Am J Transl Res 2024;16(11):6980-6990
www.ajtr.org /ISSN:1943-8141/AJTR0159437

Review Article

Therapeutic effectiveness and safety profile of lanthanum carbonate in conjunction with calcium carbonate for managing hyperphosphatemia in hemodialysis patients: a meta-analysis of randomized controlled trials

Hui Fang[1], Chunyan Chen[2]

[1]*Hemodialysis Center, The Second People's Hospital of Jiashan County, Jiaxing 314121, Zhejiang, China;*
[2]*Department of Nephrology, Jiaxing Hospital of Traditional Chinese Medicine, Jiaxing 314000, Zhejiang, China*

Received July 25, 2024; Accepted October 29, 2024; Epub November 15, 2024; Published November 30, 2024

Abstract: Objective: To comprehensively investigate the efficacy and safety of lanthanum carbonate in conjugation with calcium carbonate combination in hemodialysis patients with hyperphosphatemia via a meta-analysis of randomized controlled trials (RCTs). Method: We conducted a literature search in databases of PubMed, Embase, and Web of Science for RCTs investigating the effect of lanthanum carbonate in combination with calcium carbonate for treating hyperphosphatemia in hemodialysis patients. The search covered all studies from the inception of the database until October 2023. Data extraction and quality assessment were performed on eligible studies, followed by a meta-analysis using RevMan5.3 software. Results: Ten studies fulfilling the inclusion criteria were included, with a sample size of 475 patients (256 in the experimental group who received lanthanum carbonate and calcium carbonate; 219 in the control group who received calcium carbonate alone). The experimental group showed a significantly higher clinical response rate compared to the control group [Relative Risk (RR) = 1.21, 95% CI = (1.12, 1.30), P < 0.01]. Moreover, the serum phosphorus levels [MD = -0.34, 95% CI = (-0.39, -0.29), P < 0.01], serum calcium levels [MD = -0.09, 95% CI = (-0.14, -0.05), P < 0.01], serum intact parathyroid hormone (iPTH) levels [MD = -35.05, 95% CI = (-45.31, -24.796), P < 0.01], and the incidence of adverse reactions [RR = 1.22, 95% CI = (1.08, 1.39), P < 0.01] were all lower in the experimental group compared to those in the control group. The funnel plot exhibited symmetrical distribution, and Egger's and Begg's tests did not reveal any evidence of significant publication bias (all P > 0.05). Conclusions: The combined use of lanthanum carbonate and calcium carbonate demonstrates a superior clinical efficacy in the management of hyperphosphatemia in hemodialysis patients, as compared to the use of calcium carbonate as a standalone treatment. To corroborate these findings, it is essential to conduct additional multi-center, RCTs with substantial sample sizes.

Keywords: Lanthanum carbonate, calcium carbonate, hemodialysis, hyperphosphatemia, clinical effective rate

Introduction

Hyperphosphatemia, characterized by elevated phosphorus levels in the blood, is a common concern for individuals undergoing dialysis [1]. This is primarily because the kidneys, the organs responsible for filtering waste products and excess minerals from the blood, are unable to perform this function effectively in patients with renal impairment [2]. Consequently, patients undergoing dialysis often struggle to maintain normal phosphorus levels. To combat hyperphosphatemia, several strategies are employed, such as dietary modifications to reduce phosphorus intake, the administration of phosphate binders to facilitate the excretion of excess phosphorus, and adjustments to dialysis regimens, including increasing the frequency or duration of dialysis sessions [3, 4]. Additionally, vigilant monitoring and precise adjustments of calcium, phosphorus, and parathyroid hormone levels, are essential for effective hyperphosphatemia management [5]. In cases of severe hyperphosphatemia that can-

https://doi.org/10.62347/WXBL2590

not be controlled through non-pharmacological measures, drug therapy or other more invasive treatments may be necessary [6]. Consequently, the management of hyperphosphatemia in patients on dialysis necessitates a holistic approach, considering the patient's overall health status and treatment goals. This approach should be customized by healthcare providers to optimize outcomes.

Oral phosphorus binders are a major treatment strategy to reduce hyperphosphatemia. These agents work by binding to phosphorus in food within the gastrointestinal tract, thereby inhibiting its absorption into the bloodstream [7]. This action is crucial for mitigating the adverse effects of elevated phosphorus levels. Commonly used oral phosphorus binders include aluminum phosphate and calcium phosphate [8]. Recently, there has emerged a clinical inclination towards using non-calcium-phosphorus binders combined with calcium-phosphorus binders (such as lanthanum carbonate) for the treatment of hemodialysis hyperphosphatemia [9]. This combined approach aims to improve the efficiency and effectiveness of phosphorus binding, thereby achieving more effective control of serum phosphorus levels. Lanthanum carbonate (LC), a non-calcium phosphorus binder, effectively sequesters phosphorus without disrupting calcium metabolism [10, 11]. Additionally, LC can reduce phosphorus absorption from food, resulting in lower blood phosphorus levels [12]. Recent studies suggest that when LC is combined with calcium-containing phosphorus binders like calcium acetate or calcium carbonate, it can improve phosphorus-binding efficiency and reduce phosphorus loss during dialysis, leading to better management of hyperphosphatemia [13, 14]. However, these studies are constrained by limited sample sizes and inconsistent evaluation criteria, which hinder broader clinical recommendations.

To address these limitations, the present study conducted a meta-analysis to evaluate the efficacy and safety of combining LC with calcium carbonate in treating hyperphosphatemia in hemodialysis patients, aiming to offer a solid theoretical basis for its clinical application.

