

## Post-Thyroidectomy Hypocalcemia and Effects of Pre-Operative Calcium Supplements on its Incidence

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### ABSTRACT

**Objective:** To determine the effects of pre-operative Calcium supplements on post-total thyroidectomy hypocalcemia.

**Study Design:** Randomized Control Trial (IRCT Id20231016059739N1).

**Place and Duration of Study:** Combined Military Hospital Bahawalpur Pakistan, from Sep 2022 to Sep 2023.

**Methodology:** All the patients undergoing total thyroidectomy and having normal Calcium levels were included. Baseline demographic data, medical history, and pre-operative Calcium levels were recorded for all participants. A total of 105 patients were enrolled in the study, with 52 patients assigned to the intervention group (Group-A) and 53 patients assigned to the control group (Group-B). Group-A was given a Calcium supplement and Group-B was given a placebo. Post-operative follow-up assessments were conducted at designated time points to evaluate serum Calcium levels and monitor for the occurrence of hypocalcemia.

**Results:** The demographic characteristics, baseline Calcium levels, and surgical procedures were similar between the two groups, ensuring comparability. The mean value of the post-operative Calcium level of the interventional group was  $8.904 \pm 0.4542$  mg/dl and control group was  $8.647 \pm 0.4964$  mg/dl showing statistically significant difference ( $p$ -value 0.007). In the Group-A, 8 out of 52 patients (7.6%) developed hypocalcemia, whereas in the Group-B, 20 out of 53 patients (19%) experienced hypocalcemia showing statistically significant difference ( $p$ -value 0.009).

**Conclusion:** Preoperative Calcium supplementation may not only decrease the occurrence of hypocalcemia but also promote a faster recovery from this complication following thyroid surgery.

**Keywords:** Calcium, Hypocalcemia, Randomized controlled trial, Thyroidectomy.

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### INTRODUCTION

Total thyroidectomy is currently the most recommended surgery for thyroid diseases.<sup>1</sup> Chances of temporary hypocalcemia ranges from 19% to 38% and that of permanent hypocalcemia ranges from 0.2% to 10% after total thyroidectomy.<sup>2,3</sup> Post-thyroidectomy hypocalcemia is a common complication that occurs as a result of parathyroid gland dysfunction or damage during thyroid surgery.<sup>4</sup> Hypocalcemia, characterized by low levels of serum Calcium, can lead to various symptoms, including muscle cramps, paresthesia, tetany, and in severe cases, life-threatening complications. Preventing and managing post-thyroidectomy hypocalcemia is crucial to ensure optimal patient outcomes and quality of life.<sup>5</sup> Pre-operative Calcium supplements have been proposed as an expected technique to diminish the frequency of post-thyroidectomy hypocalcemia. These supplements aim to enhance Calcium levels and backing parathyroid function, consequently limiting the

gamble of hypocalcemia and related complexities. Nonetheless, the effectiveness of pre-operative Calcium supplementation in preventing post-thyroidectomy hypocalcemia remains a subject of continuous research and discussion.<sup>6</sup> Post-thyroidectomy hypocalcemia is principally brought about by harm or unexpected evacuation of the parathyroid organs during thyroid medical procedure.<sup>7</sup>

To relieve the gamble of post-thyroidectomy hypocalcemia, different procedures have been investigated, including the organization of pre-operative Calcium supplements.<sup>8</sup> The reasoning behind pre-operative Calcium supplementation is to give an ideal Calcium level before a medical procedure, which might uphold parathyroid function and lessen the gamble of hypocalcemia following thyroidectomy. Nonetheless, the proof with respect to the effectiveness of pre-operative Calcium supplementation in preventing post-thyroidectomy hypocalcemia is conflicting and restricted.<sup>9</sup> This study aims to add to the current information by evaluating the effects of pre-operative Calcium supplements on the rate of post-thyroidectomy hypocalcemia.

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**METHODOLOGY**

The randomized controlled trial (IRCT Id20231016059739N1) was conducted at Combined Military Hospital Bahawalpur Pakistan, in accordance with ethical guidelines and approved by the Ethical Committee (ERC Ltr No. 1516/EC/04/2023), from September 2022 to September 2023.

**Inclusion Criteria:** Patients of all ages and either gender presenting with thyroid swelling, whether multinodular or solitary, those with normal pre-op Calcium levels and with no disease related to Calcium levels were included.

**Exclusion Criteria:** Patients not undergoing total thyroidectomy, those with diseases like bone diseases, parathyroid abnormalities, and kidney diseases causing deranged Calcium levels, and patients who did not take proper Calcium supplements were excluded.

The sample size of 104 was calculated, but we recruited 123 patients. Participants were randomly assigned to one of two groups using a computer-generated randomization sequence: the intervention group (Group-A) and the control group (Group-B) (Figure). Randomization was performed by an independent researcher not involved in patient recruitment or data collection. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes. Blinding of participants, surgeons, and outcome assessors to group assignment was implemented to minimize bias.

