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Original Article

ORIGINAL ARTICLE

Real-world management of hyperphosphataemia with sucroferric oxyhydroxide: the VELREAL multicentre study

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ABSTRACT

Background. The efficacy and safety of sucroferric oxyhydroxide (SO) have been reported in clinical trials. However, real-life data are scarce. This study presents data on the use, efficacy and safety of SO in real clinical practice.

Methods. We performed a retrospective multicentre study, without any influence on the prescription decisions, that included 220 patients from 11 Spanish centres. Demographic, treatment, analytical and nutritional parameters and adherence, side effects and dropout rates were collected during 6 months.

Results. SO was initiated due to inadequate control of serum phosphate (P) in 70% of participants and in 24.5% to reduce the number of tablets. Monotherapy with SO increased from 44% to 74.1%, with a reduction in the average daily number of sachets/tablets from six to two. Serum P decreased by 20% (4.6 ± 1.2 versus 5.8 ± 1.3 mg/dL; $P < 0.001$), with a significant reduction in intact parathyroid hormone levels ($P < 0.01$). The percentage of patients with adequate serum P control at threshold levels of 5 and 4.5 mg/dL increased by 45.4% and 35.9%, respectively. Serum ferritin was not modified, while the

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transferrin saturation index increased significantly (P = 0.04). Serum albumin and normalized protein catabolic rate, when normalized by serum P, increased, averaging 37% and 39%, respectively (P < 0.001). Adherent patients increased from 28.2% to 52.7%. Adverse effects were reported by 14.1% of participants, with abandonment of treatment in 9.5%.

Conclusions. The use of SO in real-life results in better control of serum P, a reduction in the number of tablets and an improvement in therapeutic adherence. In addition, it may be beneficial with regards to secondary hyperparathyroidism and nutritional status.

Keywords: haemodialysis, hyperphosphataemia, nutritional status, sucorferric oxyhydroxide, therapeutic adherence

INTRODUCTION

Hyperphosphataemia is a practically universal complication of chronic kidney disease (CKD) and is especially frequent in the more advanced stages of the disease and the dialysis population. Serum phosphorus (P) concentrations above the recommendations of the Kidney Disease: IMproving Global Outcomes (KDIGO) and Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines have been associated with increased mortality in dialysis patients [1, 2]. Dietary control and dialysis treatment are in most cases insufficient to achieve adequate control of serum P, so the use of P binders at the intestinal level to prevent its absorption is common. This P binding is achieved using certain divalent and trivalent cations that are capable of reacting with soluble P salts present in the diet, thereby forming insoluble and non-absorbable P in the digestive tract. Ideally, these drugs should be effective with a small number of tablets, not be absorbable at the digestive level, present minimal adverse effects and be low cost [3].

One of the P binders most recently incorporated into clinical practice is sucroferric oxyhydroxide (SO) [4], a complex whose activity depends on the presence of iron in an oxidized state and which has a marked chemical capacity to react with P groups, forming insoluble salts. This process is fundamentally due to two consecutive and complementary mechanisms: the absorption of the P molecules present in the lumen of the digestive tract and the formation of ferric P.

Several clinical trials have demonstrated the efficacy and safety of SO in haemodialysis (HD) patients [5–7], although with very limited real-life data. This multicentre study aims to present data on the use, efficacy and safety of SO in patients on HD within the setting of real clinical practice.

MATERIALS AND METHODS

Study design and patients

VELphoro in REAL clinical practice (VELREAL) is an observational, retrospective multicentre study on the use of SO in HD patients in real clinical practice, without any influence on the prescription decisions of the physicians, in which 11 Spanish centres participated and a total of 220 patients were included. Informed consent was obtained from the participants. The procedures were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975 and its latest revision.

The inclusion criteria were as follows: age >18 years, CKD Stage 5D under maintenance renal replacement therapy with HD for >6 months, commencement of treatment with SO during the year prior to inclusion in the study and one of the following three conditions: a serum P concentration >4.5 mg/dL (regardless of whether or not the patient had received prior treatment with P binders); a serum P level lower than this level but with intake of an excessive number of P binder tablets that, in the opinion of the investigator, would likely be reduced by the use of SO (most of the investigators considered that four or more P binder tablets was an excessive number of pills) or ongoing treatment with another P binder that could be substituted by SO according to the investigator's criteria with respect to adverse effects or intolerance.