Methods

Search strategy

Eligible publications were retrieved from PubMed, Embase, and Web of Science from their inception up to October 2023. The search was conducted using the following terms: 'Lanthanum carbonate OR Lanthanum OR LC' AND 'Calcium Carbonate, Carbonate, Calcium OR CC' AND 'Hemodialysis Solutions OR Hemodialysis' AND 'Hyperphosphatemia OR Hyperphosphatemias'. Two authors independently performed a systematic search of the databases, with an additional manual search of all included studies to identify further relevant literature. This Meta-analysis was registered with INPLASY (International Platform of Registered Systematic Review and Meta-analysis Protocols, 202470096).

Inclusion and exclusion criteria

Inclusion criteria: (1) Type of study: Randomized controlled trials (RCTs). (2) Study population: Patients undergoing continuous hemodialysis with hyperphosphatemia (defined as a hemodialysis duration exceeding 6 months and a blood phosphorus level above 1.80 mmol/L). Patients with other preexisting conditions that might affect calcium, phosphorus, and parathyroid hormone metabolism were excluded. (3) Interventions: The control group was given calcium carbonate alone, while the observation group was given a combination of lanthanum carbonate and calcium carbonate (combined medication). (4) Outcome indicators: Blood phosphorus levels, blood calcium levels, immunoreactive parathyroid hormone (iPTH) levels, clinical effective rate, and the incidence of adverse reactions. Clinical efficacy was defined as follows: Significantly effective: Post-treatment blood phosphorus levels decreased obviously with levels ≤ 1.80 mmol/L, showing stability; Effective: Post-treatment blood phosphorus notably decreased, but with levels > 1.80 mmol/L; Ineffective: No significant change in blood phosphorus levels post-treatment. Clinical effective rate = (significant effective cases + effective cases)/the total number of cases × 100%.

Exclusion criteria: Retrospective research, animal studies, comprehensive reviews, conference abstracts or solicitations, and previously published literature.

Data extraction

Two researchers (Fang and Chen) independently screened the literature based on the pre-established inclusion and exclusion criteria and completed individual literature information col-

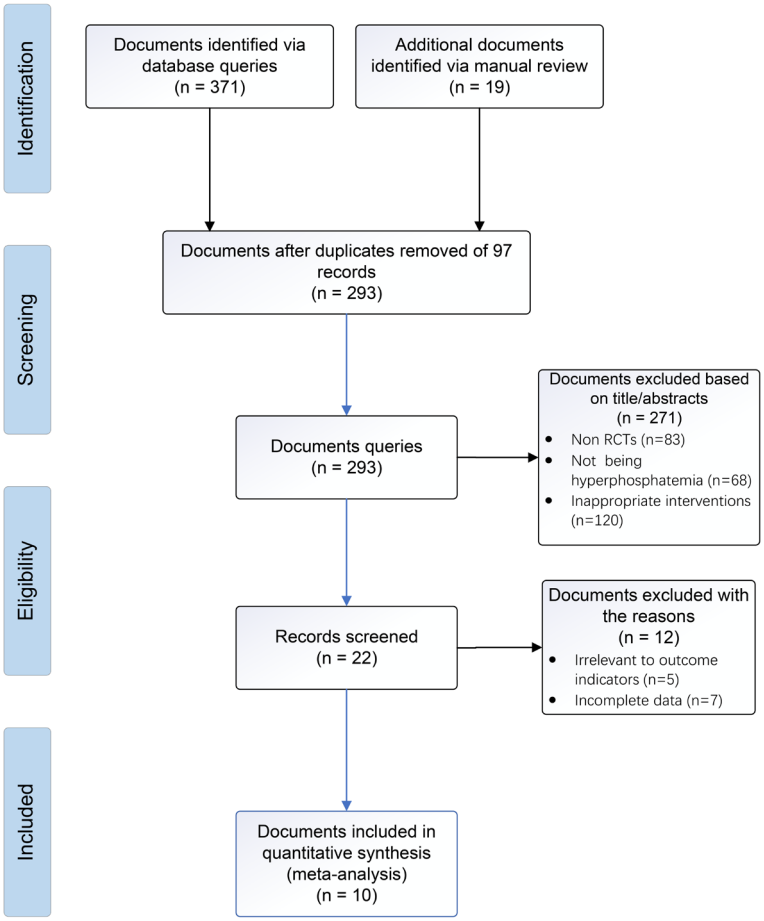

Figure 1. Flow diagram illustrating the selection process for studies included in the meta-analysis. RCT, randomized controlled trial.

lection forms. Any discrepancies were resolved through consensus. The extracted data included the title, publication time, first author, study design and methodology, intervention measures in the control group and observation group, usage and dosage of the included drugs (lanthanum carbonate and calcium carbonate), outcome measures, and evaluation methods.

Literature quality assessment

The quality of each study was evaluated using the Cochrane risk of bias assessment tool, which considers seven domains: selection bias (randomization and allocation), performance bias, detection bias, attrition bias, reporting bias, and other forms of bias. Each study was classified as having a low, high, or unclear risk of bias. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework was employed to evaluate the quality of the evidence and to determine the strength of the recommendations.

Statistical methods

Meta-analysis was carried out using RevMan 5.3 statistical software to assess clinical efficacy. The incidence of adverse reactions were analyzed as categorical data and expressed using the relative risk (RR) and its 95% confidence interval (95% CI). The blood phosphorus level, blood calcium level, and iPTH level after treatment were analyzed as continuous data and expressed using the mean difference (MD) and its 95% CI. The heterogeneity across the articles included in the study was measured using the χ^2 test, and the level of heterogeneity was measured using I^2 statistic. An $I^2 < 50\%$ indicated low heterogeneity among studies, promoting a fixed-effects model used in meta-analysis; while an $I^2 \geq 50\%$ suggested some heterogeneity among studies, and thus a random effects model was utilized. To assess the sensitivity and specificity, we employed a bivariate mixed effects model. Statistical significance was set at $P < 0.05$ for all analyses.

