Original Article

Comparison of Sevelamer and Calcium Carbonate in Prevention of Hypomagnesemia in Hemodialysis Patients

Elahe Jandaghi, Maliheh Yarmohammadi, Raheb Ghorbani[1,2], Tahereh Jalali[3], Ali Khadjeh Salehani, Peiman Mohammad Khani

Department of Internal Medicine, Semnan University of Medical Sciences, Semnan, Tehran, Iran, [1]Social Determinant of Health Research Center, Semnan University of Medical Sciences, Semnan, Tehran, Iran, [2]Department of Epidemiology and Biostatistics, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Tehran, Iran, [3]School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Background: Chronic kidney disease (CKD) is a life-threatening disease with numerous complications. Hemodialysis (HD) patients are prone to magnesium deficiency due to malnutrition, which can cause cardiovascular complications and increase mortality. The present study aimed to investigate the effects of sevelamer and calcium carbonate, as phosphate binders, on serum levels of magnesium, calcium, and phosphorus in HD patients. **Methods:** A parallel clinical trial was conducted on 54 patients undergoing HD at Kosar Hospital of Semnan. The inclusion criteria were end-stage renal disease (ESRD), alternative HD treatment for at least 3 months 3 times a week, and serum phosphate levels greater than 4.5 mg/dL. The participants were randomly assigned to two groups of sevelamer (n = 27) and calcium carbonate (n = 27). If the participants were taking a phosphate binder, they were asked to stop it for 3 weeks. Participants in the sevelamer group received 800 mg of sevelamer at most three times a day and those in the calcium carbonate group were treated with 500 mg of calcium carbonate at most 3 times a day. Before and 3 months after the intervention, the serum levels of calcium, magnesium, and phosphorus were measured through the Arsenazo method using the Pars Azmun kit in the Selectra auto-analyzer. Twenty-one patients in the sevelamer group and 22 patients in the calcium carbonate group finished the study. **Results:** The results showed that calcium carbonate and sevelamer increased serum magnesium level by 0.20 (P = 0.028) and 0.26 (P = 0.002), on average, which were statistically significant. The administration of calcium carbonate did not significantly change serum calcium levels (P = 0.53), whereas sevelamer reduced serum calcium levels by 0.23 (P = 0.017), on average. This reduction was statistically significant. The results also indicated that none of the calcium carbonate (P = 0.099) and sevelamer (P = 0.543) caused significant changes in serum phosphorus levels. The study findings showed no significant difference between the two groups in terms of changes in the serum levels of magnesium (0.590), calcium (0.116), and phosphorus (0.113). **Conclusions:** Both drugs (Sevelamer and calcium carbonate) prevented hypomagnesemia and increased serum magnesium levels, but no significant differences were found in blood levels of calcium, phosphorus, and magnesium compared to the two drugs. Considering the effect of magnesium on cardiovascular diseases, increasing the serum magnesium levels through the administration of calcium carbonate and sevelamer can prevent the likelihood of cardiovascular diseases. However, none of the studied drugs was superior to the other in this regard.

Keywords: *Calcium carbonate, hemodialysis, magnesium, phosphate binder, sevelamer*

Introduction

End-stage renal disease (ESRD) is a major life-threatening disease that requires the patient to receive alternative therapies (e.g. dialysis or transplant). Due to the limitations of kidney transplantation, many patients with ESRD require dialysis to survive.[1] Hemodialysis (HD) is the most common type of dialysis used in many countries. In addition, more than 90% of dialysis patients in Iran are under HD.[2] HD is currently being used as a vital treatment for over 3,000 patients with chronic kidney disease (CKD) in the US. According to the data published by the Foundation for Special Diseases Affairs and the Iranian Kidney Patients Support Charity, the number of patients with advanced chronic kidney disease (ACKD) reached about 35,000 in 2006 and it is estimated to exceed 40,000 by 2011 with an annual growth of 12%.[3]

As the second most abundant intracellular cation, magnesium is essential for the regulation of several enzymes and cellular functions. Among the general population,

How to cite this article: Jandaghi E, Yarmohammadi M, Ghorbani R, Jalali T, Khadjeh Salehani A, Mohammad Khani P. Comparison of sevelamer and calcium carbonate in the prevention of hypomagnesemia in hemodialysis patients. Int J Prev Med 2021;12:104.

