Open Access http://www.jparathyroid.com

Journal of Parathyroid Disease

Journal of Parathyroid Disease 2020,8, e11173

Original

See the Commentary by Zahmatkesh et al (J Parathyr Dis. 2020;8:e11183)

Comparing the effect of sevelamer carbonate versus sevelamer hydrochloride on blood level cholesterol, triglyceride and uric acid in patients undergoing maintenance hemodialysis

Milad Almasi, Bahareh Hajisalimi*

Abstract

Introduction: Hyperlipidemia and hyperuricemia are important complications of renal failure, especially in patients underlying dialysis, therefore, it is important to control these complications with more effective therapies which have lower side effects and costs. Sevelamer is an agent that binds to bile acids and impairs fat absorption and also reduces the absorption of fat-soluble vitamins.

Objectives: In this study, the effect of sevelamer carbonate and sevelamer hydrochloride was investigated on serum levels of cholesterol, triglyceride and uric acid.

Patients and Methods: In a randomized clinical trial, patients undergoing maintenance hemodialysis who were treated with sevelamer carbonate and sevelamer hydrochloride were enrolled in the study and evaluated for complications and outcomes. After one month, cholesterol, triglyceride and uric acid levels were measured. Data were analyzed at a significance level of less than 0.05 using t-test, ANOVA, Mann-Whitney U and the Kruskal-Wallis tests.

Results: In sevelamer hydrochloride group changes in levels of cholesterol, triglyceride and uric acid were 18.80 ± 28.19 mg/dL, 25.52 ± 73.80 mg/dL and 0.85 ± 2.10 mg/dL, respectively. In sevelamer carbonate group, differences for cholesterol, triglyceride and uric acid were 10.17 ±23.66 mg/dL, 3.84 ± 34.57 mg/dL and 0.60 ± 1.59 mg/dL mg/dL, respectively. Sevelamer hydrochloride reduced serum cholesterol (P = 0.321), triglyceride (P = 0.129) and uric acid (P = 0.679) levels more than sevelamer carbonate, however these differences were not significant.

Conclusion: Due to the better clinical effect of sevelamer hydrochloride, it can be recommended in patients with chronic renal failure with overload of phosphorus accompanied by lipid disorders, especially hypercholesterolemia.

Trial Registration: The trial protocol was approved by the Iranian Registry of Clinical Trial (identifier: IRCT20141016019554N13, https://en.irct.ir/trial/28916, ethical code; IR.ZUMS.REC.1397.352).

Keywords: Sevelamer carbonate, Sevelamer hydrochloride, hemodialysis, End stage renal disease

Please cite this paper as: Almasi M, Hajisalimi B. Comparing the effect of sevelamer carbonate versus sevelamer hydrochloride on blood level cholesterol, triglyceride and uric acid in patients undergoing maintenance hemodialysis. J Parathyr Dis. 2020;8:e11173.

Introduction

End-stage renal disease (ESRD) is one of the most important and life-threatening condition that requires to kidney replacement therapy (dialysis or transplant). Because kidney transplants are not available everywhere and have limitations, many patients with ESRD require dialysis to survive (1). Hemodialysis is the most common type of dialysis used in many countries. In Iran, more than 90% of dialysis patients received hemodialysis as replacement therapy (2). Since many conditions improve by dialysis, it should be noted that dialysis may worsen some uremic complications (2).

Hemodialysis is currently conducted as a vital treatment in thousands of patients with chronic renal failure in the United States, according to the charity foundation of special disease and the kidney foundation of Iran, the number of patients with chronic renal failure reached about 25 000 in 2006 and it would reach to 40 000 in 2011 with an annual increase of 13% (3).

Mortality rate due to complications in hemodialysis patients remains a concern, therefore life expectancy in 60-year-old patients was 11.9 years for men and 14.1 years for women, which has increased by 10% to 20% compared to 2003. In diabetic patients undergoing hemodialysis, life expectancy decreases to 10.8 years in men and 12.5 years in women, while in non-diabetic patients it is 13 years for men and 15 years for women. Life expectancy in those who start hemodialysis between the ages of 40 and 44 is 7 to 10 years, and if started at the ages of 60 to 64 will be 4 to 5 years. Insufficient dialysis to reduce the acceptable percentage of blood urea is also one of the important factors in increasing dialysis complications and mortality

Received: 10 May 2020, Accepted: 13 November 2020, ePublished: 26 November 2020

Internal Medicine Department, Vali-e-Asr Hospital, Zanjan University of Medical Sciences, Zanjan, Iran.
***Corresponding author:** Bahareh Hajisalimi, Email: baharehhajisalimi@yahoo.com

Implication for health policy/practice/research/medical education

Controlling of hyperlipidemia and hyperuricemia in patients with renal failure, especially in patients underlying dialysis is important for lowering the side effects and costs. Sevelamer is an agent that binds to bile acids and impairs fat absorption and also reduces the absorption of fat-soluble vitamins. In this regard, sevelamer hydrochloride has better effects and it can be recommended in patients with chronic renal failure with overload of phosphorus accompanied by lipid disorders, especially hypercholesterolemia.

in these patients (4).

