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INADEQUACY OF DIALYSIS;
HOW TO FIGHT INADEQUACY OF DIALYSIS, INCREASED BLOOD FLOW OR INCREASED DIASYLATE FLOW?

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ABSTRACT: Background: Objectives: In patients with end stage renal disease, inadequate dialysis can lead to increased morbidity and mortality. We conducted a study to analyze effects of increasing dialysate flow rate (DFR) and blood flow rate (BFR) on adequacy of dialysis. URR was used as an indicator of dialysis adequacy. **Study Design:** Prospective comparative study. **Period:** 02 months (February 2017 to March 2017). **Setting:** Department of Nephrology, Lahore General Hospital. **Method:** 40 patients on maintenance hemodialysis were included. We divided study in three phases. First phase with blood flow 300mL/min dialysate flow 500mL/min. Second phase blood flow 350mL/min dialysate flow 500mL/min. Third phase blood flow 300mL/min dialysate flow rate 800mL/min. Blood samples were collected before and after each dialysis session. Urea reduction ratio (URR) was used to measure delivered dose of dialysis and was assessed at the two levels of dialysate flow rate and two blood flow rates. Statistical analysis was done by using SPSS 23.0 software package. P values <0.05 was taken as statistically significant. **Result:** After statistical analysis we reached the conclusion that enhancing blood flow rate from 300 to 350 is associated with an increase of URR of 6.9 % as compared to increasing dialysate flow rate from 500 to 800 of 4.6%. In both settings increase in URR was clinically significant. We can also deduce that increase in dialysate flow will allow us to achieve a substantial increase in dialysis dose as assessed by urea reduction ratio for a given amount of dialysis time when we are unable to achieve a high blood flow rate. Difference in increase in URR for two groups one with increased blood flow and other with increased dialysate flow was statistically insignificant (p value >0.05). **Conclusion:** Our study shows that if we increase blood flow rate to 350 mL/min from 300 mL/min and dialysate flow rate to 800 mL/min from usual 500 mL/min there is significant increase in URR and adequacy of dialysis. We can decrease mortality and morbidity by increasing adequacy to optimal level using both methods according to patient feasibility and clinical status.

Key words: Dialysis Adequacy, URR, Blood Flow in Dialysis, Dialysate Flow in Dialysis.

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INTRODUCTION

Patients fighting end stage renal disease require dialysis support for sustaining life. [1] Adequacy of dialysis delivery is vital in prolonging survival and improving life quality.[2] Our aims are thus to achieve better quality of life, reduce morbidity, and expand total life span in hemodialysis patients.[3] It is only possible if dialysis is performed effectively. One of the important factors is effective hemodialysis (HD) that decreases morbidity and mortality in patients,[4] and when hemodialysis is not adequate it causes increase in mortality of these patients.[5] We can find a lot of surveys indicating how dose of dialysis affect mortality and morbidity in ESRD patients.[6,7,8,9,10,11,12] Sehgal,[13] and colleagues conducted a study which showed how inadequate dialysis can result in increase in cost of treatment and mortality. They reached the conclusion that ineffective dose of dialysis was a cause of increase in hospital stay and increase in total expense of treatment. So by achieving effective dialysis, we will be able to reduce total cost of medical treatment and morbidity.[13] According to the National Cooperative Dialysis Study, by increasing the efficiency of dialysis we can decrease complications of uremia and hence mortality.[5] We can use urea reduction ratio (URR) for assessing Dialysis dose.[14] The URR is assessed by measuring urea levels in blood samples obtained pre and post dialysis. In hemodialysis small solute molecules are removed by diffusion. Convection is another mechanism which is mostly involved in removal of larger molecules.[15,16,17] Ability of hemodialyzer to facilitate diffusion process determines its efficiency.[18,19,20] Factors affecting process of diffusion are temperature, membrane thickness, different dialysate and blood and flow rates, and surface area of dialyzer . By keeping all the other above mentioned factors constant, the process of diffusion will be affected by the concentration gradient between dialysate and blood.[21,22] Diffusion of particles is highly dependent on flow rate of dialysate, flow rate of blood and distribution of countercurrent flow. Efficiency of filtration process will be reduced if blood flow and dialysate flow don't match.[21] Measure of efficiency of dialyzer, in clearance of urea and different solutes of similar molecular weight is called the dialyzer mass transfer area coefficient for urea (KoA).[23] KoA can be defined as maximum theoretical clearance of dialyzer in mL /min for any solute considering flow of blood and dialysate infinite. Mass transfer area coefficient is proportional to membrane surface area in the dialyzer. But when membrane surface area is very large we observe a drop in increase in KoA.[23] Dialysis is low efficiency when KoA value is< 500 mL/min, moderate efficiency if koa of a dialyzer is 500-700 mL/min, routinely used in therapy. "High-efficiency" dialysis has a koa of > 700ml/ hr. It is useful when patient size is large and when 4 hrs of dialysis is not sufficient. If dialysate flow rate is changed from 500 to 800, KoA of a dialyzer is markedly increased but at different blood flow rates KoA of a dialyzer does not change.[24,25,26,27,28] When we increase dialysate flow rate it in turn increases penetration of dialysate in hollow bundle fibers it eventually results in increased effective surface area of dialyzer with greater urea clearance.[30,31] In our study we measured urea reduction ratio in two groups at two different dialysate flow rates keeping other conditions constant and noted increase in urr.

