MINERAL METABOLISM OUTCOMES OF A TREATMENT PROTOCOL FOR CONTROLLING SECONDARY HYPERPARATHYROIDISM IN NON-DIALYSIS CKD PATIENTS. A PROSPECTIVE COHORT STUDY.

Molina P, Beltrán S, Vizcaíno B, Climent C, Salvetti L, Alemany B, Alonso-Gómez JC, García-Masset R, Peris A, Escudero V, Fernández-Nájera JE, Górriz JL, Pallardó LM. Valencian Society of Nephrology-CKD-MBD Working Group.

INTRODUCTION & AIMS

- Although there is no one standard treatment for controlling bone metabolism parameters in non-dialysis chronic kidney disease (ND-CKD) patients, there is a concern regarding the possible harmful effects of overuse of vitamin D and calcium-based binders in this population.
- This study compared the efficacy of a paricalcitol-based regimen which limited elemental calcium intake from phosphate binders, with unrestricted conventional care (vitamin D and phosphate binders) for achieving mineral metabolism targets.

METHODS

- From 2013 through 2014, the Valencian Society of Nephrology-CKD-MBD Working Group implemented a multi-center prospective cohort study which enrolled ND-CKD stage 4-5 patients attending 10 hospitals in Valencian Community (Spain).
- All enrolled patients received a treatment protocol for controlling bone metabolism parameters based on the use of:
  1. Low doses of calcium acetate and calcium-free phosphate binders for hyperphosphatemia.
  2. Moderate doses of oral calcidiol (16000 IU monthly) for vitamin D deficiency.
  3. Paricalcitol as the only anti-parathyroid agent.

CKD-MBD TARGETS

25 OHD (ng/mL)	20–40
iPTH (pg/mL)	CKD 4: 70–110 CKD 5: 150–300
Ca_{alb}(mg/dL)	8.4–10.2
P (mg/dL)	2.3-4.7

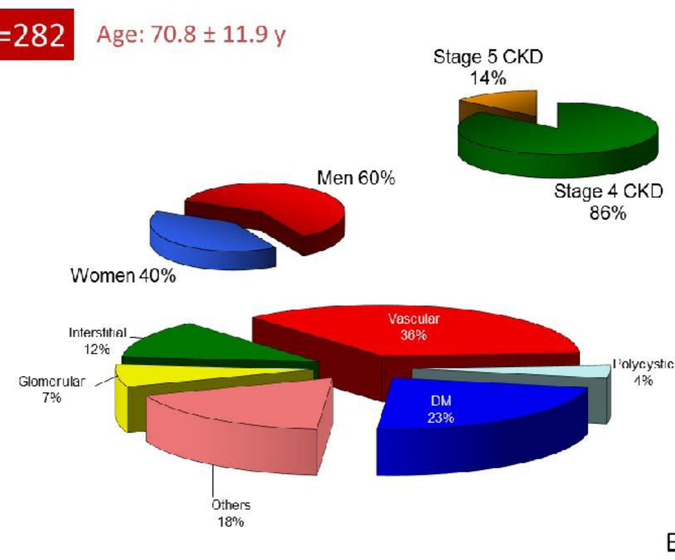
- A control cohort (n=498) without restriction on the use of calcium-based binders and vitamin D metabolites, matched for age, sex, comorbidities, CKD-stages, and calcium, phosphorus, iPTH, and 25(OH)D levels- was selected for comparison.
- The proportion of patients within mineral metabolism target ranges, and means of PTH, calcium and phosphorous values over 12 months were used to evaluate effectiveness.

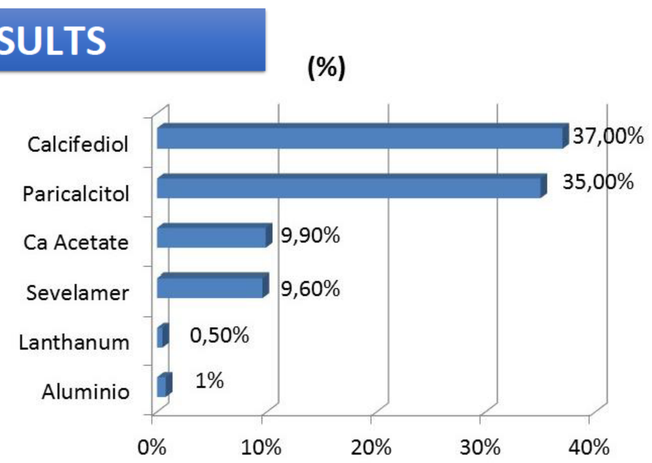
	Paricalcitol-based regimen with limited Ca intake (n=249)	Control (n=498)	p
Calcitriol	0%	32%	n.a.
Ca carbonate	0%	13%	n.a.
Nutritional VitD	37%	7%	<0.001
Paricalcitol	35%	1%	<0.001
Ca acetate	10%	20%	<0.001
Sevelamer	9%	6%	0.086
Lanthanum	0.9%	0.2%	0.237
Aluminium	1%	4%	0.016

RESULTS

Patients characteristics at baseline

N=282 Age: 70.8 ± 11.9 y





Calcium provided by the Ca Acetate: 280 mg/ d (242-508)
Calcifediol dose: 4000 UI/w (3997-4500)

*Calcitriol and Ca-Carbonate treatment was not permitted as per protocol.