Address for correspondence:
Dr. Maliheh Yarmohammadi, Kosar Hospital, Amin Street, Semnan, Iran.
E-mail: malihehyarmohamadi@yahoo.com

Access this article online

Website: www.ijpvmjournal.net/www.ijpm.ir

DOI: 10.4103/ijpvm.IJPVM_464_19

Quick Response Code:

hypomagnesemia is largely associated with an increased risk of diabetes, hypertension, and cardiac arrhythmias as well as cardiovascular stimulation and mortality. Recent studies have shown that hypomagnesemia can be one of the causes of CKD and lead to increased cardiovascular mortality in patients with ESRD (requiring dialysis).[4]

In normal glomerular filtration rate (GFR), the kidney filters 2000–2400 mg of magnesium per day and 96% of filtered magnesium is reabsorbed in the renal tubules.[5] In patients with renal failure despite the impaired capacity of kidney for Mg excretion, low serum Mg levels have commonly been reported in patients receiving HD or peritoneal dialysis (PD).[6]

Serum magnesium levels in dialysis patients depend on magnesium intake, nutritional status (serum albumin), dialysis dose, and magnesium concentration in dialysis.[4]

Sevelamer is a non-calcium phosphate binder used to control serum phosphorus levels and prevent hypercalcemia in dialysis patients. This drug is available in 400- and 800-mg forms and can be used with meals three times a day at doses of 800 mg to 1600 mg. Sevelamer also causes mild side effects such as nausea, dyspepsia, diarrhea, and constipation.

Calcium carbonate is another phosphate binder used to control phosphorus levels in patients with CKD undergoing dialysis. Some side effects of this drug include nausea, constipation, and hypercalcemia.[7]

Roza-Diez *et al*. studied the effect of sevelamer on serum magnesium levels in dialysis patients and reported that this drug prevented hypomagnesemia.[4] De-Francisco *et al*. investigated the effect of sevelamer on serum levels of magnesium and calcium and concluded that this drug increased both magnesium and calcium levels in dialysis patients. Therefore, sevelamer can be a suitable treatment for hyperphosphatemia.

Malnutrition is a major challenge to HD that makes patients prone to hypomagnesemia, causes cardiovascular complication and increases mortality. Previous studies have mostly dealt with the effect of sevelamer on phosphate levels and a few studies have investigated the effect of calcium carbonate or sevelamer on serum magnesium levels. Hence, this study aimed to investigate the effects of sevelamer and calcium carbonate, as phosphate binders, on serum levels of magnesium, calcium, and phosphorus in HD patients.

Methods

This parallel clinical trial was conducted on 54 patients undergoing HD at Kosar Hospital of Semnan in 2018. The Ethics Committee of Semnan University of Medical Sciences (IRCT20180831040912N1) approved the research. The inclusion criteria were ESRD, alternative HD treatment for at least 3 months 3 times a week, and serum phosphate levels of greater than 4.5 mg/dL. In addition, the exclusion criteria were acute cardiovascular and liver diseases, diarrhea during the last week before the intervention, history of ileostomy, colostomy or major gastrointestinal surgeries, taking cyclosporine, aminoglycoside, amphotericin B, furosemide or thiazide, and hypercalcemia.

The participants were briefed on sevelamer and calcium carbonate and their effects, they were assured that taking sevelamer and calcium carbonate did not harm them. Then a written consent form was obtained from them before assigning them to two groups and beginning the intervention. If the participants were taking a phosphate binder, they were asked to stop it for 3 weeks. Participants in the sevelamer group (n = 27) received 800 mg of sevelamer three times a day and those in the calcium carbonate group (n = 27) were treated with 500 mg of calcium carbonate at most 3 times a day. Before and 3 months after the intervention, the serum levels of calcium, magnesium, and phosphorus were measured through the Arsenazo method using the Pars Azmun kit in the Selectra auto-analyzer. Over the three months of the intervention, 11 patients were excluded from the study due to kidney transplant, a shift from HD to peritoneal dialysis, noncooperation in the intervention, and death. Finally, 21 patients in the sevelamer group and 22 patients in the calcium carbonate group finished the study [Figure 1].

The data were statistically analyzed using the Kolmogorov–Smirnov test, Chi-square test, student's *t*-test, paired sample *t*-test, and linear regression in SPSS 23. The level of significance was determined to 0.05.

