Review Article

Absorbents therapy, as a conservative option, can improve kidney function in chronic kidney disease

Abedi, B[1], Karimian, R[2], Bahari, Z[3], Iman, M[4, 5*]

1. *Faculty of Advanced Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran*
2. *Chemical Injuries Research Center, Systems Biology and poisonings institute, Baqiyatallah University of Medical Sciences, Tehran, Iran*
3. *Department of Physiology and Medical Physics, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran*
4. *Department of Pharmaceutics, Faculty of Pharmacy, Baqiyatallah University of Medical Sciences, Tehran, Iran*
5. *Nano Biotechnology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran*

How to cite this article: **Abedi B, Karimian R, Bahari Z, Iman M. Absorbents therapy, as a conservative option, can improve kidney function in chronic kidney disease. Archives of Razi Institute Journal. 2024;79(4):695-700.** DOI: 10.32592/ARI.2024.79.4.695

ABSTRACT

Chronic kidney disease (CKD), also called chronic kidney failure, is increasingly recognized as a global public health problem in the entire world. It is characterized by slow, progressive, and irreversible loss in kidney physiology. Today, the prevalence of CKD is increasing dramatically. CKD can affect almost every organ system, including the cardiovascular system. Many treatments have been attempted for CKD, such as renal transplantation, hemodialysis (HD), and peritoneal dialysis (PD). At the end stage of CKD, HD is the most widely used therapy throughout the world. However, these options can decrease volume expansion and uremic solute retention and also increase patient survival. Furthermore, there are certain complications associated with the use of these methods. Previous studies have reported that the main side effects are headaches, muscle cramps, abdominal pain, hypotension, hypertension, vomiting, and constipation. Therefore, the investigation for better and more convenient dialysis techniques should continue, as well as the search for a better material to enhance the clearance of nitrogenous waste products from the body. The intestine has a significant effect on the clearance of nitrogenous waste products from the body, making it a potentially appropriate site for CKD management. The potential mechanism of the intestinal dialysis technique is that it can absorb excess fluids, uremic toxins, and electrolytes within the gastrointestinal (GI) tract and exert them in the feces before they can be absorbed into the blood. In the present review, we will focus on different absorbents as a conservative treatment to remove uremic waste metabolites from the GI tract for the improvement of kidney function in CKD.

Keywords: Absorbents, Chronic kidney disease, Conservative treatment, GI tract

Article Info:
Received: 13 October 2023
Accepted: 11 December 2023
Published: 31 August 2024

Corresponding Author's E-Mail:
iman1359@yahoo.com

1. Context

Chronic kidney disease (CKD) is characterized as the disruption of renal structure or renal function (1). Many therapies have been suggested for CKD, including renal transplantation, hemodialysis (HD), and peritoneal dialysis (PD). However, there are certain disadvantages associated with the use of these methods. Additionally, both HD and PD are invasive and expensive (2). In HD, the waste and excess water are eliminated through an external filter called a dialyzer, which contains a semipermeable membrane. The separation of wastes is done by making a counter-current flow gradient. In PD, the peritoneum is used as a natural semipermeable membrane and eliminates waste and water into the dialyzate (the material or fluid that passes through the membrane of the dialysis). In fact, the important point involved in dialysis is the movement or diffusion of solute particles across a semipermeable membrane (3). Despite their advantages, HD and PD involve several side effects associated with the removal of uremic solutes, water, and electrolytes, all of which increase the morbidity and mortality of renal patients (4). Previous studies have reported that the main side effects are headaches, muscle cramps, abdominal pain, hypotension, hypertension, vomiting, and constipation (4). Therefore, a convenient treatment option is needed for patients with CKD who refuse to undergo HD. Conservative care can be defined as a new technique for the management of end-stage kidney disease patients who refuse to undergo HD (5). It is well-accepted that conservative therapies, such as absorbent compounds, are new treatment methods alongside HD, PD, and renal transplantation, particularly in elderly individuals with severe comorbidity (6, 7).

