Paricalcitol vs. cinacalcet for secondary hyperparathyroidism in chronic kidney disease: A meta-analysis

WEI XU[1,2], LIFENG GONG[1,2], JINGKUI LU[1,2] and WEIGANG TANG[1,2]

[1]Department of Nephrology, Wujin Hospital Affiliated to Jiangsu University; [2]Department of Nephrology, Wujin Clinical College of Xuzhou Medical University, Changzhou, Jiangsu 213000, P.R. China

Received December 14, 2019; Accepted June 17, 2020

DOI: 10.3892/etm.2020.9044

Abstract. Paricalcitol and cinacalcet have been recommended to reduce parathyroid hormone (PTH) levels for patients with secondary hyperparathyroidism (SHPT) and chronic kidney disease (CKD), and they are able to reduce the risk of hypercalcemia and hyperphosphatemia. However, to date, it has remained uncertain which is the better drug. The aim of the present meta-analysis was to evaluate the effects on PTH, calcium and phosphorus metabolism between the two drugs. The PubMed, the Cochrane Library and Embase databases were searched from inception to June 1, 2019 and eligible studies comparing paricalcitol and cinacalcet for SHPT were included. Data were analysed using Review Manager version 5.3. A total of 7 trials from six articles, comprising 456 patients in the paricalcitol group and 412 patients in the cinacalcet group, were included in the meta-analysis. There were no differences in PTH levels [mean difference (MD): 71.82, 95% CI: -185.20-328.85, P=0.58] and phosphorus levels (standard MD: 0.59, 95% CI: -0.82-2.00, P=0.41). The calcium levels in the paricalcitol group were significantly higher than those in the cinacalcet group (MD: 1.10, 95% CI: 0.92-1.28, P<0.05). In conclusion, paricalcitol and cinacalcet exhibited no difference in their efficacy to control of PTH levels, as they were similarly effective in decreasing the PTH levels. They also had comparable efficacy in the management of phosphorus levels. However, cinacalcet produced a significantly greater reduction in serum calcium levels. More large multicentre randomized controlled trials are necessary to confirm the conclusions of the present analysis.

Introduction

Secondary hyperparathyroidism (SHPT) is one of the most frequent complications in patients with chronic kidney disease (CKD) (1). SHPT is characterized by increased parathyroid hormone (PTH), which may cause vascular calcification, soft tissue calcification and bone fracture (2-4). High levels of PTH are associated with an increased risk of mortality (5-9). The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommended 'calcitriol, vitamin D analogs, calcimimetics or a combination of these drugs' to reduce PTH levels (4).

Calcitriol is a classic treatment to control PTH levels in patients with SHPT (10). However, certain patients with refractory SHPT are characterized by high levels of PTH, hypercalcaemia and hyperphosphatemia. High doses of calcitriol increase the risk of hypercalcaemia and hyperphosphatemia, which may increase mortality. Patients with SHPT have the lowest risk of mortality when their serum calcium and phosphorus levels are in the normal range (4). Recently, paricalcitol, a selective vitamin D analogue, was demonstrated to only have a minor effect on vitamin D receptors in the intestine and bone (11). Paricalcitol has been proved to be an effective treatment to control PTH levels and reduce absorption of calcium and phosphorus (12,13). In addition, cinacalcet, a kind of calcimimetic, also provides effective control of PTH levels and has the additional effect of reducing calcium and phosphate levels (14-17). Thus far, various studies have been performed to compare the effects of PTH and calcium and phosphorus metabolism between the two novel drugs; however, it has remained uncertain which is the better drug. Therefore, the present meta-analysis was performed to evaluate the effects of PTH on calcium and phosphorus metabolism between the two drugs in patients with SHPT.

Materials and methods

Search strategy. The present meta-analysis was reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (18). The PubMed, Cochrane Library and Embase databases were searched for entries from inception to June 1, 2019. The combined text and MeSH terms included the following: 'Secondary hyperparathyroidism', 'Paricalcitol', 'Cinacalcet', 'Vitamin D analogues' and 'Calcimimetics'. In addition, the cited papers and relevant references were searched manually to identify eligible studies. There were no language restrictions.

