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REVIEW ARTICLE

Efficacy and safety of sucroferric oxyhydroxide versus sevelamer carbonate: A systematic review and meta-analysis

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Abstract

Introduction: Phosphate binders are commonly used in patients receiving kidney replacement therapy (KRT), aiming to reduce and maintain serum phosphorus. Chronic kidney disease-mineral and bone disorder has been linked to reduced lifespan and worsened quality of life. This study aims to examine the efficacy and safety of sucroferric oxyhydroxide versus sevelamer carbonate in patients receiving KRT.

Methods: The data sources examined were MEDLINE (PubMed), Scopus, and the Cochrane Central Register of Controlled Clinical Trials with a search deadline of October 2023. We examined randomized controlled trials that compared sucroferric oxyhydroxide versus sevelamer carbonate in the adult population receiving KRT. We performed a meta-analysis combining the data from trials, using R-studio.

Findings: Inclusion criteria were met by five randomized trials. There was no statistically significant difference in the reduction of serum phosphorus between the two groups (MD: −0.07 mmol/L, 95% CI-random effects: −0.15 to 0.02). In the same line, a non-statistically significant difference was observed in serum i-PTH reduction between the two drugs (MD = −1.53 mg/dL, 95% CI = (−4.45, 1.4), $p = 0.26$, random effects model). No statistically significant difference was observed in all adverse events between the two groups (odds ratio: 1.11, 95% CI: 0.65–1.88, random effects model). Further analysis of gastrointestinal adverse events revealed that sevelamer carbonate increases gastrointestinal adverse events by up to 60% (odds ratio: 1.60, 95% CI: 1.31–1.97, common (fixed) effect model).

Discussion: This meta-analysis of randomized trials showed that both drugs, sucroferric oxyhydroxide and sevelamer equally and effectively controlled serum phosphorus levels, whereas sucroferric oxyhydroxide revealed a better profile in terms of gastrointestinal adverse events. Sucroferric oxyhydroxide is a valuable option for patients receiving KRT when sevelamer carbonate is more difficult to tolerate.

KEYWORDS
meta-analysis, randomized clinical trials, renal replacement therapy, sevelamer carbonate, sucroferric oxyhydroxide

INTRODUCTION

Hyperphosphatemia is a common and clinically significant complication in severe chronic kidney disease (CKD), associated with higher cardiovascular adverse events and higher mortality rates. In addition, it has emerged as an important prognostic marker, with published data to consistently demonstrate a correlation between elevated phosphate levels and increased mortality in both CKD and non-CKD populations. Particularly, individuals with elevated serum phosphate levels are at increased risk of developing cardiovascular complications, including hypertension, left ventricular hypertrophy, atherosclerosis, vascular calcification, and cardiac vascular calcification.[1]

Hyperphosphatemia and its management remain a compelling challenge to attending nephrologist, especially in dialysis patients, requiring a sophisticated approach in order to optimize phosphate control while minimizing potential adverse effects. Among various phosphate binders, sevelamer carbonate and calcium acetate are currently the most prescribed.[2]

Sevelamer carbonate, a non-calcium-based phosphate binder, has long been a mainstay in the armamentarium against hyperphosphatemia. Its ability to bind phosphate without affecting calcium levels, has made it a valuable alternative, particularly in dialysis patients where calcium balance is critically managed.[3] Sucroferric oxyhydroxide, an iron-based phosphate binder, has emerged as a novel player in the field, offering an alternative approach to phosphate control, also without impairing calcium levels.[4]

As the landscape of phosphate binder options evolves, a comprehensive understanding of the comparative effectiveness, safety profiles, and patient outcomes associated with these two, most prescribed, non-calcium phosphate binders become imperative. This meta-analysis aims to bridge current knowledge gaps by synthesizing data from randomized clinical trials, systematically assessing and comparing the impact of these two phosphate binders on phosphate levels, treatment adherence, and adverse events in dialysis patients.

MATERIALS AND METHODS

Databases

Data sources included MEDLINE (PubMed), Scopus and the Cochrane Central Register of Controlled Clinical Trials with a search deadline of October 2023 (Figure 1). We searched for randomized controlled trials comparing sucroferric oxyhydroxide with sevelamer carbonate in the adult population undergoing renal replacement therapy. The algorithm used was (sucroferric oxyhydroxide OR velphoro) AND (sevelamer carbonate) AND (dialysis) combined with the Cochrane algorithm for identifying randomized clinical trials: AND ("Clinical Trials as Topic"[Mesh] OR "randomized controlled trial"[pt] OR "controlled clinical trial"[pt] OR randomized[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab]).

Study selection

Two blinded reviewers (C.G. and A.D.) screened titles and abstracts according to the eligibility criteria, while a third independent reviewer (A.K.) resolved any disagreements that occurred with a third vote.

The inclusion criteria were, (1) randomized controlled trials in the adult population (>18 years of age) receiving KRT, both modalities, hemodialysis, and peritoneal dialysis (2) articles published in English language.

The exclusion criteria were, (1) studies with patients <18 years of age, (2) observational studies, and (3) systematic reviews.

All randomized trials that compared sucroferric oxyhydroxide versus sevelamer carbonate in the adult population undergoing dialysis met the inclusion criteria and were included in the qualitative synthesis.

