in this set-up. One reason could be that the adequate treatment time was enough in most of the cases to achieve the URR targets, whereas for Ca, P and Ca × P, the NKF-K/DOQI targets could be called as partially achieved. The reason for this may be that multiple factors were involved, such as the adequacy of the oral phosphate binders, the education on dietary phosphate reduction and the requirements of Vitamin D supplementation and the parathyroid status, to name a few. To conclude, a strict and comprehensive approach is required to achieve the latest NKF-K/DOQI targets for bone and mineral metabolism and disease to reduce the morbidity and the mortality. However, large scale studies are required to make any solid conclusions.

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