

## STUDY ON PHARMACOLOGICAL MANAGEMENT OF HYPOCALCAEMIA IN PATIENTS AFTER TOTAL THYROIDECTOMY

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### **ABSTRACT :**

#### **Background :**

Hypocalcaemia is the major postoperative complication after total thyroidectomy, causing potentially severe symptoms and increasing hospitalization time. The aim of the study is to assess the pharmacological management of hypocalcaemia in patients undergone total thyroidectomy.

#### **Methods :**

50 patients who underwent total thyroidectomy were included in the study. The incidence of hypocalcaemia was analysed with serial calcium level estimation before and after the surgery. They are randomly divided into 3 groups. Group 1 include elemental calcium 500mg every 6hrly group 2 include calcium along with vitamin-D group 3 include calcium gluconate .

#### **Results :**

Group 3 drugs affectively active against the hypocalcaemia after total thyroidectomy. The means difference of serum calcium levels before and after total thyroidectomy patients 1.6 mg/dl ,0.6 mg/dl and 0.3 mg/dl for group 2 and group 3 respectively.

**Conclusion :**

Our study suggest that group 3 drugs are more effective in treating hypocalcaemia condition after total thyroidectomy. So in severe hypocalcaemia condition group 3 drugs rapid rise in the serum calcium levels thus reduce the severe complication of hypocalcaemia .

**Keys words : Hypocalcaemia, total thyroidectomy ,calcitriol and calcium gluconate.**

**INTRODUCTION :**

Hypocalcaemia is the most common complication of total thyroidectomy , causing potentially severe symptoms and increasing hospitalization time.Hypocalcaemia is defined as the decrease in the serum calcium level(<8mg/dl).The primary cause of hypocalcaemia is secondary hypo-parathyroidism following damage or devascularisation one or more parathyroid glands during surgery. It may be transient hypocalcaemia and permanent hypocalcaemia. Most of the cases of hypocalcaemia are transient, it has been reported to occur more commonly after total thyroidectomy (1.6 %to 50%). Transient hypocalcaemia generally responds favourably to replacement therapy within a few days or weeks. Transient hypocalcaemia occur despite of careful preservation of the parathyroid and their blood supply due to temporary ischemia of parathyroid blood supply. Hypocalcaemia is considered permanent when it does not return to normal within 6 months. Permanent hypocalcaemia was reported rarely after total thyroidectomy (1.5% to 4%) .<sup>(5)</sup>The risk factors for developing hypocalcaemia are hypoparathyroidism, graves disease, hashimoto thyroiditis, renal dysfunction, hypoalbuminemia and hypomagnesemia. Hypocalcaemia can be asymptomatic particularly if calcium levels are only slightly reduced or symptomatic with typical manifestations such as Chvostek's, trousseau's sign ,muscle spasms and paresthesia. The clinical symptoms of transient hypocalcaemia are variable and include paresthesia around lips and tips of fingers, carpal spasm, convulsions, cardiac arrhythmias and laryngospasm. The assessment of hypocalcaemia biochemically by serum calcium level and clinically by trousseau's sign. Postoperatively transient hypocalcaemia was treated with oral calcium, vitamin D, calcitriol and i.v calcium gluconate. Calcium gluconate i.v will be given in titrable doses, Since it will cause adverse reactions, patient will be kept under monitoring for heart rate and base line ECG. 4<sup>th</sup> or 6<sup>th</sup> hourly calcium levels will be estimated depending upon need and patient symptoms.

Along with iv calcium supplementation oral Vitamin D3 60,000 IU given weekly once. <sup>(4)</sup> Calcium gluconate is available as 0.5g and 1.0g tablet, calcium gluconate injection

contains 100mg calcium gluconate per ml which contains 9.3mg elemental calcium. This can be administered by bolus and continuous infusion. For bolus dilute the dose of calcium gluconate injection with 5% of dextrose or normal saline to a concentration of 10-50mg/ml and for calcium gluconate infusion dilute it to a concentration 5.8-10mg/ml. The most common adverse events are local soft tissue inflammation, necrosis, calcinosis cutis, vasodilation, decreased blood pressure, bradycardia, constipation and cardiac arrest, dry mouth, increased thirst and urination.<sup>(5)</sup> To be concluded, this study aims to assess the pharmacological management of hypocalcaemia in patients undergone total thyroidectomy.