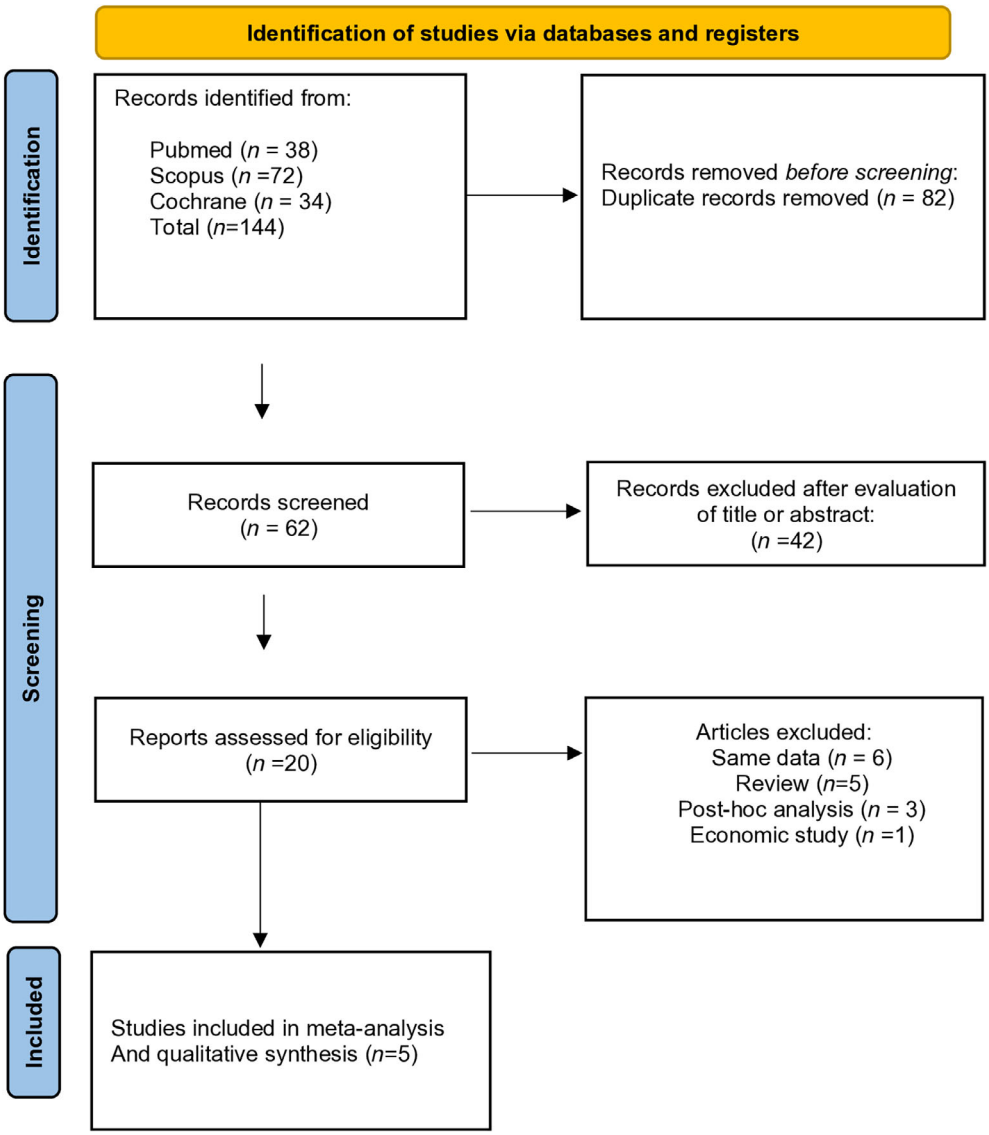

FIGURE 1 PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Data collection

Data from studies were extracted by two blinded reviewers (C.G. and A.D.) and a third independent reviewer (A.K.) resolved differences that occurred with a third vote. Data extraction followed the PICOS protocol (population, intervention, comparison, outcome, study type).[5]

Outcome

The primary endpoint of this study is the change in the serum phosphorus levels from baseline to end of treatment. Secondary outcomes were the change in the serum i-PTH levels from baseline to end of treatment as well as the adverse events ratio during the treatment study period. As gastrointestinal side effects are among the most common for both drugs and a frequent cause for drug discontinuation of patient non-adherence, a separate analysis was performed regarding the adverse events of gastrointestinal interest.

Statistical analysis

All extracted data analysis, as well as the plot formation was conducted using R-studio (Version: 2023.09.1 + 494) and the meta package.[6] The effect size was estimated using weighted mean differences for continuous outcomes (serum phosphorus, i-PTH) and odds ratio for dichotomous outcomes (adverse events).

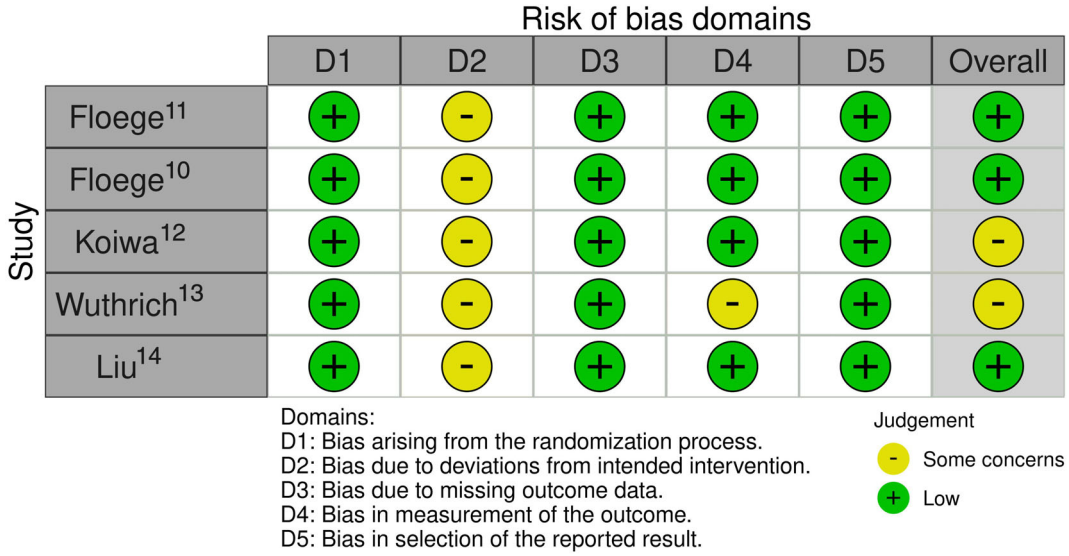

FIGURE 2 Risk of bias plot for assessing the risk of bias.

Statistically significant outcomes were considered with a p-value <0.05.

According to recent evidence the random effects model provides a more robust and conservative approach to the result of the meta-analysis compared to the common effect model, especially in this meta-analysis were it is to be expected for high heterogeneity between the studies.