Exclusion criteria included age <18 years, renal replacement therapy other than HD, hypersensitivity to drugs containing iron, history of parathyroidectomy, existence of inflammatory or immunological diseases, kidney transplant recipient, steroid or immunosuppressive therapy, active infectious processes and infection with hepatitis B, C or human immunodeficiency virus.

Biochemical analysis and other study variables

The different variables were collected at the time of initiation of SO treatment and then monthly until completion of the 6-month follow-up. Demographic data and treatment characteristics were collected, including the reasons for prescribing SO treatment and the number of tablets used throughout the follow-up. The following clinical and analytical variables were collected: bone mineral metabolism parameters [calcium (Ca), P and intact parathyroid hormone (iPTH)], ferrokinetics [ferritin and transferrin saturation (TSAT) index], haemoglobin and haematocrit levels, doses of erythropoiesis-stimulating agents, serum albumin and C-reactive protein. Ca levels were corrected for serum albumin. The erythropoietin (EPO) resistance index was defined as the weekly EPO dose (U/kg/weight) divided by the haemoglobin level (g/dL). Protein intake was estimated indirectly by calculating the normalized protein catabolic rate (nPCR), while the dialysis dose was estimated using the K_t/V according to the Daugirdas formula [8].

From the point of view of nutritional assessment, serum albumin and nPCR were each divided by serum P to calculate P-attuned albumin and nPCR (Alb/P and nPCR/P), respectively. These parameters allowed us to assess the effect of the reduction of serum P without restricting protein intake [9, 10].

Finally, adherence to SO treatment was analysed using the simplified medication adherence questionnaire (SMAQ), an instrument based on questions to the patients about their medication habits, which has been used in previous studies to evaluate compliance with P binder treatment in HD patients [11, 12]. In addition, side effects and the treatment dropout rate were analysed throughout the study.

Statistical analysis

Continuous variables were described as mean and standard deviation (SD) or median and interquartile range (IQR) according to their distribution. Categorical variables were described as means of their frequency distribution. Intragroup comparisons

were made using Student's *t*-test for paired samples or the Wilcoxon test. For intergroup comparison, the independent samples Student's *t*-test or Mann–Whitney U-test was used. The comparison between categorical variables was performed using the chi-square test or the McNemar test as appropriate. Comparisons of the same variables at different visits were analysed using a repeated measures analysis of variance test. The multivariable logistic regression analyses were performed to evaluate the factors associated with the better control of hyperphosphataemia under SO therapy. We used the achievement of a serum P concentration <5 mg/dL as the dependent variable and age, sex, presence of diabetes, time on dialysis, online haemodiafiltration (HDF), use of calcimimetics, treatment with native or active vitamin D, K_t/V, nPCR and serum concentrations of P, Ca PTH, 25-hydroxyvitamin D and albumin as baseline covariates. A P-value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS Statistics version 24 (IBM, Armonk, NY, USA).

RESULTS

Patient characteristics

The baseline characteristics of the study participants are shown in Table 1. A total of 220 patients were included: 125 males and 95 females. Their mean age was 64 ± 13 years and 25% were diabetic. The mean time on HD was 46 ± 38 months; 89 patients (40.5%) received online HDF. The Ca concentration in the dialysis fluid varied among patients, from 2.5 to 3 mEq/L; however, in each of the participants the concentration remained constant throughout the study. Most of patients (68.7%) received HD treatment through a native vascular access at baseline; this proportion did not change at the end of the study (69%). The average values of K_t/V and nPCR at baseline were 1.77 ± 0.55 and 1.15 ± 0.37 g/kg/day, respectively, without significant variations during the study.

As regards concomitant treatments at baseline, most patients (84.1%) were receiving iron supplements, in the vast majority of cases (97.2%) in the form of intravenous iron therapy, and 87.7% were being treated with erythropoiesis-stimulating agents. The mean serum level of 25-hydroxyvitamin D was 26.9 ± 7.9 ng/mL and 112 patients were receiving native vitamin D. A total of 116 patients were receiving active vitamin D treatment (62% were on paricalcitol) and 86 were being treated with calcimimetics. Throughout the study there were no significant variations in the doses of any of these drugs. The distribution of the CKD mineral and bone disorder–related drugs is shown in Table 2.

