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COMPARING PRESCRIBED AND DELIVERED DOSES IN ICU PATIENTS ON CONTINUOUS RENAL REPLACEMENT THERAPY AT KING FAHAD HOSPITAL SAUDI ARABIA.

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ABSTRACT: Purpose of this study is to find the difference among dosage of CRRT based on effluent rate prescription and actual delivered effluent rate by monitoring records of dialysis. **Study Design:** Prospective observational cohort study. **Setting:** King Fahad Hospital Medina Saudi Arabia. **Period:** 1st June 2016 to 31st December 2016. **Material & Methods:** Two hundred acute kidney injury patients admitted in ICU on CRRT at rate of 20ml/kg using pre-filter continuous venovenous hemodia-filtration (CVVHDF), among (AKI) patients prescribed doses were compared with the actual dose with in the duration of 24 hours to find out difference between prescribed and actual dose. **Results:** Findings of our study shows that. Mean average dose of dialysis delivered per day was only 16 hours which is 21% of prescription of pre-dilution CVVHDF. Patients were receiving 14ml/Kg of continues renal replacement therapy (CRRT) with the lack of 21% dilution correction factor. The average number of hours/day on continuous renal replacement therapy was 14.1±2.41, with a mean flow rate of 1.36±0.31 L/h (averaged over 24 h). The delivered doses were significantly lowered then the prescribed doses with ($P < 0.001$). 30% of doses was missing during CRRT among patients with acute kidney diseases admitted in ICU at king Fahad hospital Saudi Arabia (P-value <0.001). **Conclusions:** We concluded that during dialysis patients did not received the prescribed dose in comparison to actual delivered dose which effects the survival of critical ill patients with acute kidney injury.

Key words: CRRT, CVVHD, ICU, Prescribed Dose.

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INTRODUCTION

Acute kidney injury is a common complication and affecting approximately 2 to7% of hospitalized patients and among critical ill patients this ratio was 35% renal replacement therapy is the supportive treatment for the patients with severe acute kidney dieses. Among the critically ill patients renal replacement t therapy was reported among 5 to 6% of patients and is associated with in hospital mortality rate of 50 to 80%[1,2,3] Acute kidney injury (AKI), requiring renal replacement therapy (RRT) occurs in 5 to 6% of seriously ill patients and is related with high mortality and significant health resource utilization[4,5,6] and an important cause of increased mortality is in the intensive care unit (ICU) patients worldwide.[7] The optimum time for initiation, method and dosing of renal – replacement therapy remains uncertain more from more than 60 years after first use of hemodialysis is patients with acute kidney injury.[5,6] Different studied suggested that more intensive doses of RRT shows better outcomes in patients with acute kidney injury.[8,9] However results have been inconsistent. Disceptation exists as to what constitutes optimal RRT in this setting, there was first land mark study in which patients randomized to post-dilution continuous veno-venous hemofiltration (CVVH) at a dose of 3 ml/kg / hour or above had improved the endurance compared with those randomized to 20ml/kg /hour.[10] There are a lot of modifiable factors in the delivery of RRT modality which includes (continues or intermittent) time of initiation and dose of treatment, solute removal mechanisms (convection diffusion, adsorption or combination)[10] the relationship between treatment dose and consequences due to that dose was first introduced in landmark study in

which patients was randomized to post-dilution continue venous hemofiltration (CVVH) at 35ml/ Kg/hour or above shows good results with improvement of survival in comparison with 20ml/kg/hour[11] Some of other study shows conflicting results after exploration of this issue in the absence of any data according to this study the lower doses recommended higher doses in (CVVH) particularly among septic patients but unfortunately in outcome of different surveys suggest that this practice in not widely adopted into intensive care units (ICU)practice.[12,13] A number of factors may cause decreased solute clearance in CRRT including interruptions for radiological procedures, access change, pruning, physiotherapy, machine alarms, and clotting of filters.[14] In different studies All the measurements related with effluent rates were based on ml/ kg/h.[15] We performed a prospective observational cohort study to evaluate the prescription and actual delivered dose in ICU. Direct measurement of solute clearances was very difficult in our settings and our resources, so we calculated the prescribed dose of dialysis for a 24-hour therapy vs. the actual delivered dose keeping the exact records for continuation, interruptions and restart with special instructions to the nurses.