However, we decided to present both models in our meta-analysis, since we believe that the presentation of both models provides a better overall understanding of the underlying heterogeneity.

The Hartung-Knapp method[7] was applied to adjust the confidence intervals of the random effects and common effect model, respectively.

Heterogeneity was assessed using the I^2 and the Q statistic[8] whereas an I^2 of 0%–30% was considered as low heterogeneity, 30%–50% as medium heterogeneity and >50% as significant heterogeneity.

A Q statistic with a p-value <0.1 was considered as statistically significant for great heterogeneity.

Since only five studies were included in the overall analysis, we were reluctant to perform sub-group analysis or meta-regression since the Cochrane Handbook of systematic reviews and Interventions does not recommend it.

Assessment of bias

The assessment for bias risk was performed by two independent authors (C.G. and A.D.) using the Rob-2 tool[9] (Figure 2).

RESULTS

Selection of studies and characteristics

A total of 144 studies were identified in the initial search (Figure 1). After removing 82 duplicate records, 62 articles were screened. Of these, 42 articles were excluded based on the evaluation of title or abstract, leaving a total of 20 studies to be assessed for eligibility. Six studies were further removed because they included duplicate data, in addition to five systematic reviews, three studies of post-hoc analysis, and one economic study, resulting in five studies being included in the final analysis and qualitative synthesis.

All five studies were randomized trials, with each one mentioning randomization, and three of them describing the exact randomization process.[10–12] The treatment duration across these studies ranged from 6 to 28 weeks, with a total of 2409 patients enrolled. All five studies obtained a written informed consent from all patients.[13,14] There were no statistically significant differences in the basic characteristics of the patients between the studies (age, sex, reason for inclusion in hemodialysis, comorbidities, country of origin). In Wuthrich's study five different dosage regimens (1.25, 5, 7.5, 10.0, and 12.5 g) were used, each analyzed separately. The basic characteristics of the studies included in the meta-analysis are mentioned in Table 1.

Effects on serum phosphorus and i-PTH

No statistically significant difference was observed between the two interventions (MD = −0.07 mg/dL, 95%

TABLE 1 Characteristics of included studies.

Author	No. of patients (sucrofferic oxyhydroxide/sevelamer)	Mean age	Male (%)	HD or PD	Duration-treatment (weeks)	Race
Floege[11]	1041 (694/347)	56.3	57.8	Both	24	Caucasian/African
Floege[10]	644 (384/260)	56.8	58.5	Both	28	Caucasian/African
Wüthrich[13]	150 (126/24)	60.5	63.5	HD	6	Caucasian
Koiwa[12]	192 (100/92)	61	60	HD	12	Asian
Liu[14]	286 (142/144)	49.7	60.2	Both	12	Asian

Abbreviations: HD, hemodialysis; PD, peritoneal dialysis.

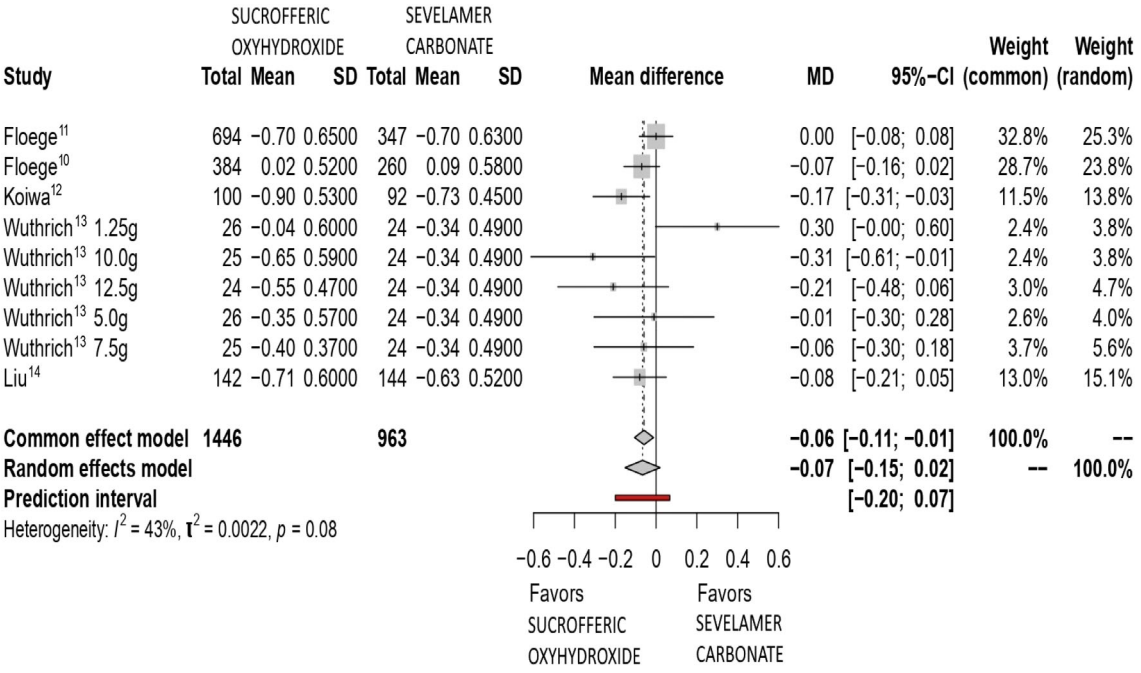

FIGURE 3 Forest plot on weighted mean difference of serum phosphorus between sucrofferic oxyhydroxide and sevelamer carbonate. Wuthrich's study contained five different dosage regimens and were analyzed separately in the final analysis.

CI = (−0.15, 0.02), $p = 0.11$, random effects model) (Figure 3). Although no significant heterogeneity was detected ($I^2 = 49\%$, p-value-Q statistic = 0.08), we believe the random effects model provides a more robust and conservative approach to these meta-analysis results. The prediction interval, as provided by the meta package, further confirms this outcome (95% CI = −0.20, 0.7), suggesting that future studies are projected to yield non-statistically significant differences in the reduction of serum phosphorus between the two drugs.