Correspondence to: Professor Weigang Tang, Department of Nephrology, Wujin Hospital Affiliated to Jiangsu University, 2 Yongning Road, Changzhou, Jiangsu 213000, P.R. China
E-mail: wjrmyysnk@163.com

Key words: secondary hyperparathyroidism, paricalcitol, cinacalcet, meta-analysis

Inclusion and exclusion criteria. The inclusion criteria were as follows: i) Randomized controlled trials (RCTs), case-control or cohort studies; ii) Haemodialysis patients with SHPT, PTH levels >300 pg/ml (reference range, 150-300 pg/ml); iii) Comparison of outcomes between paricalcitol and cinacalcet; and iv) Reported outcomes include PTH, calcium and phosphorus levels. The exclusion criteria were as follows: i) Case series, reviews, comments; ii) Patients with parathyroidectomy or kidney transplantation; and iii) Lack of relevant outcome data.

Data extraction and quality assessment. Two investigators (XWX and LFG) retrieved and independently selected all eligible records. Disagreements were resolved by discussion with a third investigator (LJK). Details including the first author's name, year of publication, location of the study, study design, sample size, sex, mean age, follow-up period, the dose of medication and treatment outcomes were extracted. The Cochrane assessment tool was used to assess the quality of RCTs (19) and the Newcastle-Ottawa scale (NOS) was used to assess the quality of non-randomized studies (20).

Statistical analysis. Data analysis was performed using Review Manager version 5.3 (Cochrane Collaboration). Treatment outcomes were summarized as odds ratios (OR) for categorical variables. Continuous data of outcomes are presented as the mean difference (MD). $P<0.05$ was considered to indicate statistical significance. Heterogeneity was assessed via I^2 statistics. $I^2>50\%$ and $P<0.10$ were considered to imply significant heterogeneity. Data with insignificant heterogeneity were analyzed using the fixed-effects model. For heterogeneous data, the random-effects model was used. Subgroup analysis or sensitivity analysis was used to assess publication bias.

Results

Study selection and characteristics. A total of 406 articles were initially selected. After the exclusion of duplicated studies, 306 studies were retained. Subsequently, 262 articles consisting of comments, reviews, case reports and content unrelated to SHPT were removed by analyzing the title and abstracts. A total of six studies (21-26) were included in the final analysis after screening the full text (Fig. 1). Of these six articles, one from Ketteler *et al* (26) involved two RCTs. The specific details of these two RCTs in the article by Ketteler *et al* (26) are listed in Table I. In total, 456 patients were included in the paricalcitol group and 412 patients were included in the cinacalcet group. The shortest follow-up time among all studies was 160 days and the longest was 12 months. The basic characteristics of the six studies are listed in Table I. According to the NOS evaluation criteria, the cohort studies scored an average of 6 points, with medium quality (Table II). However, the study by Kukavica *et al* (24) scored 5 points with low quality, where the basic PTH level in the cinacalcet group (751.07±117.74) was significantly lower compared with that in the paricalcitol group (1040.31±79.56).

The risk of bias in the included RCTs were shown in Table III. All RCTs were graded as being of moderate quality. The method of random allocation was mentioned in all RCTs.