2. Evidence Acquisition

Luijtgaarden et al. identified that conservative care has been prescribed for 10% of European CKD patients (8). In 2020, Verberne demonstrated that non-dialytic conservative care can be an alternative option for dialysis (9). Additionally, Keller et al. (10) identified a simple method for treating CKD through perspiration. It has been shown that perspiration can provide some of the most important currently recognized therapeutic goals in treating CKD, such as reducing interdialytic weight gain and serum potassium levels. In another study, intestinal dialysis (ID) and colonic dialysis were found to be successful in the treatment of CKD patients, given their minimal cost compared to the existing options (1, 11). ID can be defined as the use of a dietary supplement to shift the urinary excretion of nitrogenous waste products to intestinal excretion (12). Intestinal fluids of CKD patients have 70 g of blood urea nitrogen (BUN), 2.9 g of creatinine, and 2.5 g of uric acid in a day, which is higher than the normal amount (13). There is a negative correlation between kidney function and the concentration of nitrogenous waste products within the intestinal tract (2). The excretion of creatinine, BUN, and uric acid is higher in the gastrointestinal (GI) tract than in the urine (13). Recent evidence has proposed that different materials and techniques can remove nitrogenous waste products from the body using the GI tract. In addition, some studies have examined the application of a special polymer to improve the symptoms of CKD individuals (11). In the present review, we will focus on different absorbents as a conservative treatment to remove uremic waste metabolites from the GI tract for the improvement of kidney function in CKD.

3. Results

3.1. GI Tract Complications in CKD Patients

Patients with CKD often experience a number of GI tract complications, such as gastritis, decreased bowel mucosal permeability, delayed motility disorders, stomatitis, and microbiological floral change. In chronic renal failure, patients have a higher GI pH value than healthy individuals (14). Furthermore, Aguilera et al. identified that patients with PD usually show high levels of fecal sugar (15). Delayed GI movement in patients with HD may cause recurrent GI symptoms. It has been established that CKD patients usually experience impaired GI motility and elevated rates of glucagon and gastric inhibitory peptide levels, compared to healthy controls, which could be part of the complex multifactorial pattern of intestinal abnormalities in dialysis patients (16-18). In patients undergoing dialysis, changes in microbiome composition increase the C-reactive protein level (19). It has been demonstrated that the presence of urease and uricase bacteria changes the gut microbiome in patients with CKD (20, 21). Therefore, suppressing pathogenic species can improve the health of patients with CKD (22). It was clearly demonstrated that different factors may alter the gut microbiota, including dietary alteration, antibiotics, and pathogen infection (23).

3.2. Passing Time through the GI Tract and CKD

The GI tract is a dynamic environment, and the transport process can be affected by different factors. The passing time through the GI tract plays an important role in improving the absorption procedure (24). Usually, the transport time for small bowels is four hours, but it can range from two to six hours. In contrast, the transport time of the colon is between six and seven hours.

HD patients have longer colonic transit times than healthy individuals, particularly in the right and rectosigmoid segments. Currently, treatment options for chronic constipation are far from clear. In fact, chronic constipation is a common symptom of treatments for various diseases, such as HD in patients with CKD. Several documents have reported that 63.1% of patients undergoing long-term HD therapy experienced constipation (25).

The etiology of the higher prevalence of constipation in long-term HD patients is multifactorial. Lifestyle, phosphorus binders, a diet that includes low potassium and fluid intake, primary renal disease, and various diseases, such as diabetes, cerebrovascular disease, and heart failure, contribute to the higher prevalence of constipation in HD patients (25).

Wu et al. (26) calculated colonic transit times in HD patients and healthy control subjects. They reported that colonic transit time was effectively prolonged in HD patients, compared to healthy controls. In addition, viscosity can influence the absorption process. It has been established that the viscosity of the GI tract rises distally and can slow down absorption in semi-static conditions (24).

Here, we focus on adsorbent and absorbent agents.

3.3. Adsorbents and Absorbents

3.3.1. Starch

Starch (oxystarch) is combined with charcoal and used as a nitrogen sorbent in clinical trials (38). Starch has a high ammonia capacity (27). Starch absorbs urea at a capacity of 178-277 mmoles/mole (28). The administration of starch at a dose of 30 to 40 g/day for over two years can maintain BUN concentration (15). Unfortunately, the oxidized starch depolymerizes slowly in the buffered solution or in solutions of urea or ammonia. Therefore, this problem should be taken seriously.

3.3.2. Activated Charcoal

Activated charcoal can be used in the treatment of uremic pruritus, which is a sign of uremic toxicity. It has been established that creatinine can be adsorbed on active carbon efficiently (24). Activated charcoal binds with waste products and increases fecal nitrogen excretion (29). Active carbon is a potential non-specific adsorbent. In addition, it can reduce IS (Indoxyl Sulfate), p-cresol sulfate, and p-cresol serum levels (30). The combination of orally activated charcoal and a low-protein diet has been introduced as a new treatment for CKD patients (31).