In the analysis of serum i-PTH the random effects model shows no statistically significant difference between the interventions (MD = −1.53 pg/mL, 95% CI = (−4.45, 1.4), $p = 0.26$). Despite the lack of significant heterogeneity ($I^2 = 36\%$, p-value-Q statistic = 0.13), the variance between the two models suggests heterogeneity between the studies. This is further confirmed by the non-statistically significant prediction interval (CI = −6.18, 3.12) (Figure 4).

Estimating safety

All adverse events

The analysis of all adverse events revealed no statistically significant difference in the occurrence of adverse events between the two drugs (odds ratio = 1.11, 95% CI = [0.65, 1.88], $p = 0.67$, random effects model) (Figure 5). Significant heterogeneity was observed ($I^2 = 88\%$,

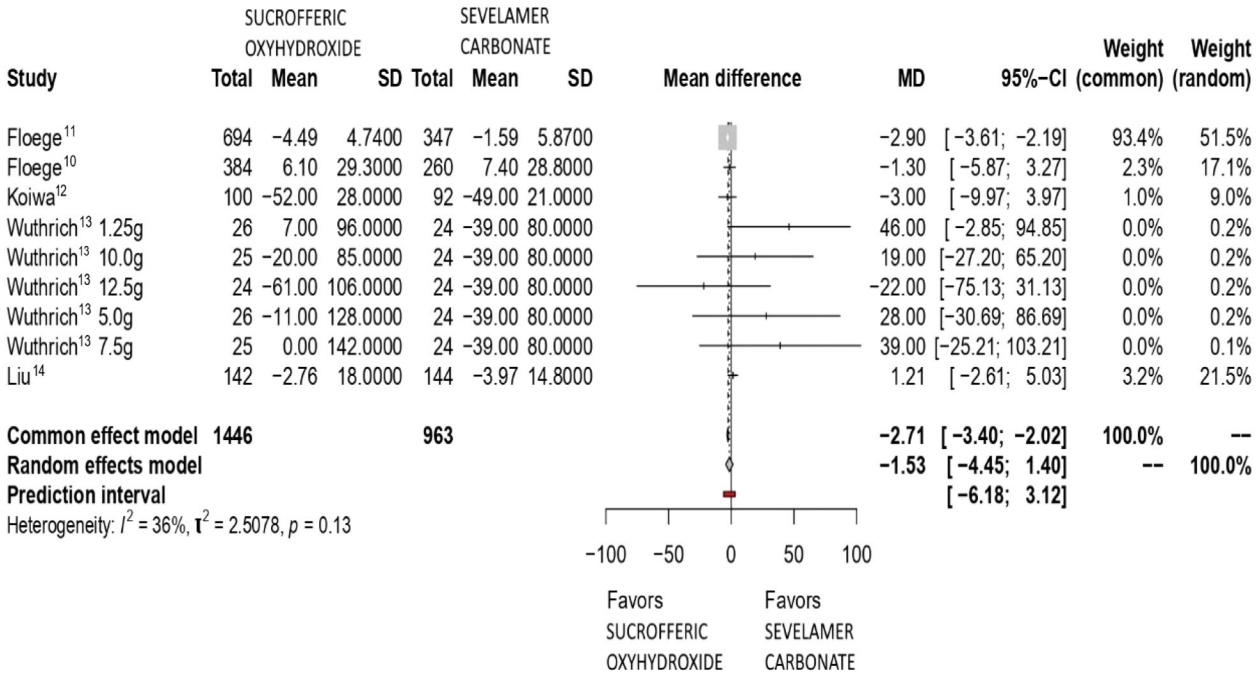

FIGURE 4 Forest plot on weighted mean difference of serum i-PTH between sucrofferic oxyhydroxide and sevelamer carbonate. Wuthrich's study contained five different dosage regimens and were analyzed separately in the final analysis.

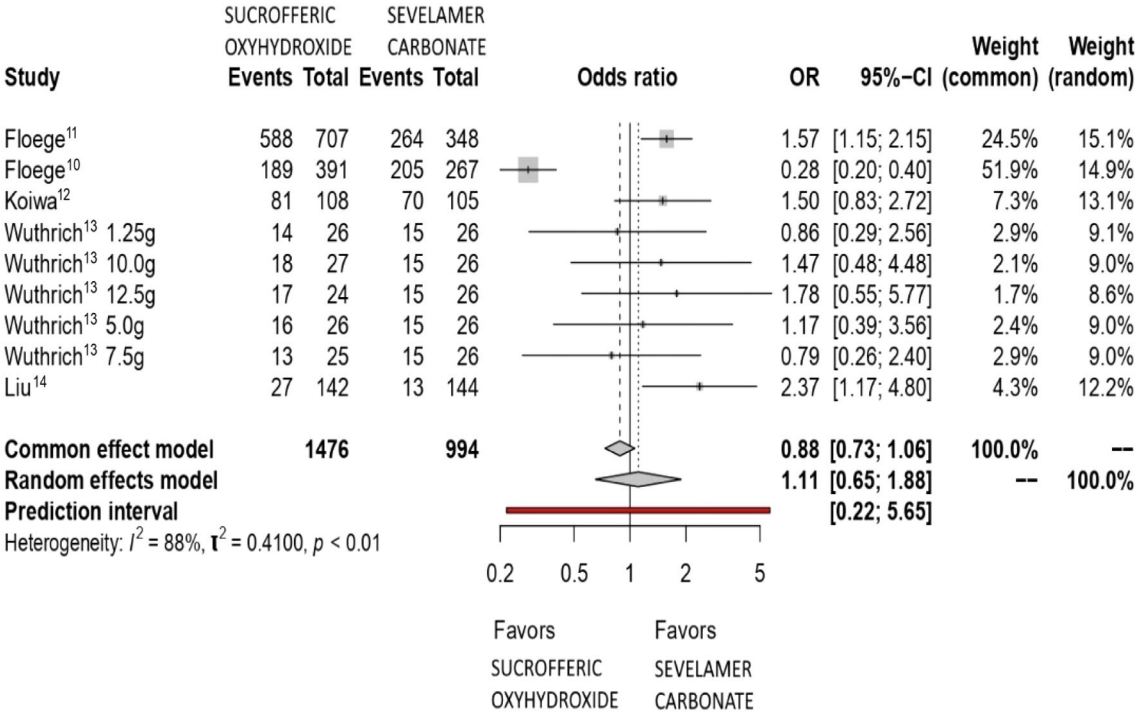

FIGURE 5 Forest plot, odds ratio for all adverse events between sucrofferic oxyhydroxide and sevelamer carbonate. Wuthrich's study contained five different dosage regimens and were analyzed separately in the final analysis.

p-value-Q statistic < 0.01), suggesting that the random effects model is more appropriate for estimating the effect size. Due to the very high heterogeneity, the prediction interval is quite large and non-statistically significant (CI = 0.22, 5.65). A list of all adverse events presented in each study is depicted in Table 2.

