

The Set Point of Intact Parathyroid Hormone-Ionized Calcium Curve during the Progression of Secondary Hyperparathyroidism among Patients Undergoing Haemodialysis

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Abstract The parathyroid gland secretes parathyroid hormone (PTH) which is a key element in the regulation of serum calcium. The PTH elevates serum calcium activities by regulating its action on the bones, kidneys and small intestine. The set point of PTH secretion defines the sensitivity of the parathyroid glands to calcium concentration. Secondary hyperparathyroidism (SHPT) is a common complication of end stage renal disease (ESRD). Ionized calcium is physiologically active form of calcium status of the body and is used for accurately monitoring calcium status in renal diseases. The present study states that the ionized calcium is the set point of secondary hyperparathyroidism undergoing haemodialysis and the range of set point lies between 2.3 – 4.8 mg/dl (0.57 – 1.2 mmol/L). The status of iPTH, set point are frequently monitored in subtotal hyperparathyroidectomy where imaging studies are not beneficial (anatomically situated on postero-lateral surface of thyroid gland) to know the appearance of parathyroid gland.

Keywords: set point, ionized calcium, Secondary hyperparathyroidism (SHPT), haemodialysis

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1. Introduction

The parathyroid gland plays a central role in controlling serum calcium concentrations by regulating secretion of parathyroid hormone (PTH). The PTH elevates serum calcium levels via its effect on the bones, kidneys and small intestine. The increased or decreased secretions of PTH are dependent on the levels of serum calcium [1,2]. Secondary hyperparathyroidism (SHPT) is a common complication of end stage renal disease (ESRD). The decrease in functioning renal mass results in hypocalcaemia, hyperphosphatemia and reduced calcitriol levels which stimulate PTH secretion leading to hyperplasia of the parathyroid gland [3]. The extracellular ionized calcium regulates the secretion of PTH, which interacts through calcium sensing receptors on parathyroid cell [4,5]. Thus, in hyperparathyroidism either primary or secondary or pseudo or idiopathic there is decreased calcium receptors [6,7,8,9]. Physiologically, the relation between PTH secretion and calcium concentration is defined by a sigmoid curve [10].

The set point of PTH secretion is defined as the concentration of calcium required to reduce maximum

PTH secretion by 50% [11,12], or it can also be defined as the serum calcium concentration required to reduce PTH secretion to half the difference between the maximum and minimum levels [13,14]. The set point of PTH secretion defines the sensitivity of the parathyroid glands to calcium concentration [15]. Ionized Calcium is normally better for accurately monitoring calcium status in renal diseases [16,17]. The advantages of measuring ionized calcium over total calcium are: [18]

- There is no effect of venous occlusion or change of posture on the ionized calcium
- More reliable indicator of calcium status of patients in certain clinical conditions
- Physiologically active form of calcium(50% of total calcium)

The measurement of ionized calcium was used to done by calculation method, but by the measurement of ionized calcium by ion-selective electrode (ISE) technology, the errors are less and this method gives accurate and precise values. The sample drawn for analysis of ionized calcium should be without anticoagulant, without air bubbles. The use of anticoagulants like heparin for measuring ionized calcium decreases the concentration of ionized calcium in the sample [19].

The aim of the present study is to determine the set point of intact parathyroid hormone – ionized calcium curve during the progression of SHPT in patients of haemodialysis.

2. Materials and Methods

50 samples of blood from haemodialysis patients with SHPT attending Nephrology OP in a multi-specialty Hospital, Karimnagar, Telangana and 11 healthy control samples were also collected. The samples were processed for iPTH, total calcium and ionized calcium.

2.1. Blood Sample Collection

The samples were collected in fasting conditions under aseptic procedure. An Informed consent was obtained from the subjects involved in the study. 5 ml blood sample without any addition of anticoagulant was collected and allowed to clot, and then centrifuged at 3000 rpm for 20 minutes. The serum obtained is used for the analysis.

2.2. Exclusion Criteria

- Hormonal Imbalance
- Diabetes mellitus
- Liver disease
- Vitamin D deficiency

2.3. Inclusion Criteria

* Chronic Kidney Disease.

Intact PTH assay - Done by Chemiluminescence method in Aborrt Chemiluminescence Analyzer (Architect)

Total calcium - Done by O-Cresphthalene Complexone method

Ionized Calcium - Done by calculation ISE procedure

3. Results

The mean and SD values of patient group of iPTH are 321.8102 and 225.9290 and control group are 49.35 and 15.45 with p value 0.0001 extremely significant. The mean and SD values of ionized calcium are 3.8410 and 0.5255 and control group are 4.34 and 0.28 with p value 0.001 statistically significant (Table 1).

The mean difference between total calcium and iPTH are 314.1792 and 95% confidence interval of this difference is from the range of 377.5877 to 250.7707. Similarly, the mean difference between ionized calcium and iPTH are 161.3970 with 95% confidence interval of this difference ranging from 193.9148 to 128.8792 (Table 1) (Figure 1).

