

CHAPTER V

DISCUSSION AND CONCLUSION

5.1 K/DOQI 2003 VS KDIGO 2009

This study was started in November, 2008 so the guideline which was used as reference is K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. (National Kidney Foundation, 2003) In August 2009, Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease – mineral and bone disorder (CKD–MBD) has been published. (Kidney Disease Improving Global Outcomes, 2009) Our study is retrospective review of the practice during June, 2006 to December, 2008 so using of K/DOQI 2003 guideline (National Kidney Foundation, 2003) is more appropriate to investigate the adherence of practice. However we reviewed the detail of those 2 guidelines and found that most of practice is the same. Frequency of clinical parameters monitoring are more flexible as shown in Table 15. If the results of the study adhere to K/DOQI 2003 guideline, they will adhere to KDIGO 2009 guideline too.

The criteria in using of phosphate binder and vitaminD₃ in KDIGO 2009 guideline are not different from K/DOQI 2003 guideline.

Table 15 Frequency of clinical parameters measurement

CKD stage	K/DOQI 2003 guideline		KDIGO 2009 guideline	
	PTH	calcium/ phosphate	PTH	calcium/ phosphate
3	Every 12 months	Every 12 months	baseline	Every 6 - 12 months
4	Every 3 months	Every 3 months	Every 6 - 12 months	Every 3 - 6 months
5 or dialysis	Every 3 months	Every 1 months	Every 3 - 6 months	Every 1 - 3 months

No calculated CaxP product target recommendation in KDIGO 2009 guideline which is different from K/DOQI 2003 guideline that less than $55 \text{ mg}^2/\text{dl}^2$ is specified. According to recommendation for CKD stage 5 in K/DOQI 2003, upper limit of targeted serum calcium is lower than normal range (9.5 VS 10.3 mg/dl) and both lower and upper limit of targeted serum phosphate is higher than normal range ($3.5 - 5.5$ VS $2.5 - 4.5 \text{ mg/dl}$). Since optimal level of serum PTH for CKD stage 3, 4 and 5 with non-dialysis is not known, so the KDIGO 2009 guideline does not recommend the PTH target level. It should be maintain within normal range ($10 - 60 \text{ pg/dl}$) (DiPiro et al., 2008). If the PTH level is above the upper normal limit, hyperphosphatemia, hypocalcemia and vitamin D deficiency should be evaluated and corrected. Suggested target of PTH level for CKD stage 5 with dialysis is 2 - 9 times upper normal limit. If serum PTH is not at target recommendation, treatment should be started. But K/DOQI 2003 guideline specifies definite value in each CKD staging as shown in Table 16. The treatment should be started in the same way, except cinacalcet is added for treatment in KDIGO 2009 guideline.

Table 16 Clinical parameters target recommendations in guidelines

CKD stage	K/DOQI 2003 guideline					KDIGO 2009 guideline		
	Serum Phosphate (mg/dl)	Serum Corrected-Calcium (mg/dl)	Serum CaxP product (mg^2/dl^2)	Serum iPTH (pg/ml)	Serum Phosphate (mg/dl)	Serum Corrected-Calcium (mg/dl)	Serum CaxP product (mg^2/dl^2)	Serum iPTH (pg/ml)
3	2.7–4.6	normal range	< 55	35-70	normal range	normal range	-	-
4	2.7–4.6	normal range	< 55	70-110	normal range	normal range	-	-
5	3.5-5.5	8.4–9.5	< 55	150-300	normal range	normal range	-	-
5D	3.5-5.5	8.4–9.5	< 55	150-300	lower toward normal range	normal range	-	2-9 times the upper normal range

CaxP produt; corrected-calcium x phosphate product, D; dialysis

5.2 Major finding

5.2.1 Study patients

Sixty percent of our patients are male and mean age is 60 years old which are the same as other studies on achievement of target recommendations for mineral and bone disorder. Most of the patients in CKD stage 5 are on continuous ambulatory peritoneal dialysis which is different from those studies that most of them are on hemodialysis. (Al Aly et al., 2004; Craver et al., 2007; Lorenzo et al., 2008; Maduell et al., 2005; Rivera et al., 2006; Verdallas et al., 2007; Younes et al., 2006)

5.2.2 Adherence to mineral and bone disorder clinical practice guideline

5.2.2.1 Clinical parameters monitoring

The percent adherence of serum calcium monitoring is more than 90% in CKD stage 3 and decrease to 80% in CKD stage 4. This is corresponding to the previous study which decreases from 91% in CKD stage 3 to 64% in CKD stage 4. Adherence to serum phosphate monitoring in our study is more than 80% in every CKD stages. But the percent adherence in CKD stage 4 is slightly lower than CKD stage 3. Our study reveals that serum phosphate monitoring is higher than the previous study which is only 26% in CKD stage 3 and 15% in CKD stage 4. So the evaluation is not adhered to the guideline in CKD stage 4. The practice in our hospital for calcium and phosphate monitoring in CKD stage 5 is around 94% adherence that is higher than 6-12% adherence in Hoy's study. The adherence to PTH monitoring is lower in previous and our study. (Hoy et al., 2007) KDIGO 2009 guideline extends the interval of PTH monitoring so the adherence to new guideline might be evaluated whether the percentage of adherence will be increased or not. (Kidney Disease Improving Global Outcomes, 2009)

The adherence data for all 12 months and recent 6 months of postindex period are not statistical significant difference which means that there is no different practicing in the nephrology unit during one year.

Laboratory test of PTH at Srinagarind hospital is available only once a week and it takes 2 weeks to report which is not in time to change the treatment for out-patient. This might be the reason for low rate of PTH monitoring.

