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HYPOMAGNESEMIA PREDICTS POSTOPERATIVE BIOCHEMICAL HYPOCALCEMIA AFTER THYROIDECTOMY

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ABSTRACT

Postoperative hypocalcemia is a common complication of total or completion thyroidectomy. P ostoperative hypocalcemia is a well-recognized complication after thyroidectomy, of which reportedly, prevalence ranges from 10% to 83% . magnesium is a crucial element in human metabolism pathway, acting as cofactor in enzymatic reaction. To investigate the role of magnesium in biochemical and symptomatic hypocalcemia, a retrospective study was conducted. For the safety of patients, the possibility of both symptomatic and biochemical hypocalcemia should be considered together before deciding early discharge. Using intact PTH for symptomatic hypocalcemia and day-1 ionized serum calcium level for biochemical hypocalcemia will be helpful for the reliable prediction of heterogeneous nature of postoperative hypocalcemia. Proper surgical techniques and identification of the parathyroid glands is important in preventing hypocalcemia after total thyroidectomy. Additionally, for predicting hypocalcemia the relative and not absolute PTH levels should be more emphasized.

Key words Hypocalcemia, Hypomagnesemia, Relative decline of iPTH, hypoparathyroidism.

INTRODUCTION

Postoperative hypocalcemia is a common complication of total or completion thyroidectomy [1, 2]. Postoperative hypocalcemia is a well-recognized complication after thyroidectomy, of which reportedly, prevalence ranges from 10% to 83% [1–7]. magnesium is a crucial element in human metabolism pathway, acting as cofactor in enzymatic reaction [8]. Reportedly, magnesium could affect calcium level via modulating PTH secretion and PTH receptor sensitivity, as well as calcium excretion in kidney [9, 10].Post-thyroidectomy hypomagnesemia has been approved to reduce the production of PTH, decrease the affinity of PTH receptor and production of vitamin D, all of which may lead to hypocalcemia [10]. So we guess magnesium will affect calcium level after thyroidectomy. Previously, a few researchers have investigated the association between magnesium and calcium level and hypothyroidism after thyroidectomy [3, 4]. But all of them had small recruitment in retro/prospective study. Moreover, literature about the effect of hypomagnesemia is limited. Therefore, value of magnesium in prediction and treatment of hypocalcemia was underestimated now. An abrupt fall in magnesium concentration leads to a reduction in the production and release of parathyroid hormone (PTH) and secondarily exacerbates the clinical manifestations of hypocalcemia. Therefore, hypocalcemic patients with hypomagnesemia will present with relative hypoparathyroidism.[11] Plasma calcium correction without concurrent normalization of magnesium may prolong the clinical manifestations.[12].Early postoperative PTH and calcium based protocols are used to guide management with calcium and/or vitamin D supplementation and subsequent weaning in many centres. Our study aim is to explore the relationship between hypomagnesemia and biochemical hypocalcemia and symptomatic hypocalcemia in the present study and to evaluate the association of hypomagnesemia with hypocalcemia after thyroidectomy.

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MATERIAL AND METHODS:

Patients who underwent thyroidectomy (total [TTx] and completion thyroidectomy [CT]) were included in the retrospective study. And preoperative and postoperative data about calcium, magnesium and PTH was extracted from the database. Exclusion criteria were lobectomy and near TTx, or any disease which would affect the level of calcium and magnesium, or patients with preoperative hyper/hypocalcemia/magnesemia. Blood was collected and tested in 6 AM in the1st postoperative Morning postoperative calcium, magnesium and iPTH was recorded. Then normal calcemic patients without any discomfort were discharged in 1st or 2nd postoperative day. The other patients were prescribed with oral calcium and/or vitamin D supplementation on case-by-case basis. Generally, whether supply with calcium and/or vitamin D was decided by the hypocalcemic symptom or biochemical hypocalcemia. Hypocalcemia means below the reference, reference: magnesium 0.67–1.04 mmol/L, calcium 2.1–2.7 mmol/L and Ipth 1.6–6.9 pmol/L.SxH means specific numbness, spasm, muscular cramp and Chevok's syndrome et al. led by hypocalcemia. Patients were followed up rigorously at outpatient department, andbegin from the end of 1st month after discharge. In terms of patients administrated with calcium and/or vitamin D were followed every month after discharge until 6 months, then 6 months thereafter. Or they were followed 1, 3, 6 month(s) after discharge until 6 months, then 6months thereafter.

