Original Research Article

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A clinical study of free T3 in breast cancer and benign breast tumours

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ABSTRACT

Background: The aim of the study was to evaluate the presence of Free T3 in women with breast cancer or benign breast tumours, and to analyse a possible relationship between FT3 and these two groups of breast diseases with emphasis to laboratory findings.

Methods: Free T3 levels of 87 women hospitalized were prospectively analyzed, using an Post hoc Tukey HSD for normally distributed continuous data, chi-square test for comparison.

Results: There was no significant association of Free T3 levels in breast cancer and benign breast tumours.

Conclusions: The association between free T3 and breast tumors was evaluated in this study. Free T3 values were not statistically significant in patients with breast cancer and benign breast tumors depicting there is no association of Free T3 and risk of breast carcinoma. However, these data must be confirmed in large patient cohorts and long duration follow-up.

Keywords: Breast carcinoma, Chemiluminescence immune assay, Free T3

INTRODUCTION

Breast carcinoma is caused by interactions of both inherited and environment risk factors that lead to progressive accumulation of genetic and epigenetic changes in tumor suppressor genes of breast epithelial Breast carcinoma and thyroid predominantly affects females and both have a postmenopausal peak incidence resulted in a search for an association between the two diseases.2 High affinity binding sites for 3-3-5 triiodothyronine (T3) have been identified in nuclei isolated from human tumours, including those in breast cancer, suggesting that thyroid hormones may play a role in the development of breast cancer at the cellular level.³ Recent studies in human breast cancer cell lines (MCF-7 and MDA-MB-231) have shown proliferative effects of thyroid hormones on breast tissue through the same signal cascade utilized by estrogens involving phosphoinositol 3-kinase (PI3K) and

the mitogen-activated protein kinase (MAPK).⁴ In estrogen receptor positive (ER+) cell lines (MCF-7), T3 mimics estradiol via its binding to ER and induces the expression of progesterone receptor (PR) and growth factor-alpha (TGF- α) mRNAs.⁴ This study was done to measure the levels of freeT3 in patients with breast cancer and benign breast tumors and to understand the role of Free T3 in breast tumors.

METHODS

The study was carried out in Saveetha Medical College and Hospital, Chennai, India. The study included healthy controls (Group 1, n=29), women with benign breast tumours (Group 2, n=29), and women with breast cancer (Group 3, n=29). All patients were without any known thyroid disease, and studied before any radio or chemotherapy. Signed informed consent was obtained

from all participants, allowing analysis of all clinical and laboratory data mentioned in this paper.

Serum free tri-iodothyronine levels (FT3), were determined in breast cancer patients, benign breast tumours and controls based on chemiluminescence immune assay designed for quantitative measurement of free T3 levels in serum. The normal ranges were 2-4.4pg/ml for free T3. Those women without any breast or thyroid disease were the control group. The clinical and laboratory details of 87 women hospitalized were prospectively analysed, using a post hoc Tukey HSD for normally distributed continuous data, chi-square test for comparison.

RESULTS

A total number of 87 patients were included in this study. Out of this, 29 women were healthy controls, 29 women with benign breast tumours and 29 women with breast cancers. The age of the patients ranged from 20 years to 92 years. All patients were without any known thyroid disease are studied. Serum free T3 were determined in healthy controls, women with benign breast tumours and breast cancer (Table 1).

Table 1: Parameters of the study population.

Parameter	Controls (group 1)	Benign tumours (group II)	Breast cancer (group III)	P- value		
Mean±SD						
FT3 (2-4.4 pg/ml)	3.06±0.82	3.29±0.41	3.01±0.61	0.206 (NS)		

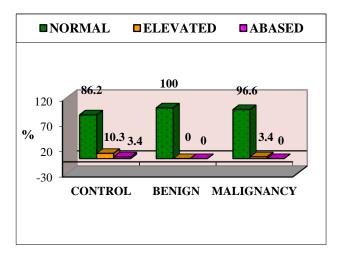


Figure 1: Comparison between free T3 and group.

Those women without any breast or thyroid disease were the control group. Out of these 29 patients in control group, 3 had elevated serum free T3 levels and 1 had abased value of serum free T3 level. Among the 29 patients with benign breast tumours there was no elevation of serum free T3 levels (Table 2), (Figure 1), which indicated no association of Free T3 with benign

breast tumours. Out of 29 patients with breast cancer, 1 had elevated serum free T3 level, which indicated Free T3 levels in breast cancer was not statistically significant.