Results

Study identification and selection

The initial database search revealed a total of 371 related publications, and 19 records were obtained through a manual search. 97 studies were excluded due to duplication and other reasons, and an additional 271 were excluded based on their titles and abstracts. The remaining 22 studies were evaluated in detail for quantitative analysis. Finally, 10 RCTs were included in the quantitative analysis. See **Figure 1** for the study selection flow chart.

Characteristics of included studies

The 10 included studies were conducted from 2010 to 2022, involving 475 patients. Among these, 256 patients in the control group

Table 1. Basic characteristics of included publications

Study	Year	Country	Interventions	Outcome	Follow-up
Ogata et al. [25]	2021	Japan	Experimental group: LC 750 mg/d + CC 1000 mg/d; Control: CC 1000 mg/d.	② ③ ④ ⑤	3.16 years
Kovesdy et al. [26]	2018	USA	Experimental group: LC 500 mg/d + CC 1334 mg/d; Control: CC 1334 mg/d.	① ② ⑤ ⑥	12-month
Takeuchi et al. [27]	2013	Japan	Experimental group: LC 750 mg/d + CC 3000 mg/d; Control: CC 3000 mg/d.	① ② ③ ⑤ ⑥	3-year
Shigematsu et al. [28]	2012	Japan	Experimental group: LC 750 mg/d (maximum 1000 mg/d) + CC 3000 mg/d; Control: CC 3000 mg/d (maximum 3400 mg/d).	① ② ④ ⑤ ⑥	16-month
Chan et al. [29]	2010	United Kingdom	Experimental group: LC 2200 mg/d + CC 3000 mg/d; Control: CC 3000 mg/d.	① ② ③ ⑤	18-month
Cui et al. [6]	2022	China	Experimental group: LC 750 mg/d + CC 1000 mg/d; Control: CC 1000 mg/d.	①–⑥	NA
Wasilewska et al. [30]	2022	Poland	Experimental group: LC 500 mg/d (maximum 1000 mg/d) + CC 1000 mg/d; Control: CC 1000 mg/d.	① ② ③ ⑤ ⑥	18-month
Gotoh [31]	2013	Japan	Experimental group: LC 750 mg/d (maximum 1560 mg/d) + CC 650 mg/d (maximum 1030 mg/d); Control: CC 1000 mg/d (maximum 1030 mg/d).	① ③ ④ ⑤ ⑥	36-month
Yu [32]	2014	China	Experimental group: LC 750 mg/d (Adjust 250 mg each time based on biochemical indicators) + CC 600 mg/d (Adjust 250 mg each time based on biochemical indicators); Control: CC 600 mg/d (Adjust 250 mg each time based on biochemical indicators).	① ② ④ ⑤ ⑥	12-month
Li [33]	2019	China	Experimental group: LC 750 mg/d + CC 600 mg/d; Control: CC 1200 mg/d.	① ② ④ ⑤ ⑥	18-month

① Serum calcium; ② Serum phosphorus; ③ Serum calcium-phosphorus product; ④ Serum iPTH; ⑤ Clinical effective rate; ⑥ Incidence of adverse reactions. CC: calcium carbonate; LC: lanthanum carbonate.

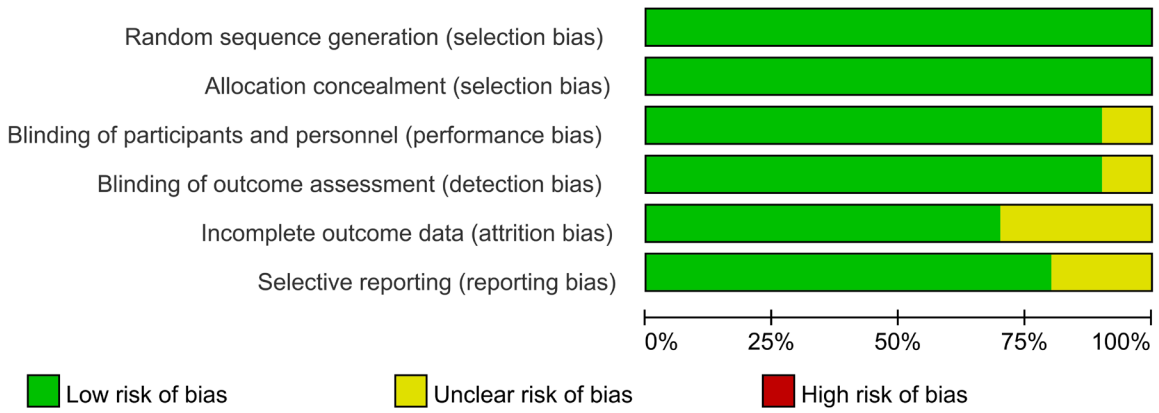

Figure 2. Risk of bias graph.

received single calcium carbonate treatment, and 219 patients in the experimental group received combined treatment with lanthanum carbonate combined and calcium carbonate. The characteristics of the included publications are demonstrated in **Table 1**.

Risk of bias of included trials

All studies included in this meta-analysis employed random allocation methods. Among them, five studies used either random number tables or computerized randomization procedures to mitigate selection bias. Additionally, three studies employed blinded outcome assessors. The data from all included studies were comprehensive, with only one study potentially displaying reporting bias. The quality evaluation of the included studies is presented in **Figure 2**. Overall, the randomization process was conducted using either a random number table or a computer-generated sequence, and most studies were considered to have a low risk of bias across all five domains.

