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EVALUATION OF CLINICALLY SIGNIFICANT HYPOCALCEMIA AFTER TOTAL THYROIDECTOMY: A PROSPECTIVE STUDY

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ABSTRACT

Purpose: Many factors are responsible for the occurrence of hypocalcemia after total thyroidectomy (TT). This study was conducted to look at the factors usually concerned in post TT clinically significant hypocalcemia (CSH). A scoring system is being developed in combination with these factors for early diagnosis of CSH.

Study Design: Institution based Prospective study.

Materials and Methods: Total 50 patients with benign goiter and early carcinoma thyroid were included in this study and all were go through total thyroidectomy. Age of the patients, pre-operative thyroid hormone status, serum Ca^{2+} level and 25 (OH) vitamin D were studied. Post-operative iPTH level at 8 hours and calcium level at 12 hours were measured. Condition of parathyroid gland and size of the nodule were studied and preserved during operation. CSH prediction score (0 to 8) was designed based on these 8 factors.

Statistical Analysis: SPSS 16 software was used. Independent samples T-test and Chi-square test was used for comparison between two groups. P value <0.05 was used as statistically significance.

Results: There were 8 males and 42females. 64% (n=32) had euthyroid multi-nodular goiters, 24%(n=12) had toxic MNG, and 12%(n=6) had an early carcinoma of thyroid. 30%(n=15) developed CSH. CSH was developed in patients with low pre-operative serum calcium (P=0.000), low 25 OH vitamin D (*P*=0.001) with low serum calcium (*P*=0.000) at 10 hours, low post-operative iPTH at 6 hours (*P*=0.001), after surgery and lesser number of parathyroid identification at surgery (*P*=0.000)and nodule size (*P* - 0.000).

Conclusions: Clinically significant hypocalcemia (CSH) after TT depends upon multiple factors and these factors (Hypocalcemia prediction score > 3) can be taken account to predict it to discharge patients within one day after surgery.

Key Words: Total thyroidectomy, 25 OH vitamin D3, Clinically significant hypocalcemia, intact PTH.

INTRODUCTION

Temporary symptomatic hypocalcemia occurs in some patients after total thyroidectomy (TT). This is a limiting factor in an early discharge of the patients from hospital[1]. The incidence has been reported to vary from 0.5% to 75%[2]. Early treatment can be started in these patients who were likely to develop clinically significant hypocalcemia (CSH), and the others, in those the incidence of hypocalcemia is unlikely and can be discharged as a day care surgery. Post-operative serum calcium, post-operative intact PTH (iPTH), serum 25 OH vitamin D levels, pre-operative serum calcium, presence of hyperthyroidism, advanced age of the patient, parathyroid preservation, and size of goiter at surgery have all been implicated in the development of post TT hypocalcemia [2-17]. It has been realized from various studies published in literature that no single factor can predict its occurrence [2-17]. The study was carried out to consider all these factors and to create a multi-factorial scoring system. We hope that this will facilitate us to predict incidence of post TT clinically significant hypocalcemia and enable us to discharge the patients within one day after surgery.

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MATERIALS AND METHODS

This prospective study was conducted at Burdwan Medcal College & Hospital a rural based medical college and hospital from February 2013 to January 2014. All patients undergo total thyroidectomy for benign thyroid swelling and stage one carcinoma thyroid (< T2/N0/M0). All surgeries were performed by a surgeon, who is well trained in thyroid surgery. Patients who developed clinically significant hypocalcemia (CSH) within 12 hours of surgery were excluded from the final analysis.

Demographics of the study population, status of hyperthyroidism, pre-operative levels of free serum Ca^{+2} and 25 (OH) vitamin D, post-operative serum parathyroid hormone (iPTH) at 6 hours and serum calcium at 10 hours, nodules size and parathyroid preservation status during operation were recorded. Hypocalcemia prediction score (0 to 8) was designed based on these factors [Table 1]. Post-operative Hypocalcemia was defined as serum calcium < 7.5 mg% occurring anytime after total thyroidectomy. Patients who have low serum calcium (< 7.5 mg %) and develope carpopedal spasm [induced within 2 minutes on eliciting the Trousseau sign (Figure 1)] after total thyroidectomy, said to have clinically significant hypocalcemia (CSH). A minimum of 0 points and maximum of 8 points were chosen to each case.

Statistical Analysis: SPSS 16 software was used. Independent samples T-test and Chi-square test was used for comparison between two groups. P value <0.05 was used as statistically significance. A logistic regression analysis model was built to assess the significant predictors.

RESULTS

Among the 50 patients included in the final analysis; there were 8 males and 42 females (16% and 84%), 64% (n=32) were euthyroid multinodular goiters, 24% (n=12) were toxic MNG, and 12% (n=6) were early carcinoma thyroid. 30% (n=15) developed clinically significant hypocalcemia (CSH) after 24 hours of surgery. Comparison of the patients who developed CSH (group B) with those who did not develop (group A) [SPSS result]. CSH was found in patients with low pre-operative serum Ca^{2+} (P=0.000), low Serum Vit D (P=0.001), low post-operative iPTH (P=0.001), and low serum Ca^{2+} (P=0.000) at 6 and 10 hours after surgery respectively. Clinically significant hypocalcemia (CSH) also occurred with lesser number of parathyroid being preserved at surgery (P=0.000) and nodule size (P-0.000). Age of the patient (P=0.3) was not significantly different between the groups. [Table 2] shows the comparison of the demographic data between groups A vs. group B. [Table 3] depicts the predictive power of the different hypocalcemia scores, which will predict clinically significant hypocalcemia.

