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Comparison of the efficacy of sucroferric oxyhydroxide and lanthanum carbonate in the hyperphosphatemia of maintainable Hemodialysis

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Abstract

Objective To study the efficacy of sucroferric oxyhydroxide (SFOH) and lanthanum carbonate (LC) in the treatment of hemodialysis hyperphosphatemia.

Methods A total of 60 hemodialysis patients with secondary hyperparathyroidism combined with hyperphosphatemia from January 2024 to April 2024 in China Rongtong Medical & Healthcare Group Tai'an 88 Hospital were selected. All patients were randomly divided into 2 groups. One group was treated with SFOH, and the other with LC. Patients in the 2 groups were treated for 3 months continuously, and clinical outcomes, serum phosphorus, serum calcium, and intact parathyroid hormone (iPTH) levels were compared before treatment, and at 1, 2, and 3 months after treatment.

Results When compared with before treatment, the serum phosphorus levels of both groups of patients decreased significantly after 1 month, 2 months, and 3 months of treatment, with statistical significance ($P < 0.01$). The degree of serum phosphorus decrease in SFOH group was higher than that in LC group ($P < 0.01$, $P < 0.05$). There was no statistically significant difference in the effect of serum calcium between the two groups ($P > 0.05$). Both groups of patients showed a significant decrease in iPTH after treatment, with a statistically significant difference ($P < 0.01$). The degree of iPTH decrease in SFOH group was more pronounced than in LC group ($P < 0.05$). After treatment, the serum hosphorus compliance rates of SFOH group and LC Group were 80% and 53.3%, respectively, and the difference in effective rates between the two groups was statistically significant ($P < 0.05$).

Conclusion SFOH was superior to LC in lowering patients' blood phosphorus and iPTH levels in patients with maintenance hemodialysis hyperphosphatemia combined with secondary hyperparathyroidism.

Keywords Sucroferric oxyhydroxide, Lanthanum carbonate, Hyperphosphatemia, Hemodialysis

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Introduction

Hyperphosphatemia is one of the common complications in hemodialysis patients, and long-term hyperphosphatemia can lead to itchy skin, hand and foot twitching, bone pain, osteoporosis, bone fracture, painful limb ulcers, and vascular calcification, which not only accelerates the progression of chronic kidney disease (CKD), but also increases the risk of cardiovascular disease and all-cause mortality [1]. Therefore, it is important to improve the management of hyperphosphatemia in clinical practice. To achieve serum phosphorus control and compliance, 3D treatment strategies are advocated in the clinic. Phosphorus binding agents (drug D) are needed along with control of dietary phosphorus intake (diet D) and intensification of dialysis (dialysis D) [2]. Domestic and international guidelines consistently recommend non-calcium-containing phosphorus-binding agents as first-line phosphorus-lowering drugs, and they limit the use of calcium-containing phosphorus-binding agents. Sucroferric oxyhydroxide (SFOH) and lanthanum carbonate (LC) entered the Chinese market in 2012 and 2023 respectively. They have been in clinical use for a relatively short time. Both are valuable in the management of serum phosphorus compliance in dialysis and non-dialysis patients [1, 2]. The study intends to compare the clinical efficacy of SFOH and LC in patients with secondary hyperparathyroidism with hyperphosphatemia, as reported below.

Methods

Object of study

Sixty hemodialysis patients with secondary hyperparathyroidism with hyperphosphatemia were selected from January 2024 to April 2024 in China Rongtong Medical & Healthcare Group Tai'an 88 Hospital. Prior to enrollment, the patient was using calcium acetate to lower serum phosphorus, but it was not effective. All of patients were older than 18 years of age and had been on dialysis for 3–10 years. The patients were divided into two groups according to the numerical randomization method, one with SFOH and the other with LC, with 30 patients in each group. In the SFOH group, there were 16 males and 14 females with a mean age of (50.8 ± 12.4) years. In the LC group, there were 20 males and 10 females with a mean age of (52.3 ± 14.6) years. All patients were adequately dialyzed and achieved target values for urea reduction rate (URR) and urea removal index (Kt/V) (URR ≥ 70%, Kt/V ≥ 1.4). All patients were followed up until July 31, 2024. In this study, patients were not restricted from using drugs such as calcium, osteotriol, and cinacalcet.