3.3.3. AST-120 (Kremezin)

The action mechanism of AST-120 is that it can absorb uremic toxins within the GI tract and excrete them in the feces (18, 32). It was found that the mean survival of nephrectomized rats increased after being treated with AST-120 (33). AST-120 can improve the severity of anemia and prolong the interval between an azotemic patient's serum creatinine level reaching 6 mg/dl and the start of maintenance HD (34). Indole is derived from the bacterial metabolism within the GI tract. It could be adsorbed by AST-120 (32). It is also effective in delaying the initiation of dialysis in patients with chronic renal failure (35). It is reported that AST-120 can delay the progression of chronic kidney and also cardiovascular disease (36). It has been reported that AST-120 can improve lipid abnormalities in experimental uremic rats. AST-120 significantly decreases the concentration of TG and cholesterol. In conclusion, AST-120 can improve the plasma lipid profile and prevent the progression of renal disease (2). It was highlighted that orally activated charcoal and AST-120 would minimize uremic toxins, such as p-cresol sulfate, IS, and p-cresol serum levels, in CKD patients (37). Chen et al. reported that early IS elimination by synergistic AST-120 administration in the early stage of acute kidney injury (AKI) is a valuable approach in the prevention of the AKI to CKD transition (38).

3. 3. 4. Lactulose

Lactulose can decrease the level of various deleterious elements. In a prospective study, the application of lactulose decreased urea concentration from 70.35 mg/dL to 64.50 mg/dL, creatinine concentration from 4.04 mg/dL to 3.45 mg/dL, and uric acid concentration from 7.31 mg/dL to 6.71 mg/dL. In addition, lactulose can increase the number of bacteria that metabolize ammonia (24).

3.3.5. Fructooligosaccharides

Fructooligosaccharides (FOS) are composed of short fructose chains. FOS occurs naturally in many plants,

such as blue agave, yacon root, and garlic. Sudhanshu assessed the beneficial effects of FOS on rats. It has also been established that FOS is a positioned product that can significantly decrease proteinuria, blood creatinine, and urea (30).

3.3.6. Inulin

Inulin is a group of naturally occurring polysaccharides produced by many types of plants, most often extracted industrially from chicory. Inulin is a type of dietary fiber called fructan.

3.3.7. Licorice (Gan Cao)

Licorice can prevent hyperkalemia in CKD patients. It can reduce plasma-potassium concentration by enhancing intestinal potassium loss (39). Licorice is one of the most prescribed herbs in Chinese traditional medicine (40). In a clinical trial, licorice reduced plasma-potassium concentration, and the frequency of hyperkalemia was also decreased from 9% to 0.6% (39).

Limitation of ID

It can be claimed that a single agent in absorbent therapy is unable to remove a wide spectrum of metabolites from the GI tract. The administration of a sorbent mixture into the intestinal bypass can effectively remove urea, potassium, and water. During the treatment of anephric animals, the administration of sorbents can stabilize the serum urea nitrogen level at about five times normal and remove nitrogen at a clearance of up to 40% of that of normal kidneys. However, larger molecules, such as creatinine and uric acid, and middle molecules are poorly removed by ID.

4. Conclusion

Conservative care, such as absorbent therapy, is suggested as a new technique for the management of CKD patients who refuse to undergo HD because of its severe complications. Absorbent therapy is described as the use of a dietary supplement to shift the urinary excretion of nitrogenous waste products to the intestinal excretion since the excretion of creatinine, BUN, and uric acid is higher in the GI tract than in the urine. Therefore, absorbent therapy can provide some of the therapeutic goals in treating CKD, such as decreasing inter-dialytic weight gain and serum potassium levels. The present study reviewed some adsorbent and absorbent agents for the improvement of kidney function in CKD patients. For example, starch, in combination with charcoal, is used as a nitrogen sorbent in patients with CKD. Additionally, activated charcoal can be used in the treatment of uremic pruritus, which is a sign of uremic toxicity. These results suggest that AST-120 delays the decline in renal function.

Acknowledgment

This study was supported by Baqiyatallah University of Medical Sciences, Tehran, Iran.

Authors' Contribution

Study concept and design: M. I.
Acquisition of data: B.A., Z.B., R. K., and M.I.
Drafting of the manuscript: B. A., Z. B., and M. I.
Critical revision of the manuscript: R. K., and M.I.

Ethics

It is declared that all ethical considerations were taken into account in the preparation of the submitted manuscript (IR.BMSU.REC.1399.296).

Conflict of Interest

The authors declare that they have no conflicts of interest.