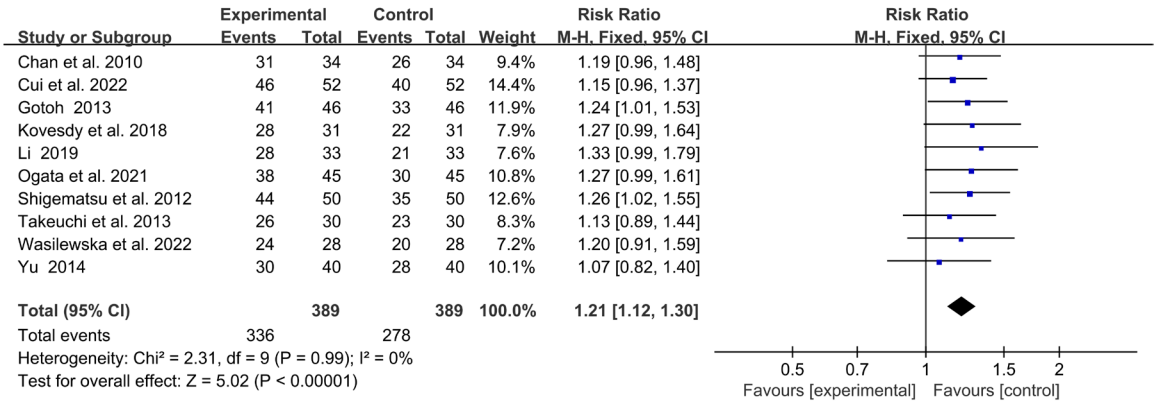

Figure 3. Forest plot of the clinical effective rate for the two treatment groups.

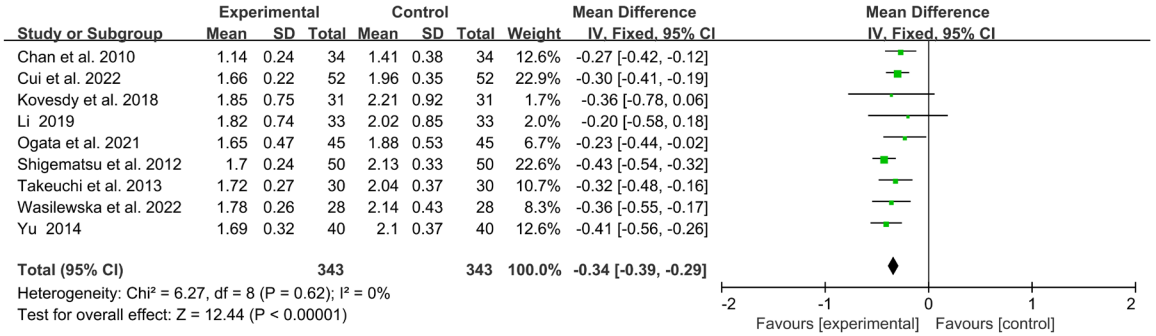

Figure 4. Forest plot of the serum phosphorus levels between the two groups.

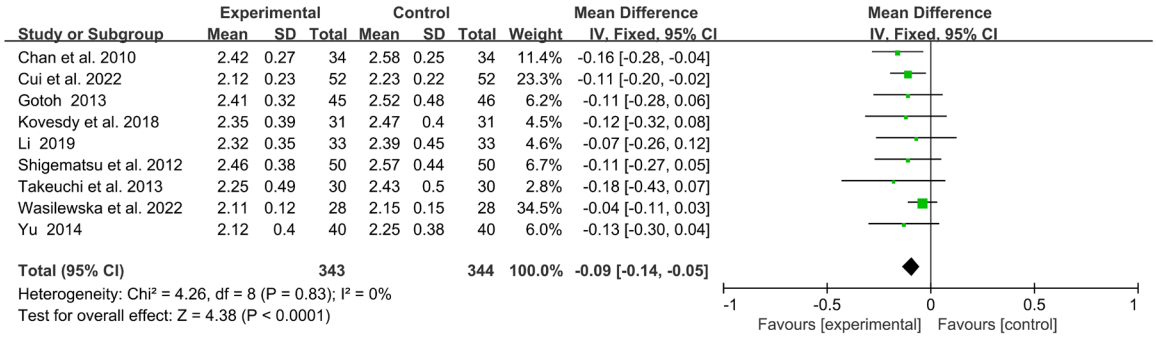

Figure 5. Forest plot of the serum calcium levels between the two groups.

Results of meta-analysis

Clinical effective rate: All the included studies assessed the clinical effective rate. The findings of this meta-analysis indicate that the observation group demonstrated a significantly higher clinical effective rate compared to the control group [RR = 1.21, 95% CI = (1.12, 1.30), P < 0.01, **Figure 3**].

Serum phosphorus levels: Nine articles mentioned serum phosphorus levels. The findings exposed that the serum phosphorus levels in the observation group were lower than those in the control group [MD = -0.34, 95% CI = (-0.39, -0.29), P < 0.01, **Figure 4**].

Serum calcium levels: Nine studies reported serum calcium levels. The results showed that the serum calcium level in the observation group was lower than that in the control group [MD = -0.09, 95% CI = (-0.14, -0.05), P < 0.01, **Figure 5**].

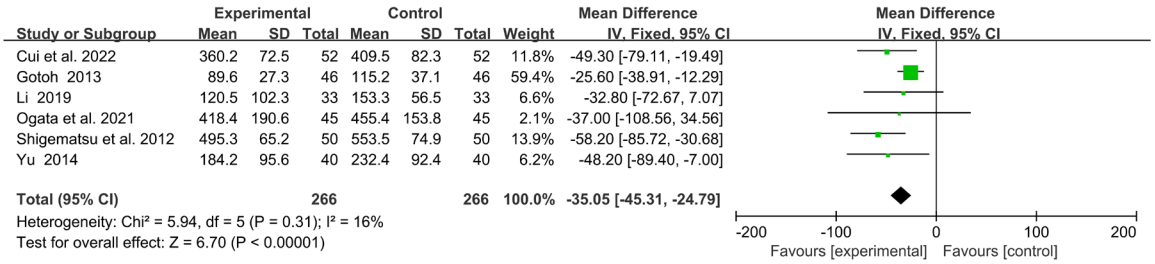

Figure 6. Forest plot of the serum intact parathyroid hormone (iPTH) levels between the two groups.

