

Relationship of Conjunctival and Corneal Calcification with Secondary Hyperparathyroidism in Hemodialysis Patients

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Abstract

Background/Objective: Hyperphosphatemia is the consequence of end stage renal failure. Inadequate control of serum phosphorus results in elevated $\text{Ca} \times \text{P}$ product with subsequent soft tissue deposition in the form of conjunctival and corneal calcification. In this study, we evaluated the relationship of conjunctival and corneal calcification with secondary hyperparathyroidism in hemodialysis patients.

Patients and methods: This is a descriptive-analytic study performed on 24 hemodialysis patients. We measured serum calcium, phosphorus, alkaline phosphatase, iPTH and conjunctival and corneal calcification using slit-lamp microscope according to a modification of Porter's criteria. The duration of hemodialysis was 30.7 ± 21.7 months.

Results: 24 patients participated in this study. The biochemical values were: Ca: 9.1 ± 0.8 mg/dl, P: 6.5 ± 2.2 mg/dl, iPTH: 488 ± 326 pg/ml, $\text{Ca} \times \text{P}$: 51.5 ± 16.6 . The mean of conjunctival and corneal calcification score was 7.1 ± 4 . There was a positive correlation between conjunctival and corneal calcification with a duration of hemodialysis ($p=0.033$, $r=0.436$), $\text{Ca} \times \text{P}$ product ($p=0.007$, $r=0.538$). P ($p=0.006$, $r=0.548$) and iPTH ($p=0.028$, $r=0.449$).

There was no correlation between conjunctival and corneal calcification with the age of the patients, serum calcium and alkaline phosphatase.

Conclusion: There is a positive correlation of serum phosphorus, $\text{Ca} \times \text{P}$ product and iPTH with conjunctival and corneal calcification and no significant correlation with serum calcium implying that there is a central role for phosphorus in calcium-phosphorus deposition in soft tissues like cornea and conjunctiva, underscoring further attention to phosphorus control in hemodialysis patients.

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Keywords • Conjunctival calcification • corneal calcification • hyperparathyroidism, secondary • hyperphosphatemia

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Table 1: The profile of the age, duration of hemodialysis, and biochemical parameters.

Results	Age (years)	Duration of dialysis (months)	iPTH (pg/ml)	Alp (IU/lit)	Ca (mg/dl)	P (mg/dl)	Ca×P	URR (%)	Conjunctival & corneal calcification score
Mean	49.7	30.7	488.1	431.4	9.1	6.5	51.5	59.4	7.1
±SD	17.1	21.7	326	234.5	0.8	2.2	16.6	5.6	4
Max	79	87	1200	1280	11	10	95	70	15
Min	17	4	25	130	4	3	30	20	2

Introduction

Hyperphosphatemia develops invariably with kidney failure. Inadequate control of serum phosphorus (P) results in an elevated calcium-phosphorus (Ca×P) product, that is associated with harmful conditions in chronic renal failure, including vascular calcifications, cardiovascular disease and soft tissue depositions.^{1,2} In this study we evaluated the relationship between the severity of conjunctival and corneal calcification with serum calcium (Ca), alkaline phosphatase (ALP), phosphorus (P), Ca×P products and intact PTH (iPTH).

Subjects and Materials

This is a descriptive–analytic study done on 24 hemodialysis patients who were on regular hemodialysis 2-3 times per week. None of the patients had any history of malignancy or primary hyperparathyroidism and none was taking drugs which might affect bone metabolism. Calcium, phosphorus and alkaline phosphatase were measured by commercial and standard kits. iPTH was done by DSL-8000 kit (RIA) manufactured in the USA. The hemodialysis adequacy was measured by Urea Reduction Rate (URR) formula. The severity of conjunctival and corneal calcification was evaluated by an ophthalmologist who was unaware of lab ex-

ams. Using slit-lamp microscope calcified deposits were classified into the following 6 grades (scores 0-5) according to a modification of Porter's criteria³ (Fig 1) 0=no deposits, 1=conjunctival deposits only, 2=conjunctival and strictly limbal deposits, 3=conjunctival deposits and irregular corneal deposits, 4=clear single line of corneal and conjunctival deposits, and 5=more extensive corneal deposits and conjunctival deposits. The severity of conjunctival and corneal calcification was determined by the total score (0-20 points) obtained at 4 regions (nasal and temporal sides of both corneas). The data were stratified as mean ± SD, and we used frequency distribution for conjunctival and corneal calcification together with Pearson Coefficient Test. All the data were analyzed by SPSS (version 11.00) software.