Data Availability

The data that support the findings of this study are available on request from the corresponding author.

References

1. Khosroshahi HT, Abedi B, Ghojazadeh M, Samadi A, Jouyban A. Effects of fermentable high fiber diet supplementation on gut derived and conventional nitrogenous product in patients on maintenance hemodialysis: a randomized controlled trial. Nutr Metab. 2019; 16(1):1-8.
2. Asadzadeh S, Khosroshahi HT, Abedi B, Ghasemi Y, Meshgini S. Renal structural image processing techniques: a systematic review. Ren Fail. 2019; 41(1):57-68.
3. Vadakedath S, Kandi V. Dialysis: a review of the mechanisms underlying complications in the management of chronic renal failure. Cureus. 2017; 9(8): e1603.
4. Pinheiro RL, de Macedo BM, de Carvalho Lira AL. Complications in patients with chronic renal failure undergoing hemodialysis. Cogitare Enferm. 2017; 22(4):e52907.
5. Abedi B, Khosroshahi HT. Excretion of nitrogenous waste products from the intestinal fluid simulator using

super absorbent polymer: a new generation dialysis. IJKD. 2023; 17(3):150.
6. Laffin MR, Tayebi Khosroshahi H, Park H, Laffin LJ, Madsen K, Kafil HS, Abedi B, Shiralizadeh S, Vaziri ND. Amylose resistant starch (HAM-RS2) supplementation increases the proportion of Faecalibacterium bacteria in end-stage renal disease patients: microbial analysis from a randomized placebo-controlled trial. Hemodial Int. 2019; 23(3):343-347.
7. Verberne WR, Dijkers J, Kelder JC, Geers A, Jellema WT, Vincent HH, Van Delden JJ, Bos WJ. Value-based evaluation of dialysis versus conservative care in older patients with advanced chronic kidney disease: a cohort study. BMC nephrology. 2018;19(1):1-11.
8. van de Luijtgaarden MW, Noordzij M, Van Biesen W, Couchoud C, Cancarini G, Bos WJ, Dekker FW, Gorriz JL, Iatrou C, Wanner C, Finne P. Conservative care in Europe-nephrologists' experience with the decision not to start renal replacement therapy. Nephrol Dial Transplant. 2013; 28(10):2604-2612.
9. Verberne WR, van den Wittenboer ID, Voorend CG, Abrahams AC, van Buren M, Dekker FW, van Jaarsveld BC, van Loon IN, Mooijaart SP, Ocak G, van Delden JJ. Health-related quality of life and symptoms of conservative care versus dialysis in patients with end-stage kidney disease: a systematic review. Nephrol Dial Transplant. 2020.
10. Keller Jr RW, Kopple JD, Kalantar-Zadeh K. Perspiration interventions for conservative management of kidney disease and uremia. Curr Opin Nephrol Hypertens. 2020. 29(1):57-63.
11. Wongrakpanich S, Susantitaphong P, Isaranuwatchai S, Chenbhanich J, Eiam-Ong S, Jaber BL. Dialysis therapy and conservative Management of Advanced Chronic Kidney Disease in the elderly: a systematic review. Nephron. 2017; 137(3):178-189.
12. Al-Mosawi A. Advances of peritoneal dialysis in the developing world: Combined intermittent peritoneal dialysis and intestinal dialysis (Chapter 3). Peritoneal Dialysis: Practices, Complications and Outcomes. Nova Science Publisher. 2017.
13. Miskowiak J. Continuous intestinal dialysis for uraemia by intermittent oral intake of non-absorbable solutions: an experimental study. Scand J Urol. 1991; 25(1):71-74.
14. Rampton DS, Cohen SL, Crammond VD, Gibbons J, Lilburn MF, Rabet JY, Vince AJ, Wager JD, Wrong OM. Treatment of chronic renal failure with dietary fiber. Clinic Nephrology. 1984; 21(3):159-163.
15. Giordano C, Esposito R, Randazzo G. Oxystarch as a gastrointestinal sorbent in uremia, in Uremia. Georg Thieme Verlag Stuttgart. 1972; 231-239.
16. Yatzidis H. Newer oral sorbents in uremia. 1979;11(2):105-6.
17. Pahl MV, Vaziri ND. The chronic kidney disease-colonic axis. Semin Dial. Wiley Online Library. 2015;28(5):459-63.
18. Stadlbauer V, Horvath A, Ribitsch W, Schmerböck B, Schilcher G, Lemesch S, et al. Structural and functional differences in gut microbiome composition in patients undergoing haemodialysis or peritoneal dialysis. Scientific Rep. 2017; 7(1):1-10.
19. Dai S, Dai Y, Peng J, Xie X, Ning J. Simplified colonic dialysis with hemodialysis solutions delays the progression of chronic kidney disease. QJM. 2019; 112(3):189-96.
20. Friedman EA. Oral Sorbents in Uremia, in Replacement of Renal Function by Dialysis. 1983; 341-353.
21. Giordano C, Esposito R, Demma G. Possibilities of reducing azotemia in humans by administration of a polyaldehyde. Boll Soc Ital Biol Sper. 1968; 44(24):2232-2234.
22. Engelhardt WV, Hinderer S, Rechkemmer G, Becker G. Urea secretion into the colon of sheep and goat. Quarterly Journal of Experimental Physiology: Translat Integ. 1984; 69(3):469-475.
23. Meyer TW, Hostetter TH. Uremic solutes from colon microbes. Kidney Inter. 2012; 81(10): 949-954.
24. Martin I, Courtney J. Oral adsorbents in the treatment of uraemia: A review. J Med Eng Technol. 1977; 1(2): 92-94.
25. Wu MJ, Chang CS, Cheng CH, Chen CH, Lee WC, Hsu YH, et al. Colonic transit time in long-term dialysis patients. AJKD; 44(2):322-327.
26. Wu MJ, Chang CS, Cheng CH, Chen CH, Lee WC, Hsu YH, et al. Colonic transit time in long-term dialysis patients. AJKD. 2004; 44(2):322-327.
27. Shen W, Zhang S, Jiang P, Liu Y. Surface chemistry of pyrolyzed starch carbons on adsorption of ammonia and carbon disulfide. Colloids Surf. 2010; 356(1-3):16-20.
28. Friedman EA. Can the bowel substitute for the kidney in advanced renal failure?. Taylor & Francis. 2009;25(8):1913-8.