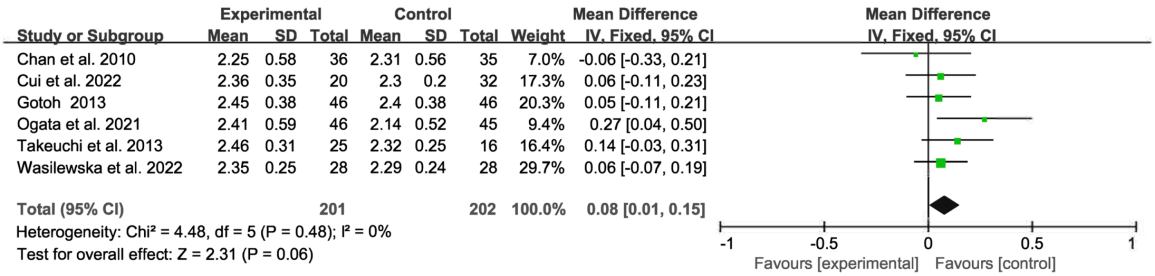

Figure 7. Forest plot of the serum calcium-phosphorus product between the two groups.

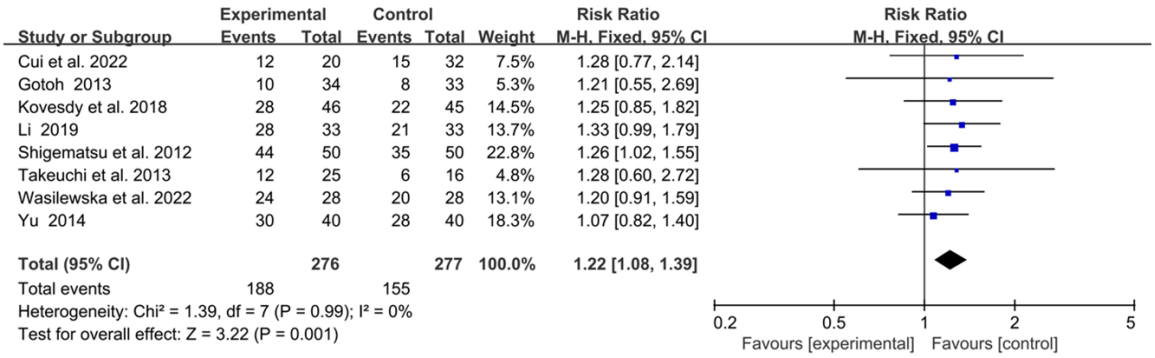

Figure 8. Forest plot of the adverse event incidence between the two groups.

Serum iPTH levels: Six articles mentioned serum iPTH levels. The results showed that the serum iPTH levels in the observation group were lower than those in the control group [MD = -35.05, 95% CI = (-45.31, -24.796), P < 0.01, **Figure 6**].

Serum calcium-phosphorus product: Six articles mentioned the serum contents of calcium-phosphorus products. The consequences indicated that there was no significant difference in calcium-phosphorus product between the two groups [MD = 0.08, 95% CI = (0.01, 0.15), P > 0.05, **Figure 7**].

Incidence of adverse events: Eight articles reported the adverse events. The primary adverse events encompassed nausea, vomiting, abdominal discomfort, and feelings of dizziness. The results showed that the incidence of adverse reactions was lower in the observation group compared to the control group [RR = 1.22, 95% CI = (1.08, 1.39), P < 0.01, **Figure 8**].

Publication bias

The funnel plots of the included studies demonstrated notable symmetry (**Figure 9**). Further Egger's and Begg's tests indicated the absence of publication bias (all P > 0.05, **Table 2**).

Discussion

Calcium carbonate is commonly used as a calcium-phosphate binder in the management of hyperphosphatemia in patients receiving he-