Results

The results showed that 45.4% of participants from the calcium carbonate group (10 patients) and 61.9% of

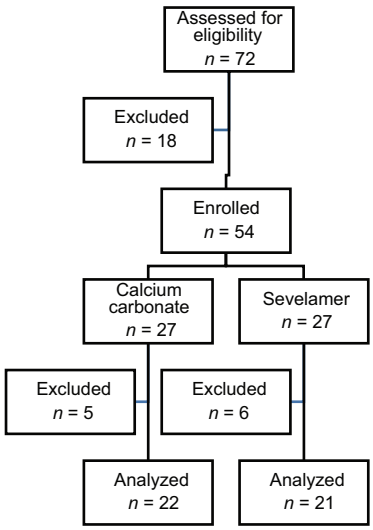

Figure 1: Consort chart of study design

participants from the sevelamer group (13 patients) were females. There was no significant difference between the two groups in this regard (P = 0.280). The mean age of participants was 66.1 ± 11.7 years in the calcium carbonate group and 57.5 ± 11.9 years in the sevelamer group. There was no significant difference between the two groups in terms of age (P = 0.22). Calcium carbonate and sevelamer increased serum magnesium levels by 0.20 (P = 0.028) and 0.26 (P = 0.002), on average, which was statistically significant [Table 1]. Administration of calcium carbonate did not significantly change serum calcium levels (P = 0.53), whereas sevelamer reduced serum calcium levels by 0.23 (P = 0.017), on average. This reduction was statistically significant [Table 1]. In addition, the results indicated that none of calcium carbonate (P = 0.099) and sevelamer (P = 0.543) caused significant changes in serum phosphorus levels [Table 1]. Linear regression was performed in this study to investigate the concurrent effect of age, gender, and drug on the studied parameters. The results indicated that the type of drug had no significant effect on changes in the studied parameters. This means that there was no significant difference between sevelamer and calcium carbonate in terms of serum levels of magnesium (0.590), calcium (0.116), and phosphorus (0.113) [Table 2]. However, there was an inverse significant relationship between age and serum levels of magnesium (P = 0.045) and phosphorus (P = 0.025).

Discussion

Serum phosphorus levels should be specially taken into account in patients with CKD, because such patients should follow a low-phosphate diet and take phosphate binders to prevent increased phosphorus levels. Many phosphate binders contain calcium. so calcium can be accumulated in some parts of the body and increases its serum levels.

Similar studies have been conducted around the world about the effects of sevelamer and other phosphate binders on serum levels of magnesium, calcium, and phosphorus. Recent recommendations of Kidney Disease: Improving Global Outcomes (KDIGO), affiliated with the International Society of Nephrology, emphasize serious administration of calcium-containing phosphate binders to HD patients with high serum calcium levels.[8] The main advantage of magnesium-containing phosphate binders such as magnesium carbonate is that they do not cause calcium overload and prevent hypercalcemia. Several studies have investigated the effects of sevelamer and other phosphate binders on serum levels of magnesium, calcium, and phosphorus and reported different results. Studies have shown that the administration of magnesium carbonate was associated with a decrease in the severity of vascular atherosclerosis and a decrease in cardiovascular mortality.[9] Prajapati *et al*. (2014) studied the effects of calcium acetate, calcium carbonate, sevelamer, and lanthanum carbonate on serum levels of phosphorus, calcium, and alkaline phosphatase 4, 8, and 12 weeks after the treatment and parathyroid hormone (PTH) levels 12 weeks after the treatment. Their findings indicated that sevelamer and calcium carbonate had the greatest and the smallest effects on the reduction of serum phosphorus levels, respectively. Sevelamer and lanthanum carbonate did not significantly change serum calcium levels, whereas calcium-containing phosphate binders significantly increased serum calcium levels, and calcium acetate had the greatest effect on raising serum calcium levels. Their results also suggested that sevelamer was more effective than other factors in reducing hypercalcemia.[10] This study also showed that the administration of sevelamer reduced serum calcium levels. However, unlike some previous studies, this study indicated that sevelamer did not significantly reduce serum phosphorus levels. The findings of this study also showed a significant increase in serum magnesium levels following treatment with sevelamer and calcium carbonate.

According to the findings of Prajapati *et al*., it can be stated that sevelamer can be effective in preventing hypercalcemia and both sevelamer and calcium carbonate are effective in preventing hypomagnesemia. However, none of them have significant effects on phosphate levels.