Results

A total of 24 patients participated in this study of which males formed 48.8 percent. The mean age was 49.7±17.1 and the duration of hemodialysis 30.7±21.7 months. The results of biochemical values were: Ca; 9.1±0.8 mg/dl, P; 6.5±2.2 mg/dl, iPTH; 488.1±326 pg/ml (normal 13-54 pg/ml), and Ca×P; 51.5±16.6. The mean conjunctival and corneal calcification score was 7.1±4. The results of biochemical parameters and conjunctival and corneal calcification are shown in Table 1. Table 2, shows the frequency distribution of conjunctival and corneal calcification. In this study, there was a positive correlation between conjunctival and corneal calcification with duration of hemodialysis (Fig1) (P=0.033, r=0.436), Ca×P product (Fig 2) (p=0.007, r=0.538), P (Fig 3) (p=0.006, r= 0.548) and iPTH (p= 0.028, r=0.449) (Fig 4).

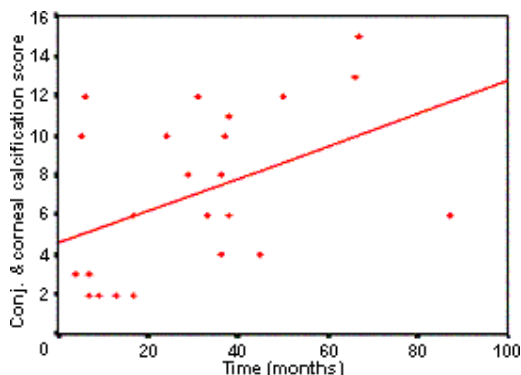


Figure1: Association of corneal and conjunctival calcification with duration of hemodialysis

Score	Number	Percent
0-3	6	25
4-7	7	29.2
8-11	6	25
12-15	5	20.8

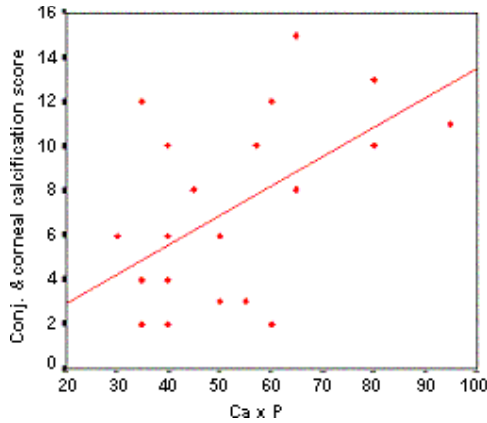


Figure 2: Association of corneal and conjunctival calcification with Ca × P product

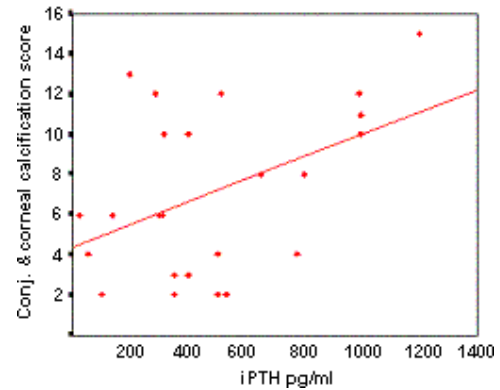


Figure 4: Association of corneal and conjunctival calcification with serum iPTH

There was no correlation between conjunctival and corneal calcification with the age of the patients ($p=0.449$, $r=-0.162$), and also no correlation with serum Ca ($p=0.809$, $r=0.052$). There was not a significant correlation between eye scores with Alp. ($p=0.903$, $r=-0.02$).

Discussion

This study showed a positive correlation between conjunctival and corneal calcification with serum phosphorus, iPTH, Ca×P-product and duration of dialysis. We could not show a significant correlation between patients' age, serum calcium and Alp with conjunctival and corneal calcification scores.