Statistical analysis:

P value <0.05 indicated significant difference. Data analysis was performed by SPSS 11.5 version (SPSS Inc., Chicago,). If normal distributed, continuous variables were presented as the mean ±standard deviation and compared by t-test; if not, variables were presented as median and compared by Mann Whitney U-test. Pearson Chi-square test or Fisher's exact test was used to compare frequency (percentage) for categorical variables. Logistic regression was used to determine the risk factor

RESULTS:

Table 1: Basic Characteristics of Patients Enrolled

Age	41.51 ± 11.42
Sex (Male/Female)	25/75
Preoperative magnesium	0.96 ± 0.11
Postoperative magnesium	0.72 ± 0.072
Preoperative calcium	2.20 ± 0.11
Postoperative calcium	2.15 ± 0.13
Preoperative iPTH	5.41 ± 2.01
Postoperative iPTH	2.22 ± 1.33

Table 2: Baseline comparison between biochemical hypocalcemia and eucalcemia patients

	Hypocalcemia (82)	**Normocalcemia**	**P Value**
Age (> 45/< 45)	11/16	23/50	0.276
Sex (male/female)	06/21	23/50	0.01
Po hypomagnesemia	12/15	18/55	0.007
Po hyperphosphatemia	13/14	30/43	0.140
Po iPTH< 1.6 pmol/L	10/17	35/38	0.055

Table 3: Risk factor identification of biochemical hypocalcemia

	Univariate		**Multivariate**		
	OR	**P value**	**OR**	**95 % CI**	**CI P Value**
Age (>45/<45)	1.348	0.246	2.147	1.125,4.101	0.020
Sex (Male/Female)	0.448	0.011	2.031	1.144,3.591	0.015
Po hypomagnesemia	2.148	0.0008			
Po hypophosphatemia	1.490	0.118			
Po iPTH<1.6 pmol/L	1.660	0.050			

Table 4: Risk factor identification of symptomatic hypocalcemia

	Univariate		**Multivariate**		
	OR	**P value**	**OR**	**95 % CI**	**CI P Value**
Age (>45/<45)	0.762	0.490			
Sex (Male/Female)	1.837	0.164			
Po hypocalsemia	2.441	0.011	2.216	1.012,4.875	0.045
Po hypomagnesemia	1.230	0.531			
Po hypophosphatemia	2.684	0.041	1.370	0.971,2.010	0.216
Po iPTH<1.6 pmol/L	4.941	0.001	1.190	0.895,1.900	0.126

Discussion:

Hypocalcemia is defined as a serum total calcium of <8.5 mg/dl.[13] Life threatening complications can develop if serum calcium levels fall below 7 mg/dl. Hypocalcemia is one of the complications after total thyroidectomy. Transient hypocalcemia occurs in up to 50% of patients and permanent hypocalcemia in 2%.[14]

The suspect nodule and the follicular adenoma are usually treated with partial thyroidectomy; therefore, the incidence of hypocalcemia was lower. However, our study shows that occurrence of hypocalcemia is independent of diagnosis and type of surgery done. The study shows that 30% of patients developed both hypocalcemia and hypomagnesemia with biochemical value S. Ca <8.5 and S. Mg <1.7. About 24% of patients developeds ymptoms of both hypocalcemia and hypomagnesemia. Magnesium is an essential cofactor of >300 enzymes. It also acts as a calcium channel antagonist and plays a key role in the modulation of any activity involving calcium, such as muscle contraction and insulin release.[13] Temporary hypoparathyroidism leads to a reduction into renal reabsorption of magnesium, and expansion of the extracellular volume increases magnesium excretion. Magnesium deficiency reduces the PTH effect in the kidneys and bones and increases its degradation in the liver and kidneys.[15]

As we know, the relation between calcium and magnesium metabolism is complicated. Magnesium deficiency is associated with impaired secretion and affinity of PTH. Magnesium may compete with calcium, and play a mimic effect on the parathyroid cell. The “calcium” receptor stimulates secretion of PTH in the presence of elevated level of calcium. However, when hypomagnesemia, calcemic ions are relative much more than usual, secretion of PTH is inhibited. Rude et al. suggested that intravenous injection of magnesium solution, when hypocalcemia secondary to hypomagnesemia, secretion of PTH would increase dramatically in 1 min after administration [13].

