ROLE OF PARATHYROID HORMONE IN THE DEVELOPMENT OF SENILE CATARACT

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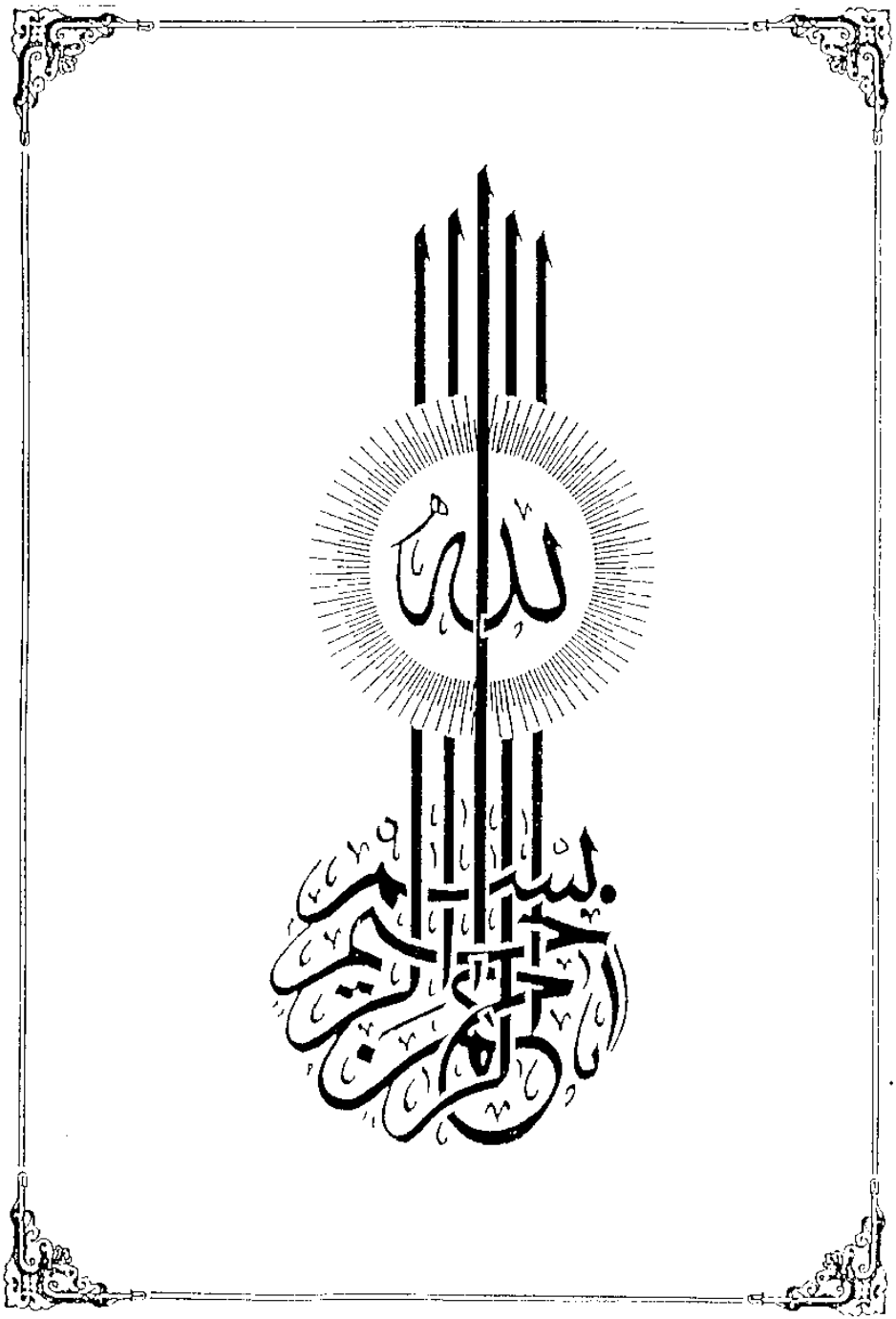

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AIM OF THE WORK

INTRODUCTION

The lens plays an important role in the process of accomodation which permits light rays that have passed through the cortex and acqueous humour to be focused toward the retina.

Loss of Transparency, or interruption of light Transmission in any portion of the lens is reffered to as cataract.