In a study conducted by Carole Nadin, sevelamer was effective in controlling the serum phosphate levels and reducing the lipids and also reduced the risk of hypercalcemia.[11] This is consistent with the findings of this study where the administration of sevelamer reduced the serum levels of calcium and phosphorus, although the

Table 1: Mean and standard deviation of parameters studied in hemodialysis patients before and after calcium carbonate and sevelamer administration

Parameters studied	Drug	After intervention		Before intervention		*P*
		Standard deviation	Mean	Standard deviation	Mean	
Magnesium	calcium carbonate	0.24	2.81	0.36	2.61	0.028
	sevelamer	0.33	2.90	0.15	2.63	0.0020
Calcium	calcium carbonate	0.44	0.488	0.82	8.35	0.530
	sevelamer	350.	8.64	0.51	878.	0.0170
Phosphorus	calcium carbonate	860.	0.754	830.	364.	0990.
	Sevelamer	0.77	70.4	1.18	864.	5430.

Table 2: Comparison of the effect of Sevelamer and Calcium Carbonate on serum magnesium, Calcium and phosphorus levels

Difference	Drug	Mean	Standard deviation	*P*
Magnesium	Calcium Carbonate	0.2000	0.39881	0.590
	Sevelamer	0.2619	0.34565	
Phosphorus	Calcium Carbonate	0.3864	1.05121	0.113
	Sevelamer	-0.1524	1.12899	
Calcium	Calcium Carbonate	0.1273	0.93411	0.116
	Sevelamer	-0.2286	0.40391	

reduction in phosphorus was not statistically significant.

Roza-Diez *et al*. investigated the effects of sevelamer, calcium carbonate, and calcium acetate on dialysis patients and concluded that serum calcium levels were lower in patients who were treated with sevelamer than other patients. There was no significant difference between the three groups in terms of phosphorus level. In addition, serum magnesium levels were higher in patients who received sevelamer ($P < 0.05$) and serum magnesium levels were normal in the majority of them ($P = 0.02$). On the other hand, hypomagnesemia was observed in patients treated with proton pomp inhibitor (PPI). They also found the protective effect of sevelamer against hypomagnesemia (OR: 0.44, 95% CI: 0.21-0.87). Their study showed the protective properties of sevelamer against hypomagnesemia, even considering the effects of PPI, although their findings questioned the effectiveness of sevelamer in the prevention of calcification.[4]

Serum magnesium levels of participants significantly increased after the administration of both drugs in this study ($P = 0.002$; $P = 0.028$), these drugs prevented hypomagnesemia and significantly increased serum magnesium levels although there was no significant difference between the two drugs in terms of changes in serum magnesium levels (0.590). Serum calcium levels significantly reduced after the administration of sevelamer ($P = 0.017$) but insignificantly increased after the administration of calcium carbonate ($P = 0.53$). This is consistent with the findings of Roza-Diez *et al*. However, there was no significant difference between the two drugs in terms of serum calcium levels ($P = 0.116$), which is inconsistent with the results of Roza-Diez *et al*. Reduced serum phosphorus levels were significant in none of the groups ($P = 0.543$; $P = 0.099$). This can be attributed to a small sample size, different laboratory methods, and different low-phosphate diets of patients or drug interactions.

Moreover, Roza-Diez *et al*. reported that a considerable number of patients with hypomagnesemia were under treatment with PPI, something which was not taken into account in this study.

The findings of Mitsopoulos *et al*. indicated that the administration of sevelamer reduced serum phosphate levels ($P < 0.001$) and iPTH ($P < 0.001$) but increased serum magnesium levels ($P < 0.001$). They also reported a significant reduction in low-density lipoprotein (LDL) and cholesterol and an increase in high-density lipoprotein (HDL) and apolipoprotein levels ($P < 0.001$) following the administration of sevelamer.[12] Consistent with these findings, there was a significant increase in serum magnesium levels but an insignificant decrease in serum phosphorus levels in HD patients treated with sevelamer in this study.

Hervas *et al*. observed a significant decrease in serum phosphorus levels of patients treated with sevelamer or calcium carbonate and also reported the lipids profile of patients who received sevelamer. Their results also demonstrated the effectiveness of sevelamer in reducing serum phosphorus levels and preventing atherosclerosis in HD patients.[13]

Savica (2008) showed that the administration of sevelamer substantiates serum phosphorus levels.[14] This is inconsistent with the findings of this study where sevelamer insignificantly reduced serum phosphorus levels. This can be attributed to the smaller size of the study population, the use of different laboratory methods and kits, different phosphate-containing diets followed by patients, and the ways phosphate binders were taken by them.