Follow-up

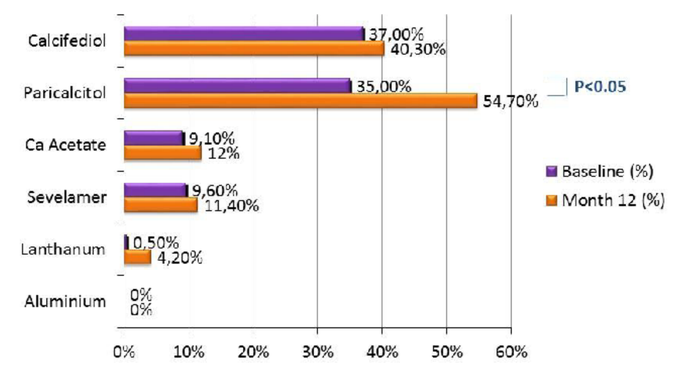
N=282 CKD 4-5

→ 11 without PTH
→ 22 lost to follow-up

N=249 CKD 4-5

- Median follow up: 12 months (IQR 10-13)

Evolution of treatment*



	BASELINE Mean / Median	BASELINE % within target range	MONTH 12 Mean / Median	MONTH 12 % within target range	*Study objectives
25D (ng/mL)	25.2 ± 13.9	**51.8**	22.4 ± 11.1	**51.2**	20–40
iPTH (pg/mL)	155 (IQR: 101-209)	**26.2**	156 (IQR: 107-212)	**34.2***	CKD 4: 70–110 CKD 5: 150–300
Ca_{alb}(mg/dL)	9.3 ± 0.6	**91.1**	9.3 ± 0.6	**91.7**	8.4–10.2
P (mg/dL)	3.8 ± 0.7	**83.0**	4.0 ± 0.8	**81.0**	2.6-4.6

*p=0.034 Vs. baseline

Matched-cohort analysis

249 patients who had received treatment with a paricalcitol-based regimen which limited elemental calcium intake from phosphate binders were matched –according to age, gender, comorbidities, CKD-stages, and calcium, phosphorus, iPTH, and 25(OH)D levels- with 498 controls with unrestricted conventional care (vitamin D and phosphate binders) for achieving control of mineral metabolism parameters.

Proportion of patients achieving calcium, phosphorous and PTH targets.

	Treatment Group (n=249)				Control Group (n=498)			
	Baseline	Month 6	Month 12	p	Baseline	Month 6	Month 12	p
Ca_{ALB} (mg/dl)								
<8.4	3%	3%	5%	0.568	3%	5%	5%	0.424
8.4-9.5	62%	65%*	64%#		55%	55%*	55%#	
>9.5	35%	33%	31%		42%	40%	40%	
P (mg/dl)								
<2.5	3%	1%	1%	0.395	1%	1%	2%	0.044
2.5-4.5	81%	80%	79%		83%	82%	84%	
>4.5	16%	19%	20%		16%	17%	15%	
PTH (pg/ml)								
<70 (stage 4) or <150(stage 5)	19%	20%	20%	0.181	22%	27%	25%	0.561
Within target range	27%	32%	35%		28%	27%	28%	
>110(stage 4) or >300(stage 5)	54%	48%	45%		50%	47%	47%	

*p=0.012 between groups at Month 6.
#p=0.046 between groups at Month 12.

1. A higher proportion of patients receiving the proposed regimen versus conventional care achieved the targets for calcium at 6 and 12 month follow-up.
2. The rate of patients with hypercalcemia at the end of the study was higher in the control group (12% Vs. 4%; p=0.001).
3. Means of PTH, calcium and phosphorous were similar in both groups.
4. The use of calcium-free phosphate binders (sevelamer:12% Vs. 5%; p=0.002; lantanum: 4% Vs. 0%; p=0.001) and paricalcitol (55%Vs.3%;p<0.001) was higher in the study group, whereas the proportion of patients under treatment with calcium carbonate (0% Vs.11%; p<0.001) and calcitriol (0% Vs. 37%; p<0.001) was greater in the control group. Use of calcium acetate was similar in both groups (14% Vs.14%; p=0.398).

CONCLUSIONS

Compared with unrestricted conventional care, a regimen based on the limited use of calcium-based binders in combination with calcium-free phosphate binders and paricalcitol as anti-parathyroid agent, increased achievement of calcium treatment targets in CKD patients, reducing the risk of hypercalcemia.

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