Table 1. Baseline characteristics of the patients

Age (years), mean ± SD	64 ± 13
Men/women, *n*/*n*	125/95
Diabetes, %	25
Time on dialysis (months), mean ± SD	46 ± 38
Online HDF, %	40.5
P (mg/dL), mean ± SD	5.8 ± 1.3
Ca (mg/dL), mean ± SD	8.9 ± 0.6
iPTH (pg/mL), mean ± SD	410 ± 300
Serum 25-hydroxyvitamin D (ng/mL), mean ± SD	26.9 ± 7.9
Albumin (g/dL), median (IQR)	3.7 (3.4–4.1)
C-reactive protein (mg/L), median (IQR)	1.15 (0.44–5)
Haemoglobin (g/dL), mean ± SD	11.6 ± 1.3
Haematocrit (%), mean ± SD	35.6 ± 4.3
Ferritin (mg/dL), mean ± SD	366 ± 243
TSAT index (%), mean ± SD	27.9 ± 9.5
K_t/V, mean ± SD	1.77 ± 0.55
nPCR (g/kg/day), mean ± SD	1.15 ± 0.37
P-normalized albumin ($\times 10^3$), median (IQR)	0.65 (0.56–0.79)
P-normalized nPCR ($\times 10^3$ dL/kg/day), mean ± SD	0.20 ± 0.08
Patients with P <5 mg/dL, %	25
Patients with P <4.5 mg/dL, %	15.9

Treatment with SO

A total of 194 patients (88.2%) had received previous treatment with other P binders, while in 26 (11.8%) the SO was the first binder used in treatment. Of the previously treated patients, 63.4% had received monotherapy, the most frequently used binders being sevelamer carbonate, Ca acetate–magnesium carbonate combination and lanthanum carbonate.

A serum P concentration at baseline <5 mg/dL was present in 25% of patients and 15.9% had a P level <4.5 mg/dL. The indications for initiation of SO treatment were lack of adequate control of serum P levels in 70% of cases, an attempt to reduce the number of tablets in 24.5% and adverse effects/intolerance to previous binders in 5.4%.

At baseline, before switching to SO, the average daily number of sachets/tablets of P binders received by the patients was 6.3 ± 2.6 (range 2–15). The SO treatment was started as monotherapy in 97 patients (44%). Among the 123 patients who started SO combination therapy, the other binders used were sevelamer (38.2% of cases), lanthanum carbonate (31.7%), Ca acetate–magnesium carbonate (23.5%) and Ca-only binders (6.5%).

After 6 months of treatment the mean number of SO tablets per day was 2 ± 1, with the maximum number of tablets administered being 3 (41.4% of cases). At the end of this period, 163 patients (74.1%) were receiving SO treatment as monotherapy, representing an increase of 30% with respect to baseline. The

Table 2. Evolution of biochemical parameters and CKD mineral and bone disorder–related drugs

Parameters	Baseline	Final	P-value
P (mg/dL), mean ± SD	5.8 ± 1.3	4.6 ± 1.2	<0.001
Ca (mg/dL), mean ± SD	8.9 ± 0.6	8.9 ± 0.7	NS
iPTH (pg/mL), median (IQR)	345 (189–525)	324 (201–456)	<0.01
Albumin (g/dL), median (IQR)	3.7 (3.4–4.1)	3.8 (3.5–4.1)	NS
C-reactive protein (mg/L), median (IQR)	1.15 (0.44–5.0)	1.18 (0.39–5.0)	NS
Haemoglobin (g/dL), mean ± SD	11.6 ± 1.3	11.7 ± 1.1	NS
Haematocrit (%), mean ± SD	35.6 ± 4.3	35.8 ± 4.6	NS
Ferritin (mg/dL), mean ± SD	366 ± 243	388 ± 290	NS
TSAT index (%), mean ± SD	27.9 ± 9.5	29.6 ± 10.6	<0.05
K_t/V, mean ± SD	1.77 ± 0.55	1.81 ± 0.46	NS
nPCR (g/kg/day), mean ± SD	1.15 ± 0.37	1.13 ± 0.30	NS
P-normalized albumin ($\times 10^3$), median (IQR)	0.65 (0.56–0.79)	0.85 (0.72–0.97)	<0.001
P-normalized nPCR ($\times 10^3$ dL/kg/day), mean ± SD	0.20 ± 0.08	0.24 ± 0.10	<0.001
CKD-mineral and bone disorder-related drugs, *n* (%)			
Native vitamin D	112 (50.9)	107 (48.6)	NS
Active vitamin D	116 (52.7)	107 (48.6)	NS
Calcimimetics	86 (39)	77 (35)	NS

NS, not significant.