MATERIALS AND METHODS

It was a prospective observational study of two hundred patents who were admitted in ICU with diagnosed of acute kidney dieses. All the prescriptions of CRRT were reviewed for a period of 6 months prospectively from 1st June 2016 to 31st December 2016 at king Fahad hospital Medina Saudi Arabia , the review from the nursing notes, regarding all documented interruptions for filter clotting, line changes, and pruning., to find out the association between the dose which was prescribed and the dose which was delivered, based on reviewing the 24-hour CRRT records documenting all interruptions and averaging down for 24 hours.as there is no official registration of hemodialysis patients each year at dialysis center. Data was collected by using specific questionnaire, which contained demographic data, date of hemodialysis and how it was started. the duration of hemodialysis and last measured hemodialysis quality index (single-pool kt/V), and numbers of hemodialysis sessions per week hemodialysis doses were recorded each time and their mean value were calculated. Hourly effluent rate/ weight of the patient and time on CRRT was used to determine the dose of Continuous renal replacement therapy which was delivered for that day. The Mean of the effluent rate (in L/h) was then calculated for every patient. 200 patients were enlisted from Medical and Surgical critical care at KFH over a 6-month period. For all the two hundred enlisted patients' hematocrit, and renal function tests were checked daily. Overall CVVHDF effluent volume and actual CVVHDF treatment time per 24 hours were calculated every day. Comprehensive data were available from all 200 enlisted patients.

Statistical Analysis

Data was analyzed by using SPSS (statically package for social scientists) (version 18, Chicago, IL USA) categorical variables were reported as frequency and continues variables as mean with their ranges and Standard deviation. Normality of the data was check through Kolmogorov-Simon test (Lilliefors modification) chi-square test was used to check association between categorical variables, the difference between prescribed and delivered dose evaluated through students-t test for continues variables. Univariate cox proportional hazards analysis was used to select variables significantly in association with missing of prescribed dose during session of CRRT. Univariate cox analysis was used to point out variables which are significantly involved in missing of prescribed dose for patients. For associated risk factors value $P<0.05$ considered as significant.

CRRT Technique

Continuous veno-Venous Hemodiafiltration (CVVHDF) was performed with Fresenius multi filtrate and polyacrylonitrile dialyzer, temporary hemodialysis catheter put into the internal jugular, subclavian or femoral vein. Continuous hemodia-filtration was carried out with blood flow rates of 180 -200 ml/min with prefilter substitution fluid. Heparin or no anticoagulation was used based on nephrologists' clinical decision. Low molecular

weight Heparin as anticoagulation was used in 33% of the cases and without anticoagulation in rest of the cases Filter and lines were switched due to the failure of the circuit from clotting, or when in use for 72 hours of use or when the patient was not on CVVHDF for more than 2 h because of some imaging study or being in a procedure. Effluent rate. All pts were prescribed 20ml/kg hour effluent rate. The prescribed effluent rate (ml/hr) was calculated by addition of the substitution fluid, dialysate flow, and ultrafiltration. For example, an 80 kg patient prescribed a dialysis dose of 20ml/kg/hr. would require an effluent rate of 1600ml/Hr (80 kg X 20 mL/kg/h) plus the UF for that hour.

The substitution fluid, dialysate flow and ultrafiltration for that patient would be calibrated to bring an effluent rate of 1600ml/hour during the study period. A dose was calculated only once and it was based on the weight of the patient on the day of CVVHDF was initiated. Prescribed dose remained the same during the period of treatment and was not fine-tuned for changes in body weight. The effluent rate would be divided equally between the substitution fluid and dialysate.

RESULTS

A suitable dose of CRRT was associated with the improvement in the survival of acute kidney injury patients, findings of our study shows that in duration of 24 hours patients on continues renal replacement therapy did not receive the desire dose which was prescribed by Nephrologist. Response rate was good Two fifty questionnaires were distributed to the study subjects out of Two fifty questionnaires, two hundred (80%) filled questionnaire was received. Due to the risk of clotting during CRRT and more chances of bleeding during therapy there was different strategies which was used to control bleeding and reduces the risk of bleeding. Which includes a) regional criteria anticoagulant b) low dose UHF (68%). In this study during CVVH. Replacement fluid was preferably administered in case of without anticoagulant. Among (60%) cases of this study heparin was delivered at the rate of 95mg/ study subjects was with different demographic characteristics in which males were 60(60%) and females was 40(40%) with the urine output of (611±792) and BUN was (76±40). As details are mentioned in following Table-I.

Gender	Male Female	60(60%) 40(40%)
		(mean ± SD)
Age		62 ± 14
Weight (kg)		91 ± 18
Creatinine (mg/dL)		4.2 ± 2.2
Urine output (ml/day)		611 ± 792
BUN (mg/dL)		76 ± 40
APACHE II		26.0 ± 6.

Table-I. Baseline characteristics of patient.

During the CVVHD among the patients with acute kidney diseases heparin was used among 66(33%) of patients and without anti-coagulant was among 134(67%) of subjects. as details are mentioned in below Table-II.

(%)	(n)	
33%	66	CVVHD_Heparin
67%	134	CVVHD_with out anticoagulation

Table-II. Anticoagulant therapy.