TABLE 2 List of treatment related adverse events per study.

Study name year population (sucrofferic oxyhydroxide/sevelamer)	Floege[11] (694/347)	Floege[10] (384/260)	Wüthrich[13] (126/24)	Koiwa[12] (100/92)	Liu[14] (142/144)
Diarrhea	21/3	32/15	7/3	27/3	17/4
Constipation	5/34	0/0	4/0	0/19	2/11
Vomiting	7/3	0/0	3/1	0/0	3/1
Nausea	7/6	23/11	0/0	0/0	9/7
Hypophosphatemia	0/0	22/14	20/3	0/0	0/0
Discolored feces	0/0	0/0	15/0	0/0	44/0
Abdominal pain	2/11	1/9	0/0	0/3	1/4
Pruritus	0/0	0/0	0/0	0/0	2/3
Death	0/0	7/7	0/0	0/0	1/0

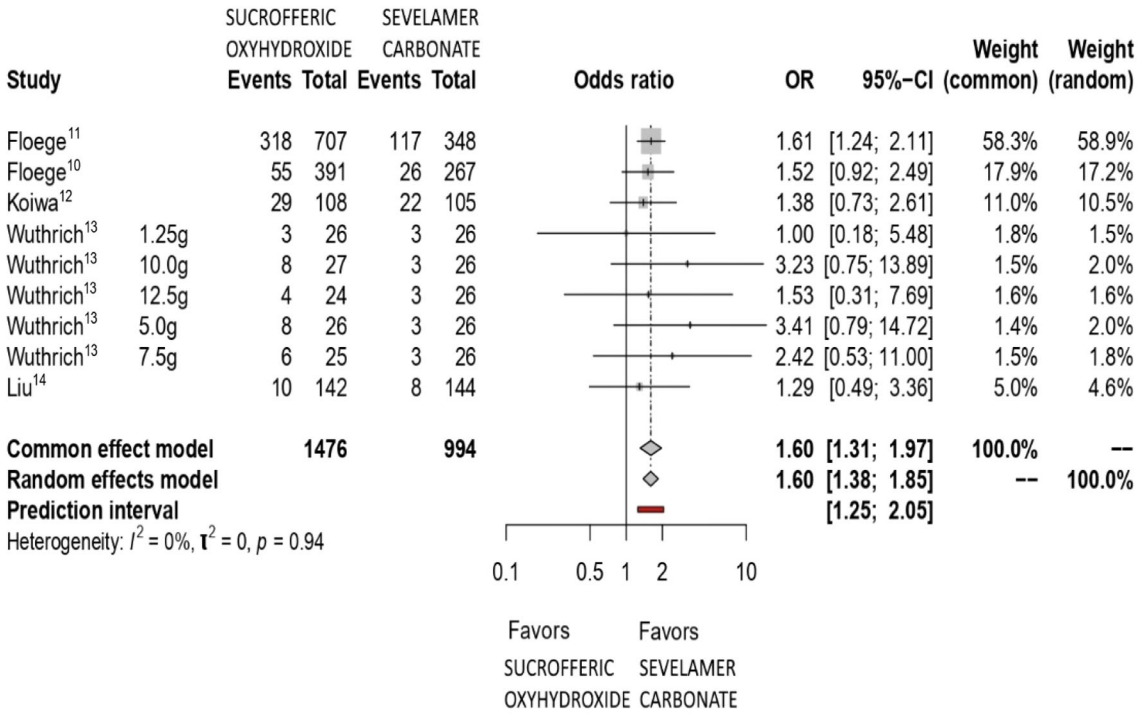

FIGURE 6 Forest plot, odds ratio for gastrointestinal adverse events between sucrofferic oxyhydroxide and sevelamer carbonate. Wuthrich's study contained five different dosage regimens and were analyzed separately in the final analysis.

Gastrointestinal adverse events

The analysis of the gastrointestinal adverse events revealed a statistically significant result favoring sucroferric oxyhydroxide in reducing adverse events up to 60% (odds ratio = 1.60, 95% CI = [1.31, 1.97], $p < 0.001$, common effect model) (Figure 6). No heterogeneity was observed ($I^2 = 0\%$, p-value-Q statistic = 0.94) and both the random effects and common effect models provided almost identical results. The prediction interval further supports this result (95% CI = 1.25–2.05), indicating that future studies are projected to yield the same results.

Sensitivity analysis

We performed a sensitivity analysis by excluding the trial with the greatest weight and observed no change in the result of heterogeneity.

Publication bias

A funnel plot was examined thoroughly for both continuous and dichotomous outcomes (Figure 7). Asymmetry in the funnel plot suggests a high likelihood of a small study