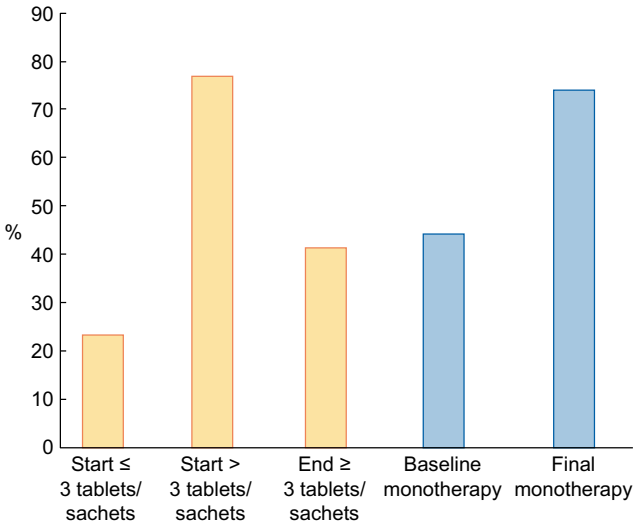

FIGURE 1: Distribution of patients according to the number of tablets/sachets of P binders at the beginning and end of the study and the percentage of monotherapy cases at baseline and at the end of the study.

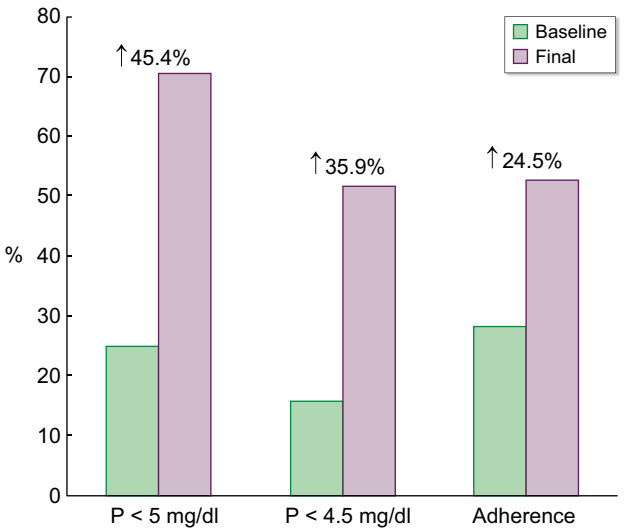

FIGURE 2: Variation in therapeutic adherence and in the percentage of patients with a serum P concentration <5 mg/dL and <4.5 mg/dL.

percentage distribution of the patients in relation to the number of tablets at the end of the study and the monotherapy treatment at baseline and the end of the follow-up period are shown in Figure 1.

Biochemical analysis

The evolution of the biochemical parameters is shown in Table 2. The mean serum concentration of P was reduced from 5.8 ± 1.3 mg/dL at baseline to 4.6 ± 1.2 mg/dL after 6 months of treatment ($P < 0.001$), representing an average decrease of 20%. There was no significant change in Ca concentration, although a slight but significant reduction in iPTH levels ($P < 0.01$) was observed. At the end of the study, the percentage of patients who obtained adequate control of serum P at threshold levels of 5 and 4.5 mg/dL increased by 45.4% and 35.9%, respectively, compared with baseline (Figure 2). The bimonthly evolution of serum P, number of tablets and percentage of patients with an adequate control of serum P at threshold levels of 5 and 4.5 mg/dL after initiation of SO therapy are shown in Table 3.

Subgroup analyses were performed to evaluate the response to SO according to sex, presence of diabetes, online HDF, Ca concentration in the dialysate fluid, baseline serum PTH and 25-hydroxyvitamin D and treatment with active vitamin D or calcimimetics (Table 4). There were no significant differences between subgroups, except for patients treated with active vitamin D, who showed a lower reduction in serum P, and subjects receiving calcimimetics, who exhibited a greater decrease in serum P.