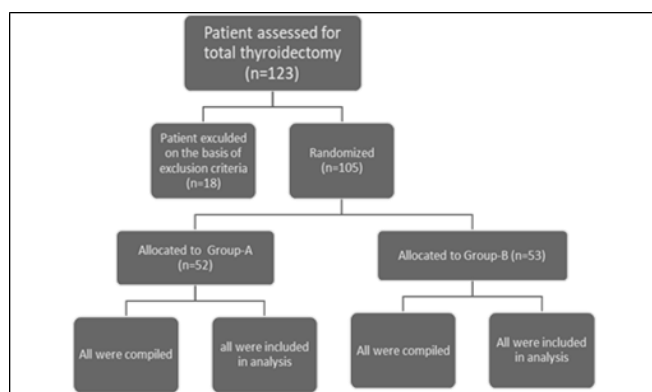


Figure: Patient Flow Diagram

All participants underwent thyroid surgery according to standard surgical techniques. The surgical approach, extent of resection, and other procedural details followed the clinical practice guidelines. Surgeons performing the procedures were experienced in thyroid surgery to ensure consistency and minimize procedural variability. The primary

outcome measure was the incidence of post-thyroidectomy hypocalcemia, defined as serum Calcium levels below the normal reference range (e.g., <8.5 mg/dL) during the post-operative period (measured after 12 hours post-operatively). Secondary outcome measures included the duration of post-operative hypocalcemia, need for post-operative Calcium and vitamin D supplementation, and the occurrence of related complications such as tetany or neuromuscular symptoms.

Baseline demographic data, medical history, and pre-operative Calcium levels were recorded for all participants. Post-operative follow-up assessments were conducted at designated time points to evaluate serum Calcium levels and monitor for the occurrence of hypocalcemia. Data were collected by trained personnel blinded to group assignment. For statistical analysis Statistical Package for Social Sciences (SPSS) version 21 was used. Quantitative variables with normal distribution were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test and Student t-test were performed to compare the incidence of hypocalcemia between the intervention and control groups and explore potential factors influencing the outcomes. The p-value lower than or up to 0.05 was considered as significant.

**RESULTS**

One hundred and five patients were enrolled in the study, with 52 patients assigned to the intervention group (Group-A) receiving pre-operative Calcium supplements and 53 to the Control Group (Group-B) receiving a placebo. A comparison of the characteristics of the groups showed more men (n=20) were randomized in the Interventional Group. The mean age in the interventional group (39.23±6.623) was more than that of the control group (37.96±6.472). The majority of the population undergoing total thyroidectomy was with multinodular goiter euthyroid (71.4%) as shown in Table-I.

Table-I: Population Characteristics of Study Groups (n=105)

| Characteristics                      | Group-A (n=52) | Group-B (n=53) | p-value  |
|--------------------------------------|----------------|----------------|----------|
| Age(years), Mean±SD                  | 39.23±6.623    | 37.96±6.472    | 0.323    |
| Gender                               | Male, n(%)     | 16(15.2%)      | 0.371    |
|                                      | Female, n(%)   | 37(35.2%)      | 0.372    |
| ASA* classification                  | Grade 1, n(%)  | 39(37.1%)      | 0.621    |
|                                      | Grade 2, n(%)  | 13(12.4%)      | 0.617    |
|                                      | Grade ≥3, n(%) | 1(0.95%)       | 1(0.95%) |
| Multinodular Goiter (euthyroid),n(%) | 37(35.2%)      | 38(36.2%)      | -        |
| Toxic Multi Nodular Goiter, n(%)     | 10(9.5%)       | 10(9.5%)       | -        |
| Suspicious Thyroid nodule, n(%)      | 2(1.9%)        | 3(1.9%)        | -        |
| Carcinoma, n(%)                      | 3(2.9%)        | 2(1.9%)        | -        |

ASA: American Society of Anesthesiologists

The primary outcome measure, the incidence of post-thyroidectomy hypocalcemia was assessed during the postoperative period. The mean value of the post-operative Calcium level of Group-A was 8.904±0.4542 mg/dl and Group-B was 8.647±0.4964 mg/dl. There was a statistically significant difference between the means of the two groups in post-op Calcium levels. During secondary outcomes measures, 4 out of 20 hypocalcemia patients got carpopedal spasms. None of the interventional group patients showed signs of hypocalcemia involving neuromuscular symptoms. Twenty percent of the total patients were given Calcium supplements postoperatively. Comparison between the two groups showed no statistically significant difference in the duration of the hospital stay (Table-II).