One of the most common complications of dialysis is changes in uric acid lipid profiles. Decreased plasma levels of high-density lipoproteins (HDLs) and elevated plasma levels of triglycerides are common in patients with chronic renal failure because HDL production is reduced due to decreased uremic lipolytic activity. Hypertriglyceridemia occurs in approximately 32%-72% of patients with chronic renal failure (5). Another important complication in chronic kidney disease (CKD) patients is hyperphosphatemia, especially in those with glomerular filtration rate (GFR) less than 60 mL/min/1.73 m^2 (6).

Conventional 4-hour thrice-weekly hemodialysis is limited in its ability to lower the phosphorus levels to normal range, thereby administration of phosphorus chelators is necessary to maintain serum levels of phosphorus at normal range. Available phosphorus chelators include calcium carbonate, calcium acetate, aluminum carbonate, aluminum hydroxide, magnesium hydroxide, and lanthanum and sevelamer. Sevelamer recipients have lower C-reactive protein (CRP) and low-density lipoprotein cholesterol (LDL-c) levels than other phosphate binder agents, however, there was no difference between them for other serum markers such as tumor necrosis factor-alpha (TNF-alpha), interleukin-6 (IL-6) and homocysteine (7).

In patients undergoing dialysis, sevelamer reduces the serum levels of phosphorus, cholesterol and LDL-c, as well as calcium-phosphorus product (Ca×P product) (8). Sevelamer is a calcium-free and non-metal containing phosphate binders and it is the best therapeutic agent in cases where serum phosphorus is high (for example, the product of phosphorus in calcium is higher than 55 mg^2/dL^2) to prevent calcium deposition in tissues, especially arteries (9).

Sevelamer is one of the agents recommended to reduce complications in dialysis patients and can prevent gastrointestinal absorption of phosphorus. It is available as a combination of sevelamer carbonate and sevelamer hydrochloride. Sevelamer hydrochloride is effective in lowering serum phosphate levels, in addition binds to bile acids, which can impair fat absorption as well as reduce the absorption of fat-soluble vitamins. Lowering serum phosphorus reduces ectopic calcification as well as total serum cholesterol (9).

A study in the United States indicated that sevelamer hydrochloride in patients with CKD who undergoing hemodialysis reduced blood bicarbonate levels. However, sevelamer carbonate does not have this effect, although, both agents are effective in lowering serum phosphate levels (10).

Objectives

Patients with CKD undergoing maintenance hemodialysis have a specific condition and are prone to numerous complications, including hyperlipidemia and hyperuricemia, therefore, control of these complications with more effective drugs can improve patient satisfaction, in addition to reducing overhead costs for insurance companies and health care system. In this study, the effects of sevelamer carbonate and sevelamer hydrochloride on the hyperlipidemia and hyperuricemia were investigated in order to select the appropriate agent to control CKD complications.

Patients and methods

Study design

In a randomized clinical trial, all patients undergoing maintenance hemodialysis at Vali-e-Asr Hospital, Zanjan in 2016 (conventional 4-hour thrice-weekly) by an appropriate vascular access, had no history of primary hyperparathyroidism or a history of parathyroidectomy, patients who did not receive any lipid-lowering agents, adherence to phosphorus restriction diet (800 to 1000 mg daily) and had no history of taking sevelamer and in them which serum phosphorus level was higher than 5.5 mg/dL were enrolled in the study. Patients were randomly (through random allocation software) divided into two groups; the first group received 800 mg of sevelamer carbonate with each meal and the second group received 800 mg of sevelamer hydrochloride with each meal. Patients were followed up for complications during the study and in case of severe complications, the drug was discontinued and the patient was excluded from the study. Cholesterol, triglyceride and uric acid levels were measured before and one month after treatment following 12 hours of fasting in a reference laboratory. Demographic data including age, sex, duration of dialysis, levels of cholesterol, triglyceride and uric acid were collected and recorded based on the information recorded in the patients' records and laboratory reports (Figure 1).