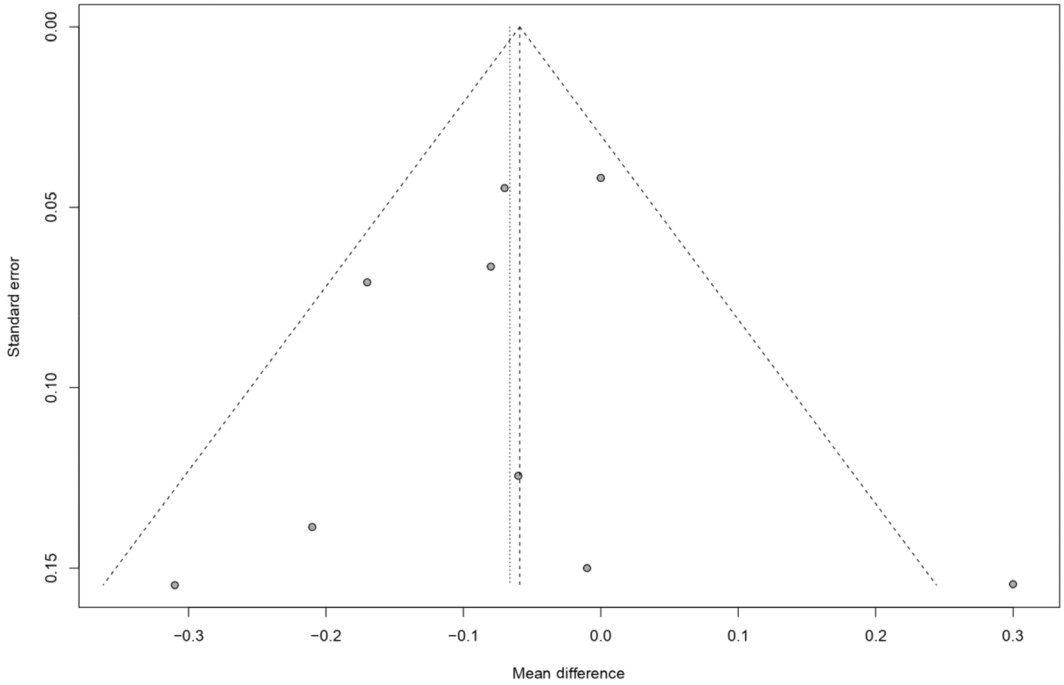

FIGURE 7 Funnel plot, assessing for small study effect and publication bias.

effect as well as publication bias. However, Egger's test could not be performed due to the limited number of studies (<10) included in the meta-analysis.

DISCUSSION

The outcomes of this meta-analysis provide vital insights into the comparative efficacy and safety of sucroferric oxyhydroxide and sevelamer carbonate in dialysis patients, especially regarding the control of serum phosphorus and related adverse events. We synthesized data from multiple randomized clinical trials, which revealed no significant difference in reducing serum phosphate and i-PTH levels between the two agents.

Two previous meta-analyses have investigated a similar primary outcome with our study. The first one, a network meta-analysis performed by Palmer et al.[15] suggested that iron-based binders may lower serum phosphorus more effectively. However, given that our meta-analysis is a direct head-to-head comparison of the two interventions, and includes two additional randomized trials conducted between 2016 and 2023, we believe that the present analysis, which relies on direct evidence, yields a statistically more robust result. Our main finding of similar efficacy in controlling serum phosphorus between sucroferric oxyhydroxide and sevelamer carbonate is also supported by a more recent meta-analysis performed by Xie et al.[16] that included four randomized trials and compared the two interventions head-to-head as well.

In the analysis of i-PTH, the random effects model seems to provide the same results. No statistically significant difference in the reduction of i-PTH between the two interventions is observed. These findings suggest that both agents are effective in addressing the primary goal of managing hyperphosphatemia and associated mineral and bone disorders in the dialysis population.

It is widely known that non-calcium containing phosphate binders compared with calcium containing binders reduce mortality among patients with CKD. A meta-analysis performed by Jamal et al.[17] reported lower all-cause mortality among patients randomly assigned to receive non-calcium-based binders compared with calcium-based binders. This analysis included patients on dialysis and those with non-dialysis CKD, showing similar reductions in mortality. Another meta-analysis performed by Patel et al.[18] also showcased a lower all-cause mortality in the sevelamer carbonate group when compared to calcium-based phosphate binders. These findings regarding mortality could derive from the well-known effect of vascular calcification of calcium-based phosphate binders leading to increased morbidity.[19]

Within the broader context of safety outcomes, our meta-analysis uncovers an intriguing pattern. While there was no statistically significant difference in the overall occurrence of adverse events between sucroferric oxyhydroxide and sevelamer carbonate, a notable

distinction arises when specifically examining gastrointestinal adverse events. While sucroferric oxyhydroxide does in fact present a greater percentage of diarrhea events, when all gastrointestinal adverse events were analyzed, a marked safety advantage emerged, reducing all gastrointestinal side effects by up to 60% compared to sevelamer carbonate. The improved safety profile of sucroferric oxyhydroxide in mitigating side effects could potentially lead to better treatment adherence and greater patient tolerability. The preferential reduction of gastrointestinal adverse events with sucroferric oxyhydroxide may be particularly relevant for patients who have previously experienced challenges or intolerances with other phosphate binders, including sevelamer carbonate. Improved tolerability is not only pivotal for patient compliance but also has implications for long-term treatment success and the overall quality of life in individuals on dialysis. The negative impact of hyperphosphatemia and uncontrolled CKD-mineral and bone disorder on the quality of life in hemodialysis patients is highlighted in a cross-sectional study by Luo et al.[20]

Adding to the similar efficacy and better gastrointestinal safety profile of sucrofferic oxyhydroxide, another advantage of this drug is its lower pill burden compared to sevelamer carbonate, as highlighted in Floege's and Wuthrich's studies.

In conclusion, the findings of this meta-analysis provide a comprehensive view of the comparative efficacy and safety of sucroferric oxyhydroxide versus sevelamer carbonate in dialysis patients. Especially in patients that struggle with gastrointestinal adverse events, our meta-analysis indicates that sucroferric oxyhydroxide may provide an overall better safety profile. The comparable efficacy in controlling phosphate and i-PTH levels, along with the superior safety profile of sucroferric oxyhydroxide for gastrointestinal adverse events, offers valuable insights for clinicians in making informed decisions about phosphate binder selection, tailoring treatment approaches aligned with patient preferences.[21–41]