Table 3. Bimonthly evolution of serum P, number of tablets and percentage of patients under control after initiation of SO

Parameters	Baseline	Month 2	Month 4	Month 6
Serum P (mg/dL), mean ± SD	5.8 ± 1.3	4.8 ± 1	4.6 ± 1	4.6 ± 1.2
Number of tablets, mean ± SD	6.3 ± 2.6	2.1 ± 0.9	2 ± 0.9	2 ± 1
Control of P at threshold level of 5 mg/dL				
Percentage of patients	25	60	69	70.4
Percent increase versus previous		35	9	1.4
Control of P at threshold level of 4.5 mg/dL				
Percentage of patients	15.9	36.8	50.7	51.8
Percent increase versus previous		20.9	13.9	1.1

Table 4. Decrease of serum P after treatment with SO in different subgroups

Parameters	Serum P reduction, median (IQR)	P-value
Gender		
Male	0.9 (0.3–2.0)	
Female	1.3 (0.3–2.2)	0.60
Diabetes		
Yes	1.2 (0.6–2.0)	
No	1.2 (0.5–2.1)	0.33
Online HDF		
Yes	1.2 (0.4–2.2)	
No	0.9 (0.2–2.0)	0.21
Dialysate Ca concentration		
2.5 mEq/L	1.1 (0.3–2.0)	
3 mEq/L	1.3 (0.3–2.2)	0.26
Serum PTH		
Tertil 1 (<251.9 pg/mL)	1.3 (0.3–2.2)	
Tertil 2 (251.9–451 pg/mL)	1.2 (0.3–2.0)	0.90
Tertil 3 (>451 pg/mL)	1.1 (0.4–2.0)	
Serum 25-hydroxyvitamin D		
≥30 ng/mL	1.1 (0.2–2.2)	
<30 ng/mL	1.0 (0.2–2.3)	0.92
Active vitamin D therapy		
Yes	0.9 (0.1–1.7)	
No	1.5 (0.3–2.3)	<0.05
Treatment with calcimimetics		
Yes	1.3 (0.5–2.3)	
No	0.8 (0.1–1.7)	0.01

Regarding haematological parameters, no significant differences were observed in haemoglobin concentration or in haematocrit level after treatment with SO. Likewise, serum ferritin concentrations were not modified, although an increase in the TSAT index was evident: 29 ± 10.6% at the end of the follow-up versus 27.2 ± 7.9% at the start of the study (P = 0.04). When analysing the change in the TSAT depending on whether patients had received treatment with iron or not, no significant differences were observed between the two groups (+2.5 ± 0.9% versus +0.3 ± 0.7%; P = 0.28). It should be noted that there was no significant change in the doses of iron or erythropoiesis-stimulating agents throughout the study, nor was there any variation in the EPO resistance index.

From the point of view of nutritional assessment, we observed that although there were no changes in serum albumin concentration or nPCR, when these parameters were normalized by the level of serum P (Alb/P and nPCR/P), significant increases averaging 37% and 39%, respectively, were evident at the end of the study (P < 0.001).

Finally, the results of the multivariate logistic regression analysis showed that better control of hyperphosphataemia under SO therapy (defined as the achievement of a serum P concentration <5 mg/dL) was positively associated with higher K_t/V {odds ratio [OR] 9.0 [95% confidence interval (CI) 1.11–73.70], P < 0.05} and the use of calcimimetics [OR 12.4 (95% CI 2.74–56.68), P < 0.05], whereas it was negatively related to baseline serum P [OR 0.61 (95% CI 0.42–0.96), P < 0.05] and treatment with active vitamin D compounds [OR 0.53 (95% CI 0.21–0.87), P < 0.01].

Adherence and safety

Assessment of adherence to treatment using the SMAQ showed that before the start of SO therapy, 28.2% of patients were adherent to therapy, a percentage that increased to 52.7% at the end of the study (Figure 2). No significant difference was observed in the percentage of non-adherent patients among the participants who did not obtain adequate control of serum P at the two threshold levels of 5 mg/dL and 4.5 mg/dL.

Regarding tolerance and safety aspects (Table 5), 31 patients (14.1%) reported an adverse effect, 21 of which led to abandonment of treatment (9.5% of patients). The most frequent adverse effects were digestive, with diarrhoea in 13 patients and constipation in 6. Most of the treatment dropouts (76%) occurred in the first 3 months after starting the drug.