Statistical analysis

Data were analyzed at a significance level less than 0.05 in SPSS version 22 software using independent *t* test, and chi-square test.

Results

The distribution of patients in terms of demographic characteristics and underlying factors including duration

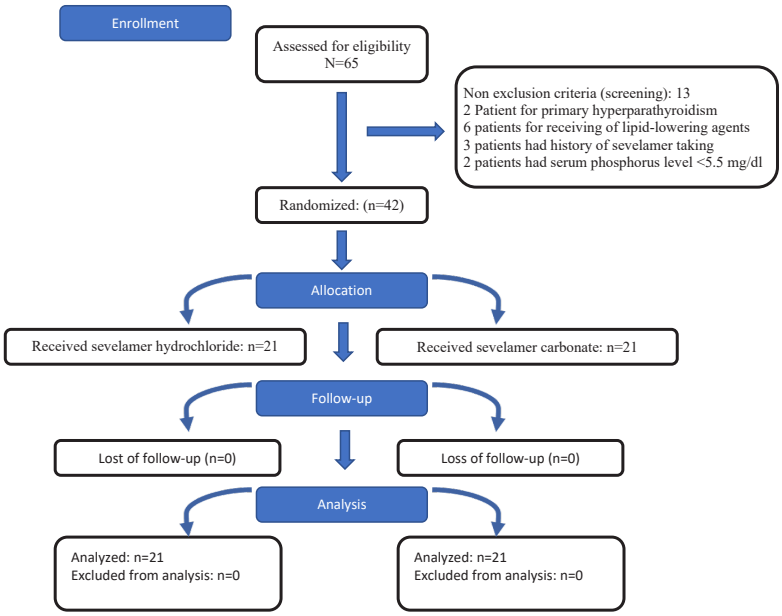

Figure 1. Consort diagram.

of dialysis, diabetes, hypertension and hyperlipidemia in the two groups were not significantly different and the two groups were homogeneous (Table 1).

Levels of cholesterol, triglyceride and uric acid before intervention (receiving sevelamer) did not show significant difference between the two groups. Similarly, repeated measurements of these parameters after intervention period did not show significant difference (Table 2). In other words, administration of both types of sevelamer did not lead to a significant change in the levels of these parameters. To examine the effects of sevelamer hydrochloride and sevelamer carbonate, the difference between two groups was compared before and after measurements of cholesterol, triglyceride and uric acid too. The results of comparing the levels of cholesterol, triglyceride and uric acid parameters showed that the two types of sevelamer, sevelamer hydrochloride and sevelamer carbonate, are not significantly different from each other, although, sevelamer hydrochloride has a better effect on reducing these parameters based on laboratory data and is preferred to sevelamer carbonate.

Discussion

In patients with chronic renal failure, special attention should be paid to serum phosphate concentrations, because in these patients, there is an increase in phosphate levels and it is necessary to use a low-phosphate diet and phosphate-chelator drugs. Many phosphate-chelating drugs contain calcium, and when taken, calcium may rise in the body and deposit in different organs.

Similar studies have been conducted worldwide about the effects of sevelamer and other phosphate-chelating

Table 1. Comparison of demographic characteristics of patients between two groups (sevelamer hydrochloride and sevelamer carbonate)

Demographic characteristics		Groups		*P* value
		Sevelamer hydrochloride % (N)	Sevelamer Carbonate % (N)	
Age (y)	<60 ≥60	47.6 (10) 52.4 (11)	47.6 (10) 52.4 (11)	>0.999
Gender	Male Female	47.6 (10) 52.4 (11)	33.3 (7) 66.7 (14)	0.346
Dialysis duration	<36 months ≥ 36 months	47.6 (10) 52.4 (11)	52.4 (11) 47.6 (10)	0.758
Residency	Urban Rural	52.4 (11) 47.6 (10)	42.9 (9) 57.1 (12)	0.537
Diabetes	+ -	33.3 (7) 66.7 (14)	52.4 (11) 47.6 (10)	0.212
Hypertension	+ -	85.7 (18) 14.3 (3)	66.7 (14) 33.3 (7)	0.147
Hyperlipidemia	+ -	28.6 (6) 71.4 (15)	0.0 (0) 100.0 (21)	0.008

Table 2. Comparison of cholesterol, triglyceride and uric acid levels before and after receiving of sevelamer carbonate and sevelamer hydrochloride