## **MATERIALS AND METHODS**

### **Study design and data collection:**

A detailed data collection form with a bilingual patient Informed Consent was prepared. Data collection was done based on the inclusion and exclusion criteria. The detailed purpose of the study and benefits are explained in the local language to the individual patients and care takers before obtaining the informed consent without any force or compulsion. All the patients with hypocalcaemia after total thyroidectomy had enrolled for the study. All the patients were examined and the demographic details, clinical features were documented and tabulated. Finally the calcium levels of all samples were categorized into before and after treatment and were then used as a criteria to describe the effectiveness of the drugs taken in the study. All the clinical details and drug related details were subjected to statistical analyses.

### **Study Materials:**

Informed consent form, patient data collection form and medication history are the essential aids used for the study.

### **Study site:**

The study site selection was done based on the availability of resources like the specific departments and study subjects so this prospective observational study was conducted in the General surgery Department, Sri Venkateswara Institute Of Medical Sciences, SPMC(W)-Tirupati, Andhra Pradesh.

**Study population :**

A total of 50 patients with total thyroidectomy were enrolled in to the study from the General surgery department, SVIMS, SPMC (W) according to the inclusion and exclusion criteria.

**Study Design:**

This is a hospital based cross sectional prospective observational study.

**Study Criteria:****Inclusion Criteria:**

- Patients with hypocalcaemia undergone total thyroidectomy.
- Patients without taking pre- operative calcium supplementation.
- Patients with symptoms of hypocalcaemia after total thyroidectomy.

**Exclusion Criteria:**

- Patients with abnormal renal function and diabetic nephropathy ,nephrotic syndrome with hypoalbuminemia.
- Patients undergoing hemithyroidectomy.
- Patients using calcium supplements before operation.
- Patients with cirrhotic liver with hypoalbuminemia and patients with hypomagnesemia.

**RESULTS:**

Hypocalcaemia is the major postoperative complication of total thyroidectomy. In this study we found 35 out of 50 patients are suffered with hypocalcaemia (70%) after total thyroidectomy. According to our study females (32 patients) are more prone to hypocalcaemia than males (3 patients), this statement was supported by many articles. Hypocalcaemia is mainly two types symptomatic and asymptomatic, the symptomatic hypocalcaemia results in parathesia, tingling sensation and carpopedal spasm. Out of 35 hypocalcemic patients 12 members develop symptomatic hypocalcemic and 23 are non symptomatic hypocalcemic.

The effectiveness of pharmacological agents can be assessed by measuring the serum calcium levels. Calcium (elemental calcium) drugs are used as prophylactic treatment for hypocalcaemia after total thyroidectomy.

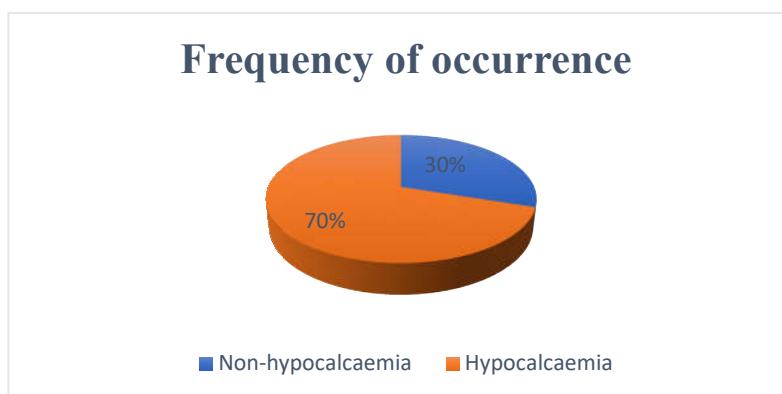
Out of 50 patients, 15 are non-hypocalcemic after total thyroidectomy and those are treated with the calcium-1 drugs as a prophylaxis treatment. For mild and moderate hypocalcaemia, calcium-2 drugs are used that include calcitriol and vitamin D3. Severe hypocalcaemia can be treated with calcium-3 drugs that include calcium gluconate. The calcium-3 drugs are more effective for the treatment of hypocalcaemia compared to calcium-1 and calcium-2 because the mean difference of serum calcium level increases to 1.6 mg/dl after treatment.

### 1. Frequency of occurrence of hypocalcaemia :

Hypocalcaemia is the most common complication of total thyroidectomy, causing potentially severe symptoms and increasing hospitalization time. The primary cause of hypocalcaemia is secondary hypo-parathyroidism following damage or devascularisation of one or more parathyroid glands during surgery. In our study, 70% of patients got hypocalcaemia after total thyroidectomy due to damage to thyroid glands during surgery.