DISCUSSION

The most common problem encountered after TT is hypocalcemia, which can either be temporary or be permanent[1]. Temporary hypocalcemia can be biochemical (BH) or symptomatic hypocalcemia (SH), which usually develops 24 to 48 hours after the thyroidectomy[3]. Thus, patients have to be observed for this time period prior to discharge in order to prevent development of clinically significant hypocalcemia. It is particularly important in India because of the poor rural health care system. Development of post total thyroidectomy (TT) hypocalcemia is depends on various factors. One of them has been post-operative serum calcium levels[4]. Pfleiderer et al[2] demonstrated that serum calcium less than 7.6 mg% on day 1 after surgery had 95% specificity in predicting SH. In this study we measured the serum calcium level at 10 hours after the TT but Lombardi et al[8] used serum calcium at 12 hours after surgery in their study. Lo CY et al[5] used serum calcium of 7.2 mg% as cut off to define hypocalcemia. The cut off value is 7.5 mg% in this study. Post-operative as well as intra-operative serum iPTH has been used in various studies to predict post TT hypocalcemia. [3,5-7]. An analysis of 9 observational studies by Noordzij et al.[3] reported that the level of PTH 6 hours after TT had 96.4% sensitivity and 91.4% specificity in detecting post-operative hypocalcemia. Payne et al[6] used iPTH at 6, 12, and 20 hours post-operatively and found the 12 hour value as most sensitive in prediction. Lombardi et al[8] used 2, 4, 6, 24, 48 hours post-operatively and found that the 4 hour and 6 hour value had the best predictive value. As there were no specific guidelines for the collection of iPTH sample, iPTH level at 6 hours after surgery was measured in this study. The mean PTH was 13.52 pg/mL in patients who developed hypocalcemia[3]. In our study, we found that the post-operative iPTH of ≤10 pg/mL at 6 hours after surgery. Literature review has shown that intra-operative PTH was less sensitive and specific than when it was checked post-operatively[3]. That's why we used only 6 hour post-operative iPTH value.

Serum vitamin D has been found to be low in Indian patients in various studies[9,10]. Since the serum vitamin D directly influences the calcium kinetics, especially in the post-thyroidectomy scenario, we included pre-operative vitamin D also as a predictive factor[11]. One study has shown that the low vitamin D levels are associated with 28-fold increase in chances of post TT clinically significant hypocalcemia[12].

Hyperthyroidism has been shown to have significant impact over bone turn over even after euthyroid status is restored[13]. Longer duration of Grave's disease

and low vitamin D were shown as factors contributing to hypocalcemia[14]. Pre-operative calcium levels have been used to predict hypocalcemia post-operatively[11]. Yamashita et al[15] have reported that lower pre-operative calcium levels in patients underwent total thyroidetomy shown early development of hypocalcemia. Erbil et al[14] and Dedivitis et al[16] observed that elderly patients have significant risk factor for post-operative hypocalcemia. Ageing is said to be associated with decreased intestinal calcium absorption, decreased renal 1α hydroxylase, decreased dermal synthesis of vitamin D, these contribute to susceptibility to hypocalcemia after TT[14]. In this study, we found post-menopausal women and men > 60 years are susceptible to hypocalcemia. We also found that the age was insignificant parameter in predicting clinically significant hypocalcemia .

Preservation of parathyroid gland is inversely proportional for the development of post total thyroidectomy (TT) hypocalcemia. Some authors have suggested that at least 3 parathyroids are to be saved while others opined that 2 functional glands are enough to prevent post TT hypocalcemia[17]. In our study, in patients with 2 or <2 parathyroid gland developed clinically significant hypocalcemia. It has been shown that the post-operative hypocalcemia is also dependant on the surgeons experience and the operative technique used[17].

CONCLUSION

CSH after TT depends upon multiple factors and these factors can be taken account to predict it to discharge patients within one day after surgery. Further studies are needed to authenticate the scoring system.

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Table 1: Showing predictor and scoring

Variable	Yes	No
Men with age more than 60 years and post-menopausal female	1	0
Presence of hyperthyroidism at initial diagnosis	1	0
Pre-operative calcium <8 mg%(Range:8.4-10.2mg%)	1	0
Pre-operative Vit D <20ng/ml (<15ng/mL=severe deficiency)	1	0
Serum iPTH at 8 hours <10 pg/mL (range:13-88.2 pg/ml)	1	0
Post-operative calcium <7.5 mg% at 12 hours	1	0
Number of parathyroid preserved (n≤2)	1	0
Pre-operative nodule size ≥ 4 cm	1	0
Total score	08	

Table 2: Showing demographic data of Study population

Variable		Without post operative hypocalcimia (Group A: n=35)	With post operative CSH (Group B:n=15)	P value
Age (years)		35.37± 4.466	35.93 ± 9.04	0.769*
Sex	Male	14.28%(n=5)	20%(n=3)	0.452**
	Female	85.71%(n=30)	80%(n=12)	
Nodule size(cms)		3.30±0.354	4.16±0.792	0.000*

*Independent sample T test, **Chi square test

Table 3: Predictive power of the hypocalcemia score

Hypocalcemia score	Group A(n=35)	Group B(n=15)	Sensitivity(95% CI)	Specificity(95% CI)	PPV(95% CI)	NPV(95% CI)
>4	Nil	08	0.53(0.40-0.68)	0.971(0.95-.99)	0.99(0.83-0.99)	0.82(0.76-0.89)
>3	06	13	0.866(0.78-0.96)	0.828(0.75-0.9)	0.684(0.59-0.82)	0.93(0.89-0.98)
>2	19	15	0.989(0.9-0.99)	0.45(0.36-0.55)	0.44(0.35-0.54)	0.989(0.9-0.99)
>1	29	15	0.989(0.9-0.99)	0.17(0.10-0.24)	0.34(0.26-0.42)	0.98(0.76-0.99)

Figure 1: Showing Trousseau Sign