We found that the mean CRRT dose prescribed for these patients was 20.±.96mL/Kg/h but delivered dose was only 14±2.41 mL/Kg/h. The average dose of dialysis delivered per day was only with in the duration of 16 hours which is 14ml/kg and in this 21% of dilution factors was not applied the average numbers of hours for CRRT is 24 hours in prescription by consultant but delivered dose in this time was only 14.1±2.41 with flow rate of 1.36±0.31 L/h.

	Doses
Prescribed clearance	20.±.96mL/Kg/h
Estimated clearance	14±2.41 mL/Kg/h

Table-III. Results as per dialysis dose prescription and delivered dose.

The vascular accesses for RRT among the study subjects are mentioned in Table-IV.

Vascular access,	(n)	(%)
Femoral vein	106	53%
Right-sided jugular vein	51	25.5%
Left-sided jugular vein	43	21.5%

Table-IV. Vascular access for RRT.

DISCUSSION

Association between dialysis dose adequacy and patient's outcomes have been studies for the first time in Saudi Arabia. our results suggested that due to some of the factors delivered does to patients was less than prescribed dose and this prescribed doses were for the period of 24 hours, among the study subjects males were 60(60%) and females were 40(40%), body weight of subjects was (91 ± 18). And creatinine in mg/dl was (4.2 ± 2.2). urine out-put in ml/day was (611±792), BUN was (76±40), APACHEII was (26.0±6). finding of our study is in similarity with the study conducted by Etienne Macedo their findings report that males were greater than females and creatinine was (4.5±2.2) and average weight of study subjects (90±20) and BUN was (70±45).[16] As results our study shows that delivered doses was less than the prescribed dose and duration of time was also very less in which dose was delivered as compared to the prescribed dose. Prescribed clearance was within the duration of 24 hours with 20.±.96mL/Kg/h and the delivered estimated clearance was 14±2.41 mL/Kg/h within the duration of 16 hours. this finding of our study is in similarity with the findings of the study conducted by Zhabg and Zhingheng in their trail patients with AKI admitted in ICU and on renal replacement therapy, did not received the prescribed doses and even due to other issue dose delivery time is also less and this difference was increases progressively over period of time[17] one of another study conducted by Mentz and Philips G their findings show that acute kidney diseases patients undergoing renal replacement therapy present excessive risk in hospital death and this was due to the CRRT delivered dose because required dose was not delivered to the patients and in a results patients expired.[18] One of another study by william D. Lyndon at nephrology and dialysis department which shows that prescribed doses differed significantly from the measured TEV dose (P<0.001). Due to which urea and creatinine clearance not achieved.[19] Claure-Del granado et al. published in last few years they report that urea, creatinine was not cleared form the body during CRRT therapy and there was a big delay duration of time between prescribed and delivered and factors involved in this delay of clearance includes mechanical disorder and issues related with membrane of the filter due to which prescribed doses was not delivered.[20]

Results of our study shows that anticoagulation therapy was not used in majority of the study subjects. heparin was used among 66(33%) of cases and the study subjects without heparin was 134(67%). This results are in similarity with results of the study conducted by A.n Berbece according to finding of their study heparin was used as an anticoagulant among in 29% cases and majority was without anticoagulant[21] According to the results of our study majority was on femoral vein106 (53%) for RRT access and then right-sided jugular vein 51(25.5%) and then left sided jugular vein 43(21.5%). In our study the majority was on femoral site for CRRT because most of the study reported that jugular site is note the safe site. This finding is in similarity with the findings of the study conducted by Domenico santoro adnfillppo Benedetto their findings report that femoral vein is the major and big vein and have less chance for the clots formation due to which it's the favorable site for the patients of dialysis.[22]

One of the another study conducted by Bloom Rans martensson J their findings reports that femoral vein was the first access site in 937(67%) of 1399 patients this patient had higher acute physiology and chronic health evaluation and sequanritoal organ failure assessment score was (P=0.009) and lower PH (P<0.001) and on other hand mortality due to non_femoral vein was (44vs, 45%: P=0.63).[23] Overall study results of over study and findings of some other study. This was highlighted that prescribed dose was not delivered to the patient in duration of renal replacement therapy due to Which patients with acute kidney diseases was unable to survive

for large duration of time. And there are allot of different factors involved due to which patients were unable to receive the prescribed dose.

CONCLUSIONS

Our study reveals that delivered dose of dialysis was 70 percent of the prescribed dose which represents flaws in our CRRT practice because it is not routinely measured and CRRT is frequently interrupted among the patients with acute kidney diseases. Due to which patients survival rates will not improve.

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A **small** leak can sink a **great** ship.

"Benjamin Franklin"

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Adil Manzoor	Design of study, and receiving of IRB latter from the ethical review board.	
2	Ahmed Bhatt	Collection of data.	
3	Gurdeep Singh	Data analysis and write up of research paper.	
4	Faisel Yunus	Revision of research paper.	