Cataract may develop as a result of various insults to the lens, but the exact mechanism that affects the lens and disturbs its clarity is not fully understood. many factors have been blamed, of which changes in ca^{++} level and parathyroid function. This thesis asses variations in the level of parathyroid hormone and function in patients with senile cataract and in normal senile persons as a control.

The assessment include level of ca^{++}, p^{+++}, alkaline phosphatase, total protein and parathormone hormone in the serum.

It aims at throwing light upon the possible role of parathyroid gland and function in the development of senile cataract.

THE PARATHYROID

Emberyology:-

The superior parathyroids arise from the fourth branchial pouch, and migrate caudally together with the thyroid to reach their final position on its posterior surface.

The inferior pair arise with the thymus from the third branchial pouch and must, therefore, cross the superior pair during their migration. (Reginald Hall, 1974).

Anatomy

The normal glands vary in size, shape, and location. In 88% of individual four glands are present.

(Reginald Hall, 1974).

The4 glands are embeded in the posterior surface of the thyroid gland and weight about 0.05 - 0.3 gm.

(Aurbach et al., 1970).

They are small brown bodies, measuring about 6 m.m. in length, 3 to 4 m.m in breadth, and 0.5 to 2 m.m in thickness.

Blood and nerve supply:

The parathyroid glands receive blood supply from the inferior

thyroid arteries in humans, (Aurbach et al., 1970), or from anastomoses between superior and inferior thyroid vessels. (Reginald Hall,1974).

Their nerve supply is derived from the sympathetic nervous system, either directly from the superior or middle cervical ganglia, or indirectly from the plexus in the fascia on the posterior surface of the thyroid gland.

Histology:

With increasing age, the colour of the gland changes from brown to yellow, due to deposition of fat, and the compact epithelial complexes are divided even more by connective tissue stroma.

Four types of cells are present in the gland:-

1. **Chief cell:**

   (principal cell, light chief cell)

   * Rich in glycogen, small golgi apparatus, scanty Endoplasmic reticulum, few secretory granules, and dark nuclei with definite chromatin network.
   * Secrete parathyroid hormone.

2. **Transitional cell:**

   (Dark chief cell)

   * Poor in glycogen, prominent Endoplasmic reticulum and golgi apparatus, and many secretory granules.
   * Main source of parathyroid hormone.

3. **Oxyphil cell:**

(Eosinophil cell)

* No glycogen, granular cytoplam, smaller denser nuclei and vary in size but larger than chief cell.
* Secrete parathyroid hormone.

4. **Water clear cell**

* **Large polyhydral cell up to 40 u. and** vaculated cytoplasm.
* Non assigned function but capable of secreting parathyroid hormone. (Reginal Hall, 1974).

THE PARATHYROID HORMONE

The parathyroid hormone secreted by the parathyroid glands , and its primary function is to maintain the concentration of ionized calcium in the plasma within the narrow range characteristic of this electrolyte despite wide variation in calcium intake, excretion, and deposition in bone. (Harper , 1973).

Chemistry :

Parathyroid hormone is a linear polypeptide consisting of 84 amino-acids. (Harper, 1973).

The human parathyroid hormone differs in the sequence of their amino-acids from the bovine hormone at position 1, 7 and 16.

of the human peptide constitutes a sequence difference unique to human parathyroid hormone.

The sequence of the first 37 amino acids of the human parathyroid hormone has been determined, and a peptide consisting of the first 34 amino-acids has been synthesized and shown to have both phosphaturic, and calcium mobilizing activity (Reginald Hall, 1974).

The hormone is formed as preprohormone and is cleaved to a pro-hormone (90 amino-acids) and to its final active form (84 amino-acids), as it is transformed from the endoplasmic reticulum to golgi apparatus to secretory granules. (Thomasm, 1982).

Control of release of parathyroid Hormone:

In contrast to many protein hormones, the parathyroid hormone is not stored in the gland, no storage granules are present. It is thus synthesized and secreted continously (Harper, 1973).

Secretion of the hormone was regulated through a feed back control mechanism (Verinon B. Mountcastle, 1974).