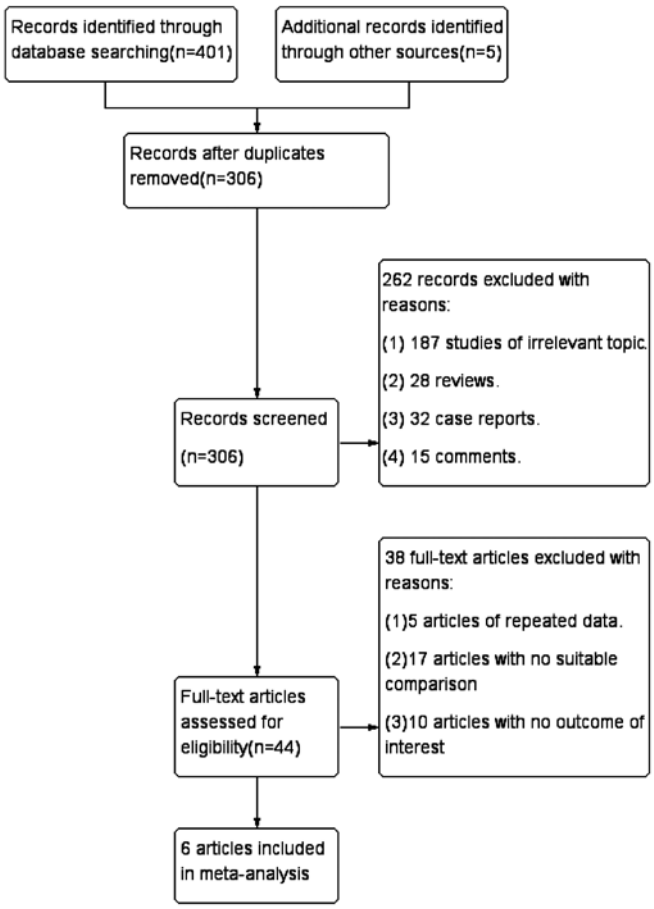

Figure 1. Flow diagram of the literature search.

However, none of the RCTs elaborated on the methods of random sequence generation, allocation concealment or blinding. The completeness of the outcomes was unclear in the studies by Sharma *et al* (21) and Sprague *et al* (23).

Meta-analysis results.

PTH. Data regarding PTH levels were reported by six trials included in five articles (22-26). There was significant heterogeneity among the six trials ($P<0.10$, $I^2=100\%$); therefore, the random-effects model was used for the meta-analysis. There was no significant difference between the paricalcitol and cinacalcet groups regarding PTH levels (MD: 71.82, 95% CI: -185.20-328.85, P=0.58; Fig. 2).

A total of 3 trials included in two studies reported data on the proportion of subjects with PTH levels of 150-300 pg/ml at the end of follow-up (21,26). The heterogeneity among these experiments was not significant ($P=0.52$, $I^2=0\%$); therefore, the fixed-effects model was used for the meta-analysis. The proportion of subjects treated with paricalcitol who had PTH values of 150-300 pg/ml was significantly greater (90/160, 56.3%) than the respective proportion in the cinacalcet group (55/149, 37.0%). There was a statistically significant difference between the two groups (OR: 2.19, 95% CI: 1.39-3.46, $P<0.05$; Fig. 3).

Calcium levels. Data regarding calcium levels were reported in five trials included in four articles (22,23,25,26). There was

Table I. Characteristics of the included studies.

Author (year)	Country	Design	Follow-up period	Sample size	Mean age (years)	Males, n (%)	Creatinine (mg/dl)	Calcium (mg/dl)	Phosphorus (mg/dl)	PTH (pg/ml)	Dose of medication	(Refs.)
Sharma (2014)	US	RCT	28 wk	Paricalcitol: 51 Cinacalcet: 47	61.0±11.5 60.7±11.6	31 (60.8) 28 (59.6)	8.1±2.3 9.0±2.5	9.0±0.5 9.1±0.4	4.8±1.0 5.0±1.0	516.6±147.9 524.3±149.7	-	(21)
Zawierucha (2019)	Poland	Cohort study	52 wk	Paricalcitol (IV): 60 Cinacalcet (oral): 50	66 63	39 (65.0) 31 (62.0)	-	8.5±0.9 7.1±3.2	5.1±1.4 5.7±1.5	1130 1271	6.76 μg/dialysis 0.6 mg/kg	(22)
Sprague (2015)	US	RCT	12 m	Paricalcitol (IV): 157 Cinacalcet (oral): 155	55 53	95 (61) 93 (60)	-	9.5±0.5 9.6±0.5	5.8±1.5 5.7 ±1.6	815.7±427.9 845.7±431.3	21.4 ±1.5 μg/wk 85.6 ±5.4 mg/d	(23)
Kukavica (2011)	Bosnia and Herzegovina	Cohort study	160 d	Paricalcitol: 41 Cinacalcet: 13	48.08±7.4	-	-	-	-	1040.31±79.56 751.07±117.74	-	(24)
Kaperonis (2012)	Greece	Cross-over design	6 m	Paricalcitol (IV): 13 Cinacalcet (oral): 13	57	11 (84)	-	9.3 9.4	-	-	13.2 μg/wk 40.4 mg/d	(25)
Ketteler (2012)	12 countries	RCT	28 wk	Paricalcitol (oral): 72 Cinacalcet (oral): 70	65.7±13.5 65.1±12.5	49 (68.1) 43 (61.4)	8.9±2.6 8.4±2.6	9.0±0.6 9.0±0.7	4.9±1.1 4.4±1.1	494.8±170.3 509.5±138.5	3.5±3.5 μg/dialysis 31.8±28.7 mg/d	(26)
Ketteler (2012)	12 countries	RCT	28 wk	Paricalcitol (IV): 62 Cinacalcet (IV): 64	61.2±12.7 59.9±12.0	38 (61.3) 38 (59.4)	8.2±2.4 8.6±2.5	9.0±0.6 9.0±0.7	4.9±1.1 4.9±1.1	526.3±153.1 521.1±149.2	5.5±3.7 μg/dialysis 61.6±44.8 mg/d	(26)

RCT, randomized controlled trial; IV, intravenous administration; d, day; wk, week; m, month; PTH, parathyroid hormone.

