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ROLE OF RED CELL CALCIUM AND MAGNESIUM IN THYROID FUNCTION

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ABSTRACT

Many previous studies have established the role of metal ions like calcium (Ca) and magnesium (Mg) in controlling the thyroid hormones production as well as metabolism and hence an association may exist between thyroid hormones and the above two metals. Although many studies have been done to evaluate the role of the two principle macrometals calcium and magnesium, but all the studies were based on plasma levels of these metals which are variable. Very few studies have been done to find out the red cell content of these two metals in a variety of clinical conditions associated with altered thyroid function. The main aim of this study is an attempt to find out the association of red cell Ca and Mg to the principle thyroid hormones TSH, FT4 and FT3. Very Good correlations were observed between red cell Ca and Mg to TSH and FT4 indicating that both TSH and FT4 are indeed Ca and Mg dependent suggesting the role of both red cell Ca & Mg in regulating thyroid function. More studies are required to establish the role of red cell Ca & Mg to evaluate all types of thyroid diseases.

KEYWORDS: Ca, Mg, FT4, FT3, TSH, Cell Ca, Cell Mg.

INTRODUCTION

Ca and Mg belong to a group of parasympathetic elements that exhibit anti inflammatory or degenerative properties at higher amounts, Just as the human body needs adequate amounts

of water and air for survival it also needs minerals or it will die. Ca and Mg are extremely important minerals that are often out of balance in persons with thyroid diseases. Thyroid function is controlled by these macro metals. The objective of this study is find out the role of red cell macro metals Ca and Mg in thyroid function.

Calcium carbonate, the most recommended form of calcium supplement can interfere with thyroid medication, since Ca can prevent the absorption of thyroxin. Taking thyroid supplements for hypothyrodisim in the morning and Ca supplements at night may prevent problem like osteoporosis.[1] Thyroid diseases have widespread systemic manifestations including their effect on bone metabolism. On one hand, the effects of thyrotoxicosis including subclinical disease have received wide attention from researchers over the last century as an important cause of secondary osteoporosis. On the other hand, hypothyroidism has received lesser attention as its effect on bone mineral metabolism is minimal.[2]

Basal Erythrocyte Ca^{2+}-ATPase enzyme activity was significantly increased in the hyperthyroid group and decreased in the hypothyroid group. *In vitro* responsiveness of the enzyme to calmodulin, the activator protein for Ca^{2+}- TPase, was decreased in both hyper- and hypothyroid.[3] Thyroid hormone augments transsarcolemmal Ca influx, at least in part via slow Ca channels associated with increased numbers of these channels. T3-treated cells appear to be more responsive to the effects of BAY k 8644 or isoproterenol on [Ca]i.[4] In L-thyroxine-induced hyperthyroidism condition, it shows a significant decrease in erythrocyte Ca, Mg, and Zn concentrations, and a significant decrease in plasma Mg concentration. Significant positive correlations were found for Mg and Zn both in plasma and in erythrocytes, suggesting that the homeostasis of Ca, Mg, and Zn is altered during experimental hyperthyroidism.[5]

Plasma and red cell Mg concentrations were low in half of the hyperthyroid subjects, but mean values were not significantly different from controls. Urinary excretion and clearance of Mg were lower in hypothyroid subjects, but differences were removed when expressed relative to Chromium (Cr) excretion and clearance.[6] Peripheral thyroid hormone metabolism is altered in Mg deficiency, but this effect is dependent on the age at which the deficiency occurs.[7]