Table 2: FT3 levels within study population.

Groups	Control group	Benign tumours	Breast cancer	Total
Normal	25	29	28	82
range	(86.2%)	(100.0%)	(96.6%)	(94.3%)
Elevated	3 (10.3%)	0(0.0%)	1(3.4%)	4(4.6%)
Abased	1(3.4%)	0 (0.0%)	0(0.0%)	1(1.1%)
Total	29	29	29	87
	(100.0%)	(100.0%)	(100.0%)	(100.0%)

DISCUSSION

Thyroid hormones are important regulators of growth, development and metabolism in higher animals and humans.5 They act as major physiological regulator of mammalian development through specific effect on the rate of cell differentiation and gene expression.⁶ Thyroid hormones and cognate nuclear receptors are involved in cell growth and differentiation of many cell types.⁷ Free T3 play an important role in the normal development of breast by stimulating ductal branching and alveolar budding.⁸ Growing and developing breasts require the coordinated action of several hormones such as estrogen (E2), progesterone, Fress T3, adrenal steroids, insulin, and prolactin.⁹ The biological activity of thyroid hormones and estradiol are only manifested in cells expressing thyroid hormone and estrogen receptors respectively. These receptors belong to the nuclear receptor superfamily. They share a common mechanism of action whereby hormone-receptor complexes bind to cis acting DNA elements and enhance or repress transcription of target genes. 10 Estrogen is considered to be a potent mitogen for the normal mammary gland, whereas thyroid hormones appear to stimulate lobular development, contributing to the differentiation of normal breast tissue. 11 Consistent with the proposal that thyroid hormones act on the breast, thyroid receptors have been described in breast carcinoma.¹² There are reports on interference between estradiol and thyroid hormones. Studies suggested a cross talk between estrogen receptors and thyroid receptors in neuroendocrine tissues leading to inhibition of estrogenic effects by thyroid hormone.¹³ Excess proliferation of breast epithelial cells is caused by unopposed action of estrogen and various mitogenic growth factors like EGF and IGF, by stimulating the growth factor signalling pathway leading to the development and progression of breast carcinoma. Thyroid hormone, by causing differentiation of breast epithelial cells antagonizes the proliferative effect of estrogen and mitotic growth factors. Thyroid receptors can also alter expression of genes that do not contain a hormone response element through positive or negative interference of other transcription factors and signalling pathways. Increasing evidence shows that loss of

expression and or function of the thyroid hormone receptors could result in a selective advantage for tumor development, as transformed or immortalized cells in general express very low levels of thyroid receptors. Hypothyroidism affects tumor growth and invasiveness differentially.¹⁴ The anti-tumor role Free T3 in liver carcinomas is also supported by the observation that hypothyroidism is a possible risk factor for hepatocellular carcinoma in patients with no known underlying cause of liver disease. 15 We evaluated the association between thyroid dysfunction and breast tumors in this study. The levels of free T3 were not statistically significantly among the breast carcinoma patients and the benign breast tumor patients. The non-significant p-value of FreeT3 between benign breast tumor patients and controls suggest a possibility that the pathogenesis of benign breast neoplasia involves other unidentified mechanism not involving thyroid hormones. Another intriguing possible role in breast carcinogenesis may be ascribed to iodide, based on its protective antioxidant mechanism. This theory has been postulated based on the capacity of breast tissue to transport and concentrate iodide similar to thyroid. Both organs require a method of oxidizing iodide to iodine in order to produce iodoproteins and iodolipids. 16 Iodolipids like 6iodolactones which act via peroxisomal proliferator activator receptors - gamma (PPAR-y) and prevent proliferation of mammary epithelial cells. Cross talk between PPARs and thyroid receptors may also be mediated indirectly by modulating the gene of deiodinase-2 enzyme involved in T3 metabolism.¹⁷

CONCLUSION

The association between free T3 and breast tumors was evaluated in this study. Free T3 values were not statistically significant in patients with breast cancer and benign breast tumors depicting there is no association of Free T3 and risk of breast carcinoma. However, these data must be confirmed in large patient cohorts and long duration follow-up.

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Institutional Ethics Committee

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