Parameters		Sevelamer carbonate Mean (SD)	Sevelamer hydrochloride Mean (SD)	*P* value
Cholesterol (mg/dL)	Before	138.50 (44.4)	158.90 (37.3)	0.128
	After	128.53 (31.7)	140.10 (26.1)	0.226
	Mean difference	-10.17	-18.80	0.321
Triglyceride (mg/dL)	Before	120.94 (60.7)	173.38 (112.1)	0.085
	After	124.89 (60.6)	147.86 (56.8)	0.230
	Difference	3.94	-25.52	0.129
Uric acid (mg/dL)	Before	6.53 (1.3)	7.46 (1.6)	0.123
	After	5.93 (1.0)	6.46 (1.4)	0.211
	Mean difference	-0.60	-0.85	0.679

drugs on serum magnesium, phosphorus and calcium levels.

New recommendations of KDIGO (kidney disease: improving global outcomes) and world nephrology association emphasizes the serious restrictions of calcium-contained phosphorus-binders in hemodialysis patients with high serum calcium level (11).

Absence of calcium overload and prevention of hypercalcemia is the main advantage of magnesium-contained phosphorus-binders such as magnesium carbonate. Magnesium carbonate has been associated with a reduction in the severity of vascular atherosclerosis and a reduction in cardiovascular mortality (12).

In patients with chronic renal failure, a decrease in plasma levels of HDLs and an increase in plasma levels of triglycerides could occur due to decreased production of HDL resulting from lipolytic activity which is caused by uremia (5). Another important complication in these patients is hyperphosphatemia (6), which is the reason for prescription of phosphorus chelators including calcium carbonate, calcium acetate, aluminum carbonate, aluminum hydroxide, magnesium hydroxide, lanthanum and sevelamer (7). Sevelamer is a phosphate-binding agent that acts in the gut to prevent phosphate uptake without being absorbed. Its use has been associated with reduced cardiovascular mortality. This effect is due to the binding ability to phosphate and reduce its compatibility mechanisms, such as fibroblast growth factor-23 (FGF23) and PTH (parathyroid hormone; parathormone). Lowering LDL-c, phenols, uric acid, or endotoxins, all of them which have intestinal origin, appears to reduce inflammation and oxidation. These functions have significant effects on complications such as anemia, vascular calcification, atherogenesis and endothelial dysfunction, which in turn improves the survival of patients with CKD (13).

Sevelamer hydrochloride, is effective on serum phosphate levels, in addition to binds to bile acids, which can impair fat absorption as well as reduce the absorption of fat-soluble vitamins. Decreased serum phosphorus reduces ectopic calcification as well as lowers total serum cholesterol (9).

The present study compared effects of sevelamer hydrochloride with sevelamer carbonate on serum lipid levels including triglyceride, cholesterol and uric acid. The results showed that sevelamer hydrochloride and sevelamer carbonate had statistically significant effect on serum cholesterol, triglyceride and uric acid levels; however, they have no preference over each other.

Hamida et al evaluated the effect of sevelamer on the level of lipid profile and reported that sevelamer had no significant effect on the level of triglyceride and HDL-c (14).

Following binding to bile acids, sevelamer inhibits the absorption of fats and thus can lower serum lipid levels. However, in the study by Hamida et al (14), it was found to be ineffective in reducing the lipid profile. In our study, the amount of cholesterol and triglyceride reduction in patients receiving sevelamer hydrochloride and sevelamer carbonate was not significantly different, although it was higher after the administration of sevelamer hydrochloride, this finding is considered clinically somewhat important.

Sevelamer binds to negatively charged bile acids and acts as a bile acid binder that may reduce the concentration of LDLs. Beneficial effects attributed to sevelamer include reduced mortality due to cardiovascular complications is in part attributed to hypolipemic function (15). The ability of sevelamer to lower intestinal cholesterol is known by several studies that reported this effect (16,17). The effect of sevelamer on the lowering of phosphorus and cholesterol levels in peritoneal dialysis has been identified (18). In another study, it was indicated that this effect reduced the need for statins in patients with chronic renal failure (19).

In the present study, the effects of sevelamer hydrochloride and sevelamer carbonate on uric acid level, were also compared. The results showed that sevelamer hydrochloride and sevelamer carbonate had no statistically significant effect on blood uric acid levels and compared to each other.

