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Original Article

Comparison of Online Clearance Monitoring and Daugirdas Formula for The Assessment of Haemodialysis Adequacy

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ABSTRACT

Objective: To determine if urea kinetic modelling (Kt/V) by online clearance monitoring (OCM) could be used as an alternative to Kt/V calculated using Daugirdas equation.

Study Design: Cross-sectional study

Place and Duration of Study: Dialysis Unit, Combined Military Hospital Peshawar, Pakistan, Nov 2019 to Feb 2020.

Methodology: Outdoor patients on maintenance thrice-weekly hemodialysis were selected using non-probability convenience sampling. Body weight was measured and serum urea levels were checked before and after each haemodialysis session. Kt/V-Daugirdas was calculated using Calculate by QxMD android application. Kt/V online clearance monitoring was determined using the built-in online clearance monitoring module of Fresenius F4008 haemodialysis machines.

Results: Amongst 47 patients aged 55.47±13.66 years, 34(72.34%) were males. Patients were assessed during 63 hemodialysis sessions. Kt/V was 1.21±0.24 and 1.44±0.46 by online clearance monitoring and Daugirdas formula respectively (p<0.001). There was a positive correlation between the two (r=0.373, p=0.003). In 24(38.10%) sessions, both Kt/V online clearance monitoring and Kt/V Daugirdas targets of 1.2 (minimum) were achieved. Kt/V Daugirdas target was achieved more frequently than Kt/V online clearance monitoring (66.67% vs 46.03%; p=0.012). Kt/V Daugirdas targets were better attained amongst patients with arteriovenous fistula as compared to those tunneled dialysis catheters (74.00 vs 38.46%; p=0.015). This was not true for Kt/V online clearance monitoring targets (p=0.992).

Conclusion: Online clearance monitoring is non-invasive and can reliably be used to screen for hemodialysis adequacy even though it slightly underestimates Kt/V as compared to the Daugirdas formula.

Keywords: End Stage Renal Disease, Haemodialysis, Renal Clearance, Renal Replacement Therapy

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INTRODUCTION

End stage renal disease (ESRD) is a major cause of disability and death, and affects people from the developing world disproportionately more.[1] Around 22000 new patients require haemodialysis (HD) each year in Pakistan.[2, 3] Burden of CKD/ ESRD will continue to multiply in coming years since both diabetes mellitus and hypertension, the two major risk factors, are epidemic now. This disease is a major public health problem in Pakistan, where poverty and lack of equitable access to healthcare counters effective medical treatment. The vast majority of patients are managed with HD here, and considering the cost (almost four times the per capita income), many patients cannot afford regular HD three times a week.[4]

Adequacy of HD is generally assessed by urea reduction ratio (URR) or urea kinetic modelling, referred to as Kt/V. As compared to URR, Kt/V offers the additional advantage of taking into account intradialytic urea generation as well as extra urea removed because of ultrafiltration. A single pool Kt/V of at least 1.2 is considered a marker of adequate urea clearance and is a strong predictor of outcomes/ mortality for patients on chronic HD treatment.[5] Whereas Kt/V is generally calculated using equations dependent on repeated blood sampling, online clearance monitoring (OCM) can also be used for this purpose. The latter is a non-invasive technique, hence is economically feasible and convenient for patients. It works on the principle of measuring conductivity of dialysate before and after entering the dialyser to determine the ionic dialysance of sodium, which is a surrogate marker of Kt/V.

We carried out this study to determine if Kt/V by OCM could be used as an alternative to Kt/V calculated using Daugirdas equation. The results would allow us to adopt a more convenient method that could place lesser burden on human resources as well.

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METHODOLOGY

This cross-sectional study was carried out at the Dialysis Unit of Combined Military Hospital Peshawar, Pakistan, from November 2019 to February 2020. Permission from Institutional Ethics Review Committee was obtained before starting data collection (Approval No. 03, dated 29 October 2019).

Inclusion Criteria: Patients of chronic kidney disease on haemodialysis of either gender, aged 18 years and above, undergoing maintenance HD for ESRD for at least a week were included.

Exclusion Criteria: Patients recently started on HD and undergoing one of the first three sessions and those on HD less frequently than 3 times a week were excluded.