Table II. Quality assessment of cohort studies.

	Selection				Comparability		Outcome				
Author (year)	Representativeness of the exposed group	Representativeness of the non-exposed group	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Controls for the most important factor	Controls for any additional factors	Assessment of outcome	Follow-up period sufficient for the measurement of outcomes	Adequacy of follow-up of cohorts	Score	(Refs.)
Zawierucha (2019)	*	*	*	*	*	-	*	*	-	7	(22)
Kukavica (2011)	*	-	-	*	*	-	*	*	-	5	(24)
Kaperonis (2012)	*	*	-	*	*	-	*	*	-	6	(25)

The Cohort studies were evaluated using the Newcastle-Ottawa scale. A total of 9 points. *, 1 point; -, 0 point.

significant heterogeneity among these experiments (P=0.02, I^2=66%); therefore, the random-effects model was ultimately used for the meta-analysis. The calcium levels of the paricalcitol groups were higher than those of the cinacalcet groups, and the difference was statistically significant (MD: 1.10, 95% CI: 0.92-1.28, P<0.05; Fig. 4).

Phosphorus levels. Data regarding phosphorus levels were reported in five trials included in four studies (22-24,26). There was significant heterogeneity among these studies (P<0.10, I^2=98%); therefore, the random-effects model was used for the meta-analysis. There was no significant difference between the groups regarding phosphorus levels (SMD: 0.59, 95% CI -0.82-2.00, P=0.41; Fig. 5).

Sensitivity analyses and publication bias. To evaluate the robustness of the estimated pooled effect size for PTH, calcium, phosphorus levels and the rate of reaching the PTH standard, a sensitivity analysis was performed by sequentially deleting one study at a time and redetermining the pooled effect size of the remaining studies. The results revealed that none of the individual studies affected the overall results on PTH, calcium, phosphorus levels and the rate of reaching the PTH standard, which suggested that the pooled effects on PTH, calcium and phosphorus levels were stable (Tables SI-SIV).

Discussion

Vitamin D supplementation is the traditional strategy for SHPT management. However, the application of vitamin D is limited in certain patients due to hypercalcemia, hyperphosphatemia and high levels of PTH (27,28). As a novel selective vitamin D receptor agonist, paricalcitol is able to effectively inhibit PTH synthesis and parathyroid hyperplasia, but its effect on the intestine and bone is only 1/10 of that of calcitriol (29). Thus, paricalcitol is advantageous in reducing PTH levels and lowering the risk of hypercalcemia and hyperphosphataemia. Furthermore, as a calcimimetic, cinacalcet activates calcium-sensitive receptors of the parathyroid (30). Certain studies have suggested that cinacalcet is able to significantly inhibit PTH secretion so as to reduce the number of parathyroidectomy operations (31,32). With the application of cinacalcet, the present analysis indicated that there was a significant decreasing trend of serum calcium. The present systematic review aimed to appraise the effects on PTH and calcium and phosphorus metabolism between the two novel drugs for SHPT.

The studies included in the present meta-analysis indicated that paricalcitol and cinacalcet were both beneficial in decreasing the PTH levels and the efficacy was not significantly different. The Kidney Disease Outcomes Quality Initiative recommends a PTH target of 150-300 pg/ml (33), while the KDIGO guidelines suggest maintaining PTH levels in the range of 130-600 pg/ml (2-9X the upper limit of normal) (4). The present meta-analysis indicated that paricalcitol was more effective than cinacalcet in achieving the target level of PTH (150-300 pg/ml). Of note, the studies of Kukavica *et al* (24) and Kaperonis *et al* (25) reported a significant advantage of cinacalcet treatment in decreasing the PTH levels compared with that of paricalcitol treatment, but they did not report

Table III. Risk of bias of randomized controlled trials[a].