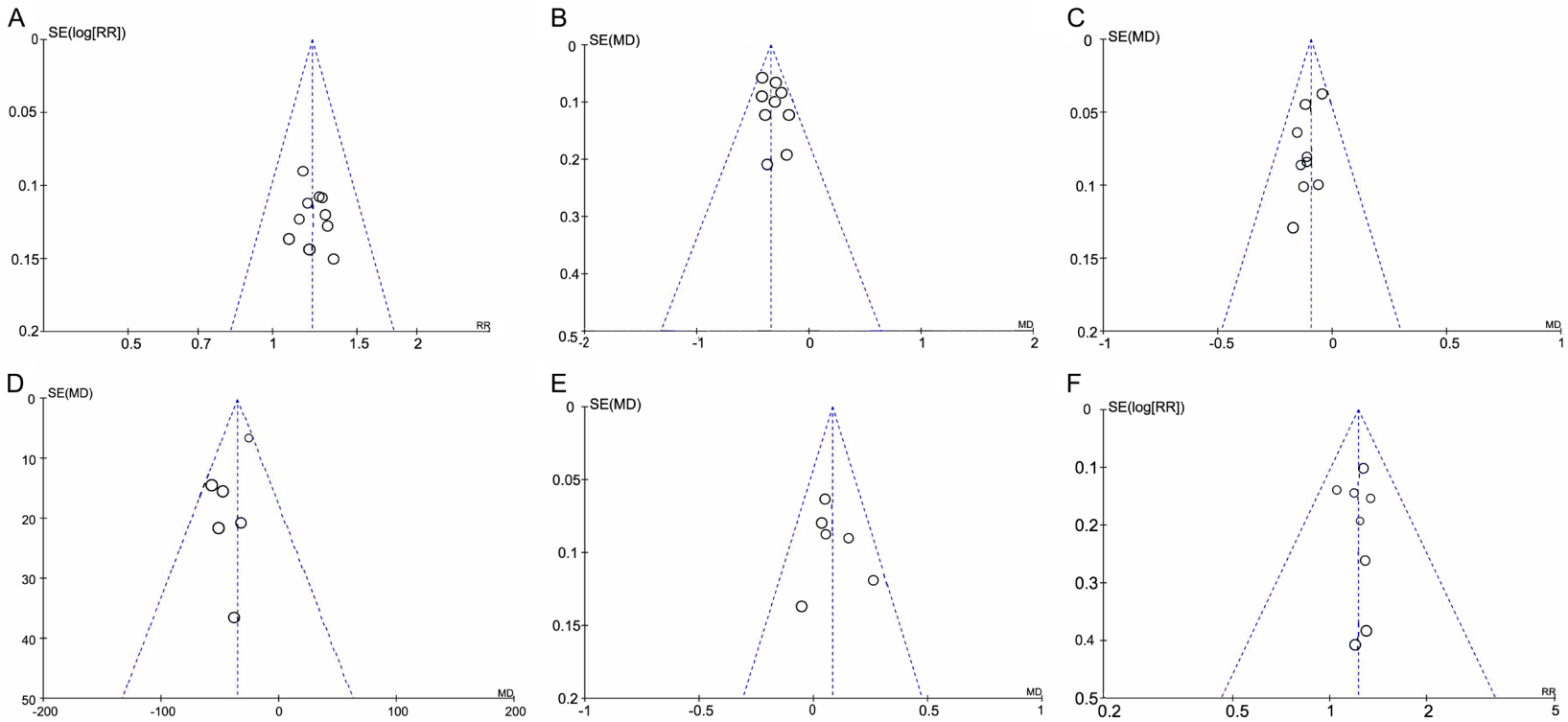

Figure 9. Publication Bias evaluation. A. Funnel plot of studies reporting clinical effective rate; B. Funnel plot of studies reporting serum phosphorus levels; C. Funnel plot of studies reporting serum calcium levels; D. Funnel plot of studies reporting serum iPTH levels; E. Funnel plot of studies reporting serum calcium-phosphorus product; F. Funnel plot of studies reporting incidence of adverse events.

Table 2. The publication bias provided by the outcomes of Egger's and Begg's tests

	PE	PB
Clinical effective rate	0.078	0.122
Serum phosphorus levels	0.059	0.273
Serum calcium levels	0.071	0.731
Serum iPTH levels	0.067	0.901
Serum calcium-phosphorus product	0.290	0.615
Incidence of adverse events	0.099	0.681

PE: *P* value for the Egger's test; PB: *P* value for the Begg's test.

modialysis [15]. Hyperphosphatemia, marked by elevated phosphate levels in the bloodstream, is a common complication in individuals with chronic kidney disease (CKD), especially among those on hemodialysis [16]. Calcium carbonate works by binding with dietary phosphate in the gastrointestinal tract, thereby reducing its absorption into the blood. By doing so, it aids in controlling blood phosphate levels and managing hyperphosphatemia. Often, calcium carbonate is prescribed concurrently with dialysis therapy to regulate phosphate levels and mitigate the progression of kidney disease [17]. However, while calcium carbonate offers some clinical benefits, it also carries potential risks and limitations. One notable concern is its association with hypercalcemia, particularly when used without careful monitoring or in patients with renal impairment. Excessive calcium intake can raise blood calcium levels [18], which may lead to complications such as vascular calcification, soft tissue calcification, and cardiac arrhythmias.

Lanthanum carbonate is a novel, calcium-free phosphorus binder that lowers serum phosphorus levels without causing hypercalcemia. It also prevents the excretion of toxic substances in urine and inhibits the activation of mononuclear macrophages in the urine [19]. These properties endow lanthanum carbonate with distinct clinical advantages in managing phosphorus metabolic disorders in patients. However, the cost of lanthanum carbonate is relatively high, and the dosage of the medication must be incrementally adjusted according to the patient's blood phosphorus levels, which could pose an additional financial burden on patients. Theoretically, the combination of lanthanum carbonate with calcium carbonate could potentially reduce the risk of hypercalcemia and alleviate the economic burden for patients.

Currently, there is a lack of definitive, authoritative guidelines for the combined use of calcium-based and non-calcium phosphorus binders for managing hyperphosphatemia in hemodialysis patients. Our study revealed a marked increase in clinical effectiveness in patients received combination medications compared to those treated with calcium carbonate alone. This underscores the considerable clinical benefits achieved through combination therapy. Emerging evidence suggests that the combination therapy can mitigate the risk of drug resistance or adverse effects commonly associated with monotherapy. By utilizing a combination of medications, treatment becomes more effective, with fewer complications, ultimately improving patients' quality of life. The findings provide important guidance for medical practice, encouraging doctors to consider the potential benefits of combination drug therapy when developing treatment plans and to incorporate these strategies into clinical practice [20]. Future studies should further explore the effects of different drug combinations to refine treatment protocols and provide superior patient care.

The findings from our study provide compelling evidence supporting the benefits of combination treatment over calcium carbonate alone. Notably, our analysis revealed significant reductions in serum phosphorus, calcium, and iPTH levels in the group receiving the combined treatment, as compared to the group receiving calcium carbonate alone. Elevated serum phosphorus levels are often associated with increased cardiovascular risk and mineral bone disorders, particularly in individuals with CKD. Lowering phosphorus levels can help to mitigate these risks and improve overall health outcomes [21]. Furthermore, maintaining the calcium balance is crucial for diverse physiological processes, including bone health, muscle function, and neural transmission. The combined treatment, by lowering serum calcium levels, may help prevent complications associated with hypercalcemia, while still ensuring sufficient calcium intake [22]. Moreover, the observed decrease in iPTH levels is noteworthy, as elevated iPTH levels are indicative of parathyroid gland dysfunction, commonly seen in

conditions like secondary hyperparathyroidism. By effectively lowering iPTH levels, the combination treatment may contribute to better calcium and phosphorus homeostasis, thereby reducing the risk of bone disease progression and related complications [23]. Furthermore, the lower incidence of adverse reactions in the combination treatment group highlights the favorable safety profile and tolerability of this therapeutic approach. Minimizing such adverse events is crucial for ensuring patient adherence and overall treatment effectiveness [24]. Our findings highlight the superior efficacy and safety of combination treatment compared to calcium carbonate alone in managing serum mineral levels and reducing adverse reactions. These results have significant implications for clinical practice, offering guidance to healthcare providers on refining treatment protocols for patients suffering from mineral metabolism and bone health.