Table- II: Post-Operative Outcome Measures (n=105)

| Measures  | Group-A Mean±SD (n=52) | Group-B Mean±SD (n=53) | Total Mean±SD | p-value |
|---|------------------------|------------------------|---------------|---------|
| Pre-Operative Calcium level (mg/dl)               | 9.144±0.4956           | 9.234±0.4265           | 9.190±0.4620  | 0.322   |
| Post-Operative Calcium level (mg/dl)              | 8.904±0.4542           | 8.647±0.4964           | 8.774±0.4909  | 0.007   |
| Severe symptoms, n(%)                             | 0(0.0%)                | 4(3.8%)                | 4(3.8%)       | 0.04    |
| Need for post-operative Calcium supplements, n(%) | 7(6.7%)                | 14(13.3%)              | 21(20.0%)     | 0.09    |
| The average duration of stay (days), Mean±SD      | 4.08±0.904             | 4.13±0.810             | 4.10±0.854    | 0.74    |

Post-Operative hypocalcemia was found among 28 patients. There was also a statistically significant difference (<0.009) between the patients of the two groups who developed hypocalcemia (Table-III).

Table-II: Frequency Distribution of Post-Operative Hypocalcemia (n=105)

| Hypocalcemia | Group-A n(%) | Group-B n(%) | p-value |
|--------------|--------------|--------------|---------|
| Yes          | 8(7.6%)      | 20(19.0%)    | 0.009   |
| No           | 44(41.9%)    | 33(31.4%)    |         |
| Total        | 52(49.5%)    | 53(50.5%)    |         |

No statistically significant difference was found between hypocalcemic and normocalcemic patient when focused on age, gender, ASA classification and disease of the patient (Table-IV).

**DISCUSSION**

The present study investigated the effects of pre-operative Calcium supplements on the incidence of post-thyroidectomy hypocalcemia in patients with thyroid disorders. Our findings revealed a significantly lower occurrence of hypocalcemia in the

intervention group, along with absence of severe symptoms like tetany, neuromuscular disorders as compared to the control group. This lines up with previous examinations that have announced comparative findings.<sup>10,11</sup> This protective effect of Calcium supplements could be credited to their capacity to increment Calcium saves, upgrade parathyroid chemical emission, and work on the responsiveness of Calcium-detecting receptors.<sup>12,13</sup>

Our study found that preoperative Calcium supplementation may lessen the frequency as well as advance a quicker recuperation from hypocalcemia following thyroidectomy. This corresponds with another study, where preoperative Calcium supplementation diminished requirement for delayed postoperative Calcium and vitamin D supplementation.<sup>14</sup>

The definition of postoperative hypocalcemia in view of demographic factors, like age and orientation, uncovered fascinating patterns. We noticed a higher frequency of hypocalcemia in the younger (18-40 years) cohort contrasted with their older (41-65 years) counterparts in both Groups A and B.<sup>15</sup>

While considering the ASA grade, there was a non-significant pattern towards a higher occurrence of hypocalcemia in patients with higher ASA grades (Grade 2) contrasted with those with lower ASA grades (Grade 1). This is in concurrence with other studies.<sup>16-18</sup>

Table-IV: Characteristics of Post-Operative Patients on the basis of Calcium level (n=105).

| Characteristics                       | Post-Operative Hypocalcemic (n=52) | Post-Operative Normocalcemic (n=53) | p-value   |       |
|---------------------------------------|------------------------------------|-------------------------------------|-----------|-------|
| Age(years), Mean±SD                   | 37.07±5.48                         | 39.14±6.84                          | 0.153     |       |
| Gender,                               | Male, n(%)                         | 9(8.6%)                             | 27(25.7%) | 0.780 |
|                                       | Female, n(%)                       | 19(18.1%)                           | 50(47.6%) | 0.780 |
| ASA* classification                   | Grade 1, n(%)                      | 17(16.2%)                           | 58(55.2%) | 0.143 |
|                                       | Grade 2, n(%)                      | 11(10.5%)                           | 17(16.2%) | 0.78  |
|                                       | Grade ≥3, n(%)                     | 0(0)                                | 2(1.9%)   | 0.389 |
| <b>Reason for Surgery</b>             |                                    |                                     |           |       |
| Multinodular Goiter (euthyroid), n(%) | 22(21.0%)                          | 53(50.5%)                           | 0.329     |       |
| Toxic Multi Nodular Goiter, n(%)      | 4(3.8%)                            | 16(15.2%)                           | 0.454     |       |
| Suspicious Thyroid nodule, n(%)       | 2(1.9%)                            | 3(2.9%)                             | 0.490     |       |
| Carcinoma, n(%)                       | 0(0%)                              | 5(4.8%)                             | 0.167     |       |

\*ASA: American Society of Anesthesiologists

**CONCLUSION**

In conclusion, our study findings suggest that preoperative Calcium supplementation may not only

decrease the occurrence of hypocalcemia but also promote a faster recovery from this complication following thyroid surgery.

**Conflict of Interest:** None.

### Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

EK & MSA: Data acquisition, critical review, approval of the final version to be published.

KN & WIA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MAM & MSR: Conception, data analysis, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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