METHODOLOGY

In this prospective comparative study 40 patients on maintenance hemodialysis were included (mean age 44.42 ± 13.18, 62% male, 38% female). Total study period was 2 months (February 2017 to March 2017). No subjects dropped out of this study. The procedure was explained and consent was signed by the patients. Data about age, comorbidities, albumin, weight, height, duration of hemodialysis was collected for all patients. We used same dialysis machines and dialyzer for all patients. The BFR was maintained at 300 mL/min in the first and 350mL/min during second session, respectively. We completed our study in two months. We divided study in three phases. In first phase we kept blood flow at 300 mL/min and dialysate flow at 500 mL/min. Second phase was with blood flow 350 mL/min dialysate flow 500 mL/min. Third phase included blood flow of 300 mL/min and dialysate flow rate of 800 mL/ min. We collected blood samples before starting and after completion of each dialysis session. The reliability and validity of collected data was checked time and again. All emergency cases reporting to dialysis unit, patients without av fistula patients unable to tolerate 4 hr sessions and with hemodynamic instability were excluded. We included patients having patent and working arteriovenous fistula, patients registered at our dialysis units with proper follow up having proper history with all clinical record, having 4 hrs dialysis two times a week, they were on hemodialysis for at least 1 year and those who were fully cooperative and willing to enroll for the study. Explained informed consent was obtained. The presence of comorbidities diabetes mellitus (DM), hypertension (HTN), and chronic liver disease (CLD) was confirmed from clinical record. We calculated URR by following formula: (Urea pre dialysis - Urea post dialysis /Urea pre dialysis X 100%).[32] The pre-dialysis samples for blood urea level were drawn immediately prior to hemodialysis, whereas we collected post-dialysis samples 45 min after the patient's blood had been reinfused. Our patients received dialysis twice a week in 4 hour sessions. We kept dialysate temperature in all treatments 36-37°C. The dialysate composed of following elements: potassium 2.0 mmol/L, sodium 138 mmol/ L , magnesium 0.50 mmol/L, calcium 1.25 mmol/L, acetate 3.0 mmol/L chloride 108.5 mmol/L and bicarbonate 32.0 mmol/L. We used Freseniuss model

4008S dialysis machine in all dialysis sessions. Pre dialysis and post dialysis urea levels were noted keeping treatment time and rate of blood flow constant.

The average values of blood urea levels were taken for each patient. Urea reduction ratio (URR) was used to measure delivered dose of dialysis and was assessed at the two levels of dialysate and blood flow rates. Statistical analysis was done by using SPSS 23.0 software package. P values< 0.05 was taken as statistically significant.

RESULTS

After statistical analysis we reached the conclusion that enhancing BFR from 300 to 350 is associated with an increase of URR of 6.9 % as compared to increasing DFR from 500 to 800 of 4.6%. In both settings increase in URR is clinically significant. We can also deduce that increase in dialysate flow will allow us to achieve a substantial increase in dialysis dose as assessed by urea reduction ratio for a given amount of dialysis time when we are unable to achieve a high blood flow rate. Difference in increase in URR for two groups one with increased blood flow and other with increased dialysate flow was statistically insignificant (p value >0.05).

Variable	Frequency	Percentage
Male	25	62.5%
Female	15	37.5%
Age 18-40	16	40%
41-60	20	50%
>60	4	10%
Hep B positive	3	7.5%
Hep C positive	18	45%
HTN	20	50%
DM	6	15%
Blood Flow 300	40	100%
Blood Flow 350	40	100%
Dialysate flow 500	40	100%
Dialysate flow 800	40	100%

