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## COMPARISON OF CORRECTED SERUM CALCIUM CHANGES FOLLOWING THYROID AND NON THYROID NECK SURGERIES

### Objective:

To compare the corrected serum calcium changes following thyroid and non thyroid neck surgeries.

### Material and Methods:

It was a prospective, longitudinal and comparative study, done in Ganesh Man Singh Memorial Academy of ENT and Head and Neck Studies, Tribhuvan University, Teaching hospital, Kathmandu, Nepal. Convenient sample size was taken of patients undergoing thyroid and non thyroid neck surgeries under general anaesthesia, between 1<sup>st</sup> November 2009 to 30<sup>th</sup> April 2011.

### Result:

Total 87 cases were included which comprises 41 cases of thyroid and 46 cases of non thyroid neck lesions. Total females in thyroid cases were 39 out of 41 and in non thyroid cases 25 out of 46. The mean corrected calcium in thyroid cases were  $2.04 \pm 0.07$ ,  $1.75 \pm 0.26$ ,  $1.92 \pm 0.16$  and  $2.00 \pm 0.07$  in pre-operative, recovery room (immediate post-operative), post-operative day-1(POD 1) and post-operative day-4(POD- 4) respectively. The mean calcium changes in non thyroid cases were  $2.04 \pm 0.09$ ,  $1.89 \pm 0.19$ ,  $1.94 \pm 0.13$  and  $1.99 \pm 0.04$  in pre-operative period, recovery room (immediate post-operative), post-operative day-1(POD-1) and post-operative day-4 (POD- 4) respectively. In both thyroid and non thyroid group, the calcium drop was statistically significant ( $< 0.05$ ) in recovery. Rest were not significant statistically. The mean differences from pre-operative to recovery and preoperative to POD-1 corrected calcium changes were also significant in both thyroid and non thyroid groups. The mean difference between preoperative to POD-4 was not significant in both groups.

### Conclusion:

After comparing the corrected serum calcium changes following thyroid and non thyroid neck surgeries, the transient post-operative hypocalcaemia is not a thyroid surgery dependent phenomenon. Haemodilution is the main factor for hypocalcaemia in immediate postoperative period in all major neck surgeries.

**Key word:** Non thyroid neck Surgery, Serum calcium, Thyroid surgery

## INTRODUCTION:

Calcium regulation is maintained by parathyroid hormone, Vitamin D and calcitonin through complex feedback loops. These compounds act primarily at bone, renal and gastrointestinal sites. It is also affected by albumin, magnesium and phosphorus. Total calcium concentration in plasma is 4.5-5.1 mEq/L (9-10.2 mg/dL) of which 50 % is ionized, 40% binds with proteins of which, 90% binds to the albumin and 10% is bound to anions (eg. phosphate, carbonate, citrate, lactate, sulfate). Clinical signs and symptoms of hypocalcaemia appear when there is a decrease in ionized calcium concentration. Hypocalcaemia is a well known sequel of thyroid surgery. It can be transient or permanent. It usually manifests in the first 24 hours after the surgery. The incidence ranges from 5.4%-68% and is highly variable due to differences in both definition and surgeon's experience. The most significant aetiology of hypocalcaemia following thyroid surgery is thought to be a combination of haemodilution and parathyroid dysfunction. However, studies have shown that haemodilution from intra-operative fluid replacement is a temporary cause of hypocalcaemia.<sup>1</sup> Post operative hypocalcaemia is a concern after thyroid surgery because it lengthens the duration of hospital stay, need for biochemical tests and increases the overall cost of thyroidectomy.<sup>2</sup>

In other neck surgeries like superficial parotidectomy, submandibular gland excision, excision of various neck swellings; transient post-operative hypocalcaemia may be observed immediately. This change is attributed mainly to haemodilution. Fall in ionized calcium have been reported during standard surgical procedures and have been mostly attributed to changes in pH due to

mechanical respiration also. Rarely, in some cases of head and neck surgery, hypercalcaemia have also been observed in post operative period. Probable cause of this hypercalcaemia was pseudohyperparathyroidism.<sup>3</sup> The biologic effect of calcium is determined by the amount of corrected calcium rather than the total calcium. Total calcium measurement leads to overestimation of hypocalcaemia, called as factitious hypocalcaemia. There is a common practice of giving oral and intravascular calcium supplement looking at total serum calcium level which leads to overdose of these supplements causing undesirable side effects like constipation, dry mouth and loss of appetite. It is useful to measure the ionized calcium level when the serum albumin level is not within normal ranges or when a calcium disorder is suspected despite a normal total calcium level.<sup>4,5</sup>

