International Journal of Biotechnology and Clinical Medicine ISSN 2583-4665
Vol.2, No.1, Jan - Mar 2023, pp. 20~24

PROTEIN CATABOLISM AND UREA MANAGEMENT IN DIALYSIS PATIENTS – A MINI-REVIEW

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Article Info

Article history:

Received February 18th, 2023
Revised March 12th, 2023
Accepted March 24th, 2023

Keyword:

Uremia
Dialysis
Protein catabolism
Comorbidity
Health science

ABSTRACT

Chronic Kidney Disease patients undergoing hemodialysis need thrice weekly dialysis to get good control and prevent morbidity and mortality. In certain comorbid conditions like HCV, cardiac failure, diabetes, and hypertension, URR can be improved by increasing the time of dialysis and blood flow in the dialyzer.

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How to Cite:

Senthil R. Protein catabolism and Urea management in dialysis patients – A mini Review. IJBTCM. 2023; Volume 2 (Issue 1): Page 20-24.

1. INTRODUCTION

Current dialysis techniques provide only about 15% of the urea clearance compared to the normal real function. Dialysis patients have mortality rates 5-20 times higher than a normal individual of similar age [1]. Numerous studies have demonstrated a link between mortality and measures to quantify dialysis efficiency, including clearance of Urea, Creatinine [2]. Measurement of the dialysis dose (duration & frequency of dialysis) has mostly relied on the estimation of urea clearance. An indicator of fractional urea clearance is the ratio Kt/V. It's calculated utilizing UKM (Urea Kinetic Modelling) [3]. Since the relative decrease in urea concentration during dialysis is the main factor affecting Kt/V, calculating the dialysis dosage directly from the URR is simpler than using more complicated calculations [4]. Numerous research studies have established a link between poor outcomes of hemodialysis patients and insufficient urea reduction ratio (URR). The mortality rate was decreased from 22.5 to 18.1 percent annually by raising the URR from 61 to 70% [5]. 5S l As a result, URl is performed once per 12–14 cycles of dialysis, or roughly once every month. The session-to-session variation in URR and Kt/V is small in stable hemodialysis patients. So URR can be used to assess dialysis adequacy m hemodialysis patients [6].

2. PROTEIN CATABOLIZATION AND UREA

Protein catabolization produces urea. Proteolysis is the process that converts protein into amino acids [7–9]. Ammonia is created through the transamination and oxidative deamination of amino acids. To create urea, ammonia enters the urea cycle [10]. Kidneys are responsible for the body's primary urea removal. Since the kidneys eliminate more than 90% of urea, urea buildup in the blood is a sign of renal illness. Tubules do not actively reabsorb or emit urea; the glomerulus filters it freely. In a healthy kidney, 40–70% of highly diffusible urea passively exits the renal tubule, enters the interstitium, and then returns to the plasma [11]. Less enters the interstitium at high flow rates due to this reverse diffusion. The glomerular filtration rate is thus typically

underestimated by urea clearance. The osmotic diuresis in the remaining functioning nephrons in end-stage renal disease limits back diffusion of urea, bringing urea clearance closer to inulin clearance [12]. It ought to be simple to measure. It should build up in uremia and be simple to eliminate by dialyzer. Urea best satisfies these criteria in end-stage renal failure. Because urea measures dialyzer clearance rather than toxicity, it is utilized as a marker. [13].