Author (year)	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Incomplete outcome data	Selective reporting	Other bias	(Refs.)
Sharma (2014)	?	?	?	?	+	?	(21)
Sprague (2015)	?	?	?	?	+	?	(23)
Ketteler (2012)	?	?	?	+	+	?	(26)

[a]Evaluated using the Cochrane assessment tool. +, low risk of bias; ?, unclear risk of bias; -, High risk of bias.

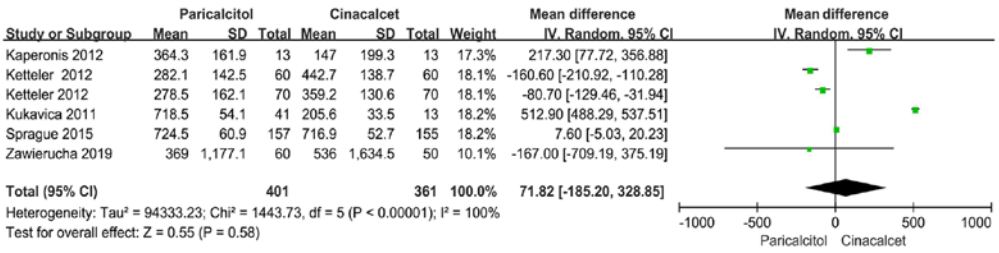

Figure 2. Forest plot comparing parathyroid hormone levels between the paricalcitol and cinacalcet groups. IV, inverse variance; SD, standard deviation; df, degrees of freedom.

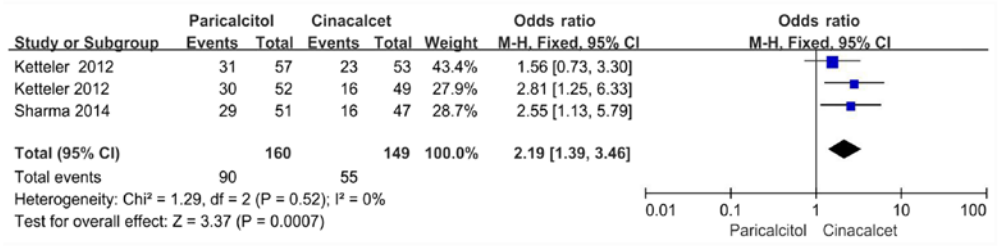

Figure 3. Forest plot comparing the proportion of subjects with a parathyroid hormone level of 150-300 pg/ml between paricalcitol and cinacalcet. M-H, Mantel-Haentzel; df, degrees of freedom.

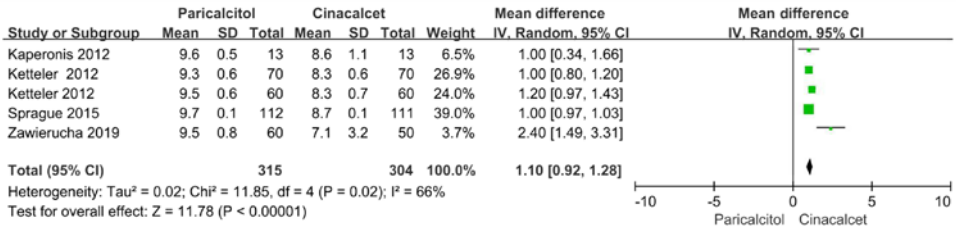

Figure 4. Forest plot comparing calcium levels between paricalcitol and cinacalcet. IV, inverse variance; SD, standard deviation; df, degrees of freedom.

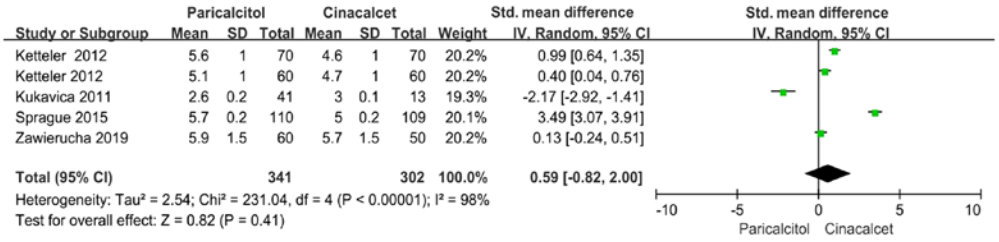

Figure 5. Forest plot comparing phosphorus levels between paricalcitol and cinacalcet. IV, inverse variance; SD, Std. deviation; Std, standard; df, degrees of freedom.

any data on the proportion of subjects with PTH levels of 150-300 pg/ml. In addition, certain studies included suggested that when the average baseline PTH levels were >800 pg/ml, both drugs were able to decrease the PTH levels but did not decrease the average PTH levels to 2-9X the upper limit of normal (4).