A clinico-biochemical performa has been prepared to note down the corrected calcium level in preoperative, immediate post-operative, first post-operative and fourth post-operative day. The corrected calcium levels were recorded in the performa in the patients who were planned for surgery. Very few studies till date have been done in the literature to see the comparison of true calcium changes after thyroid and non thyroid neck surgeries. This study is first of its kind in Nepal. This study is going to prevent the unnecessary and inadvertent use of post-operative calcium supplementation and prolonged hospital stay.

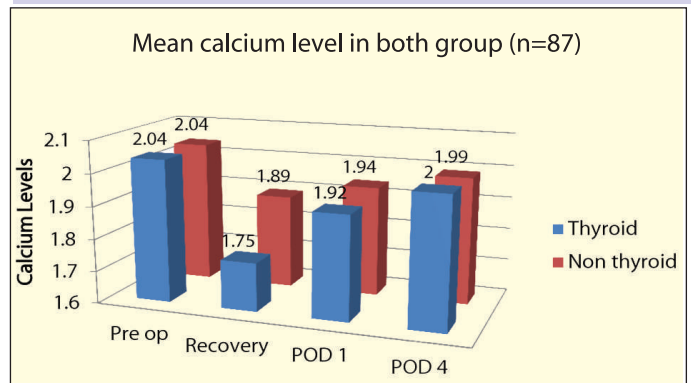
## MATERIALS AND METHODS:

Prospective, longitudinal and comparative study of cases undergoing thyroid and non thyroid neck surgery was carried out at Ganesh Man Singh memorial academy of

Otorhinolaryngology and Head and Neck Studies, Institute of Medicine, Tribhuvan University, Teaching Hospital, Maharajgunj, Kathmandu, Nepal for 18 months (from 1st November 2009 to 30th April 2011). Ethical approval was taken from institutional review committee. Patients undergoing thyroid and non thyroid neck surgeries under general anaesthesia, age more than twelve years and all gender were included in this study. Patients having primary, secondary or tertiary hypercalcaemia/hypocalcaemia, patients taking oral calcium pre-operatively, patients with history of previous parathyroid surgery, patients received radiation treatment over the neck in the past were excluded from study. Patients were selected from the outpatient department and surgery was decided by the faculties of ENT Head and Neck surgery department. All the patients underwent base line investigations along with serum calcium and serum albumin at least 3-4 days prior to surgery. All thyroid patients were made euthyroid before the surgery if they were hypothyroid or hyperthyroid. Patients were admitted and posted for surgery. Classical steps of surgery were used in all cases. Surgery was performed only by the faculty members. Patient's details were noted in clinico-biochemical performa. Use of tourniquet was contraindicated for the right calculation of post operative calcium level. Blood samples were sent for estimation of serum calcium and albumin from the recovery room (immediate post-operative) and post-operative day-1 (POD-1) and post-operative day-4 (POD-4). Fully automated analyzer, BT 3000, Rome, Italy was used for the calculation of serum albumin and calcium in all cases.

The pre-operative mean corrected calcium level was 2.04 in both the groups. In recovery, it was 1.75 in thyroid and 1.89 in non thyroid. Again, in post-operative day-1(POD-1) and post-operative day-4(POD-4), the corrected mean calcium was almost similar in both the groups. Fisher's exact test was applied and a statistically significant fall was observed in the mean calcium level in recovery which is similar in both the thyroid and non thyroid cases. Figure 1 is an illustrative representation of the above table 1.