3. FATE OF UREA

Urea is simple to test and highly concentrated in uremic patients. You may think urea clearance as a signal for removing other, more harmful solutes [14]. Studies have connected prognosis in hemodialysis patients to factors determined by urea clearance. Compared to other solutes, urea's low molecular weight makes it considerably simpler to forecast the clearance rate and fluctuations in blood concentration [7]. It is a small globular protein with a molecular weight of 66.3 kDa. It is most prevalent in plasma (up to half of plasma protein mass). The majority of extracellular bodily fluids, including CSF, interstitial fluid, urine, and amniotic fluid, include it as a significant protein. It lacks a carbohydrate side chain, but since it has a large net negative charge at physiological pH, it is very soluble in water [15]. A gene on the long arm of the chromosome codes for albumin. The hepatic parenchymal cells in the liver produce albumin. Consumption of protein and colloidal osmotic pressure both influence the rate of synthesis. All tissues undergo catabolism, primarily by pinocytosis [16]. The acquired free amino acids are then utilized to create new proteins in living things. The preservation of colloidal osmotic pressure in extravascular space and blood vessels [17]. Many different substances, including free fatty acids, phospholipids, metallic ions, amino acids, medicines, hormones, and bilirubin, are bound and transported by albumin. Analbuminemia: Rare genetic disorder <0.5g/dl. Complications are related to abnormal lipid transport.

4. INFLAMMATION AND UREA

Both acute and long-lasting inflammations lower albumin levels in the blood due to hemodilution, extravascular space loss, increased cell consumption, and reduced production [18]. Reduced owing to reduced production and loss into extravascular space in hepatic illness. Albumin is generally tiny and spherical. Therefore a large proportion filters into the glomerulus during urination. The proximal tubule absorbs the majority of it. Up to 20 mg of albumin per gram of creatinine can be found in normal voided urine [19]. Excretion over this point demonstrates greater tubular or glomerular filtration. Physical activity and fever both show physiological increases. 3.5 to 5.2 gm/dl is the normal range [20].

It is cyclic anhydride of creatine produced as the product of the decomposition of phospho creatine is excreted in the urine. Creatinine is synthesized in the kidneys, liver, and pancreas [21–23]. Two enzymatically mediated reactions are seen. Transamidation of arginine & glycine to form guanidino acetic acid occurs in the kidneys. Methylation of guanidino acetic acid with s- adenosyl methionine as methyl donor occurs in the liver [24]. Creatine is transported to the muscle's brain, where it 1s phosphocreatine. A distinctive aspect of the metabolic process that causes muscular contraction is the interconversion of phosphocreatine and creatine. Muscle tissue spontaneously and permanently transforms a part of its free creatine to its anhydride waste product, creatinine. As a result, the daily production of creatinine is generally stable and correlated with muscle mass [25]. In good health, the blood's level of creatinine is largely stable. Endogenous production of creatinine and continual release into bodily fluids. Glomerular filtration is the principal mechanism by which its plasma concentration is kept within strict bounds [26].

5. GLOMERULLAR FILTRATION RATE AND UREA

Both plasma creatinine concentration and renal clearance have been utilized to measure the glomerular filtration rate. Even when serum creatinine is normal or hardly abnormal, significant renal impairment may still exist [27]. When creatinine clearance drops below 253/c> of normal, renal function gradually diminish, although symptoms frequently do not become noticeable until severe renal failure. Although serum creatinine is frequently used to estimate creatinine clearance, it is a poor predictor of glomerular filtration rate because assay techniques, endogenous and exogenous substances, renal tubular handling of creatinine, and other factors can all have unpredictable effects on serum creatinine (age, sex, body weight, muscle mass, diet, drugs) [28].

Because of left ventricular hypertrophy, cardiac failure happens. Two kinds of left ventricular hypertrophy exist. It can be left ventricular dilatation or concentric hypertrophy [29]. Congestive heart failure results from the diastolic or systolic dysfunction caused by this. Left ventricular failure first appears in chronic renal failure due to hypertension, followed by anemia [29]. Fluid overload is also a risk for left ventricular hypertrophy in patients who are dialysis dependent. Renal damage 1s brought on by persistent hypertension l4J Renal function rapidly declines when malignant hypertension is present. The cause of renal injury is arterial necrosis [30].