Limitations of the study

While this meta-analysis offers valuable insights into the comparative efficacy and safety of the intervention's studies, it is crucial to interpret the findings within the context of its inherent limitations. The limited inclusion of only five studies may affect the generalizability and robustness of the results, consequently limiting the statistical power and precision of the observed effects. The lack of subgroup analysis or meta-regression, due to the small sample size further, restricts our ability to explore potential sources of heterogeneity and identify subtle patterns within the data. Moreover, the open-label design of the included studies may introduce performance and detection bias, which could influence both the reported outcomes and the interpretation of adverse events. The presence of a small study effect and publication bias also raises concerns about the reliability of the observed effect sizes, as smaller studies with significant findings may be overrepresented in the literature. Further research with larger, more diverse cohorts is necessary to strengthen the evidence base.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

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REFERENCES

1. Ruospo M, Palmer SC, Natale P, Craig JC, Vecchio M, Elder GJ, et al. Phosphate binders for preventing and treating chronic kidney disease-mineral and bone disorder (CKD-MBD). Cochrane Database Syst Rev. 2018;8(8):CD006023. https://doi.org/10.1002/14651858.CD006023.pub3
2. Berner T, Ferro C, Dieguez G, Metz S, Moore J, Szabo E, et al. Real-world phosphate binder use among dialysis-dependent patients with CKD. Nephron. 2023;147(10):583–90. https://doi.org/10.1159/000530230
3. Scialla JJ, Kendrick J, Uribarri J, Kovesdy CP, Gutiérrez OM, Jimenez EY, et al. State-of-the-art management of hyperphosphatemia in patients with CKD: an NKF-KDOQI controversies perspective. Am J Kidney Dis. 2021;77(1):132–41. https://doi.org/10.1053/j.ajkd.2020.05.025
4. Bousher A, Al-Makki A, Sutton J, Shepler B. A review of sucroferric oxyhydroxide for the treatment of hyperphosphatemia in patients receiving dialysis. Clin Ther. 2014;36(12):2082–93. https://doi.org/10.1016/j.clinthera.2014.09.021
5. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst Rev. 2019;10(10):ED000142. https://doi.org/10.1002/14651858.ED000142
6. Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. Evid Based Mental Health. 2019;22(4):153–60. https://doi.org/10.1136/ebmental-2019-300117
7. Jackson D, Law M, Rücker G, Schwarzer G. The Hartung-Knapp modification for random-effects meta-analysis: a useful refinement but are there any residual concerns? Stat Med. 2017;36(25):3923–34. https://doi.org/10.1002/sim.7411

8. Huedo-Medina TB, Sánchez-Meca J, Marín-Martínez F, Botella J. Assessing heterogeneity in meta-analysis: Q statistic or I^2 index? Psychol Methods. 2006;11(2):193–206. https://doi.org/10.1037/1082-989X.11.2.193
9. Luchini C, Veronese N, Nottegar A, Shin JI, Gentile G, Granziol U, et al. Assessing the quality of studies in meta-research: review/guidelines on the most important quality assessment tools. Pharm Stat. 2021;20(1):185–95. https://doi.org/10.1002/pst.2068
10. Floege J, Covic AC, Ketteler M, Mann JFE, Rastogi A, Spinowitz B, et al. Long-term effects of the iron-based phosphate binder, sucroferric oxyhydroxide, in dialysis patients. Nephrol Dialysis Transplant. 2015;30(6):1037–46. https://doi.org/10.1093/ndt/gfv006
11. Floege J, Covic AC, Ketteler M, Rastogi A, Chong EM, Gaillard S, et al. A phase III study of the efficacy and safety of a novel iron-based phosphate binder in dialysis patients. Kidney Int. 2014;86(3):638–47. https://doi.org/10.1038/ki.2014.58
12. Koiwa F, Yokoyama K, Fukagawa M, Terao A, Akizawa T. Efficacy and safety of sucroferric oxyhydroxide compared with sevelamer hydrochloride in Japanese haemodialysis patients with hyperphosphataemia: a randomized, open-label, multicentre, 12-week phase III study. Nephrol Ther. 2017;22(4):293–300. https://doi.org/10.1111/nep.12891
13. Wüthrich RP, Chonchol M, Covic A, Gaillard S, Chong E, Tumlin JA. Randomized clinical trial of the iron-based phosphate binder PA21 in hemodialysis patients. CJASN. 2013;8(2):280–9. https://doi.org/10.2215/CJN.08230811
14. Liu J, Zuo L, Walpen S, Bernard L, Marty M, Enoiu M. Efficacy and safety of sucroferric oxyhydroxide compared with sevelamer carbonate in Chinese dialysis patients with Hyperphosphataemia: a randomised, open-label, multicentre, 12-week phase III study. Nephron. 2023;148:22–33. https://doi.org/10.1159/000531869
15. Palmer SC, Gardner S, Tonelli M, Mavridis D, Johnson DW, Craig JC, et al. Phosphate-binding agents in adults with CKD: a network meta-analysis of randomized trials. Am J Kidney Dis. 2016;68(5):691–702. https://doi.org/10.1053/j.ajkd.2016.05.015
16. Xie D, Ye N, Li M. A systematic review on the efficacy and safety of PA21 versus sevelamer in dialysis patients. Int Urol Nephrol. 2018;50(5):905–9. https://doi.org/10.1007/s11255-017-1774-9
17. Jamal SA, Vandermeer B, Raggi P, Mendelssohn DC, Chatterley T, Dorgan M, et al. Effect of calcium-based versus non-calcium-based phosphate binders on mortality in patients with chronic kidney disease: an updated systematic review and meta-analysis. Lancet. 2013;382(9900):1268–77. https://doi.org/10.1016/S0140-6736(13)60897-1
18. Patel L, Bernard LM, Elder GJ. Sevelamer versus calcium-based binders for treatment of hyperphosphatemia in CKD: a meta-analysis of randomized controlled trials. Clin J Am Soc Nephrol. 2016;11(2):232–44.
19. Di Iorio B, Molony D, Bell C, Cucciniello E, Bellizzi V, Russo D, et al. Sevelamer versus calcium carbonate in incident hemodialysis patients: results of an open-label 24-month randomized clinical trial. Am J Kidney Dis. 2013;62(4):771–8. https://doi.org/10.1053/j.ajkd.2013.03.023
20. Luo L, Chen Q. Effect of CKD–MBD phenotype on health-related quality of life in patients receiving maintenance hemodialysis: a cross-sectional study. J Int Med Res. 2020;48(2):30006051989584. https://doi.org/10.1177/0300060519895844
21. Bataille P, Delattre V, Daroux M. Oxyhydroxyde sucroferrique, un nouveau chélateur des phosphates à base de fer. Quelle utilisation chez le patient dialysé? Nephrol Ther. 2017;13:S103–8. https://doi.org/10.1016/j.nephro.2017.01.004
22. 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(5):438–41. https://doi.org/10.1038/sj.ki.5002059
23. Cernaro V, Santoro D, Lacquaniti A, Costantino G, Visconti L, Buemi A, et al. Phosphate binders for the treatment of chronic kidney disease: role of iron oxyhydroxide. Int J Nephrol Renovasc Dis. 2016;9:11–9. https://doi.org/10.2147/IJNRD.S78040
24. Covic AC, Floege J, Ketteler M, Sprague SM, Lisk L, Rakov V, et al. Iron-related parameters in dialysis patients treated with sucroferric oxyhydroxide. Nephrol Dial Transplant. 2017;32(8):1330–1338. https://doi.org/10.1093/ndt/gfw242
25. Covic AC, Sprague SM, Rastogi A, Ketteler M, Walpen S, Perrin A, et al. Characteristics of patients who achieve serum phosphorus control on sucroferric oxyhydroxide or sevelamer carbonate: a post hoc analysis of a phase 3 study. Nephron. 2020;144(9):428–39. https://doi.org/10.1159/000507258
26. Coyne DW, Sprague SM, Vervloet M, Ramos R, Kalantar-Zadeh K. Sucroferric oxyhydroxide for hyperphosphatemia: a review of real-world evidence. J Nephrol. 2022;35(3):875–88. https://doi.org/10.1007/s40620-021-01241-5
27. Ferreira A, Pinto B, Navarro D, Aniceto J, Neves PL, Ponce P. Effectiveness of sucroferric oxyhydroxide in patients on on-line hemodiafiltration in real-world clinical practice: a retrospective study. J Bras Nefrol. 2019;41(2):224–30. https://doi.org/10.1590/2175-8239-jbn-2018-0142
28. Floege J. Phosphate binders in chronic kidney disease: a systematic review of recent data. J Nephrol. 2016;29(3):329–40. https://doi.org/10.1007/s40620-016-0266-9
29. Floege J. Phosphate binders in chronic kidney disease: an updated narrative review of recent data. J Nephrol. 2020;33(3):497–508. https://doi.org/10.1007/s40620-019-00689-w
30. Floege J, Covic AC, Ketteler M, Mann J, Rastogi A, Spinowitz B, et al. One-year efficacy and safety of the iron-based phosphate binder sucroferric oxyhydroxide in patients on peritoneal dialysis. Nephrol Dialysis Transplant. 2017;32(11):1918–26. https://doi.org/10.1093/ndt/gfw460
31. Floege J, Sprague S, Rastogi A, Ketteler M, Covic A, Rakov V, et al. Mp381 characteristics of responders and non-responders to treatment with sucroferric oxyhydroxide: a post hoc analysis of a phase 3 study. Nephrol Dialysis Transplant. 2016;31-(suppl_1):i466. https://doi.org/10.1093/ndt/gfw190.38
32. Greig SL, Plosker GL. Sucroferric oxyhydroxide: a review in hyperphosphataemia in chronic kidney disease patients undergoing dialysis. Drugs. 2015;75(5):533–42. https://doi.org/10.1007/s40265-015-0366-1
33. Ketteler M, Block GA, Evenepoel P, Fukagawa M, Herzog CA, McCann L, et al. Executive summary of the 2017 KDIGO chronic kidney disease–mineral and bone disorder (CKD-MBD) guideline update: what's changed and why it