The relation between calcium and magnesium metabolism is a complex one and relates mainly to the interaction of these cations with PTH. There lacks an illustration of continuing change of magnesium, calcium and iPTH, blood only was collected in the 1st morning after surgery. We believe it would be interesting to observe the change of electrolyte and iPTH in days after surgery. And we will investigate whether correction of hypomagnesemia could alleviate hypocalcemia, including symptoms in further prospective studies. Finally, we did not take the impact of proton pump inhibitor (PPI) on hypocalcemia and hypomagnesemia post-thyroidectomy. Several cases and researches found the potential link between chronic use of PPI and hypomagnesemia in small proportion of patients, though mechanism is not well-recognized [16-18].

A prospective database about thyroidectomy patients is maintained, though it is a retrospective study. It records the symptoms and biochemical data prospectively. Besides, all of less than to al thyroidectomy is excluded from the final analysis. And all of operations were performed by one surgeon. Additionally, data integrity is well in our study, every patient had perioperative data about electrolyte and iPTH. It was found that both magnesium and calcium were associated with symptoms. This demonstrates that hypomagnesemia may well contribute to postoperative tetany after total thyroidectomy, especially with concomitant hypocalcemia.

Magnesium may compete with calcium, and play amimic effect on the parathyroid cell. The “calcium” receptor stimulates secretion of PTH in the presence of elevated level of calcium. However, when hypomagnesemia, calcemicions are relative much more than usual, secretion of PTH is inhibited. Rude et al. suggested that intravenous injection of magnesium solution, when hypocalcemia secondary to hypomagnesemia, secretion of PTH would increase dramatically in 1 min after administration [19]. While, postoperative iPTH in eumagnesemia patients was lower than that in hypomagnesemia patients significantly in the present study. Clinically, limited literature had investigated the role of hypomagnesemia after thyroidectomy. Wilson et al. reported that hypomagnesemia indeed had a significant relation with hypocalcemia in a prospective study in a series of 50 patients with total thyroidectomy[20] and Hammerstad et al. suggested that decreasing degree of magnesium level in 48 h after operation may predict development of permanent hypoparathyroidism combined with preoperative serum calcium and postoperative PTH [21]. In our present study, we also found that the significant relation between hypomagnesemia and hypocalcemia. Being different from the Cherian's research, in which the prevalence of hypomagnesemia pre/post-thyroidectomy was about24% and70% respectively, only 23.36% patients developed hypomagnesemia after surgery, and no patient had hypomagnesemia [22]. The obvious statistic gap may attribute tothe totally different environment and dietary habit. In addition, gender (female) was proved to be an independent risk factor for hypocalcemia in the present study.

A consensus was nearly reached that it would be more reasonable to take the baseline function of parathyroidinto consideration, rather than the absolute number. Additionally, here lacks an illustration of continuing change of magnesium, calcium and iPTH, blood only was collected in the 1st morning after surgery [23]. We believe it would be interesting to observe the change of electrolyte and iPTH in days after surgery. And we will investigate whether correction of hypomagnesemia could alleviate hypocalcemia, including symptomsin further prospective studies. Symptoms and biochemical data prospectively. Besides, all of less than to al thyroidectomy. Is excluded from the final analysis. And all

of operations were performed by one surgeon. Additionally, data integrity is well in our study, every patient had perioperative data about electrolyte and iPTH (24-27).

Conclusion

Hypomagnesemia is not a rare complication successive to thyroidectomy. There is an association of hypomagnesemia with hypocalcemia after thyroidectomy. Some patients show symptomatic hypomagnesemia and hypocalcemia. Hence, if a patient had persistent symptoms postoperatively, then iv/oral magnesium supplementation can be given as a partin the management of hypocalcemia with hypomagnesemia. Hypomagnesemia, which proved to be independent risk factor for biochemical hypocalcemia in the study, other than the variable sex. And relative decline of iPTH, outweighed absolute value of iPTH and magnesium, was identified to be risk factor of symptomatic hypocalcemia.

Risk factors for the occurrence of PoSH may be classified as modifiable or treatable (such as Vitamin D deficiency orhypomagnesemia) or non-modifiable (such as postoperative PTH level or Graves' disease). A more accurate understanding of risk at tributable to individual risk factors would help in a better prediction of risk of PoSH and this can be factored into the discussions regarding the risks and benefits of surgery. a reliable predictor for biochemical hypocalcemia. Using both iPTH and postoperative iCa++levels will increase the diagnostic accuracy for the early and reliable prediction of postoperative hypocalcemia. Hypomagnesemia is not a rare complication successive to thyroidectomy. To be independent risk factor for biochemical hypocalcemia in the study, other than the variable sex. And relative decline of iPTH, out weighed absolute value of iPTH and magnesium, was identified to be risk factor of symptomatic hypocalcemia.

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