Cystatin C Reduction Ratio as an Indicator for Adequacy of Hemodialysis

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Abstract: Accurate measurement of adequacy of haemodialysis is essential for evaluation of the care provided to patients with end stage renal disease on regular haemodialysis. Adequacy of haemodialysis is often measured using urea reduction ratio or kt/v. The usefulness of serum cystatin C reduction as an indicator of adequacy of haemodialysis is not known with certainty, therefore the present study will be undertaken in order to evaluate the potential clinical utility of serum cystatin C determination in patients undergoing haemodialysis**.** Aim of the work: This study will be conducted on 40 patients with end stage renal disease on regular haemodialysis by measurement of serum cystatin C before and after dialysis session to evaluate cystatin C reduction ratio as an indicator for adequacy of haemodialysis compared to urea reduction ratio, and serum creatinine.
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1. Introduction

Chronic kidney disease (CKD) and end-stage renal disease (ESRD) are major health problems worldwide with dramatically increasing incidence and prevalence. The evaluation of glomerular filtration rate (GFR) is very important to diagnosis of CKD (Zhang and Rothenbacher, 2008).

Adequacy of hemodialysis improves patient survival, quality of life and biochemical outcomes and minimizes disease complications and hospitalizations. Blood tests, body weight and blood pressure are measured before and after hemodialysis. Single-pool Kt/V and urea reduction ratio (URR) are calculated. The targets based on the National Kidney Foundation Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines are Kt/V > 1.2 and URR>65% Attempts to achieve the desired goals are necessary. It is important to calculate Kt/V or URR and individualize the dialysis doses for each patient (Adas et al., 2012).

Serum cystatin C (Scys-C) recently was proposed as a promising alternative marker of GFR owing to better specificity and sensitivity for detecting residual kidney function. However, several studies have reported that Scys-C was superior to serum creatinine as a marker of GFR (Pei et al., 2012).

Currently the determination of serum cystatin C has been proposed as an additional parameter for assessment of renal function. Cystatin C is a single non- glycosylated polypeptide chain consisting of 120 amino acid residues with a molecular mass of 13 kDa. Low molecular weight proteins are now recognized as a distinct class of uremic toxins and numerous compounds in this category have been identified including cystatin C. Serum cystatin C is produced at a constant rate by all nucleated cells and freely filtered by the glomerulus, it is neither secreted nor reabsorbed and has been known to be unaffected by non- renal factors. Therefore serum cystatin C is known to be an excellent surrogate marker of glomerular filtration rate (Ledson et al., 2008).

The usefulness of serum cystatin C levels as an indicator of the efficacy of hemodialysis is not known with certainty (Krishnamurthy et al., 2010). Therefore the present study will be undertaken in order to evaluate the potential clinical utility of serum cystatin C determination in patients undergoing hemodialysis.

2. Materials and Methods

Inclusion crieteria:

-End stage renal disease on regular haemodialysis
-Duration of haemodialysis more than one year
-Age =30 – 60 years
-Gender: male and female

Exclusion crieteria:

-Patients with sepsis

All patients will be subjected to the following:

1-Full history including duration of haemodialysis
2-Clinical examination
3-Investigations:
-Serum creatinine
-Blood urea

-Urea reduction ratio (URR): By measurement of blood urea before and after haemodialysis cession

-Glumerular filtration rate (GFR): By Cockroft Gault equation

-Cystatin C reduction ratio: By measurement of serum cystatin C before and after haemodialysis cession

-Complete blood count (CBC)

-Serum calcium

-Serum phosphorous

3. Result:

The study proved that serum cystatin C reduction ratio is highly significant as an indicator for adequacy of haemodialysis compared to urea reduction ratio and kt\v

The mean age of the studied sample was 49.78 ± 7.1 years and ranged from 31 – 59 years.

Table (1): Pre-dialysis and post-dialysis laboratory findings among the studied group

Parameter	Pre-dialysis		Post-dialysis	
	Mean ± SD	Range	Mean ± SD	Range
Albumin	3.45 ± 0.51	(2.3 – 4.3)	ND	ND
Hemoglobin	10.28 ± 1.83	(7.1 – 14.2)	ND	ND
Calcium	8.43 ± 1.16	(5.7 – 10.3)	ND	ND
Phosphorus	4.42 ± 1.34	(1.5 – 6.9)	ND	ND
Creatinine	9.71 ± 2.36	(4.8 – 13.6)	ND	ND
Blood urea	127.95 ± 33.48	(56 – 212)	48.68 ± 16.7	(21 – 94)
Urea reduction ratio	61.74 ± 8.88 (33.71 – 78.38)			
Cystatin C	9.53 ± 7.46	(1.5 – 50)	4.13 ± 2.45	(0.7 – 11.7)
Cystatin reduction ratio	49.77 ± 28.12 (1.89 – 89.6)			

Table (2): Effectiveness of dialysis calculated in referral to Urea reduction ratio and Kt/V ratio

Parameter		Frequency	%
Urea reduction ratio	*Effective ≥ 65*	14	35
	Not effective < 65	26	65.0
Kt/V ratio	*Effective ≥ 1.2*	40	100.0

Table (3): Correlation between blood chemistry before dialysis at one side and blood Urea & Cystatin before dialysis on the other hand