The mean Triiodothyronine (T3) and serum Thyroid Stimulating Hormone (TSH) levels in cases were found to be significantly different from the control group. Patients in both groups had serum Mg level more than 2 mg/dL with no significant difference. There was a significant association between type I diabetes and serum TSH and T3 and hence assessment of thyroid hormones in diabetic children is recommended.[8] Plasma Magnesium (P-Mg) was significantly lower in hyperthyroid patients than in euthyroid or hypothyroid individuals. Erythrocyte Magnesium (E-Mg) was significantly higher in hypothyroid patients than in hyperthyroid or euthyroid individuals. In the entire series of 84 subjects, both P-Mg and E-Mg showed significant negative correlations with thyroidhormone levels, but the correlations were greater in P-Mg than E-Mg. In hyperthyroid patients, both P-Mg and E-Mg were negatively correlated with the duration of illness, but this correlation was greater in E-Mg than P-Mg. Also, both P-Mg and E-Mg were significantly higher in patients with destructive thyroiditis with a short duration of half a month such as subacute or painless thyroiditis than in patients with Graves' disease (5 months). These results suggest that Mg metabolism in thyroid dysfunction is affected not only by thyroid hormone levels but also by the duration of illness.[9]

Mg increases Free Triiodothyronine (FT3) values and reduces Total Triiodo Thyronine (TT3) values in all groups. After supplementation, sedentars receiving 10 mg/Kg/day had higher Thyroxine (T4) values than sedentars and control subjects practicing sports but receiving Mg supplement and the sportsperson receiving Mg supplement for 90-120 min/day had higher T4 values than the third group. Results of this research show that training until exhaustion causes reduction in thyroid hormone activity in sedentars and sportsperson. It has been established that Mg supplementation however, prevents reduction in thyroid hormone activity in sedentars and sportsperson.[10] There was no significant difference in ionized or total serum Mg concentration between the 2 groups, but there was a significant difference in the ratio of ionized to total serum Mg concentrations between the healthy cats and the hyperthyroid cats with T4 concentrations at or above the median. There was a significant correlation between the ionized and total Mg concentrations in the hyperthyroid cats. The hyperthyroid cats had a significantly lower total serum protein concentration than the healthy cats. A significant negative correlation was detected between Mg and logarithmically transformed T4 concentrations in the hyperthyroid cats, which suggests that the severity of hyperthyroidism may contribute to a decrease in the Mg concentration.[11]

Parameters of bone turnover showed a decrease when hyperthyroid patients became euthyroid: serum Ca, acid phosphatase, alkaline phosphatase, the Ca/creatinine ratio and the hydroxyproline/creatinine ratio in the urine. These parameters showed an increase when hypothyroid patients became euthyroid: serum Ca, alkaline phosphatase and the hydroxyproline/creatinine ratio in the urine. Changes in the Ca regulating hormones, parathyroid hormone, calcitonin and vitamin D metabolites were not observed when hyperthyroid patients became euthyroid. When hypothyroid patients were treated a decrease in serum levels of 1.25-dihydroxyvitamin D was observed. Serum growth hormone levels decreased when hypothyroid patients became euthyroid. An additional factor could be somatomedin, that might also be involved in changes in bone turnover in hyper- and hypothyroidism.[12]

Increased thyroid activity causes more Mg to be consumed by the tissue, thus favoring hypomagnesaemia. T4 diminishes Mg content in serum, but Mg content of the ratio containing the high dosage of T4 is increased and its effect is cancelled and Mg content of the serum is more or less to normal.[13] Serum T4 response to TRH challenge was reduced in Mg deficient due to an impaired T4 synthesis or release in Mg deficient rats.[14]

MATERIALS AND METHODS

50 patients in the age group of 17-70 years consisting of males and female were selected for this study. All 50 patients who attended the Master Health Checkup and who were investigated for Thyroid function (FT3, FT4 and TSH) were included for the study. The main aim of this study was to find out the role of red cell Ca and Mg in thyroid function.

Diuri CS 1300 B fully automatic analyser and Dialab reagents were used to measure Ca and Mg and Siemens Advia Centaur CP fully automatic analyser and their reagents were used to analyse FT4, FT3 & TSH. The accuracy of all analytes were validated by the use of Bio-Rad accuracy controls at two levels for Ca & Mg and trilevel for thyroid hormones.

Inclusion Criteria

Patients who attended Endocrinology Clinic and who were investigated for Thyroid function tests and routine Master Health Checkup patients who were investigated for the analytes used in this study were included.