Online calculator provided by University of California San Francisco Clinical and Translational Science Institute was used to calculate a sample size of 63.[6,7]

Patients were recruited using non-probability convenience sampling. Written informed consent was also taken from the participants beforehand. A total of 63 sessions were monitored and some patients had their data collected during more than one session. Basic demographic data was noted down during the initial interaction with the patients. We also recorded data on type of vascular access, including arteriovenous fistula (AVF) and long-term tunneled HD catheters. HD was done for 3.5 hours on Fresenius 4008S haemodialysis machines, following standard protocols. The blood pump speed was set at 300 ml/minute and dialysate blood flow at 500ml/minute for all patients. Fresenius Polysulfone F8 High Performance Stem dialysers were during all HD sessions. All this was done to ensure consistency. Ultrafiltration was done as per dry weight of patients. A record of ultrafiltration volumes was also made. Sampling was done from the arterial port of the dialyser tubing to collect blood samples for pre and post dialysis serum urea levels as well as pre dialysis hematocrit. Patients also had their weight measured before and after HD sessions. Using these different parameters, we calculated Kt/V- Daugirdas with android-based Calculate by QxMD app. Kt/V- OCM was determined using the built-in OCM module. For this purpose, we estimated total body water using dry weight- based Watson formula.

Data was analysed using Statistical Package for Social Sciences (SPSS) version 24. Continuous variables were described as mean± standard deviation. Relationship between Kt/V- Duagridas and Kt/V-OCM was evaluated using linear regression analysis. Chi-square test was used to compare proportions of patients achieving minimum recommended single pool Kt/V target (≥1.2) measured by the two techniques. Frequencies of patients with temporary or permanent vascular access achieving Kt/V goals by different estimation techniques were also calculated and compared using Chi-square test. For all comparisons, $p<0.05$ was considered statistically significant.

RESULTS

There were 63 patients aged 55.47± 13.66 years, including 72.3% males and 27.6% females. Most of the patients (76.6%) had arteriovenous fistulas, while the remaining ones had long term tunneled HD catheters. These patients underwent a total of 63 monitored HD sessions during the study period. Mean weight of the patients before and after these HD sessions was 59.89±8.99 kg and 57.48± 11.25 kg respectively. Pre and post HD serum urea levels were 23.59±7.46 and 7.03±3.35 mmol/l respectively. This gave a urea reduction ratio (URR) of 69.38±11.85%. URR ≥65% was achieved in 43(68.35%) sessions.

There was a significant positive relationship between Kt/V by OCM and Daugirdas equation (R=0.373, $p=0.003$). Kt/V by OCM was 1.21±0.24, whereas Kt/V by Daugirdas equation was 1.44± 0.46. This difference was statistically significant ($p<0.001$). For this comparison, the degree of bias was 15.97%. Target Kt/V by both OCM and Daugirdas equation was achieved in 24(38.10%) HD sessions only. However, Kt/V by Daugirdas equation was achieved in a greater proportion of HD sessions as compared to that by OCM (66.67% vs 46.03%; $p=0.012$). Details are depicted in Figure.

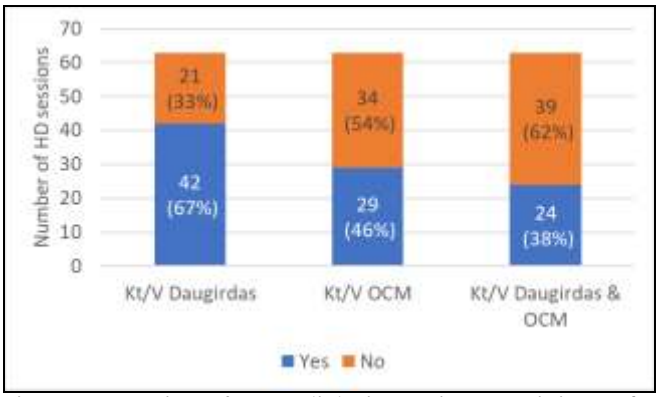

Figure: Proportion of Hemodialysis Sessions Attaining Kt/V Targets

As shown in Table, outcomes for Kt/V by Daugirdas equation were better with arteriovenous fistula as compared to long term tunneled HD catheters (74.00 vs 38.46%; *p*=0.015). Fulfilment of targets for Kt/V by OCM was not affected by the type of vascular access (*p*=0.992).

Table: Effect of vascular access on Attainment of Kt/V targets (n=63)

Baseline Characteristics	Study Groups		*p*
	Fistula (n=50)	Catheter (n=13)	
Kt/V Daugirdas, n(%)			
Achieved	37(74.00%)	5(38.46%)	0.015
Not achieved	13(26.00%)	8(61.54%)	
Kt/V OCM, n(%)			
Achieved	23(46.00%)	6(46.15%)	0.992
Not achieved	27(54.00%)	7(53.85%)	

DISCUSSION

The results of this study have proven urea kinetic modelling (Kt/V) by online clearance monitoring (OCM) to be a reliable indicator of HD adequacy, though the results underestimate this slightly, as compared to Kt/V Daugridas, which is currently believed to be the gold standard tool. However, it does not require any special blood sampling and laboratory analysis.

