Hormones affecting Calcium Metabolism

Objectives:

1. To verify the chemical structure and effects of parathyroid hormone.

2. To verify the effects of calcitriol on calcium metabolism.

3. To verify the effects of calcitonin on calcium metabolism.

5. To illustrate the disorders of plasma calcium.

4. To illustrate the disorders of parathyroid hormone secretion.

Calcium in the body:

A round 99 % of Calcium in the body is present in the bone and teeth, and only 1 % present in the rest of the body.

Functions:

1. Structural, in bone and teeth.

2. Neuromuscular activity.

3. Coenzyme for blood coagulation.

4. Second messenger for hormone action.

Calcium in the plasma:

Forms of calcium in the plasma:

1. Bound to albumin (30 - 45%)

2. Free (ionized calcium), (50 - 60%)

3. Bound to citrate and phosphate (5 - 10%)

Normal values:

Total plasma calcium: 8.5 - 10.5 mg/dl (2.1 - 2.6 mmol/L)

Ionized plasma calcium: 4.4 - 5.2 mg/dl (1.1 - 1.4 mmol/L)

Corrected Calcium (Adjustment of measured plasma Calcium):

Adjusted " Corrected" Plasma Calcium:

= measures Ca + (40 - plasma albumin 'g/L') x 0.02

Parathyroid Hormone (PTH)

Parathyroid Glands: There are 4 parathyroid glands which are situated posterior to the thyroid gland.

Parathyroid H. (PTH) :- an 84-amino acid peptide is secreted from the chief cells of the 4 parathyroid glands in response to changes in serum calcium.

	- 25 Amino acids	-6 Amino acids
PrePro PTH →	Pre PTH →	mature PTH
(115 A.As)	(90 A.As)	(84 A.As)

Calcium-Sensing Receptor (CaSR):

There is an inverse relationship between ambient calcium levels and PTH release. Changes in ECF calcium levels are transmitted through CaSR. The exact by which the activation of the CaSR inhibits PTH secretion is unknown.

- **PTH and vitamin D control calcium and phosphate homoeostasis.**
- **A fall in ECF calcium triggers PTH secretion. PTH directly acts on the kidney to promote renal calcium reabsorption and conversion of 25(OH)D to 1,25$(OH)_2$D.**
- **1,25$(OH)_2$D increases intestinal absorption of calcium (and phosphate) and, with PTH, mobilizes calcium (and phosphate) from bone.**
- **Thus ECF calcium is restored to normal, neutralizing the signal initiating PTH release.**
- **PTH inhibits renal phosphate reabsorption, promoting phosphaturia**

Effects of PTH:

PTH Normalizes ECF Calcium by :-

1. **Increases the rate of bone resorption which moves Calcium into ECF.** ***" Direct"***
2. **Decreases renal Calcium excretion.** ***" Direct"***
3. **Increases Intestinal Calcium absorption (by promoting calcitriol synthesis).** ***" Indirect"***

PTH reduces ECF P level by:

Decreasing renal Phosphate reabsorption, thus Increasing renal Phosphate excretion.

The net effect of PTH on bone and kidney is to:

1. **↑ ECF Calcium concentration**
2. **↓ ECF Phosphate concentration**

Calcitriol

Effects of Calcitriol:

1. Increases Intestinal Calcium and Phosphate absorption.

2. Increases the rate of bone resorption which moves Calcium and Phosphate into ECF

3. Decreases renal Calcium excretion (mild effect).

Calcitonin (CT)

Is a 32 amino acid peptide secreted by the para follicular cells (C- cells) of the thyroid gland .

Effects of CT:-

It lowers circulating Calcium and Phosphate levels by inhibiting bone resorption. However, the exact role of CT in human physiology is still unknown.

CT is therapeutically used in:

1. Treatment of hypercalcaemia (especially that associated with malignancy)

2. Treatment of osteoporosis

Pathophysiology

Causes of hypercalcaemia:

A. Conditions with normal or elevated PTH:

1. Primary or tertiary hyperparathyroidism
2. Lithium-induced hyperparathyroidism
3. Familial hypocalciuric hypercalcaemia

B. Conditions with low PTH:

1. Malignancy: (lung, breast, renal, lymphoma, multiple myeloma)
2. Elevated 1,25(OH)2 vitamin D: (Vitamin D intoxication, HIV, Sarcoidosis)
3. Thyrotoxicosis
4. Paget's disease (with prolonged immobilization)
5. Milk-alkali syndrome
6. Drugs (Thiazide diuretics)

Causes of hypocalcaemia:

1. Hypoalbuminaemia
2. Vitamin D deficiency
3. Chronic renal failure
4. Hypoparathyroidism
5. Pseudohypoparathyroidism
6. Acute pancreatitis
7. Hypomagnesaemia

Hypoparathroidism:

Insufficient PTH production:-

- **↓ S. Ca**
- **↑ S. P**
- **↓ PTH**

Pseudohypoparathyroidism:

There is PTH production, *however*, there is end organ resistance to it's effects.

Features: **Carpo pedal spasm, convulsions and stridor.**

Hyperparathyroidism:

A: Primary hyperparathyroidism:

Excessive PTH production by the parathyroids (usually due to adenoma):

- **↑ S. Ca**
- **↓ S. P**
- **↑ PTH**

B. Secondary hyperparathyroidism :-

Threre is physiological compensatory hypertrophy of all parathyroids because of hypocalcaemia, such as occurs in renal failure, malabsorption or vitamin D deficiency:

- **↓ S. Ca**
- **↑ S. P**
- **↑ PTH**

C. Tertiary hyperparathyroidism :-

Autonomous parathyroid hyperplasia after long- standing secondary hyperparathyroidism, most often in renal failure:

- ✓ **↑ S. Ca**
- ✓ **↑ S.P**
- ✓ **↑ PTH**