Table 1. The statistical data of iPTH, Total calcium and ionized calcium

Parameter	Mean +/- SD		P value
	Control	Patient	
Intact PTH	49.35+/-15.45	321.81+/-225.9	0.001*
Total Calcium	8.68+/-0.56	7.63+/-1.24	0.001*
Ionised Calcium	4.34+/-0.28	3.84+/-0.52	0.001*

* Highly significant

The statistical analysis was done using Graph pad prism software.

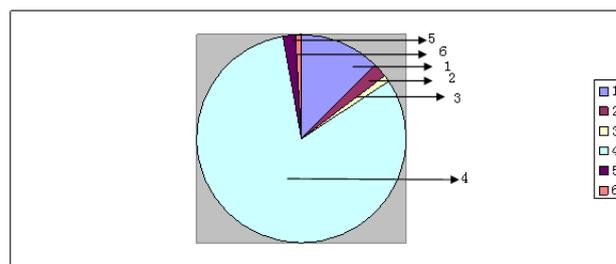
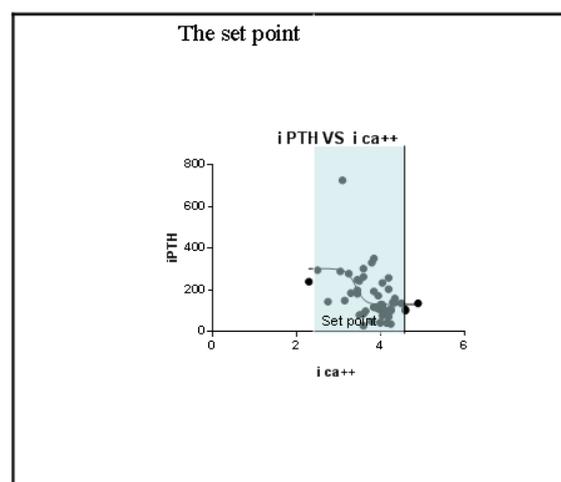


Figure 1. The pie diagram of intact PTH, Total Calcium and Ionized calcium of Patients and control group

- 1- Intact PTH control group.
- 2- Total calcium control group.
- 3- Ionised calcium control group.
- 4- Intact PTH of patient group.
- 5- Ionised calcium patient group.
- 6- Total calcium patient group.

The set point of intact PTH – Ionized calcium curve among SHPT patients undergoing hemodialysis (shown in graph). From the graph it is concluded that the set point in this study lies in the range of 2.3 to 4.8 mg/dl (0.57 – 1.2 mmol/L).



Graph. The set point of SHPT among hemodialysis (shown in colored region)

4. Discussion

The results of our study indicate that the ionized calcium is the set point for the patients undergoing haemodialysis with chronic kidney disease and the range of this set point lies between 2.3 – 4.8 mg/dl (0.57 – 1.2 mmol/L). The influence of SHPT on the set point of the PTH – calcium curve is controversial. The in-vitro experiments showed an increased set point in SHPT (20) however clinical studies with haemodialysis patients provided a variety of results. Ramirez et. al., and Goodman et al., reported no change in the set point with SHPT [21,22]. Malberti et al. and Goodman et al. found no change in set point of patients with moderate SHPT but described an increase in set point in patients with severe SHPT [23,24] contrast to this Borrego et al. and Cardinal et al. observed a decrease in set point in uremic patients [25,26]. The decrease in calcium receptors (CR) with primary hyperparathyroidism correlated with the increase

in the set point [27] but the reduction in CR occurs in the course of SHPT. A decrease in vitamin D receptor (VDR), reduces the ability of calcitriol to inhibit parathyroid gland proliferation is an important etiopathogenic factor in both primary and secondary hyperparathyroidism [28,29]. There were some studies which states that the set point of the PTH- calcium curve changes with variation in extracellular calcium i.e., decreases with hypocalcaemia and increases with hypercalcaemia [30,31,32,33].

In a study conducted to know the difference between set point in-vivo and in-vitro it is concluded that the set point in vivo calcium is more related to the serum calcium concentration than the base line (level of PTH before hypo or hypercalcaemia) PTH concentration [10]. In clinical studies on dialysis patients showed no correlation between set point of PTH secretion and magnitude of hyperparathyroidism, but in-vitro studies in dialysis patients with SHPT on removal of parathyroid gland hypercalcaemia was demonstrated which caused an increase in set point of PTH stimulated by calcium, suggesting intrinsic abnormality of hyper plastic parathyroid cell [34].

5. Conclusion

The set point defines the sensitivity of parathyroid gland to calcium concentration, the present study states that the ionized calcium is the set point of secondary hyperparathyroidism undergoing haemodialysis and the range of set point lies between 2.3 – 4.8 mg/dl (0.57 – 1.2 mmol/L). The levels of intact PTH, set point is frequently monitored in subtotal hyperparathyroidectomy where imaging studies are not beneficial (anatomical position – postero-lateral to thyroid gland) to know the size of parathyroid gland. It highlights the significance of measuring iPTH and ionized calcium activities among haemodialysis patients in the diagnosis of hyperparathyroidism.

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