Fig. 1: Mean calcium level in both thyroid and non thyroid cases



The mean difference in calcium levels (a fall of serum calcium levels) seen from our observations calculated in recovery (immediately following surgery) and on first (POD-1) and fourth (POD-4) post-operative days were analysed for distribution at a confidence interval of 95% using an independent sample t-test and the results obtained were as follows:

Table 2: Comparison of different readings of calcium level in thyroid cases

Days	Thyroid (n=41)		Remarks
	Mean difference (95% CI)	'p' value	
Recovery	0.284 ± 0.27	p<0.05	Statistically significant
POD-1	0.126 ± 0.19	P<0.05	Statistically significant
POD-4	0.04 ± 0.10	p>0.05	Statistically not significant

The fall in serum calcium levels (mean 0.284±0.27) in

Table 3: Comparison of different readings of calcium level in non thyroid cases

Days	Non Thyroid (n=46)		Remarks
	Mean difference (95% CI)	'p' value	
Recovery	0.15 ± 0.22	p<0.05	Statistically significant
POD-1	0.10 ± 0.17	P<0.05	Statistically significant
POD-4	0.04 ± 0.12	p>0.05	Statistically not significant

Corrected calcium levels were calculated using the formula:  
 Corrected calcium (mg/dL) = measured total Ca (mg/dL) + 0.8 (4.0 - serum albumin [g/dL]) Or  
 Corrected calcium (mmol/L) = measured total Ca (mmol/L) + 0.02 (40 - serum albumin [g/L])

**RESULTS:**

There were 87 cases included in the study. The thyroid cases were 41 and non thyroid were 46. The mean age of thyroid cases was 38.6 years which is older as compared to non thyroid, which was 29 years.

Table1: Mean value of corrected Ca++ in both groups (n=87)

Days	Thyroid surgery mean calcium levels (mmol/l)	Non-Thyroid Surgery mean calcium levels (mmol/l)	p-value (Fisher's exact)	Remarks
Pre-op	2.04 ± 0.07	2.04 ± 0.09	>0.05	Not significant
Recovery	1.75 ± 0.26	1.89 ± 0.19	<0.05	significant
POD- 1	1.92 ± 0.16	1.94 ± 0.13	>0.05	Not significant
POD- 4	2.00 ± 0.07	1.99 ± 0.05	>0.05	Not significant

Table 1 shows the mean value of corrected calcium on pre-operative day, recovery (immediate post-operative), post-operative day-1 (POD-1) and post-operative day-4 (POD-4) in both groups i.e. thyroid and non thyroid neck



patients undergoing thyroid surgery as calculated from samples collected in the recovery room was found to be statistically significant ( $p < 0.05$ ). The mean value for calcium were found to increase (with a concurrent decrease in mean difference, as calculated from the pre-operative values) on the first post-operative day (POD-1) ( $p < 0.05$ ) and the values came close to their pre-operative values on the fourth post-operative day (POD-4) with no major difference ( $p > 0.05$ ) from the first day ( $0.04 \pm 0.10$ ) as shown in table 2.

Similarly, patients undergoing neck surgery other than thyroid were also assessed separately for a fall in calcium levels. The mean difference in calcium levels in the samples collected from the recovery room and the first and fourth post-operative days were analysed for statistical significance at a confidence interval of 95%. The fall in serum calcium levels (mean  $0.15 \pm 0.22$ ) in patients undergoing non thyroid neck surgery as calculated from samples collected in the recovery room was found to be statistically significant ( $p < 0.05$ ). The mean values for calcium were found to increase (with a concurrent decrease in the mean difference, as calculated from the pre-operative values) on the first post-operative day (POD-1) ( $p < 0.05$ ) and the values came close to their pre-operative values on the fourth post-operative day (POD-4) with no major difference ( $p > 0.05$ ) from the first day (mean difference  $0.04 \pm 0.12$ ). (Table 3) Comparison of mean difference of corrected calcium from pre-operative day to recovery room, pre-operative day to post-operative day-1 (POD-1) in both thyroid and non thyroid group was found to be statistically significant from pre-operative day to post-operative day-4 (POD-4) for both groups.