Ethical consideration

We received approval from the Medical Ethics Committee of the China Rongtong Medical & Healthcare Group Tai'an 88 Hospital for undertaking this study. The study was designed to be secure and fair to patients while minimizing risk of harm to participants. The included partici pants provided written informed voluntary consent. Participants had the right to withdraw from the study at any time.

Therapeutic regimen

One group was treated with SFOH (Velphoro, 0.5 g/tablet), 1 tablet chewed with a meal 3 times/day, and the other group was treated with LC (Fosrenol, 500 mg/tablet), 1 tablet chewed with a meal 3 times/day. Patients in both groups were treated for 3 months. During the treatment period, patients in both groups were put on a low-phosphorus diet, with phosphorus intake less than 7 mg/(kg·d).

Clinical observation indicators

In both groups, blood was collected before treatment, at 1 month, 2 months, and 3 months of treatment. Serum phosphorus, serum calcium, and intact parathyroid hormone (iPTH) were measured using an automated biochemical analyzer. The serum phosphorus compliance rate of the two groups after 1 month, 2 months and 3 months of medication were counted separately. And to compare the adverse effects during the treatment of the two groups. Both KDIGO and CKD-MBD guidelines recommend using phosphate binders to lower elevated serum phosphorus levels towards the normal range (typically 2.5–4.5 mg/dL) [2]. However, most dialysis centers use a serum phosphate target value of ≤ 1.78 mmol. In this study, serum phosphorus ≤ 1.78 mmol/L was judged to be effective.

Statistical methods

SPSS 24.0 software was used to statistically analyze the data of the two groups. Measurement information was expressed by $\bar{x} \pm s$, and the t-test was used between the groups. Counting information was expressed by %, and the χ^2 test was used. $p < 0.05$ indicated that the difference was statistically significant.

Results

Comparison of serum phosphorus, serum calcium, and iPTH between the two groups of patients before and after treatment

Compared with the serum phosphorus level before treatment, serum phosphorus decreased significantly in both groups after 1, 2 and 3 months of treatment, and the difference was statistically significant ($P < 0.01$). Among them, the SFOH group showed a significant decreasein

Table 1 Comparison of serum phosphorus before and after treatment in two groups of patients ($\bar{x} \pm s$)

Group	Number	Serum phosphorus(mmol/L)			
		Pre-treatment	1 month	2 months	3 months
SFOH	20	2.33 ± 0.12	1.79 ± 0.15[①②]	1.70 ± 0.14[①②]	1.65 ± 0.13[①③]
LC	20	2.31 ± 0.10	1.94 ± 0.15[①]	1.83 ± 0.11[①]	1.70 ± 0.12[①]

Comparison with pre-treatment, [①]*P*<0.01;comparison of SFOH group and LC group at the same time point after treatment, [②]*P*<0.01, [③]*P*<0.05

Table 2 Comparison of serum calcium before and after treatment in two groups of patients ($\bar{x} \pm s$)

Group	Number	Serum calcium(mmol/L)			
		Pre-treatment	1 month	2 months	3 months
SFOH	20	2.21 ± 0.06	2.19 ± 0.04	2.18 ± 0.05	2.17 ± 0.04
LC	20	2.20 ± 0.03	2.19 ± 0.03	2.18 ± 0.03	2.17 ± 0.03

Comparison with pre-treatment, *P* > 0.05

Table 3 Comparison of iPTH before and after treatment in two groups of patients ($\bar{x} \pm s$)

Group	Number	iPTH/(pg/mL)			
		Pre-treatment	1 month	2 months	3 months
SFOH	20	418 ± 24	381 ± 19[①②]	344 ± 21[①②]	318 ± 19[①②]
LC	20	416 ± 24	398 ± 21[①]	362 ± 26[①]	337 ± 25[①]

Comparison with pre-treatment, [①] *P*<0.05;comparison of SFOH group and LC group at the same time point after treatment, [②] *P*<0.05

serum phosphorus compared with the LC group ($P < 0.01$, $P < 0.05$) (Table 1). The difference between the two groups on serum calcium was not statistically significant ($P > 0.05$) (Table 2). The iPTH decreased significantly in both groups after treatment, and the difference was statistically significant ($P < 0.01$). The decrease in iPTH was greater in the SFOH group compared with the LC group ($P < 0.05$) (Table 3).