The included literature comprised RCTs, which are essential in reducing bias, balancing unknown confounding factors, and offering a high level of recommendation. However, certain limitations should be acknowledged. First, the sample size of the literature included is fairly small. Second, variations in the usage, dosage, and treatment duration across different studies may contribute to the heterogeneity observed in blood phosphorus levels, blood calcium levels, and iPTH levels.

In conclusion, the therapeutic efficacy of lanthanum carbonate in conjunction with calcium carbonate for the management of hyperphosphatemia in hemodialysis patients was superior to that of calcium carbonate alone. Furthermore, it exhibited enhanced safety profiles and significantly improved prognosis. However, this study is constrained by the scope of the included literature. Therefore, future research should focus on conducting high-quality RCTs with larger sample sizes and multiple centers to further validate these findings.

Disclosure of conflict of interest

None.

Address correspondence to: Chunyan Chen, Department of Nephrology, Jiaxing Hospital of Traditional Chinese Medicine, No. 1501 Zhongshan East Road, Jiaxing 314000, Zhejiang, China. E-mail: chenchunyan0602@126.com

References

[1] Zamper R, Prempeh A, Iglesias I and Fayad A. Intraoperative transesophageal echocardiography following mitral valve repair: a systematic review. Braz J Anesthesiol 2022; 72: 379-397.

[2] Zhou C, Shi Z, Ouyang N and Ruan X. Hyperphosphatemia and cardiovascular disease. Front Cell Dev Biol 2021; 9: 644363.

[3] Cernaro V, Longhitano E, Calabrese V, Casuscelli C, Di Carlo S, Spinella C, Gembillo G and Santoro D. Progress in pharmacotherapy for the treatment of hyperphosphatemia in renal failure. Expert Opin Pharmacother 2023; 24: 1737-1746.

[4] Daoud K, Badran H, Anwar N and Nguyen T. The role of iron-based phosphate binder in the treatment of hyperphosphatemia. Nephrol Nurs J 2023; 50: 140-144.

[5] Koiwa F, Sato Y, Ohara M, Nakanishi K, Fukagawa M and Akizawa T. Long-term safety and decrease of pill burden by tenapanor therapy: a phase 3 open-label study in hemodialysis patients with hyperphosphatemia. Sci Rep 2023; 13: 19100.

[6] Cui X, Jiang S, Liu L, Tang X and Chen Y. Effect of low-dose lanthanum carbonate on calcium and phosphorus metabolism in Asian patients with end-stage renal disease, maintenance hemodialysis and hyperphosphatemia. Afr Health Sci 2022; 22: 362-368.

[7] Ding X, Sun S, Zhang J, Zhao H, Lun F, Liu X, Zhen Y, Dong J and Wu J. Ferric citrate for the treatment of hyperphosphatemia and iron deficiency anaemia in patients with NDD-CKD: a systematic review and meta-analysis. Front Pharmacol 2024; 15: 1285012.

[8] Barrera-Baena P, Rodríguez-García M, Rodríguez-Rubio E, González-Llorente L, Ortiz A, Zoccali C, Locatelli F, Floege J, Cohen-Solal M, Ferreira MA, Ketteler M, London GM, Gorriz-Teruel JL, Sánchez-Álvarez E, Hevia-Suárez MÁ, Fernández-Gómez JM, Martín-Carro B, Gómez-Alonso C, Alonso-Montes C, Cannata-Andia JB and Fernández-Martín JL; COSMOS. Serum phosphate is associated with increased risk of bone fragility fractures in haemodialysis patients. Nephrol Dial Transplant 2023; 39: 618-626.

[9] Makowka A and Nowicki M. Different effect of lanthanum carbonate and sevelamer hydrochloride on calcium balance in patients with moderate to advanced chronic kidney disease. Ther Clin Risk Manag 2021; 17: 1145-1151.

[10] Nain P, Nayak N, Maj MC, Singh RK, Kaur J, Jeong Y, Maity S, Nath R, Hilgers RH, Nauhria S and Nauhria S. Efficacy of lanthanum carbonate and sevelamer carbonate as phosphate