Hyaline (pink, amorphous, homogenous substance) builds up in the walls of tiny arteries and arterioles in the kidneys as a result of benign arterial hypertension, causing the thickening of their walls and the narrowing of the lumina (hyaline arteriolosclerosis) [31]. Tubular atrophy, interstitial fibrosis, glomerular changes (smaller glomeruli with varying degrees of hyalinization - from moderate to sclerosis of glomeruli), and periglomerular fibrosis are all effects of subsequent ischemia [32]. Renal failure will happen at a later stage. Tubules in functional nephrons are dilated and frequently exhibit hyaline casts in the lumen. The glomerular damage that causes proteinuria and hematuria due to hypertensive nephropathy also frequently results in additional problems [33,34].

95% of CKD patients develop hypertension, which is brought on by sodium chloride retention, abnormally high renin levels compared to the amount of extracellular fluid that has been expended, sympathetic stimulation via renal afferent reflexes, and impaired renal endothelial function with low nitric oxide and increased endothelin production [35]. If left untreated, this kind of hypertension is far more likely than essential hypertension to progress to the malignant phase. There is ample evidence that shows that chronic hypertension worsens renal function. Regardless of the patient's gender, race, age, or kidney disease etiology, high blood pressure causes the kidneys to fail more quickly [36]. However, there is proof that renal damage can be delayed by properly managing high blood pressure. One of the finest things a person can do to prolong the life of their kidneys is to reduce blood pressure [37]. Renal injury in hypertension individuals is a gradual process that takes decades to manifest. Renal failure, therefore, arises in older hypertension individuals [38].

6. BENEFITS OF HOME HEMODIALYSIS

In addition, in 1964, the University of Washington created a program for home hemodialysis (HHD). The families found the twice-weekly 12- to 16-hour schedule to be challenging, and some patients continued to experience the same medical issues with nerve damage and insufficient blood pressure regulation [39]. The families found it easier when the dialysis schedules were adjusted thrice weekly and shifted to overnight sessions lasting 8 to 10 hours. The patient's total stamina increased thanks to this nocturnal routine, which improved blood pressure management, reduced nerve damage, loosened food limitations, and significantly improved patient rehabilitation [40]. Another benefit of HHD was that it was more economical. Because of a lack of funding, not all patients underwent dialysis. There were undoubtedly several variables involved in the change from the lengthy three-times-per-week program to the present routine. Free-standing dialysis units and for-profit dialysis firms proliferated when Medicare began to fund dialysis in 1973. With a three-times-weekly plan, dialysis sessions were shortened to accommodate three and occasionally four shifts of patients per day [41].

7. CONCLUSION

Dialysis times were shortened to treat more patients in less time when high flux/more efficient dialyzers were available. Given that it maximized convenience, the patients favored this. The first consideration is the community's economic situation, which the medical center serves. In areas where state funding or insurance benefits are available, ESRD care is frequently consistent, but in areas where there is no government assistance for the treatment of ESRD, the frequency of dialysis is based on the ability of the patient to pay. Therefore, a diverse picture frequently comes to light when discussing a nation like India.

ACKNOWLEDGEMENTS

The encouragement and support from Bharath University, Chennai, are gratefully acknowledged for providing the laboratory facilities to conduct the research.