Parameter	Blood Urea		Cystatin	
	Pearson correlation	p-value	Pearson correlation	p-value
Hemoglobin	-0.14	0.39	0.09	0.6
Albumin	-0.12	0.47	0.04	0.79
Creatinin	0.61	0.000	0.12	0.46
Calcium	-0.38	0.016	0.17	0.3
Phosphorus	0.482	0.002	-0.17	0.3

Table (4): Correlation between blood chemistry before dialysis at one side and blood Urea & Cystatin after dialysis on the other hand

Parameter	Blood Urea		Cystatin	
	Pearson correlation	p-value	Pearson correlation	p-value
Hemoglobin	-0.19	0.24	-0.32	0.048
Albumin	0.04	0.83	-0.07	0.66
Creatinin	0.28	0.08	0.16	0.32
Calcium	-0.31	0.05	-0.17	0.3
Phosphorus	0.33	0.037	-0.26	0.1

Table (5): Correlation between blood chemistry before dialysis at one side and Urea RR & CysCRR on the other hand

Parameter	Urea RR		CysCRR	
	Pearson correlation	p-value	Pearson correlation	p-value
Hemoglobin	0.053	0.75	0.316	0.047
Albumin	-0.184	0.26	0.014	0.93
Creatinin	0.252	0.12	-0.092	0.57
Calcium	0.081	0.62	0.19	0.24
Phosphorus	0.03	0.86	-0.012	0.94

Table (6): Correlation between blood Urea and Cystatin levels before and after dialysis

Parameter	Pearson Correlation	p-value
Blood urea # Cystatin (before)	-0.07	0.68
Blood urea # Cystatin (after)	0.00	1.0
Urea reduction ratio # Cystatin reduction ratio	0.29	0.07

Table (7): Correlation between Urea reduction ratio & Cystatin reduction ratio with Kt/V ratio

Parameter	Pearson Correlation	p-value
Urea reduction ratio # Kt/V	0.26	0.11
Cystatin reduction ratio # Kt/V	0.43	0.006

Table (8): Mean CysCRR in relation to abnormalities among laboratory tests done before dialysis

Parameter		CysCRR Mean ± SD	Significance	
			t-test	p-value
Hemoglobin	normal (n=16)	63.2 ± 24.27	2.65	0.012
	abnormal (n=24)	40.8 ± 27.35		
Albumin	normal (n=25)	48.4 ± 29.98	0.395	0.7
	abnormal (n=15)	52.1 ± 25.56		
Calcium	normal (n=28)	52.55 ± 26.56	0.96	0.35
	abnormal (n=12)	43.27 ± 31.73		
Phosphorus	normal (n=28)	50.86 ± 28.13	0.37	0.71
	abnormal (n=12)	47.23 ± 29.17		

Variable	Effective dialysis URR ≥ 65% (n= 14)	Non effective dialysis URR < 65% (n= 26)
Cystatin reduction ratio	63.96 ± 24.35	42.13 ± 27.42
	t-test = 2.49 P-value = 0.017	
ROC curve (AUC)*	0.717	
Sensitivity in relation to URR	0.71	
Specificity in relation to URR	0.62	

Table (9): Comparison between mean Cystatin reduction ratio among the studied group regarding the resultant Urea reduction ratio (OR: according to dialysis effectiveness calculated by Urea RR)
* ROC = Receiver Operating Characteristic – AUC = area under the curve

4. Discussion

Cystatin C is a low molecular mass plasma protein, which is synthesized and secreted constantly by all nucleated cells, it is freely filtered through the glomerulus and almost completely reabsorbed and catabolized by tubular cells, such that it will not return to the blood in an intact form **(Ogawa et al., 2008).**

There is strong association of serum cystatin C with mortality and cardiovascular disease than serum creatinine, particularly in studies of older adults **(Lesely et al., 2009).**

This prospective study was conducted in January 2016 on end stage renal disease patients that were on regular haemodialysis in Sidnawy health insurance hospital in Cairo.

Total number of cases was 40, our study was performed to assess usefulness of the use of cystatin C reduction ratio as an indicator of adequacy of haemodialysis.

In this study, our patients were chosen according to specific crieteria such as:

Inclusion crieteria:

1- End stage renal disease on regular haemodialysis for a period longer than one year.

2- Age between 30 – 60 years old

3- Gender: male and female

Exclusion crieteria:

1- Patients with acute renal failure

2- Pregnancy

3- Patients with sepsis

Our patients were informed about the study, they gave consent then we started our study

1- Full history including clinical diseases, duration of haemodialysis, cause of renal failure.

2- Clinical examination, general and abdominal examination

3- Laboratory investigations:

-Before starting haemodialysis session: blood haemoglobin, blood urea, serum creatinin, serum calcium, serum phosphorous, serum cystatin C.

-After haemodialysis session: Blood urea, serum cystatin C.

4- After collecting lab results, calculation of urea reduction ratio (URR), kt\v and cystatin C reduction ratio was done and results are listed and then, by statistical analysis the following results were obtained:

Conclusion:

We conclude that serum cystatin C reduction ratio can be a useful marker for assessment of adequacy of haemodialysis in patients with end stage renal disease on regular haemodialysis.

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