Table-I. Patient's characteristics chart

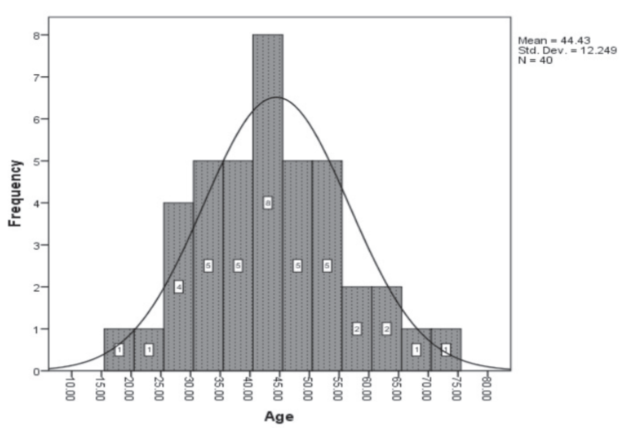

Figure-1. Means plots

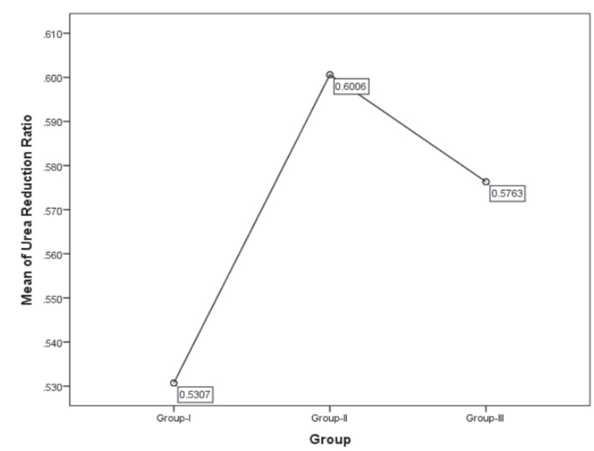

Figure-2.

	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.
Tukey HSD	Group-I	Group-II	-.069888*	.016372	.000
		Group-III	-.045606*	.016259	.016
	Group-II	Group-I	.069888*	.016372	.000
		Group-III	.024283	.017300	.342
	Group-III	Group-I	.045606*	.016259	.016
		Group-II	-.024283	.017300	.342
LSD	Group-I	Group-II	-.069888*	.016372	.000
		Group-III	-.045606*	.016259	.006
	Group-II	Group-I	.069888*	.016372	.000
		Group-III	.024283	.017300	.163
	Group-III	Group-I	.045606*	.016259	.006
		Group-II	-.024283	.017300	.163

Table-II.

Further Research Findings

We observed that in our set up we are not getting optimum dialysis dose and URR on usually practiced blood flow of 300mL/min and dialysate flow of 500mL/min.

CONCLUSION

Our study shows that if we increase rate of blood flow to 350 mL/ min from 300 mL/min and rate of dialysate flow to 800 mL/ min from usual 500 mL/ min there is significant increase in URR and adequacy of dialysis. We can decrease mortality and morbidity by increasing adequacy to optimal level using both methods according to patient feasibility and clinical status. Hemodialysis is major modality to treat patients with ESRD who require renal replacement therapy. Scientists since 1970 have been trying to decrease treatment time and increase urea clearance these efforts led to development of high efficiency dialysis. Dose of treatment is not totally decided by time of treatment, it is also determined by dialyzer characteristics like dialysate and blood flow rate. In old times we used to estimate quantity of dialysis by time of treatment when we had low efficiency dialysis and low blood flow rates. Now a days we do not use time of treatment to express quantity of treatment as efficiency is very variable. KOA for a dialyzer decides the mass transfer barrier between the dialyzer and blood pathways in a hemodialyzer. We can reduce the thickness of stagnant fluid layer for both blood compartment and dialysate compartment by increasing respective flow rates.[25] In this study we investigated the changes in urea clearance on different flow rates for dialysate and blood. In our local hospital settings, we studied dialysis efficiency over two different blood flow rates 300 & 350 mL/min and dialysate flow rates 500 & 800 mL/min in Pakistani population. We collected blood samples just before initiation of dialysis and 45 minutes after completion of dialysis. The increase in URR with increased flow rate of dialysate depicts that dialysate stagnant fluid layer offers a significant resistance to urea transfer. An improved flow distribution in the dialysate compartment secondary to increased flow rate of dialysate might be the cause for increase in URR.[21] A flow rate of 800 mL/ min caused an increase in URR by about 4.6% when a high-efficiency dialyzer is used. These increases in URR are clinically important and would permit significant increases in dialysis dose given a fixed treatment time.

We observed that in our set up we are not getting optimum dialysis dose and URR on usually practiced blood flow of 300 mL/min and dialysate flow of 500 mL/min. Thus it can be concluded that these results are in concordance with the observation that both increased flow rates of dialysate and blood, increase the efficacy of dialysis which ultimately reduces the cost of treatment, morbidity and mortality of patients on maintenance hemodialysis.

Limitations of the Research

1. Number of patients was not very large.
2. Association of different comorbidities with dialysis adequacy and association with urr after increasing blood flow and dialysate flow were not established.
3. We observed that in our set up we are not getting optimum dialysis dose and URR on usually practiced blood flow of 300mL/min and dialysate flow of 500mL/min.

Conflict of Interest

The authors of the study declare no financial or any other conflict of interest related with the study.

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You cannot push anyone up the ladder unless he is willing to climb.

– Andrew Carengie –

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Aurangzeb Afzal	Conceived idea, Designed Research, Manuscript, Final reading and approval.	
2	Adnan Shabbir	Literature search, Data collection, Manuscript writing, Assessed parameters.	
3	Maira Iqbal Malik	Literature search statistical analysis, Data interpretation manuscript writing.	