The present meta-analysis indicated that cinacalcet significantly decreased the serum calcium levels compared with paricalcitol. The KDIGO guidelines recommend avoiding hypercalcemia (4). In all studies included, the average serum calcium levels were still in the ideal range (8.4-10 mg/dl) (4) after paricalcitol treatment. Only one study included reported on the incidence of hypercalcaemia, which was significantly higher in the paricalcitol group (12.7%) than in the cinacalcet group (0.7%). Although the effect of paricalcitol on the intestine and bone is only 1/10 of that of calcitriol, paricalcitol treatment still poses a risk of hypercalcemia, which is proportional to the dosage of paricalcitol (29). In three of the included trials (22,26), the average serum calcium levels were below the ideal range after cinacalcet treatment. Only one of the articles included reported on the incidence of hypocalcemia, which was significantly higher in the cinacalcet group (20.1%) than in the paricalcitol group (0%). The reason is that cinacalcet mimics the effect of Ca^{2+} on parathyroid cells so that it reduces PTH and serum calcium (17,30). However, cinacalcet combined with vitamin D reduces the incidence of hypocalcemia (34).

The present results revealed that the serum phosphate levels were relatively higher in the paricalcitol groups than in the cinacalcet groups but there was no significant difference. There is an increasing risk of mortality with increasing levels of serum phosphate (4). In certain studies included, the average serum phosphate levels of paricalcitol or cinacalcet were above the upper limit of normal at the end of follow-up. In other words, both drugs are associated with the risk of causing hyperphosphataemia.

Only one of the studies included reported on the incidence of adverse events, which were all higher in the cinacalcet group (26). Therefore, only a descriptive analysis was performed in the present study. The incidence rates in the cinacalcet group were as follows: Nausea (6.7%), vomiting (4.5%), constipation (3.0%) and muscle spasms (2.2%). The incidence rates in the paricalcitol group were as follows: Nausea (0%), vomiting (1.5%), constipation (0%) and muscle spasms (0%). In addition, only one included article from the US reported on the cost of treatment (26). The study revealed that paricalcitol was more cost-effective than cinacalcet and that paricalcitol was simultaneously more effective in achieving the target levels of PTH. In a word, paricalcitol appeared to have an advantage in terms of adverse events and cost.

There were certain limitations to the present meta-analysis. First, only one study compared paricalcitol and cinacalcet in terms of hypocalcemia, hypercalcemia, hyperphosphataemia, adverse events and cost; thus, it was not possible to perform a meta-analysis for these points. Furthermore, additional studies reporting on the proportion of subjects with PTH levels in the target range after treatment with these two drugs are required.

In conclusion, the present meta-analysis revealed that paricalcitol and cinacalcet were effective for decreasing PTH levels. There was no difference between the two novel drugs concerning the management of PTH and phosphorus levels. Cinacalcet significantly reduced the serum levels of calcium. To further confirm these conclusions, further large multicenter RCTs comparing these two drug treatments are necessary.

Acknowledgements

Not applicable.

Funding

No funding received.

Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

WX and WGT contributed to this work by designing the study, reviewing literature, interpreting the analyses and writing the manuscript. LFG and JKL contributed to the literature review, data collection and analysis, and writing the manuscript. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Davies EW, Matza LS, Worth G, Feeny DH, Kostelec J, Soroka S, Mendelssohn D, McFarlane P and Belozeroff V: Health state utilities associated with major clinical events in the context of secondary hyperparathyroidism and chronic kidney disease requiring dialysis. Health Qual Life Outcomes 13: 90, 2015.
2. Lewis R: Mineral and bone disorders in chronic kidney disease: New insights into mechanism and management. Ann Clin Biochem 49: 432-440, 2012.
3. Wei Y, Lin J, Yang F, Li X, Hou Y, Lu R, Shi X, Liu Z and Du Y: Risk factors associated with secondary hyperparathyroidism in patients with chronic kidney disease. Exp Ther Med 12: 1206-1212, 2016.
4. Isakova T, Nickolas TL, Denburg M, Yarlagadda S, Weiner DE, Gutiérrez OM, Bansal V, Rosas SE, Nigwekar S, Yee J, *et al*: KDOQI US commentary on the 2017 KDIGO clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Am J Kidney Dis 70: 737-751, 2017.
5. Goettsch C, Iwata H and Aikawa E: Parathyroid hormone: Critical brigde between bone metabolism and cardiovascular disease. Arterioscler Thromb Vasc Biol 34: 1333-1335, 2014.
6. Grams ME and Coresh J: Assessing risk in chronic kidney disease: A methodological review. Nat Rev Nephrol 9: 18-25, 2013.
7. Ye H, Ye P, Zhang Z, Hou A, Liang Z and Kong Y: A bayesian network analysis on comparative efficacy of treatment strategies for dialysis patients with secondary hyperparathyroidism. Exp Ther Med 17: 531-540, 2019.