Garg et al showed that sevelamer significantly reduced serum uric acid relative to calcium-based phosphate binder (20). Ohno et al also point out that sevelamer reduces serum uric acid levels through urate uptake in

patients undergoing maintenance hemodialysis (21).

Uric acid is a factor that causes oxidative stress and endothelial damage in patients with CKD (22). There is controversy as to whether sevelamer is able to lower serum uric acid levels. Ohno et al (21) and Garg et al (20) reported the effect of sevelamer on reducing uric acid in patients on hemodialysis, since Evenepoel et al reported such an effect in patients on peritoneal dialysis (23). However, in the study by Brandenburg et al, the results did not show such an effect (24).

Sevelamer is an oral phosphate binder that significantly reduces serum urate levels in maintenance hemodialysis patients with hyperuricemia. The mechanism of urate reduction by sevelamer is thought to be intestinal urate uptake, while changes in urate are associated with changes in phosphate and calcium-phosphate product, since sevelamer significantly absorbs urate, in vitro. This indicates the usefulness of sevelamer in reducing urate in hemodialysis patients (21).

Conclusion

Sevelamer hydrochloride and sevelamer carbonate were effective on cholesterol, triglyceride and uric acid levels. Although there was no significant difference between them, sevelamer hydrochloride had a better effect in reducing these parameters and was clinically and laboratory superior to sevelamer carbonate.

Limitations of the study

The low-sample size prevented the analysis of results based on age, sex and other underlying factors.

Recommendations

Due to the decreasing effect of sevelamer on cholesterol, triglyceride and uric acid levels, despite the statistically insignificant relationship, it is suggested to conduct studies in a clinical trial with a longer follow-up period and larger sample size to obtain more accurate results.

Authors' contribution

BH and BF participated in conceptualization, validation, investigation, resources, supervision, project administration and funding acquisition. BF contributed to data curation and writing (original draft preparation). BH contributed to methodology and formal analysis. Both authors participated in preparing the final draft of the manuscript, review and editing.

Conflicts of interest

The authors declare that they have no competing interests. Patients received the drugs free of charge. Additionally, patients received the drugs free of charge. The authors had not any relation with the company which distributing the drugs, since the drugs were purchased directly from the market.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. This study was conducted by approval of the Research Council of Zanjan University of Medical Sciences with the design code A-11-969-7 and the approval of the ethics committee of Zanjan University of Medical Sciences (code IR.ZUMS.REC.1397.352). The study protocol was registered in the Iranian Registry of Clinical Trials (identifier: IRCT20141016019554N13, https://en.irct.ir/trial/28916). Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/ Support

This work was supported by the Deputy of Research and Technology of the Zanjan University of Medical Sciences.

References

1. van de Luijtgaarden MW, Jager KJ, Segelmark M, Pascual J, Collart F, Hemke AC, et al. Trends in dialysis modality choice and related patient survival in the ERA-EDTA Registry over a 20-year period. Nephrol Dial Transplant. 2016;31:120-8. doi: 10.1093/ndt/gfv295.
2. Chazot C, Jean G. End-Stage Kidney Patients Require Hemodialysis Therapy Full Start. Blood Purif. 2019;47:214-222. doi: 10.1159/000494582.
3. Mousavi SS, Mousavi MB, Motemednia F. Baclofen-induced encephalopathy in patient with end stage renal disease: Two case reports. Indian J Nephrol. 2012;22:210-2. doi: 10.4103/0971-4065.98762.
4. Nakai S, Wada A, Wakai K, Abe M, Nitta K. Calculation of expected remaining lifetime of dialysis patients in Japan. Renal Replacement Therapy. 2020;6:58. doi: 10.1186/s41100-020-00301-z.
5. Thakar CV, Christianson A, Himmelfarb J, Leonard AC. Acute kidney injury episodes and chronic kidney disease risk in diabetes mellitus. Clin J Am Soc Nephrol. 2011;6:2567-72. doi: 10.2215/cjn.01120211.
6. Stevens PE, Levin A. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. Ann Intern Med. 2013;158:825-30. doi: 10.7326/0003-4819-158-11-201306040-00007.
7. Shantouf R, Budoff MJ, Ahmadi N, Tiano J, Flores F, Kalantar-Zadeh K. Effects of sevelamer and calcium-based phosphate binders on lipid and inflammatory markers in hemodialysis patients. Am J Nephrol. 2008;28:275-9. doi: 10.1159/000111061.
8. Sturtevant JM, Hawley CM ,Reiger K, Johnson DW, Campbell SB, Burke JR, et al. Efficacy and side-effect profile of sevelamer hydrochloride used in combination with conventional phosphate binders. Nephrology (Carlton). 2004;9:406-13. doi: 10.1111/j.1440-1797.2004.00338.x.
9. Bargman JM, Skorecki KL. Chronic Kidney Disease. In: Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, eds. Harrison's Principles of Internal Medicine, 20e. New York, NY: McGraw-Hill Education; 2018.
10. Pai AB, Shepler BM. Comparison of sevelamer hydrochloride and sevelamer carbonate: risk of metabolic acidosis and clinical implications. Pharmacotherapy. 2009;29:554-61. doi: 10.1592/phco.29.5.554.
11. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl. 2009:S1-130. doi: 10.1038/ki.2009.188.
12. Block GA, Raggi P, Bellasi A, Kooienga L, Spiegel DM. Mortality effect of coronary calcification and phosphate binder choice in incident hemodialysis patients. Kidney Int. 2007;71:438-41. doi: 10.1038/sj.ki.5002059.
13. Rodríguez-Osorio L, Pazmiño Zambrano D, Gracia-Iguacel C, Rojas-Rivera J, Ortiz A, Egido J, et al. Use of sevelamer in chronic kidney disease: beyond phosphorus control. Nefrologia.