DISCUSSION

The results of this study show that, in real clinical practice, SO treatment in patients previously treated with other P binders achieves a significant reduction in serum P levels, with an increase in the percentage of patients who achieve adequate control of serum P, with a smaller number of tablets and with an improvement in therapeutic adherence.

Table 5. Adverse effects and causes of treatment dropout

Adverse effects, *n* (%)	
Diarrhoea	13 (5.9)
Digestive discomfort (nausea, flatulence, meteorism and abdominal pain)	12 (5.7)
Constipation	6 (2.7)
Treatment dropout, *n* (%)	
Adverse effects	15 (6.8)
Rejection of organoleptic properties	5 (2.3)
Kidney transplant	1 (0.5)

The reason for the prescription of SO was lack of adequate control of serum P levels in more than two-thirds of the patients, while in almost 25% of cases SO was prescribed to reduce the number of tablets administered. In this respect, two facts should be highlighted. First, with the prescription of SO, the average number of tablets decreased from six at the beginning of the study to two at the end of the study. Importantly, the mean number of tablets at the initiation of SO was two per day, which did not change throughout the study. Second, almost 60% of patients received only one or two tablets per day at the end of the study, representing a reduction in the average number of tablets of >65%. Also, 74% of the patients received SO as the only P binder at the end of the study, which represents a 30% increase in SO prescription as monotherapy compared with baseline.

The preceding data are even more relevant in the context of the evolution of the parameters of bone mineral metabolism since after treatment with SO a significant reduction, averaging 20%, was observed in serum P concentration. Importantly, the percentage of patients who achieved a P concentration <5 mg/dL at the end of the study rose from 25.1% to 70.5%, while for a P threshold of 4.5 mg/dL this percentage increased from 15.9% to 51.8%. It is noteworthy that there was a progressive increase in the number of patients who achieved adequate serum P control throughout the study, although the most significant increment was observed within the first 2 months of treatment.

These results are consistent with those observed in clinical trials and in previous studies on the use of SO in real life, both in HD and in peritoneal dialysis, in which the reduction in P concentration has been verified by an increase in the percentage of patients reaching adequate levels, together with a decrease in the number of tablets [5, 9, 10, 13]. Finally, these data are especially relevant with regard to a P level of 4.5 mg/dL, the value denoting the upper limit of the normal range in most laboratories. On the other hand, the guidelines of the Spanish Society of Nephrology for the management of bone mineral metabolism disorders in CKD patients recommend that the serum P concentration should be <4.5 mg/dL in all stages of CKD but that levels up to 5 mg/dL should be tolerated in dialysis patients [14].

Considering a serum concentration <5 mg as a threshold for adequate serum P control, logistic multivariate analysis was performed to identify factors associated with the response to SO. The results showed that the better control of hyperphosphataemia under SO therapy was positively associated with K_t/V and the use of calcimimetics, whereas it was negatively related to baseline serum P and treatment with active vitamin D compounds. Although insufficient in most cases, P removal by dialysis is a main factor in the management of hyperphosphataemia in patients under renal replacement therapy. Thus a higher K_t/V, reflecting better dialysis optimization, results in increased P removal capacity, explaining the positive association with a better response to SO. However, online HDF was not related to this response, a finding in agreement with studies that have shown no beneficial effect of HDF compared with high-flux HD on the control of mineral metabolism parameters, including P levels [15, 16]. Another factor influencing serum P levels is the use of drugs for treating secondary hyperparathyroidism, which can affect the response to P binders. Available drugs differ in their effects on serum P. Thus active vitamin D derivatives increase intestinal P absorption and

increase its serum levels [17], while calcimimetics lower serum P [18]. These divergent effects may explain the different associations with the response to SO observed in our study.

It is worth noting the reduction of iPTH levels in our study after SO treatment, which, although moderate, reached statistical significance. This is an aspect that distinguishes our study from previous works in which an increase in the concentrations of this hormone was observed [9, 13]. A probable explanation for this difference relates to Ca levels, since while in our study there was no variation, in previous studies a slight but significant decrease in Ca concentrations was observed, which could have provided a stimulus for iPTH production. This finding suggests that SO potentially has an adjuvant effect on the control of secondary hyperparathyroidism, but on the condition that serum Ca concentrations remain stable.