Exclusion Criteria

Patients who attended Endocrinology Clinic and Master Health Checkup and who were not investigated for thyroid function tests were excluded.

Preparation and Analysis of Haemolysate for red cell Ca and Mg measurements

1) Centrifuge the EDTA blood sample at 2500 rpm at 5 minutes.
2) Separate the plasma and buffy coat completely with the use of a teat pipette.
3) Wash the blood cells with 0.9% ice cold sodium chloride. Mix well and centrifuge at 2500 rpm.
4) Repeat the above washing procedures two times. Finally remove the supernatant completely and to the washed cells add equal volume of deionized water to lyse the cells.
5) Store it at -5^0C for overnight.
6) Bring the lysed cells to room temperature.
7) Add 0.2 mL of haemolysate to 0.8 mL of 3% Tri-Chloroacetic Acid (TCA).
8) Mix well and leave for 5 minutes.
9) Centrifuge at 2500 rpm and collect the filtrate to analyse red cell Ca and Mg.
10) Ca was measured using Arsenazo III dye binding and Mg by Xylidyl blue dye binding.

For Statistical analysis of data, a software downloaded from the website http:// www.graphpadqucikcalcs.com was used to calculate Student 't' distribution (t) and probability (p) between analytes.

Table I. Mean & SD for all study groups n=50.

		TSH	FT4	FT3	CELL.Ca	CELL.Mg
All patients n=50	Mean	6.73	1.19	256.42	1.72	3.65
	SD	19.25	0.26	74.61	0.81	1.89
Males n=18	Mean	2.74	1.27	270.06	1.97	3.79
	SD	2.28	0.25	67.94	0.75	2.39
Females n=32	Mean	12.29	1.11	252.71	1.44	3.78
	SD	23.86	0.25	78.1	0.82	1.58

Table I shows the Mean & SD for all the patients studied. An observation of this Table gives a rough idea about the correlation that may be predicted from the difference in mean values of the metals and hormones.

Table II. Statistical Parameters (t & P): for the study group.

	Analytes compared	t	P
All Patients (n=50)	C.Ca VS TSH	1.8387	0.0690
	C.Ca Vs FT4	4.4054	<0.0001
	C.Ca Vs FT3	24.1374	<0.0001
	C.Mg Vs TSH	1.1260	0.2629
	C.Mg Vs FT4	9.1177	<0.0001
	C.Mg Vs FT3	23.948	<0.0001
All Males (n=18)	C.Ca VS TSH	1.3611	0.1824
	C.Ca Vs FT4	3.7566	<0.0001
	C.Ca Vs FT3	16.7404	<0.0001
	C.Mg Vs TSH	1.3487	0.1864
	C.Mg Vs FT4	4.4491	<0.0001
	C.Mg Vs FT3	16.6175	<0.0001
All Females (n=32)	C.Ca VS TSH	2.5709	<0.05
	C.Ca Vs FT4	2.1776	<0.05
	C.Ca Vs FT3	18.1987	<0.0001
	C.Mg Vs TSH	2.0132	<0.05
	C.Mg Vs FT4	9.4419	<0.0001
	C.Mg Vs FT3	18.0265	<0.0001

Ca = Cell Calcium, C.Mg = Cell Magnesium

Table II presents the statistical parameters viz t and p between individual cell content of the metals and the hormones. In the case of all patients a highly significant correlations were observed between cell content of Ca & Mg to both FT4and FT3, and only a moderate significance was see between cell Ca and TSH.

In Males, both C.Ca & C.Mg shows highly significant correlations to both FT4 & FT3, while TSH does not show any correlation. In Females, C.Ca shows a moderate association to both TSH and FT4and a highly significant association to FT3. C.Mg shows a moderate association to TSH, but highly significant association to both FT4 & FT3.