De-Francisco *et al*. compared the effects of sevelamer and calcium acetate/magnesium carbonate in 326 patients under dialysis. Their results indicated that phosphorus levels dramatically reduced in both groups but there was no significant difference between them. Administration of calcium acetate/magnesium carbonate pills led to a slight increase in the total serum calcium levels but caused no change in ionized calcium levels. In addition, there was a non-symptomatic increase in serum magnesium levels in patients who were treated with calcium acetate/magnesium carbonate.[15] Consistent with this finding, calcium carbonate increased serum calcium levels in the present study. Calcium carbonate also insignificantly increased serum phosphorus levels. In addition, the administration of sevelamer caused an insignificant decrease in serum phosphorus levels. Increased serum phosphorus levels in the calcium carbonate group can be probably attributed to the small sample size and different diets of participants in this study. Both sevelamer and calcium carbonate increased serum magnesium levels but there was no significant difference between them in this regard.

In another study, De-Francisco *et al*. (2014) reported that optimal serum phosphate levels were achieved by administering magnesium carbonate and stated that magnesium carbonate was more effective than calcium acetate in this regard.[16]

Arroyo *et al*. studied the effects of magnesium carbonate as a replacement for aluminum hydroxide and showed that this drug significantly reduced phosphate (P = 0.027) but had no effects on serum levels of calcium and PTH.[17]

Luci Setiani *et al*. investigated the effects of calcium-based phosphate chelators on serum levels of calcium and phosphorus in patients under HD and showed that 23%, 42.7%, and 34.3% of participants exhibited hypocalcemia, normocalcemia, and hypercalcemia, respectively. However, hypophosphatemia, hyperphosphatemia, and normophosphatemia were observed in 14.6%, 53.1%, and 32.3% of participants. They also stated that the way phosphate binders are taken affects therapeutic results.[18]

Since the above-mentioned research was a qualitative study, its results cannot be compared with the findings of this study. However, given that phosphate binders caused no significant decrease in serum phosphorus levels in this study, it can be stated that the results were somewhat similar. In the study by Luci Setiani *et al*., 46.9% of participants exhibited normal or low levels of phosphorus after treatment with phosphate binders and serum phosphorus levels were high in half of them. This can be consistent with the findings of this study where there were no significant difference between the pre- and post-intervention serum phosphorus levels. Administration of calcium carbonate caused hypercalcemia in this study, although this change was not statistically significant. Moreover, 34% of participants in this study were hypercalcemic. Different results of these two studies can be attributed to different sample sizes and different phosphate-containing diets of participants.

In a systematic review and meta-analysis through 20 original papers and abstracts in 2019, the association between magnesium and mortality in chronic renal failure and dialysis patients was assessed.[19]

According to the KDIGO guideline, the diagnosis and treatment of calcium and phosphorus disorders have been identified but magnesium disorders were not considered.[8] With due attention to the association between magnesium and mortality in HD patients and chronic renal failure, nephrologists should have greater attention to magnesium monitoring in these patients. The importance of our study demonstrates the preventive effects of sevelamer and calcium carbonate on hypomagnesemia.

Some of our research limitations were: few number of patients who met the inclusion criteria and a single center study. It recommended that further studies with a larger sample size and multicenter should be performed.

Conclusions

Administration of sevelamer to patients with CKD increased serum magnesium levels and decreased serum calcium levels but had no significant effect on serum phosphorus level. In addition, calcium carbonate increased serum magnesium levels but had no significant effect on serum levels of phosphorus and calcium in patients with CKD. The results demonstrated no significant difference between these two drugs in terms of their effects on serum levels of calcium, magnesium, and phosphorus. Considering the effect of hypomagnesemia on cardiovascular diseases, the administration of calcium carbonate and sevelamer can prevent cardiovascular disease. However, none of the studied drugs was superior to the other in this regard. Since the results were not statistically significant in some cases such as serum phosphorus levels, there is a need for similar studies with larger sample sizes.

Acknowledgments

The authors would like to thank the Clinical Research Development Department of Kosar Hospital of Semnan, affiliated with Semnan University of Medical Sciences, for financing the present research project, the staff of the Dialysis Department of this hospital, especially Ms. Bahraminasab, who provided us with medical records of patients, and Research and Technology Deputy of Semnan University of Medical Sciences that financially supported this research project

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Received: 12 Dec 19 **Accepted:** 07 Mar 20
Published: 24 Aug 21