**Table 1:** Frequency of occurrence of hypocalcaemia

Frequency of occurrence	Percentage
Non-hypocalcaemia	30 %
Hypocalcaemia	70%



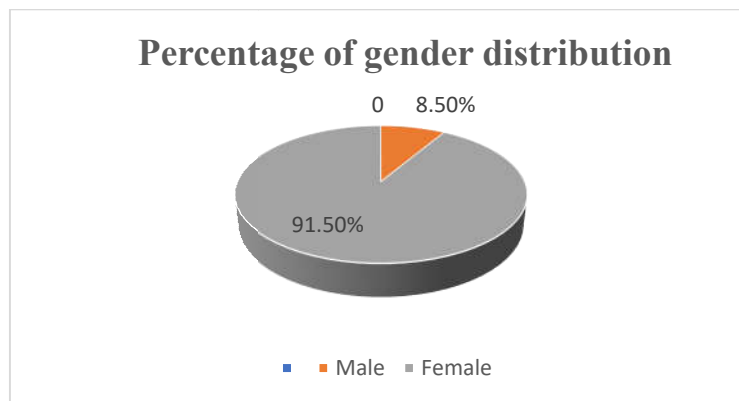
**Figure 1 :** Frequency of occurrence of hypocalcaemia

### 2. Gender distribution of hypocalcaemia :

Females are more prone to hypocalcaemia than males. So many articles supports that same statement. Our research also confirms the same as females are more prone to the hypocalcaemia than males. In our research out of 35 hypocalcaemia patients 3(8.5%)are male and 32(91.5%) are females.

**Table 2:**Gender distribution of hypocalcaemia

Gender distribution of hypocalcaemia :	percentage
Male	8.5%
Female	91.5%



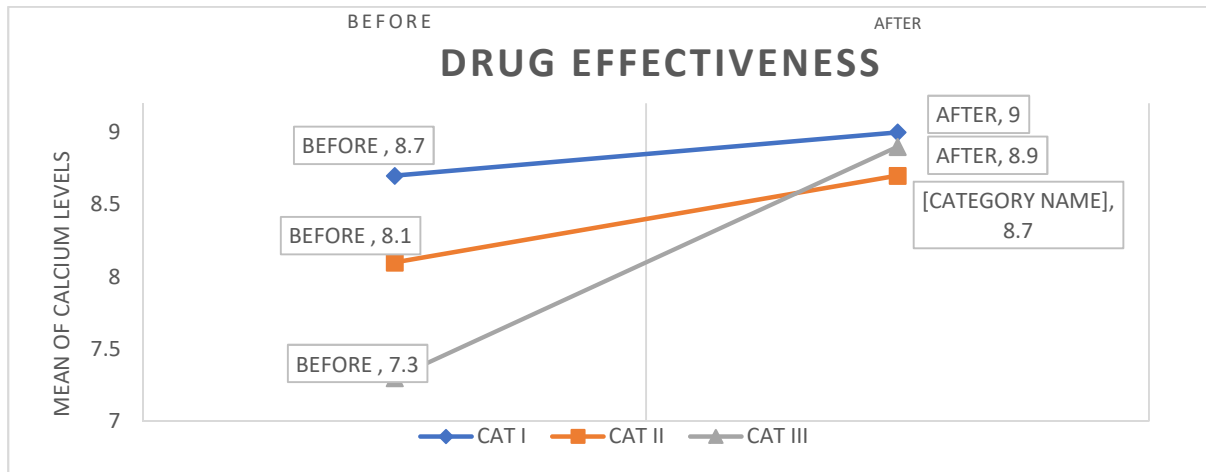
**Figure 2 :** Gender distribution of hypocalcaemia

### 3. Assessment of effectiveness of the Pharmacotherapy of hypocalcaemia in total thyroidectomy:

The effectiveness pharmacological agents can be assessed after total thyroidectomy by measuring the serum calcium levels before treatment and after treatment with calcium supplements. By measuring the mean difference of calcium levels we can conclude the effectiveness of pharmacological agents.

**Table 3:** Improvement of Serum Calcium By Various Pharmacological Agents

		Mean	Mean difference
Cat -I	Before	8.7	0.3
	After	9	
Cat -II	Before	8.3	0.6
	After	8.9	
Cat -III	Before	7.3	1.6
	After	8.9	



**Figure 3:** Improvement Of Serum Calcium By Various Pharmacological Agents

**4. Stastical Analysis:**

Statistical evaluation of the change in serum Ca<sup>2+</sup> level has been done with the help of spss 18 version statistical fool .the main method to find out the t value and p value is paired sample test. The degree of freedom is 49 (50 -1) .the level of significant as taken as 0.05 %.