binders in chronic kidney disease-a comparative clinical study. Pharmacy (Basel) 2023; 11: 27.
[11] Shimma S, Makino Y, Kojima K and Hirata T. Quantitative visualization of lanthanum accumulation in lanthanum carbonate-administered human stomach tissues using mass spectrometry imaging. Mass Spectrom (Tokyo) 2020; 9: A0086.
[12] Zhou Q, Yu M, Chang X, Shang S, Li M and Xu W. A 47-year-old man with hyperphosphatemia due to chronic renal failure treated with lanthanum carbonate tablets presenting acutely with partial large bowel obstruction. Am J Case Rep 2023; 24: e942113.
[13] Maemoto M, Hirata Y, Hosoe S, Ouchi J, Uchii M, Takada H, Akizawa E, Yanagisawa A and Shuto S. Development of potent non-acylhydrazone inhibitors of intestinal sodium-dependent phosphate transport protein 2b (NaPi2b). Bioorg Med Chem 2022; 71: 116944.
[14] Yaguchi A, Akahane K, Tsuchioka K, Yonekubo S, Yamamoto S, Tamai Y, Tatemichi S and Takeda H. A comparison between the combined effect of calcium carbonate with sucroferric oxyhydroxide and other phosphate binders: an in vitro and in vivo experimental study. BMC Nephrol 2019; 20: 465.
[15] Scialla JJ, Kendrick J, Uribarri J, Kovesdy CP, Gutiérrez OM, Jimenez EY and Kramer HJ. State-of-the-art management of hyperphosphatemia in patients With CKD: an NKF-KDOQI controversies perspective. Am J Kidney Dis 2021; 77: 132-141.
[16] Ulaya G and İla HB. In vitro cytogenetic analysis of two different anti-phosphates (sevelamer hydrochloride and calcium carbonate) agents used by patients with hyperphosphatemia. Drug Chem Toxicol 2023; 46: 699-707.
[17] Mason DL, Godugu K, Nnani D and Mousa SA. Effects of sevelamer carbonate versus calcium acetate on vascular calcification, inflammation, and endothelial dysfunction in chronic kidney disease. Clin Transl Sci 2022; 15: 353-360.
[18] Chen W, Liu HF, Chen QK, Zhao MH, Chen XN, Liu H, Wan JX, Li SM, Chen MH, Dai C, Shi HB, Wei JL, Zhao HW, Wang LH, Long G, Lu WH, Tang Y, Yang JW, Cao LY, Tang DX, Yang YQ and Yu XQ. Efficacy and safety of sevelamer carbonate in chinese nondialysis chronic kidney disease patients with hyperphosphatemia: a randomized, double-blind, parallel-group study. Kidney Dis (Basel) 2023; 9: 82-93.
[19] Nakamura K, Nagata Y, Hiroyoshi T, Isoyama N, Fujikawa K, Miura Y, Matsuyama H and Kuro OM. The effect of lanthanum carbonate on calciprotein particles in hemodialysis patients. Clin Exp Nephrol 2020; 24: 323-329.
[20] Plana D, Palmer AC and Sorger PK. Independent drug action in combination therapy: implications for precision oncology. Cancer Discov 2022; 12: 606-624.
[21] Villa-Bellosta R. Vascular calcification: key roles of phosphate and pyrophosphate. Int J Mol Sci 2021; 22: 13536.
[22] Sotorník R. Hypoparathyroidism. Cas Lek Cesk 2023; 162: 136-147.
[23] Zeng Q, Zhong Y and Yu X. Meta-analysis of the efficacy and safety of sevelamer as hyperphosphatemia therapy for hemodialysis patients. Ren Fail 2023; 45: 2210230.
[24] Gérard AO, Merino D, Charbinat A, Fournier J, Destere A, Loschi M, Cluzeau T, Sicard A and Drici MD. CAR-T Cells and the kidney: insights from the WHO safety database. BioDrugs 2023; 37: 521-530.
[25] Ogata H, Fukagawa M, Hirakata H, Kagimura T, Fukushima M and Akizawa T; LANDMARK Investigators and Committees. Effect of treating hyperphosphatemia with lanthanum carbonate vs calcium carbonate on cardiovascular events in patients with chronic kidney disease undergoing hemodialysis: the LANDMARK randomized clinical trial. JAMA 2021; 325: 1946-1954.
[26] Kovesdy CP, Lu JL, Wall BM, Gyamlani G, Naseer A, Wallick A, Han Z, Thomas F, Quarles LD and Jarmukli N. Changes with lanthanum carbonate, calcium acetate, and phosphorus restriction in CKD: a randomized controlled trial. Kidney Int Rep 2018; 3: 897-904.
[27] Takeuchi K, Matsuda E, Sekino M, Hasegawa Y, Kamo Y, Kikuchi N and Sekino H. Three-year follow-up of lanthanum carbonate therapy in hemodialysis patients. Ther Apher Dial 2013; 17 Suppl 1: 15-21.
[28] Shigematsu T and Negi S; COLC Research Group. Combined therapy with lanthanum carbonate and calcium carbonate for hyperphosphatemia decreases serum FGF-23 level independently of calcium and PTH (COLC Study). Nephrol Dial Transplant 2012; 27: 1050-1054.
[29] Chan WL, Rounsley K, Chapman E, Collings K, Dale C, De Waal S, Patel V, Tanner J, Turner E, Moore J and Borrows R. Lanthanum carbonate is an effective hypophosphatemic agent for hemodialysis patients intolerant of other phosphate binders. J Ren Nutr 2010; 20: 270-277.
[30] Wasilewska A, Murray RA, Sundberg A, Uddin S, Achenbach H, Shavkin A, Szabó T, Vergani A and Umeh O. An open-label phase 2 trial to assess the efficacy, safety and pharmacokinetics of lanthanum carbonate in hyperphosphatemic children and adolescents with chronic kidney disease undergoing dialysis. BMC Nephrol 2022; 23: 84.

[31] Gotoh J, Kukita K, Tsuchihashi S, Hattori M, Iida J, Horie T, Onodera K, Furui H, Tamaki T, Meguro J, Yonekawa M and Kawamura A. Study of prolonged administration of lanthanum carbonate in dialysis patients. Ther Apher Dial 2013; 17 Suppl 1: 9-14.

[32] Yu HB, Jiang AL and Wei F. Effect of lanthanum carbonate combined with calcium carbonate on hyperphosphatemia in hemodialysis patients. Chinese Journal of Nephrology 2014; 30: 656-659.

[33] Li GF and Zhu ZD. Effect of calcium acetate and lanthanum carbonate in the treatment of uremic hemodialysis hyperphosphatemia. Practical Clinical Practice of Integrated Traditional Chinese and Western Medicine 2019; 19: 20-21.