matters. Kidney Int. 2017;92(1):26–36. https://doi.org/10.1016/j.kint.2017.04.006
34. Ketteler M, Sprague SM, Covic AC, Rastogi A, Spinowitz B, Rakov V, et al. Effects of sucroferric oxyhydroxide and sevelamer carbonate on chronic kidney disease–mineral bone disorder parameters in dialysis patients. Nephrol Dialysis Transplant. 2019;34(7):1163–70. https://doi.org/10.1093/ndt/gfy127
35. Koiwa F, Yokoyama K, Fukagawa M, Akizawa T. Efficacy and safety of sucroferric oxyhydroxide and calcium carbonate in hemodialysis patients. Kidney Int Rep. 2018;3(1):185–92. https://doi.org/10.1016/j.ekir.2017.10.003
36. Lioufas NM, Pascoe EM, Hawley CM, Elder GJ, Badve SV, Block GA, et al. Systematic review and meta-analyses of the effects of phosphate-lowering agents in nondialysis CKD. JASN. 2022;33(1):59–76. https://doi.org/10.1681/ASN.2021040554
37. McCullough PA. Phosphate control: the next frontier in dialysis cardiovascular mortality. Cardiorenal Med. 2021;11(3):123–32. https://doi.org/10.1159/000516286
38. Molony DA, Parameswaran V, Ficociello LH, Mullon C, Kossmann RJ. Sucroferric oxyhydroxide as part of combination phosphate binder therapy among hemodialysis patients. Kidney360. 2020;1(4):263–72. https://doi.org/10.34067/KID.0000332019
39. Perry CM, Plosker GL. Sevelamer carbonate: a review in hyperphosphataemia in adults with chronic kidney disease. Drugs. 2014;74(7):771–92. https://doi.org/10.1007/s40265-014-0215-7
40. Sprague SM, Covic AC, Floege J, Ketteler M, Botha J, Chong EM, et al. Pharmacodynamic effects of sucroferric oxyhydroxide and sevelamer carbonate on vitamin D receptor agonist bioactivity in dialysis patients. Am J Nephrol. 2016;44(2):104–12. https://doi.org/10.1159/000447600
41. Sprague SM, Ketteler M, Covic AC, Floege J, Rakov V, Walpen S, et al. Long-term efficacy and safety of sucroferric oxyhydroxide in African American dialysis patients. Hemodial Int. 2018;22(4):480–91. https://doi.org/10.1111/hdi.12663

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