**4.1 Paired Sample Statistics:**

**Table 4 :** Paired Sample Statistics

	mean	SD	Mean difference	confidence interval	t	Degree of freedom	p. value
<b>BEFORE</b>	8.1	0.0290	0.83	95%	217.388	49	0.000
<b>AFTER</b>	8.93	0.03010					

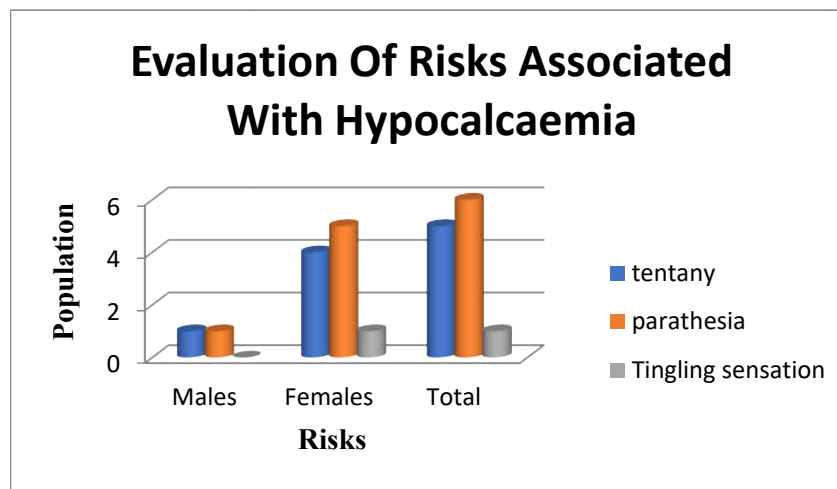
At 0.05% level of significance (confidence interval 95%) p value below 0.05 found for this study reflecting that the study is significant for two failed test. It implies that the use of pharmacological agents in management of hypocalcaemia is found effective.

**5. Evaluation Of Risks Associated With Hypocalcaemia:**

The risk factors of hypocalcaemia are paraesthesia of upper limb and lower limb , tingling sensation around the mouth, spontaneous tetany and carpopedal spasms .This is due to the condition of hypocalcaemia .In this study we observed 12 patients with these risk factors ,out of 12 patients 5 patients with tetany and 6 patients are with paraesthesia and one member with tingling sensation around the mouth .

**Table 5.**Evaluation Of Risks Associated With Hypocalcaemia

Tetany	1	4	5
Paraesthesia	1	5	6
Tingling sensation	0	1	1

**Figure 5:**Evaluation Of Risks Associated With Hypocalcaemia

#### 6. Assessment Of ADRs Associated With Calcium Gluconate :

Calcium gluconate iv is indicated for patients for the treatment of acute symptomatic hypocalcaemia. Calcium gluconate is a form of calcium combined with glucuronic acid. The following ADRs with the use of calcium gluconate are arrhythmias, end organ damage, tissue necrosis, hypotension, bradycardia, and cardiac arrest. In our study we did not find any adverse events because of proper administration of the drug with titrable doses and regular patient monitoring under the guidance of the physicians and 24 hourly care taking nurse.

### DISCUSSION

Hypocalcaemia is one of the major post-operative complications followed by total thyroidectomy which can increase the duration of the hospital stay and escalates financial burden for the patient, warranting, readmission and more number of hospital visits.

Many literatures and surveys concluded that females are more prevalent in thyroid disorders than males. A study conducted by Arumugam, et.al titled hypocalcaemia after



thyroidectomy explains that females are with 92% and males are with 8% calcium level abnormalities. Our study population also reflected the same that prevalence of thyroid abnormalities is more in females (84%) than in males (16%). The sex ratio between males and females are 1:5.25 and that females are 5 times are more prone to the thyroid disorders .

We understood that age is also one of the important risk factor for getting thyroid problems. A study conducted by viswanathan ,et.al named post- operative hypocalcaemia after thyroidectomy explained that patients above 40 years are more prone to thyroid problems (56%). In our study we observed that 27 members in between 31-50 years of age ,15 members in 51-65 years and 8 members in 18-30 years of age are with thyroid disorders .By using this data ,so that we conclude that age group between 31-50 years are more favour to thyroid disorders and in this 27 members females are 20 members and 7 members are males .