FUNDING

Nil

ETHICAL APPROVAL

Nil

COMPETING INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Turner NN, Lameire N, Goldsmith DJ, Winearls CG, Himmelfarb J, Remuzzi G, editors. Oxford textbook of clinical nephrology. Oxford University Press; 2015.
2. Painter P. Physical functioning in end-stage renal disease patients: Update 2005. Hemodial Int. 2005;9(3):218–235.
3. Casino FG, Marshall MR. Simple and accurate quantification of dialysis in acute renal failure patients during either urea non-steady state or treatment with irregular or continuous schedules. Nephrol Dial Transplant. 2004;19(6):1454–66.
4. Chertow GM, Owen WF, Lazarus JM, Lew NL, Lowrie EG. Exploring the reverse J-shaped curve between urea reduction ratio and mortality. Kidney Int. 1999;56(5):1872–1878.
5. Parker III TF, Husni L, Huang W, Lew N, Lowrie EG, Associates DN. Survival of hemodialysis patients in the United States is improved with a greater quantity of dialysis. Am J kidney Dis. 1994;23(5):670–680.
6. Kloppenburg WD, Stegeman CA, Hooyschuur M, Van Der Ven J, De Jong PE, Huisman RM. Assessing dialysis adequacy and dietary intake in the individual hemodialysis patient. Kidney Int. 1999;55(5):1961–1969.
7. Ikizler TA, Sezer MT, Flakoll PJ, Hariachar S, Kanagasundaram NS, Gritter N, et al. Urea space and total body water measurements by stable isotopes in patients with acute renal failure. Kidney Int. 2004;65(2):725–732.
8. Ganesh PS, Veena K, Senthil R, Iswamy K, Ponmalar EM, Mariappan V, Girija AS, Vadivelu J, Nagarajan S, Challabathula D, Shankar EM. Biofilm-associated Agr and Sar Quorum sensing systems of Staphylococcus aureus are inhibited by 3-Hydroxybenzoic acid derived from Illicium verum. ACS omega. 2022;7(17):14653-65.
9. Rajasekaran E, Rajadurai M, Vinobha CS, Senthil R. Are the proteins being hydrated during evolution?. J. Comput. Intelli. Bioinfo. 2008;1(2-3):115-9.
10. Gupta A. Metabolism of proteins and amino acids. In: Comprehensive Biochemistry for Dentistry. Springer; 2019. p. 377–393.
11. Thompson S, James M, Wiebe N, Hemmelgarn B, Manns B, Klarenbach S, et al. Cause of death in patients with reduced kidney function. J Am Soc Nephrol. 2015;26(10):2504–2511.
12. Marsh DJ, Segel LA. Analysis of countercurrent diffusion exchange in blood vessels of the renal medulla. Am J Physiol Content. 1971;221(3):817–828.
13. Twardowski ZJ. We should strive for optimal hemodialysis: a criticism of the hemodialysis adequacy concept. Hemodial Int. 2003;7(1):5–16.
14. Depner TA. Prescribing hemodialysis: a guide to urea modeling. Springer Science & Business Media; 2012; 29.
15. Ali M. A Study of Reference Ranges for Biochemical and Hematological Parameters in the Healthy Population of Bangladesh. University of Rajshahi; 2016.
16. Miller MA, Zachary JF. Mechanisms and morphology of cellular injury, adaptation, and death. Pathol basis Vet Dis. 2017;2.
17. Matsushita S, Chuang VTG, Kanazawa M, Tanase S, Kawai K, Maruyama T, et al. Recombinant human serum albumin dimer has high blood circulation activity and low vascular permeability in comparison with native human serum albumin. Pharm Res. 2006;23(5):882–891.
18. Hankins J. The role of albumin in fluid and electrolyte balance. J Infus Nurs. 2006;29(5):260–265.
19. Fan S-L, Bai S. Urinalysis. In: Contemporary Practice in Clinical Chemistry. Elsevier; 2020. p. 665–80.
20. Ahmad S, Maqbool A, Srivastava A, Gogoi S, Siddiqui FA, Panwar S. Urine analysis revisited: A review. Ann Int Med Dent Res. 2018;5(1):22.
21. Nogdallah NAA. Assessment of Plasma Creatinine and Urea Level among Fuel Benzene Station Workers in Khartoum State. Sudan University of Science & Technology; 2015.
22. Manivannan C, Meenakshi Sundaram K, Sundararaman M, Renganathan R. Investigation on the inclusion and toxicity of acriflavine with cyclodextrins: A spectroscopic approach. Spectrochim Acta - Part A Mol Biomol Spectrosc. 2014;122:164–170.
23. Viswanathan A, Kute D, Musa A, Konda Mani S, Sipilä V, Emmert-Streib F, et al. 2-(2-(2,4-dioxopentan-3-ylidene)hydrazineyl)benzonitrile as novel inhibitor of receptor tyrosine kinase and PI3K/AKT/mTOR signaling pathway in glioblastoma. Eur J Med Chem. 2019;166:291–303.
24. Ardalan M, Batista ED, Titgemeyer EC. Effect of post-ruminal guanidinoacetic acid supplementation on creatine synthesis and plasma homocysteine concentrations in cattle. J Anim Sci. 2020;98(3):skaa072.
25. Gropman AL, Pappa B, Mew NAH. The urea cycle disorders. Neurobiol Dis. 2016;440.
26. Conrad KP, Stillman IE, Lindheimer MD. The kidney in normal pregnancy and preeclampsia. In: Chesley's hypertensive disorders in pregnancy. Elsevier; 2015:335–77.
27. Lopez-Giacoman S, Madero M. Biomarkers in chronic kidney disease, from kidney function to kidney damage. World J Nephrol. 2015;4(1):57.
28. Huttner A, Von Dach E, Renzoni A, Huttner BD, Affaticati M, Pagani L, et al. Augmented renal clearance, low β-lactam concentrations and clinical outcomes in the critically ill: an observational prospective cohort study. Int J Antimicrob Agents. 2015;45(4):385–392.
29. Lovic D, Narayan P, Pittaras A, Faselis C, Doumas M, Kokkinos P. Left ventricular hypertrophy in athletes and hypertensive patients. J Clin Hypertens. 2017;19(4):413–417.
30. Unver S, Kavlak E, Gümüsel HK, Celikbilek F, Esertas K, Muftuoglu T, et al. Correlation between hypervolemia, left ventricular hypertrophy and fibroblast growth factor 23 in hemodialysis patients. Ren Fail. 2015;37(6):951–956.
31. Le HT, Murugesan A, Ramesh T, Yli-Harja O, Mani SK, Kandhavelu M. Molecular interaction of HIC, an agonist of P2Y1 receptor, and its role in prostate cancer apoptosis. Int J Biol Macromol. 2021;189:142-150.