References

1. Valderrábano F, Berthoux FC, Jones EH, Mehls O. Report on management of renal failure in Europe, XXV, 1994 end stage renal disease and dialysis report. The EDTA-ERA Registry. European Dialysis and Transplant Association-European Renal Association. Nephrol Dial Transplant 1996;11(Suppl 1):2-21.
2. Beladi Musavi SS, Hayati F, Alemzadeh Ansari MJ, Valav E, Cheraghian B, Shahbazian H, *et al*. A survival at 1, 3, and 5 years in diabetic and nondiabetic hemodialysis patients. Iran J Kidney Dis 2010;4:74-7.
3. Mousavi SSB, Mousavi MB, Motemednia F. Baclofen-induced encephalopathy in patient with end stage renal disease: Two case reports. Indian J Nephrol 2012;22:210-2.
4. Rosa-Diez G, Negri AL, Crucelegui MS, Philippi R, Perez-Teysseyre H, Sarabia-Reyes C, *et al*. Sevelamer carbonate

reduces the risk of hypomagnesemia in hemodialysis-requiring end-stage renal disease patients. Clin Kidney J 2016;9:481-5.
5. Blaine J, Chonchol M, Levi M. Renal control of calcium, phosphate, and magnesium homeostasis. Clin J Am Soc Nephrol 2015;10:1257-72.
6. Eisenman K, Holley JL. A higher magnesium dialysate concentration treats hypomagnesemia 2005;25:604-5.
7. Daugirdas John T, Blake P, Ing T. Handbook of dialysis fifth edition. In: Coyne D, Larson D, Delmez J, editors. Bone Disease. Philadelphi: Wolters Kluwer Health; 2015. Ch. 36, p. 674-5.
8. KDIGO clinical practice guideline Update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Kidney Int Suppl 2017;7:1-59.
9. Block GA, Raggi P, Bellasi A, Kooienga L, Spiegel DM. Mortality effect of coronary calcificationand phosphate binder choice in incident hemodialysis patients. Kidney Int 2007;71:438-41.
10. Prajapati V, Galani V, Shah P. A comparative study of phosphate binders in patients with end stage kidney disease undergoing hemodialysis. Saudi J Kidney Dis Transpl 2014;25:530-8.
11. Nadin C. Sevelamer as a phosphate binder in adult hemodialysis patients: An evidence-based review of its therapeutic value. Core Evid 2005;1:43-63.
12. Mitsopoulos E, Griveas I, Zanos S, Anagnostopoulos K, Giannakou A, Pavlitou A, *et al*. Increase in serum magnesium level in haemodialysis patients receiving sevelamer hydrochloride. Int Urol Nephrol 2005;37:321-8.
13. Hervas JG, Prados D, Cerezo S. Treatment of hyperphosphatemia with sevelamer hydrochloride in hemodialysis patients: A comparison with calcium acetate. Kidney Int Suppl 2003:S69-72.
14. Savica V, Santoro D, Monardo P, Mallamace A, Bellinghieri G. Sevelamer carbonate in the treatment of hyperphosphatemia in patients with chronic kidney disease on hemodialysis. Ther Clin Risk Manag 2008;4:821-6.
15. de Francisco AL, Leidig M, Covic AC, Ketteler M, Benedyk-Lorens E, Mircescu GM, *et al*. Evaluation of calcium acetate/magnesium carbonate as a phosphate binder compared with sevelamer hydrochloride in haemodialysis patients: A controlled randomized study (CALMAG study) assessing efficacy and tolerability. Nephrology, dialysis, transplantation: Official publication of the European Dialysis and Transplant Association-European Renal Association 2010;25:3707-17.
16. de Francisco AL, Belmar L, Pinera C, Kislikova M, Seras M, Serrano M, *et al*. Effect of calcium acetate/magnesium carbonate in the treatment of hyperphosphataemia in dialysis patients in real clinical practice. One year follow up. Nefrologia 2014;34:617-27.
17. Arroyo D, Panizo N, Abad S, Vega A, Perez-de Jose A, Lopez-Gomez JM. The effect of replacing aluminium hydroxide with calcium acetate/magnesium carbonate on serum phosphorus control in haemodialysis patients. Nefrologia 2014;34:199-204.
18. Setiani Agus L, Effendi I, Abdillah S. Influence of the use of phosphate binders on serum levels of calcium phosphate in patients with chronic kidney disease undergoing hemodialysis: A retrospective and prospective study. Saudi Pharm J 2014;22:333-7.
19. Xiong J, He T, Wang M, Nie L, Zhang Y, Wang Y, *et al*. Serum magnesium, mortality, and cardiovascular disease in chronic kidney disease and end-stage renal disease patients: A systematic review and meta-analysis. J Nephrol 2019;32:791-802.