The reasons for the risk of hypocalcaemia after total thyroidectomy are revascularization of the parathyroid glands, recurrent laryngeal nerve injury, ageing and hemorrhage. Studies reported that 0.5% to 75 % patients are developing with hypocalcaemia after total thyroidectomy. In our prospective study of 50 patients the result demonstrates that 70 % (35) of the subjects are experienced hypocalcaemia after total thyroidectomy. Kasev jagadesan et.al conducted a study entitled incidence of hypocalcaemia in 30 patients after total thyroidectomy and the observed result was 6.66%. The hypocalcaemia may be symptomatic and asymptomatic, the symptomatic hypocalcaemia includes paresthesia, spontaneous tetany, tingling sensation around the mouth and carpodeal spasm .Our subjects experienced that 12 were with symptomatic hypocalcaemia and other 38 were with asymptomatic hypocalcaemia. EL-Shinawi et.al conducted a study entitled oral calcium and vitamin D supplementation after total thyroidectomy has observed 8 of their patients are exhibited with symptomatic hypocalcaemia out of the 50 patients.

The initial features of perioral numbness and tingling sensation of fingers which often go unnoticed can prove fatal due to cardiac arrest, if prompt action is not taken at appropriate moment. Benign diseases show less incidence of post-thyroidectomy hypocalcaemia than malignant diseases. The incidence of post-thyroidectomy hypocalcaemia is more in toxic thyroid disorders than in non-toxic thyroid disorders.

Parathyroid glands reduce parathyroid hormone which is intimately involved in the regulation of serum calcium. PTH increases serum calcium levels by causing bone resorption,

increasing renal absorption of calcium and stimulating the synthesis of biologically active form of vitamin D in kidneys.

The most dramatic effect of vitamin D is to facilitate intestinal absorption of calcium even in healthy individuals with no apparent vitamin D deficiency. Some authors suggested the use of routine prophylactic vitamin D or calcium as an alternative strategy to decrease the rate of hypocalcaemia based on the principle that offering prophylaxis to all patients will help all susceptible patients even those that are not detected by serum tests.

The dosages and durations of calcium and vitamin D given to our patients were within standard pharmacological limits. Hypercalcaemia, hypercalciuria or other side effects were not observed. In the absence of vitamin D dietary calcium is not absorbed at all efficiently. The vitamin D hormone stimulates the synthesis of epithelial calcium channels and plasma membrane calcium pumps and induces the formation of calbindins. It is an intracellular protein that ferries calcium across the intestinal epithelial cell. Thus vitamin D increase the overall rate of transcytosolic diffusion of calcium.

Inadequate production of PTH leads to hypocalcaemia due to inadequate production of active form of vitamin D. Serum calcium levels begin to recover in parallel with the increase of PTH levels. Calcium and vitamin D supplements will effectively reduce the incidence and progression of hypocalcaemia. Calcitonin is produced by the thyroid and inhibits bone breakdown while stimulating renal excretion of calcium.

The effectiveness of pharmacological agents for the management of hypocalcaemia after total thyroidectomy is assessed by calculating the mean difference of measured serum calcium levels before and after calcium supplementation. Since the sample size is very less, the statistical results were not found significant, even the mean difference of Serum calcium level was found (0.3) for elemental calcium, (0.6) and (1.6) for calcium vitamin D and calcium gluconate respectively shows the effectiveness of various pharmacological agents .

The clinical risk associated with symptomatic hypocalcaemia are paraesthesia of upper limb and lower limb , tingling sensation around the mouth , spontaneous tetany and carpedal spasms. The frequency of occurrence of the above risks in our study are tetany (5), paraesthesia (6) and tingling sensation around the mouth(1).

Since the risk and prevalence of hypocalcaemia is more after total thyroidectomy and the risks associated with hypocalcaemia are complicated, the role of health care team in predicting and preventing the hypocalcaemia by prophylactic calcium supplementations and management of hypocalcaemia after total thyroidectomy are found relevant. By this study we also evaluate the effectiveness of various pharmacological agents involved in management of hypocalcaemia.

## **CONCLUSION:**

Due to sedentary life style changes, food habits etc, thyroid disorders became one among the life style disorders. Total thyroidectomy is found to be the only refined surgical technique (because of reoccurrence of thyroid disorders are absent) that can completely manage some thyroid disorders like multi nodular goiter and grave disease etc. Preservation of parathyroid glands and RLN is essential to avoid the complication of hypocalcaemia in total thyroidectomy. Our study results suggest that post-operative oral calcium, vitamin D and inj.calcium gluconate are effective in the prophylaxis and management of hypocalcaemia after total thyroidectomy. This ultimately lead to improve the patient condition.

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