32. Seccia TM, Caroccia B, Calò LA. Hypertensive nephropathy. Moving from classic to emerging pathogenetic mechanisms. J Hypertens. 2017;35(2):205–212.
33. Vujkovic M, Keaton JM, Lynch JA, Miller DR, Zhou J, Tcheandjieu C, et al. Discovery of 318 new risk loci for type 2 diabetes and related vascular outcomes among 1.4 million participants in a multi-ancestry meta-analysis. Nat Genet. 2020;52(7):680–691.
34. Jayaraj V, Vijayasarathy M, Geerthana R, Senthil R, Rajasekaran E. Pattern recognition in proteins based on carbon content. J Comput Intell Bioinform. 2009;2:99-102.
35. Hall JE, do Carmo JM, da Silva AA, Wang Z, Hall ME. Obesity, kidney dysfunction and hypertension: mechanistic links. Nat Rev Nephrol. 2019;15(6):367–385.
36. Morrell NW, Aldred MA, Chung WK, Elliott CG, Nichols WC, Soubrier F, et al. Genetics and genomics of pulmonary arterial hypertension. Eur Respir J. 2019;53(1):1801899.
37. Vanmassenhove J, Kielstein J, Jörres A, Van Biesen W. Management of patients at risk of acute kidney injury. Lancet. 2017;389(10084):2139–2151.
38. Kellum JA, Romagnani P, Ashuntantang G, Ronco C, Zarbock A, Anders H-J. Acute kidney injury. Nat Rev Dis Prim. 2021;7(1):1–17.
39. Saravanan KM, Selvaraj S. Performance of secondary structure prediction methods on proteins containing structurally ambivalent sequence fragments. Peptide Science. 2013;100(2):148-153.
40. Saravanan KM, Kannan M, Meera P, Bharathkumar N, Anand T. E3 ligases: a potential multi-drug target for different types of cancers and neurological disorders. Future Medicinal Chemistry. 2022;14(3):187-201.
41. Govindaraj S, Renganathan S. Molecular characterization and phytochemical studies of Pleurotus sp to unveil species diversity and pharmacological activities. J Pure Appl Microbiol. 2017;11:891-902.