## DISCUSSION:

In this study, it was clearly observed that there was significant fall in corrected serum calcium in the recovery room (immediate post-operative) in both thyroid and non thyroid neck surgery group; but the fall in thyroid surgery was more than non thyroid neck surgery. The mean corrected serum calcium level was 2.04 mmol/l in both thyroid and non thyroid neck surgery pre-operatively but in post-operative day-1 (POD-1), it became 1.75 and 1.89 mmol/l respectively. In contrast, on post-operative day-4 (POD-4) it became almost same i.e. 2.0 & 1.99. This result was comparable to the study done by Mehta et al.<sup>6</sup> According to de Andrade Sousa et al. Ionized calcium concentrations  $< 1.03$  mmol/l on postoperative day 1 (POD-1) are indicative of the presence of symptoms and the need for treatment.<sup>7</sup> Routine calcium supplements may not be necessary if serum calcium level is more than 1.81 mmol/l.<sup>8</sup> Most of the studies showed the decline of the serum calcium level after major surgery.<sup>9,10,11</sup> Reason behind have been described multifactorial. Most common cause of this decline was thought to be haemodilution along with hypoparathyroidism, hypomagnesaemia. Some studies say the only reason behind hypocalcaemia is hypoparathyroidism. Contrary to this, hypercalcaemia may occur at the time of diagnosis in patients found to have epidermoid carcinoma of the

head and neck. Pseudo-hyperparathyroidism was the suspected cause in those patients.<sup>12</sup> The effect of hypoparathyroidism seems to be less likely in our study, because, in all the thyroid and non thyroid cases, the mean value of corrected calcium on POD-4 became 1.99 and 2.0 from 2.04. Although immediately in recovery, the thyroid cases had lower value than non thyroid, both were significant statistically. Measuring or calculating ionized calcium level post thyroidectomy, to avoid unnecessary calcium supplementation resulting from diagnosing hypocalcaemia from measuring total calcium level alone is more accurate and more appropriate.<sup>13</sup> In our study, the difference between pre-operative corrected serum calcium level to POD-4 value was 0.03mmol/l which was not statistically significant ( $p = > 0.05$ ) in 29 cases of hemithyroidectomy. This was comparable to study done by Cannon et al who specifically studied 107 patients of hemithyroidectomy.<sup>14</sup> First time, Mehta et al<sup>6</sup> in their study, compared the thyroid neck surgeries with non thyroid neck surgeries, to see the change of corrected serum calcium level using albumin. This study is similar to our study in many respects. He compared the peri-operative calcium changes following total and completion thyroid surgery with a control group undergoing non thyroid neck surgery. All three groups showed a significant decrease in corrected serum calcium from pre-operative to POD-1. Study done by Snow et al<sup>15</sup> may be taken as a better explanation to our result. He mentioned that, Hypoalbuminemia, thyroidectomy, hypoparathyroidism, hypomagnesaemia, estrogen replacement therapy, oral contraceptives, blood transfusions, hyperventilation alkalosis, depression, emotional stress and diet are some of the etiological factors in hypocalcaemia secondary to the operations for carcinoma of pharynx and larynx. He also proved in his study that onset of symptoms and signs of hypocalcaemia occur within 24 to 48 hours after the operation. Lepage et al.<sup>16</sup> also proved our results in his study over hypocalcaemia produced during major and minor abdominal surgeries by mentioning, an important part of this fall in ionized serum calcium was apparently associated with falls in albumin resulting from acute haemodilution by physiological saline. In this way, this study could be a good platform for the further research and study for the role of hypoparathyroidism in cases of total thyroidectomies.

## CONCLUSION:

Both thyroid and non thyroid neck surgeries have similar risk of hypocalcaemia after surgery. Transient post-operative hypocalcaemia is not a thyroid surgery dependent phenomenon. It is observed in both groups. It is observed more in thyroid cases contrary to the non thyroid neck surgeries in recovery and postoperative day one. Probable role of hypoparathyroidism in total thyroidectomy cannot be determined in this study due to less number of cases. Corrected serum calcium is a better baseline tool to evaluate post-thyroidectomy parathyroid dysfunction. So it serves as a marker for feasibility of short stay after thyroid surgery and unnecessary calcium supplement is avoided in all thyroid surgeries.

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