Studies concerning the conjunctival and corneal calcification during recent years, have shown variable results. In a study by Pahor et al. on 14 hemodialysis patients, a 79% rate of typical conjunctival and corneal calcification was found. This study showed that, patients treated longer with hemodialysis, had a higher grade of calcification.⁴ Similar to our study Emmerrich et al. studying 72 dialysis patients, showed a statistically significant correlation with the duration of hemodialysis yet no correlation with alkaline phosphatase or the patient's age.⁵ Moreover Vignanelli M et al. showed that conjunctival calcification developed in patients suffering from high mathematical product of $\text{Ca} \times \text{PO}_4$ ⁶ while Pahor et al. found that product of calcium and phosphate and also parathyroid hormone concentration did not differ in patients with or without calcifications. In the study of Emmerrich et al., no correlation was found between deposition of calcium salts on conjunctiva and $\text{Ca} \times \text{PO}_4$ product. Kelenhegyic et al. working on 27 hemodialysis patients elaborated on the role of hyperphosphatemia.⁷ In a recent study by Takuyama et al, in contrast to our data, no correlation was observed between conjunctival and corneal calcification and Alp.⁸ However, we, in concordance with Takuyama et al., could not show any correlation between serum calcium and conjunctival and corneal calcification, implying that there ought to be a central role for phosphorus in calcium-phosphorus deposition in soft tissues like cornea and conjunctiva. In addition, alkalosis of the ocular surface may increase the severity of conjunctival and corneal calcification.^{8,9} Other investigators have also shown abnormal Ca and P values in conjunctival and corneal calcification in hemodialysis patients.¹⁰⁻¹² Thus, chronic renal fail-

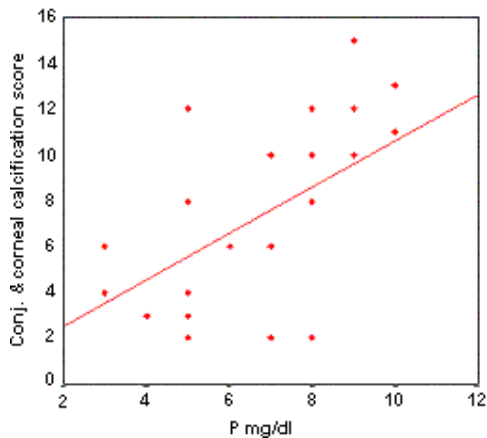


Figure 3: Association of corneal and conjunctival calcification with serum phosphorus

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ure alters the Ca and P balance and results in secondary hyperparathyroidism.^{1,13}

The most important problem in hemodialysis patients is the control of hyperphosphatemia.^{1,2} Hyperphosphatemia has a central role in ectopic calcifications caused by an abnormal balance of Ca and P metabolism in hemodialysis patients.¹ Also it seems that a relatively high alkalinity results from the diffusion of carbon dioxide (CO₂) from the exposed eye surface, which promotes the precipitation of Ca-phosphate salts in high serum Ca×P product cases of conjunctival and corneal calcification.⁸⁻¹² Because of improved treatment modalities in dialysis therapy, we rarely find patients with severe conjunctival and corneal calcification developing band keratopathy.¹² However, the increased frequency of conjunctival and corneal calcification in patients undergoing prolonged hemodialysis indicates the presence of secondary hyperparathyroidism and bone metabolic disorder in hemodialysis patients, as is also reflected in our study.⁸ In this study, we have underscored the serious problem of hyperphosphatemia and secondary hyperparathyroidism in hemodialysis patients. In fact, every patient entering dialysis treatment should be investigated and counseled by dieticians in order to improve nutrition in terms of energy, protein and phosphorus intake.¹ On a standard thrice-weekly dialysis schedule, hyperphosphatemia and positive phosphorus balance are frequent despite the use of phosphate binders, especially in well-nourished patients.^{1,2,13} As the course of conjunctival and corneal calcification can be easily followed, the evaluation of the clinical courses of conjunctival and corneal calcification is very useful for assessing the severity of Ca and P imbalance and bone metabolic disorder in hemodialysis patients.^{8,13}

Further evaluation of the relationship between conjunctival and corneal calcification and other sites of soft tissue calcification like heart and cardiovascular system appears recommendable.

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