Intermittent maintenance HD is at the forefront of treatment options for patients with ESRD. Together with other aspects of disease management such as pharmacological therapy and dietary modifications, it plays an important role in sustaining life. There is ample evidence to prove improved survival with better HD adequacy. A number of studies focusing on this aspect have been carried out both regionally and internationally. Amongst 18242 dialysis dependent patients in Korea, Hong *et al*. showed that HD adequacy was associated with patient survival.[8] It is therefore imperative to monitor HD adequacy regularly. For patients undergoing regular HD three times a week, National Kidney Foundation/ Kidney Disease Outcomes Quality Initiative recommends a minimum delivered single pool Kt/V of 1.2, whereas the ideal target is 1.4.[9]

These targets were achieved in two thirds of the HD sessions carried out as a part of this study. The proportions of sessions during which Kt/v- Daugirdas and URR targets were attained were nearly the same, but lower for Kt/V OCM. Kt/V OCM was lower than Kt/V Daugirdas in another study on 1076 patients from the Czech Republic.[10] The degree of bias (15%) was also very close to what we found in our study. The results are also quite similar to those presented by Fazal-e-Mateen *et al*.,[11] They compared Kt/V values obtained by OCM, Daugirdas formula and normogram on 60 patients at Mayo Hospital Lahore. Though the absolute Kt/V values obtained by Daugirdas formula and OCM were slightly higher in our cohort of patients, the trends and the degree of bias between the two parameters were the same. Incidentally, the patients reported by Fazal-e-Mateen *et al*., were much younger and far more of them had AVF rather than temporary lines.[11]

The quality of life and survival is better amongst patients with AVF rather than temporary vascular access.[12] Similarly, it was previously believed that HD adequacy is also better with fistulas and grafts as compared to central venous access.[13] However, more recent studies provide contrary evidence suggesting that the vascular access type does not affect adequacy of HD.[14,15] In our study, a greater proportion of HD sessions carried out using arteriovenous fistulas attained adequacy targets defined by Daugirdas formula, in contrast to tunneled HD catheters. This is most likely due to recirculation, since all patients had uniform blood flow rates to ensure consistency of prescription during dialysis sessions. However, this phenomenon was not observed when dialysis adequacy was assessed by OCM. The most plausible explanation for this is the general underestimation of Kt/V by OCM.

Reliable output from OCM is critically dependent on the values of total body water volume which is equivalent to the volume of distribution of urea. This volume is generally estimated from Watson formula that relies on patient's age, gender, height and weight. Alternatively, volume calculated with other techniques such as bioimpedance spectroscopy may be directly fed into the HD machine for calculation of Kt/V. Variability in estimates by these techniques is well known, with both having their own pros and cons.[16] Fernández *et al*. showed this variation to be >10% in up to 60% cases from Spain.[17] As per Alayoud *et al*., there are two reasons for the overestimation of total body water by Watson formula in dialysis dependent population: loss of muscle mass and the non-inclusion of urea generation rate in Watson formula.18 This explains why OCM generally underestimates Kt/V as compared to the Daugirdas formula.

The results of this study have proven that OCM is a reliable choice for assessment of HD adequacy in

clinical practice. It is very easy to use and does not need any extra effort on part of dialysis technicians. Any progressive decrease in Kt/V as detected by OCM can be further investigated to determine cause of decrease in HD adequacy. Potential analytical errors during estimation of blood urea levels for use with Daugirdas formula are also not a concern with OCM.

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LIMITATIONS OF STUDY

We did not compare our results with the normogram, since this is not being done routinely in most of the dialysis units. This was a single center study done only on one make of HD machines, such that generalization to other makes of dialysis machines such as Gambro would need additional evidence.

DISCLOSURE

This data was presented as a poster titled 'Comparison of Kt/V estimation by online clearance monitoring and Daugirdas formula' at 1st International Conference of Pakistan Society of Internal Medicine, held at Lahore in March 2020.

CONCLUSION

Though OCM slightly underestimates Kt/V as compared to the conventional Daugirdas formula, it may be safely used in routine clinical practice, especially once the clinicians are aware of the shortcomings and interpret the results accordingly.

Conflict of Interest: None.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

ARA & MB: Conception, study design, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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