2015;35:207-17. doi: 10.1016/j.nefroe.2015.05.011.
14. Hamida FB, Fatma LB, Barbouch S, Kaaroud H, Helal I, Hedri H, et al. Effect of sevelamer on mineral and lipid abnormalities in hemodialysis patients. Kidney Dis Transpl. 2008;19:183-8.
15. Iimori S, Mori Y, Akita W, Takada S, Kuyama T, Ohnishi T, et al. Effects of sevelamer hydrochloride on mortality, lipid abnormality and arterial stiffness in hemodialyzed patients: a propensity-matched observational study. Clin Exp Nephrol. 2012;16:930-7. doi: 10.1007/s10157-012-0640-4.
16. Ramos R, Moreso F, Borras M, Ponz E, Buades JM, Teixidó J, et al. Sevelamer hydrochloride in peritoneal dialysis patients: results of a multicenter cross-sectional study. Perit Dial Int. 2007;27:697-701. doi: 10.1177/089686080702700618.
17. Burke SK, Dillon MA, Hemken DE, Rezabek MS, Balwit JM. Meta-analysis of the effect of sevelamer on phosphorus, calcium, PTH, and serum lipids in dialysis patients. Adv Ren Replace Ther. 2003;10:133-45.
18. Suñer M, Guerrero A, Montes R, Rivera M, Ruiz A, Martínez-García M, et al. Treatment of hyperphosphatemia with sevelamer in patients with chronic renal failure. Nefrologia. 2004;24:142-8.
19. Chue CD, Townend JN, Moody WE, Zehnder D, Wall NA, Harper L, et al. Cardiovascular effects of sevelamer in stage 3 CKD. J Am Soc Nephrol. 2013;24:842-52.
20. Garg JP, Chasan-Taber S, Blair A, Plone M, Bommer J, Raggi P, et al. Effects of sevelamer and calcium-based phosphate binders on uric acid concentrations in patients undergoing hemodialysis: a randomized clinical trial. Arthritis Rheum. 2005;52:290-5. doi: 10.1002/art.20781.
21. Ohno I, Yamaguchi Y, Saikawa H, Uetake D, Hikita M, Okabe H, et al. Sevelamer decreases serum uric acid concentration through adsorption of uric acid in maintenance hemodialysis patients. 2009;48:415-20.
22. Yelken B, Caliskan Y, Gorgulu N, Altun I, Yilmaz A, Yazici H, et al. Reduction of uric acid levels with allopurinol treatment improves endothelial function in patients with chronic kidney disease. Clin Nephrol. 2012;77:275-82. doi: 10.5414/cn107352.
23. Evenepoel P, Selgas R, Caputo F, Foggensteiner L, Heaf JG, Ortiz A, et al. Efficacy and safety of sevelamer hydrochloride and calcium acetate in patients on peritoneal dialysis. Nephrol Dial Transplant. 2009;24:278-85. doi: 10.1093/ndt/gfn488.
24. Brandenburg VM, Schlieper G, Heussen N, Holzmann S, Busch B, Evenepoel P, et al. Serological cardiovascular and mortality risk predictors in dialysis patients receiving sevelamer: a prospective study. Nephrol Dial Transplant. 2010;25:2672-9. doi: 10.1093/ndt/gfq053.