5.2.2.2 Using of phosphate binders

Adherence to using of phosphate binders are more than 90% in CKD stage 3 and 4 but decrease to lower than 70% in CKD stage 5. In the previous study (Shastri J. et al., 2008), using of calcium-base phosphate binder in 283 hemodialysis patients was 29% non adherence. The criteria in assessment of using phosphate binders in CKD stage 5 is different form CKD stage 3 and 4 which serum calcium has to be evaluated apart from Ca x P product. We found that serum calcium did not meet the standard criteria.

5.2.2.3 Using of vitaminD₃

The criteria of using vitaminD₃ base on all of serum calcium, phosphate and PTH. As we found that monitoring of PTH is lower than 10% in CKD stage 3 and 4 and lower than 40% in CKD stage 5, so the adherence to using of vitaminD₃ could be evaluated in only 33% of all patients. The adherence in these patients is 72.2%. But in CKD stage 3 is only 40.0% due to only 5 patients that serum calcium, phosphate and PTH monitored at the same time for evaluation. Serum PTH is monitored more frequent in CKD stage 4 and 5 which more than 70% adherence is found.

5.2.3 Achievement of K/DOQI target recommendations

At the end of study total achievement of Ca x P product is 95% which is higher than serum calcium (74%) and serum phosphate (76%). This might be the reason why KDIGO 2009 changes the target achievement guideline to serum calcium and phosphate without determining of Ca x P product. In CKD stage 5 achieving of calcium and phosphate target recommendations are lower than 50% but Ca x P product achievement is higher (84%). Our results correspond with the new target recommendation that we should strictly achieve target for both calcium and phosphate more than CaxP product. PTH achievement could not be determined due to low percentage of monitoring. The results from our study are the same as previous study. Most of studies discussed that it is difficult to achieve target recommendation for clinical parameters in CKD stage 5. (Al Aly et al., 2004; Craver et al., 2007; Lorenzo et al., 2008; Maduell et al., 2005; Rivera et al., 2006; Verdallas et al., 2007; Younes et al., 2006)

The total percentage of patient achieving 100% target recommendation during 12 months of postindex period for serum calcium and phosphate are more than 50%. The study in hemodialysis patients (Al Aly Z. et al., 2004) found that there was less than 50% achievement of 50% target recommendation. Our study in CKD stage 5, there is more than 50% achievement if we determine at 50% target recommendations. The 100% achievement of Ca x P product is higher than 70% in each CKD stage.

5.2.4 Comparison of percentage of target recommendation achievement between adherent and non-adherent patients.

Our finding was indicated that the patient who met only clinical parameter monitoring according to MBD – CPG the target recommendations achievement was not increased. KDIGO 2009 guideline was published the new criteria which suggests to extending the interval of clinical parameters measurement. This new criteria agrees with our results. (Kidney Disease Improving Global Outcomes, 2009) The target recommendations will be achieved if the patients meet 100% adherence to using of phosphate binder in MBD – CPG. However the clinical parameters monitoring are needed to help in selection type of phosphate binder.

5.3 Limitations and Suggestions

The reference guideline that used in our study was not the recent updating because the new guideline was published after the study had been started.

The results of adherence to using of vitaminD₃ and serum PTH achievement can not be analyzed due to low rate of PTH monitoring. The limitation of PTH investigation in the hospital might be an important factor.

In our study the criteria that used for evaluation of adherence during postindex period were according to CKD staging at the index date. The CKD staging in some patients (less than 15%) had been changed during our study. So the adherence data might be slightly lower than the results compare to the real CKD staging at the end of study.

The odd ratio of 100% achievement of target recommendations during 12 months of the study period between 100% and less than 100% adherence to mineral

and bone disorder clinical practice guideline in some category can not be statistical calculated due to small number of sample.

Further study should consider in new surrogate outcome that is recommended in KDIGO 2009 guideline, such as alkaline phosphatase and calcidiol. Therapeutic end point for cardiovascular and bone diseases should be investigated in long term study.

5.4 Conclusions

The results from our study are determined.

The mean percentages of adherence in each patient are 89.5% for calcium monitoring, 88.6% for phosphate monitoring and 17.1% for PTH monitoring.

The mean percentage of adherence to using of phosphate binder in each patient is 84.6%.

The mean percentage of adherence to using of vitaminD₃ in each patient is 72.2%. This value is analyzed from only 68 patients who had all of serum calcium, phosphate and PTH monitoring.

Using of vitaminD₃ and PTH monitoring are still far from recommendations.

The K/DOQI target recommendation achievements at the end of study are 73.7% for serum calcium, 76.1% for serum phosphate, 94.6% for calculated CaxP product and 23.7% for serum PTH. Moreover the mean percentage of K/DOQI target recommendation achievement in each patient during 12 months of postindex period are 79.3% for calcium achievement, 78.1% for phosphate achievement, 95.8% for serum CaxP product achievement and 26.3% for PTH achievement.

The achievement of serum calcium, phosphate and CaxP product target recommendations are statistical significant difference in using of phosphate binder, when compare between 100% and less than 100% of adherent patients, odd ratio 5.43 for 100% serum calcium achievement (95% CI 2.43 – 12.11), 11.33 for 100% serum phosphate achievement (95% CI 4.63 – 27.72) and 11.75 for 100% serum CaxP product achievement (95% CI 2.92 – 47.24) in comparison between 100% and 75.0-99.9% adherence group. Using of phosphate binders is one of an important factor to achieve target recommendation.