DISCUSSION

As already stated in the abstract, studies linking red cell macrometals to thyroid hormones are scares. Only few studies have been done. A study done in 1989 has found an association of red cell Mg in patients with hyperthyroid induced by thyroxin supplements and our study has linked both red cell Ca & Mg to the three principle thyroid hormones TSH, FT4 & FT3.[5] Many studies carried out previously have linked only plasma levels and predicted low values of these two metals in hyperthyroidism but no association was found between plasma levels

of Ca & Mg to thyroid hormones.[6,7] Our study has established that red cell content of both Ca & Mg may be very useful compared to plasma level to evaluate the role of these two metals to study the functions of thyroid gland and its hormones.

CONCLUSION

The outcome of this study strongly suggests that both the macro metals Ca & Mg may play a significant role in the functioning of thyroid gland and that there exists an inverse correlation between the thyroid hormones TSH, FT4 & FT3 to both cell Ca & Mg. Further studies with a large number of population are to be done to recommend the measurement of red cell Ca & Mg for augmenting the diagnosis of thyroid disorders and to suggests their supplementation. Further, routine measurement of these two macro metals in erythrocyte may be included along with thyroid profile tests.

CONFLICT OF INTEREST: None

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REFERENCE

1. Don’t take Calcium and thyroid mestogether. JAMA, 2000; 21(283): 2822-2825.
2. Dinesh Kumar Dhanwal. Thyroid disorders and bone mineral metabolism. Indian J Endocrinol Metab, 2011; 15(2): S107–S112.
3. Marjory P. Dube, Faith B. Davis, Paul J. Davis, Marion Schoenl, and Susan D. Blas. Effects of Hyperthyroidism and Hypothyroidism on Human Red Blood Cell Ca^{2+}-ATPase Activity. The Journal of Clinical Endocrinology & Metabolism, February 1986; 62(2): 253.
4. D Kim, T W Smith, and J D Marsh. Effect of thyroid hormone on slow calcium channel function in cultured chick ventricular cells. J Clin Invest, 1987; 80(1): 88–94.
5. Gönül Simsek, Gülnur Andican, Ethem Ünal, Hüsrev Hatemi, Günnur Yigit, Gülden Candan. Calcium, magnesium, and zinc status in experimental hyperthyroidism. Biological Trace Element Research, May 1997; 57(2): 131-137.

6. Dolev E, Deuster PA, Solomon B, Trostmann UH, Wartofsky L, Burman KD. Alterations in magnesium and zinc metabolism in thyroid disease. Metabolism, 1988; 37(1): 61-7.
7. Mahoney CP, Alster FA, Carew LB Jr. Growth, thyroid function, and serum macromineral levels in magnesium-deficient chicks. Poult Sci., 1992; 71(10): 1669-79.
8. Derakhshan R, Balaee P, Darakhshan S, Masoodpoor N, Banihosseini SS. Lipid profile, thyroid function, and serum magnesium level in type I diabetic children. Minerva Pediatr, 2011; 63(1): 27-33.
9. Shibutani Y, Yokota T, Iijima S, Fujioka A, Katsuno S, Sakamoto K.Plasma and erythrocyte magnesium concentrations in thyroid disease: relation to thyroid function and the duration of illness. Jpn J Med., 1989; 28(4): 496-502.
10. Cinar V.The effects of magnesium supplementation on thyroid hormones of sedentars and Tae-Kwon-Do sportsperson at resting and exhaustion. Neuro Endocrinol Lett., 2007; 28(5): 708-12.
11. Cornelia V. Gilroy, Barbara S. Horney, Shelley A. Burton, and Allan L. MacKenzie. Evaluation of ionized and total serum magnesium concentrations in hyperthyroid cats. Can J Vet Res. 2006; 70(2): 137–142.
12. Bijlsma JW, Duursma SA, Roelofs JM, der Kinderen PJ.Thyroid function and bone turnover. Acta Endocrinol (Copenh), 1983; 104(1): 42-9.
13. S. Swaminathan1, G. Priya and Mitra Ghosh. Association Between Thyroid Hormones And Macro Metals Calcium And Magnesium. JPBMS, 2010; 4: 17.
14. Mecafffrey C, Quamme,G A : Effects of thyroid status on renal Calcium and Magnesium handling. Can J Comp Meed, 1984: 1: 51-57.