Comparison of the efficacy of the two groups of patients after treatment

After 3 months of treatment, the standardized rate of serum phosphorus in the LC group was 53.3%. The early phosphorus compliance rate was significantly higher in the SFOH group, with 33.3% of serum phosphorus compliance rate after 1 month of treatment, 56.6% after 2 months of treatment, and up to 80% after 3 months of treatment. The SFOH group had significantly higher serum phosphorus compliance rates than the LC group after 1, 2 and 3 months of treatment (all $P < 0.05$) (Table 4).

Comparison of adverse reactions in the treatment of the two groups of patients

During the treatment, 2 cases of gastrointestinal flatulence occurred in the SFOH group. Two cases of nausea and vomiting and one case of constipation occurred in the LC group. Symptomatic treatment was given to

Table 4 Serum phosphorus compliance rate in two groups [n(%)]

Group	1 month		χ^2	*P*	2 months		χ^2	*P*	3 months		χ^2	*P*
	Achieved	Not met			Achieved	Not met			Achieved	Not met		
SFOH	10(33.3)	20(66.6)	4.812	0.0258	17(56.6)	13(43.3)	4.344	0.037	24(80)	6(20)	4.8	0.028
LC	3(10)	27(90)			9(30)	21(70)			16(53.3)	14(46.6)		

both groups, and the medication was continued after the symptoms were relieved. The rates of gastrointestinal adverse reactions in the SFOH group and LC group were 6.6% (2/30) and 4/30 (13.3%), respectively, and the differences in the incidence of adverse reactions between the groups were not statistically significant when compared ($\chi^2 = 0.671$, $P > 0.05$).

Discussion

Hyperphosphatemia is common in end-stage CKD, which occurs as a result of impaired renal phosphate excretion. Elevated serum phosphorus levels directly exacerbate vascular calcification and secondary hyperparathyroidism, which in turn leads to increased cardiovascular morbidity and mortality [1]. Studies [1, 2] have shown that hyperphosphatemia is an independent risk factor for cardiovascular morbidity and mortality in patients with chronic kidney disease stages 3–5. For every 0.32 mmol/L increase in serum phosphorus levels, the risk of cardiovascular death increased by 10% and the risk of all-cause mortality increased by 18% [3]. National and international guidelines state that serum phosphorus management should be initiated in CKD stage 3a to reduce serum phosphorus to near normal range [1, 4].

The current treatment of hyperphosphatemia follows the 3D principles: reduction of phosphorus intake, adequate dialysis, and medication. However, limiting dietary phosphorus intake is difficult to maintain in daily life and it is not sufficient to normalize serum phosphorus concentrations in most patients. As well, standard intermittent hemodialysis performed three times a week is usually not sufficient to maintain serum phosphorus concentrations at appropriate levels. Therefore, in addition to limiting dietary phosphorus intake and undergoing dialysis, patients with CKD need oral phosphorus-lowering drugs to control serum phosphorus concentrations.

SFOH is an iron-based phosphate binder, and its use has been widely expanded since its initial approval in 2013 [5]. It officially enters the Chinese market in February 2023. In the gastrointestinal tract, phosphate binding is formed by ligand exchange between hydroxyl groups in sucrose hydroxyl iron oxide or water and dietary phosphate. The bound phosphate is excreted in the feces, reducing gastrointestinal phosphorus absorption and thus effectively lowering serum phosphorus concentrations [5, 6]. Studies [7, 8] have shown that SFOH has 1.6 times the phosphorus binding capacity of LC.

LC [9] is a compound of the heavy metal lanthanum ion, whose efficacy depends on the high affinity of the lanthanum ion for phosphates. Lanthanide ions are released from carbonates in the acidic environment of the stomach. It can combine with phosphorus in food throughout the digestive tract (stomach, duodenum, jejunum) to form insoluble lanthanum phosphate complexes, which cannot pass through the intestinal wall into the bloodstream and are excreted by the body [10–12]. This reduces the absorption of phosphorus in the gastrointestinal tract. Therefore, LC must be chewed with food and swallowed. The phosphorus-lowering effect of LC is dose-related, and patient compliance and tolerance may be compromised by increasing the dose [13].