29. Kajbafzadeh, AM, Sabetkish N, Sabetkish S. Establishment of colonic dialysis model in uremic rats by right nephrectomy and left partial nephrectomy. J Pediatr Urol. 2018;14(2):159.e1-159.e8.
30. Andersen AH. Experimental Studies on the Pharmacology of Activated Charcoal. III. Adsorption from Gastro-Intestinal Contents. Acta Pharmacol Toxicol. 1948; 4(3-4):275-84.
31. Musso CG, Michelangelo H, Reynaldi J, Martinez B, Vidal F, Quevedo M, et al. Combination of oral activated charcoal plus low protein diet as a new alternative for handling in the old end-stage renal disease patients. SJKDT. 2010; 21(1):102.
32. Asai M, Kumakura S, Kikuchi M. Review of the efficacy of AST-120 (KREMEZIN) on renal function in chronic kidney disease patients. Ren Fail. 2019; 41(1):47-56.
33. Miles AM, Fleischacker J, Hyppolite G, Zhao ZH, Distant D, Friedman EA. Oral sorbent (AST-120) slows uremia progression in 7/8th nephrectomized rats. JASN. 1995;21201-2436.
34. Sanaka T, Akizawa T, Koide K, Koshikawa S. Protective effect of an oral adsorbent on renal function in chronic renal failure: determinants of its efficacy in diabetic nephropathy. Ther Apher Dial. 2004; 8(3):232-240.
35. Yamakado M, Ise M. Mechanism of oral absorbent AST-120 in lipid abnormalities in experimental uremic rats. Kidney Inter. 1999; 56:190-192.
36. Niwa T. Role of indoxyl sulfate in the progression of chronic kidney disease and cardiovascular disease: Experimental and clinical effects of oral sorbent AST-120. Ther Apher Dial. 2011; 15(2):120-124.
37. Liu WC, Tomino Y, Lu KC. Impacts of indoxyl sulfate and p-cresol sulfate on chronic kidney disease and mitigating effects of AST-120. Toxins. 2018; 10(9):367.
38. Chen JH, Chao CT, Huang JW, Hung KY, Liu SH, Tarng DC, et al. Early Elimination of Uremic Toxin Ameliorates AKI to CKD Transition. Clin Sci. 2021.
39. Kwon YJ, Son DH, Chung TH, Lee YJ. A review of the pharmacological efficacy and safety of licorice root from corroborative clinical trial findings. J Med Food. 2020; 23(1):12-20.
40. Ferrari P. Licorice: a sweet alternative to prevent hyperkalemia in dialysis patients? Kidney Int. 2009; 76(8):811-812.