SO was developed as an iron-based P binder with low iron-releasing capacity [19–21]. Previous studies have shown varying results in relation to changes in the concentration of ferritin and in TSAT, as well as in the use and doses of iron or erythropoiesis-stimulating agents [9, 10, 13, 22]. The majority of patients in our study received intravenous iron supplementation, being treated with erythropoiesis-stimulating agents in almost 90% of cases, with no change observed in either the number of patients or the doses of these therapies at the end of the study. Regarding haematological parameters, after SO treatment there were no significant changes in haemoglobin or haematocrit or in serum ferritin. However, a small but significant increase was observed in the TSAT, with no difference according to whether the patients received iron treatment. This change in the TSAT is consistent with the changes previously reported in a *post hoc* analysis of a Phase 3 clinical trial [19], as well as in studies of the use of SO in actual clinical practice [9, 10, 13]. The increase in the TSAT has been related to the low level of absorption of iron from SO, which presents a minimal risk of accumulation or overload of iron in the long-term but which may be beneficial since the TSAT reflects the circulating iron available for the production of haemoglobin [23–25].

Dietary management is a very important element in the achievement of adequate control of serum P in HD patients. Diet must be closely monitored to avoid excessive restriction of protein intake with subsequent reduction in nPCR and serum albumin and the development of a protein-energy wasting syndrome, which has been associated with a reduction in quality of life and an increase in mortality [26–28]. In our study we did not observe variations in nPCR or serum albumin concentration, indicating that there was no significant change in protein intake. To assess the impact of P reduction without restriction of protein intake, new nutritional analysis parameters based on normalization of albumin and nPCR values by serum P concentration have recently been introduced: Alb/P and nPCR/P [9, 10]. Similar to observations in previous studies with SO in actual practice [9, 10, 29], these parameters increased significantly by the end of the study period, indicating achievement of control of serum P without a reduction in protein intake.

Lack of adequate therapeutic adherence is a significant issue in patients with CKD; this is especially true in relation to P binders, with the frequency of inadequate adherence exceeding 60% in those receiving dialysis [30]. An appropriate level of compliance is essential in achieving adequate control of serum P and the high number of tablets received by these patients is a determining factor in inadequate therapeutic adherence [31, 32]. In our study, a notable reduction in the number of tablets received by patients was found. In addition, we specifically analysed adherence using the SMAQ, which showed that SO therapy led to a 24.5% increase in the percentage of patients adhering to treatment.

The observational and multicentre nature of this study ensured provision of information relating to actual clinical practice in a broad geographic context. However, some limitations must be recognized. First, although a database was designed to collect all the variables of interest, this was a retrospective study where data collection was carried out from previously existing electronic records not specifically established to meet the objectives of the study. Regarding nutritional data, we did not have direct information from patients or dieticians on the dietary intake of P or proteins, and a definitive causal relationship between intake of SO and the change in nutritional parameters could not be established. Another limitation stems from the fact that not all measurements were done during the same dialysis shift, either morning, noon or evening, and therefore the circadian variation of phosphataemia may have affected the results. Finally, we did not have information on parameters such as acute phase reactants or residual renal function.

In conclusion, SO is an effective P binder for the treatment of hyperphosphataemia in real clinical practice. It results in an increase in the percentage of patients who achieve adequate control of serum P levels, as well as a significant reduction in the number of tablets taken and an improvement in therapeutic adherence. In addition, it has associated effects that may be beneficial in relation to secondary hyperparathyroidism and nutritional parameters.

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AUTHORS' CONTRIBUTIONS

J.F.N.G. and J.B. were responsible for the conception and design of the study. M.D.A., M.J.L., P.M., L.E. and E.S. contributed to the final design of the database. M.D.A., F.H.P., M.J.L., P.M., F.R.M., M.A.M.L., L.E., E.S., M.L. and A.C. collected the data. J.F.N.G. performed the statistical analysis and wrote the article. J.F.N.G., M.D.A., P.M., E.S. and J.B. contributed to the interpretation of results and discussion. All authors have read and agreed to the final version of the manuscript.

CONFLICT OF INTEREST STATEMENT

The results presented in this article have not been published previously in whole or part, except in abstract format at the XLVII Congress of the Spanish Society of Nephrology and the 56th ERA-EDTA Congress.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

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