The concentration of ionized calcium in blood regulate the secretion of parathyroid hormone, a low level of calcium leads to increased output of the hormone. If the serum ionized calcium is raised by mechanisms other than hyperparathyroidism, parathyroid hormone secretion is reduced, though the immediate lowering of serum calcium is probably mediated by calcitonin. (Reginald Hall, 1974).

Even the slightes decrease in the extracellular calcium causes the parathyroid gland to increase their rate of secretion within minutes , and if the decreased calcium concentration persists, the glands will hypertrophy sometimes as much as five fold or more. On the other hand any condition that increase the calcium ion concentration causes decreased activity and reduced size of the parathyroid glands. Such conditions include:

1. Excess quantities of the calcium in the diet.
2. Increased vitamine -D in the diet and
3. Bone resorption caused by factors other than parathyroid hormone . (Guton, 1981).

Action Of The Parathyroid Hormone:

Excess of parathyroid hormone result in:

1. Hypercalcaemia.
2. Hypophosphataemia.
3. Hyperphosphaturia.
4. Hypercalcuria.
5. Increased urinary hydroxyproline excretion.

The main function of parathyroid hormone is to regulate the concentration of the ionized calcium in body fluids, by its action on bone, the small intestine and the kidneys.

Rapid regulation of serum calcium level probably depends on simple buffering by the large exchangeable calcium pool in bone.

Intermediate regulation probably involves both bone and the kidney, whereas Long-term regulation is probably mediated by renal and intestinal mechanism. (Reginald Hall, 1974).

Action on bone :

Bone has been considered the principal tissue influenced by parathyroid hormone in maintaining blood calcium, and it has been believed that the influence of the hormone on the tissue relatively slow.

Only recently the relatively rapid effects of the hormone on the bone has been recognized. Indeed the effect of parathyroid hormone on bone in tissue culture develop in two phases.

The earlier phase is more rapid, is manifested by the increased release of calcium into the medium within the first 2 to 3 hours of the hormone action, and does not depend on the protein synthesis. (Raisz, L.G., 1976).

The second later phase involves activation and synthesis of new proteins, particularly lysosomal enzymes including collagenase and other hydrolytic enzymes, (Raisz, L.G., 1976), and is blocked by Actinomycin D.

Parathyroid hormone requires vitamine D to bring about its effect on bone. (Harper, 1973).

It is therefore comparatively depressed in subjects with rickets .

Action on the kidney :

Parathyroid extract adminstered in vivo causes avery rapid increase in the rate of excretion of phosphate in urine. (Foster, et al., 1964).

Parathyroid hormone has two independent actions:-

It inhibits proximal renal tubular reabsorption of phosphate which leads to phosphaturia and hypophosphataemia.

Parathyroid hormone also decreases calcium excretion by a different mechanism at a different site.

This action can be obscured by the effect of parathyroid hormone on bone, where by enhanced calcium mobilization increase serum calcium concentration and provide a greater filitered load with resultant hypercalcuria. (Reginald Hall, 1974).

Action on small intestine :

The action of parathyroid hormone on the intestine may be important in long-term adaptation to low calcium intake (Reginald Hall, 1974).

Recent evidences indicates that the influence of parathyroid hormone on intestinal absorption of calcium is indirect and involves a mechanism regulating synthesis of 1,25 dihydroxycholecalciferol in the kidney. (Deluca, H.F., 1971).

Mechanism of Action of Parathyroid Hormone:

The mode of action is on adenyl cyclase in the cells of target tissue.

Stimulation of enzyme activity in target-cell membranes by the hormone leading to an increased in the intracellular 3',5' cyclic AMP. (Aurbach et al., 1972).

The postulated sequence of events in parathyroid hormone - one driven, cyclic AMP mediated calcium and phosphorus transport can be summarized as follows :

Cyclic AMP binds to surface binding protein causing it to dissociate from and thereby activate protein kinase. The protein that, in turn is phosphorylated by kinase is unknown, but certain evidences suggest that microtubular proteins are the sites of phosphorylation. (Aurbach et al., 1972).

The initial effect, within minutes of parathyroid hormone administration, is hypocalcaemia caused by flow of calcium out of blood into the cells, apparently skeletal cells. Thus, both cyclic AMP and calcium may serve as "second messangers" for mediating parathyroid hormone effects in receptor cells.