8. Naves-Díaz M, Passlick-Deetjen J, Guinsburg A, Marelli C, Fernández-Martín JL, Rodríguez-Puyol D and Cannata-Andía JB: Calcium, phosphorus, PTH and death rates in a large sample of dialysis patients from Latin America. The CORES Study. Nephrol Dial Transplant 26: 1938-1947, 2011.
9. Komaba H, Taniguchi M, Wada A, Iseki K, Tsubakihara Y and Fukagawa M: Parathyroidectomy and survival among Japanese hemodialysis patients with secondary hyperparathyroidism. Kidney Int 88: 350-359, 2015.
10. Ifudu O: Care of patients undergoing hemodialysis. N Engl J Med 339: 1054-1062, 1998.
11. Martin KJ, González EA, Gellens M, Hamm LL, Abboud H and Lindberg J: 19-Nor-1-α-25-dihydroxyvitamin D2 (paricalcitol) safely and effectively reduces the levels of intact parathyroid hormone in patients on hemodialysis. J Am Soc Nephrol 9: 1427-1432, 1998.
12. Ross EA, Tian J, Abboud H, Hippensteel R, Melnick JZ, Pradhan RS, Williams LA, Hamm LL and Sprague SM: Oral paricalcitol for the treatment of secondary hyperparathyroidism in patients on hemodialysis or peritoneal dialysis. Am J Nephrol 28: 97-106, 2008.
13. Mittman N, Desiraju B, Meyer KB, Chattopadhyay J and Avram MM: Treatment of secondary hyperparathyroidism in ESRD: A 2 -year-single-center cross-over study. Kidney Int (Suppl 8): S33-S36, 2010.
14. Block GA, Martin KJ, de Francisco AL, Turner SA, Avram MM, Suranyi MG, Hercz G, Cunningham J, Abu-Alfa AK, Messa P, *et al*: Cinacalcet for secondary hyperparathyroidism in patients receiving hemodialysis. N Engl J Med 350: 1516-1525, 2004.
15. Block GA, Zeig S, Sugihara J, Chertow GM, Chi EM, Turner SA, Bushinsky DA; TARGET Investigators: Combined therapy with cinacalcet and low doses of vitamin D sterols in patients with moderate to severe secondary hyperparathyroidism. Nephrol Dial Transplant 23: 2311-2318, 2008.
16. Fishbane S, Shapiro WB, Corry DB, Vicks SL, Roppolo M, Rappaport K, Ling X, Goodman WG, Turner S and Charytan C: Cinacalcet HCl and concurrent low-dose vitamin D improves treatment of secondary hyperparathyroidism in dialysis patients compared with vitamin D alone, the ACHIEVE study results. Clin J Am Soc Nephrol 3: 1718-1725, 2008.
17. Block GA, Zaun D, Smits G, Persky M, Brillhart S, Nieman K, Liu J and St Peter WL: Cinacalcet hydrochloride treatment significantly improves all-cause and cardiovascular survival in a large cohort of hemodialysis patients. Kidney Int 78: 578-589, 2010.
18. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J and Moher D: The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. BMJ 339: b2700, 2009.
19. Higgins JP and Green S: Cochrane handbook for systematic reviews of interventions. Cochrane Book Series, 2008.
20. Wells GA, Shea B, O'Connell D, Petersen J, Welch V, Losos M and Tugwell P: The Newcastle-Ottawa Scale(NOS) for assessing the quality of nonrandomized studies in meta-analyses. Ottawa Hospital Research Institute, Ottawa, 2015. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
21. Sharma A, Marshall TS, Khan SS and Johns B: Cost effectiveness of paricalcitol versus cinacalcet with low-dose vitamin D for management of secondary hyperparathyroidism in haemodialysis patients in the USA. Clin Drug Investig 34: 107-115, 2014.
22. Zawierucha J, Malyszko J, Malyszko JS, Prystacki T, Marcinkowski WP and Dryl-Rydzynska T: Three therapeutic strategies: Cinacalcet, paricalcitol or both in secondary hyperparathyroidism treatment in hemodialysed patients during 1-year observational study-A comparison. Front Endocrinol (Lausanne) 10: 40, 2019.
23. Sprague SM, Wetmore JB, Gurevich K, Da Roza G, Buerkert J, Reiner M, Goodman W and Cooper K: Effect of cinacalcet and vitamin d analogs on fibroblast growth factor-23 during the treatment of secondary hyperparathyroidism. Clin J Am Society Nephrol 10: 1021-1030, 2015.
24. Kukavica N, Resic H, Ajanović S, Groša E, Prohić N, Ćorić A and Mašnić F: Comparative effectiveness of cinacalcet (sensipar/mimpara) versus paracalcitol in treatment of secondary hyperparathyroidism in patients on hemodialysis. Acta Med Croatica 65: 128-129, 2011.
25. Kaperonis N, Kourvelou C, Sgantzosl A, Nastoul D, Ntatsis G, Ziakka S, Karakasis F, Nikolopoulos V, Zoubaniotou V, Koutsovasili A, *et al*: Cinacalcet vs. paricalcitol in hemodialysis patients. Nephrol Dial Transplant 27: 497-498, 2012.
26. Ketteler M, Martin KJ, Wolf M, Amdahl M, Cozzolino M, Goldsmith D, Sharma A, Marx S and Khan S: Paricalcitol versus cinacalcet plus low-dose vitamin D therapy for the treatment of secondary hyperparathyroidism in patients receiving haemodialysis: Results of the IMPACT SHPT study. Nephrol Dial Transplant 27: 3270-3278, 2012.
27. Andress D: Nonclassical aspects of differential vitamin D receptor activation, implications for survival in patients with chronic kidney disease. Drugs 67: 1999-2012, 2007.
28. Dusilová-Sulková S: Vitamin D metabolism and vitamin D traditional and nontraditional, target organs, implications for kidney patients. J Ren Care 35: 39-44, 2009.
29. Matuszkiewicz-Rowińska J and Żebrowski P: Paricalcitol-a selective vitamin D receptor activator for secondary hyperparathy-roidism in patients with chronic kidney disease. Wiad Lek 69: 756-759, 2016.
30. Zawierucha J, Małyszko J, Małyszko J, Prystacki T, Marcinkowski W and Dryl-Rydzyńska T: Treatment of secondary hyperparathyroidism in hemodialysed patients-paricalcitol with or without cinacalcet. Przegl Lek 73: 229-232, 2016 (In Polish).
31. Soliman AR, Maamoun HA, Soliman MA, Darwish H and Elbanna E: Cinacalcet versus parathyroidectomy in the treatment of secondary hyperparathyroidism post renal transplantation. Rom J Intern Med 54: 184-189, 2016.
32. Block GA, Bushinsky DA, Cheng S, Cunningham J, Dehmel B, Drueke TB, Ketteler M, Kewalramani R, Martin KJ, Moe SM, *et al*: Effect of etelcalcetide vs. cinacalcet on serum parathyroid hormone in patients receiving hemodialysis with secondary hyperparathyroidism: A randomized clinical trial. JAMA 317: 156-164, 2017.
33. National Kidney Foundation: K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis 42 (4 Suppl 3): S1-S201, 2003.
34. Ureña-Torres P, Bridges I, Christiano C, Cournoyer SH, Cooper K, Farouk M, Kopyt NP, Rodriguez M, Zehnder D and Covic A: Efficacy of cinacalcet with low-dose vitamin D in incident haemodialysis subjects with secondary hyperparathyroidism. Nephrol Dial Transplant 28: 1241-1254, 2013.