In the present study, we found that both drugs improved serum phosphorus and iPTH levels in patients. The effect was more pronounced in the SFOH group. One study reported that the median time to SFOH blood phosphorus compliance was shorter, at only 1.9 weeks [14]. Hypercalcemia did not occur in both groups during treatment. LC has greater gastrointestinal adverse effects such as constipation, nausea, vomiting, and flatulence. Long-term use of LC may pose a risk of metal accumulation. However, it is absorbed in extremely minute amounts of less than 0.002% [12]. And the effects of lanthanum on the body after accumulation have not been found yet [13]. SFOH has a better taste and it is less irritating to the gastrointestinal tract [15]. SFOH may also provide additional benefits to CKD patients. Studies [14–16] have reported that patients treated with SFOH have increased ferritin levels and transferrin saturation (TSAT), reducing the use of intravenous iron and erythropoiesis-stimulating agents (ESAs) while maintaining hemoglobin levels. Despite the iron content of SFOH, no significant signs of iron accumulation were observed and iron metabolism parameters were generally stable, further supporting the safety of its long-term use. And in this 3-month study, changes in ESA and IV iron use were not investigated. This is a limitation that should be addressed in our future studies. SFOH was generally well tolerated and had a low incidence of serious adverse events [14]. It has been demonstrated that during the administration of SFOH, CKD patients can be allowed to moderately increase their dietary protein intake, thereby increasing serum albumin levels, and not affecting vitamin D absorption [7, 15]. Moreover, SFOH can be used to treat hyperphosphatemia in pediatric patients with CKD aged 12 years and older with CKD stage 4–5 (defined as glomerular filtration rate < 30 mL/min/1.73 m2) or undergoing dialysis. SFOH fills the gap of phosphorus-lowering drugs for CKD pediatric patients aged 12–18 years old with CKD stage 4–5 or receiving dialysis treatment in China, which is expected to further improve the quality of life of dialysis patients, and bring a new choice of drug for phosphorus-lowering treatment for CKD dialysis patients in China [8, 14].

Additionally, hyperphosphatemia stimulates iPTH secretion, whereas SFOH and LC indirectly inhibit iPTH overproduction by decreasing phosphorus uptake to reduce phosphatemia [13, 16]. Studies [14, 18] have shown that FGF-23 is also significantly lower in patients

with serum phosphorus attainment. In CKD patients, FGF-23 levels are elevated. It is not only associated with mineral metabolism disorders, but also closely related to endothelial cell dysfunction and the development of atherosclerosis. Moreover, FGF-23 levels are strongly associated with mortality risk in hemodialysis patients. Some studies [7, 13, 18] have reportedthat SFOH and LC can also reduce fibroblast growth factor (FGF)-23, delay the degree of calcification of coronary arteries, and improve the long-term prognosis of patients. FGF-23 levels were not monitored because no relevant kit was available. In the future, we need to expand the sample size, increase the clinical observables, extend the follow-up period, and explore more studies on the clinical efficacy and complications of the drugs.

Conclusions

In summary, SFOH and LC can effectively reduce serum phosphorus and iPTH levels in patients with maintenance hemodialysis hyperphosphatemia combined with secondary hyperparathyroidism, and SFOH has better effect. It is recommended that it can be used in hemodialysis patients clinically according to the actual situation.

Abbreviations

CKD	Chronic kidney disease
SFOH	Sucroferric Oxyhydroxide
LC	Lanthanum carbonate

Author contributions

XQN and CZ conceived of the study and participated in the design. ML was responsible for collecting samples and statistical analysis. YJK helped to perform the statistic analysis, draft the manuscript and modify the article. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The protocol of this study was approved by the Ethics Committee of China Rongtong Medical & Healthcare Group Tai'an 88 Hospital. The study is in line with the World Medical Association Declaration of Helsinki. Before their admission to the study, a signed and dated informed consent was obtained from each patient. They were totally voluntary and could withdraw from the study at any time. We can get information that could identify individual participants during or after data collection.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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