

Original Research Article

Effect of Radiotherapy on Thyroid and Parathyroid Gland FunctionsAvinash S¹, Gupta R², Mohindroo NK³, Thakur JS⁴, Azad R⁵¹Department Of ENT, Indira Gandhi Medical College, Shimla, Himachal Pradesh²Department of ENT, Indira Gandhi Medical College, Shimla, Himachal Pradesh³Professor, Department Of ENT, Indira Gandhi Medical College, Shimla, Himachal Pradesh⁴Assistant Professor, Department Of ENT, Indira Gandhi Medical College, Shimla, Himachal Pradesh⁵Department of ENT, Indira Gandhi Medical College, Shimla, Himachal Pradesh***Corresponding author**

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Abstract: Radiotherapy is one of the most important modalities of treatment in cancer of the head and neck region. Collateral damage to surrounding tissues and vital organs is inevitable in radiotherapy. The thyroid and parathyroid gland come within the field of radiation in case of radiotherapy for head and neck cancer. This study aims to evaluate the effect of radiotherapy on the function of thyroid and parathyroid gland. The objective was to study the effect of radiotherapy on thyroid and parathyroid gland functions in head and neck cancer patients. We conducted a one year prospective study taking diagnosed cases of head and neck cancer with radiotherapy as the primary modality of treatment. The evaluation of PTH, thyroid function test and calcium was done prior to the start, immediately after completion and 6 months after completion of radiotherapy. The results were compared thereafter. The study included 25 patients diagnosed with head and neck cancer with radiotherapy as the primary treatment. 76 percent (n=19) were male and rest were female (n=6). Mean age group of the patients was 58.6 years. On evaluating the results obtained, it was noted that there was significant lowering to serum PTH value ($p < 0.05$) but no significant difference was noted in the values of calcium and thyroid function tests ($p > 0.05$). The effect of radiotherapy on the vital organs is a well discussed topic. Even then its effect on the thyroid and parathyroid is understudied. Serum Calcium is likely to remain unaffected as it is regulated by the homeostatic mechanisms by other hormones. Variable response of thyroid hormones during the early phase is well documented. Very little has been studied about the effect of radiotherapy on parathyroid hormone. Our study showed significant effect of radiation on the parathyroid gland functions but not as much on the thyroid functions and calcium levels. Parathyroid hormone levels were found to be decreased after the completion of radiotherapy and further decreased on follow up. The effect on these organs is likely due to the hampering of their blood supply due to damage to the vascularity. To conclude, the collateral effect of radiation is an important factor in the prognosis of the patient. They should be monitored on a regular basis. However, larger studies and longer follow ups to definitively know about the long term effects of radiation on the thyroid and parathyroid glands.

Keywords: radiotherapy, Collateral damage, neck cancer

INTRODUCTION

Head and neck cancers are among the ten most frequent cancers in the world [1]. Laryngeal cancer is a common head and neck cancer with incidence of 12,700 new cases each year [2]. There is a concern that the incidence is increasing particularly in younger patients and in women [3]. In India, head and neck cancer accounts for 23% of all cancers in males and 6% in females [4]. This higher prevalence of head and neck neoplasia in relation to other malignancies in India may

be due to the use of tobacco in various forms, consumption of alcohol and poor oral hygiene resulting from lower education and socioeconomic status [5]. The primary and most influential etiological factor for squamous cell carcinoma is tobacco use and alcohol [6].

Head and neck cancer includes cancer of hypopharynx, larynx, oral cavity, nasopharynx, oropharynx, nose and paranasal sinus, salivary glands, thyroid, and parathyroid glands. Radiotherapy, surgery and

chemotherapy are three main types of treatment modalities for head and neck cancers, and optimal combination of these modalities depends on the site and stage of the cancer. Common adverse effects of radiotherapy to head and neck cancer patients include loss of appetite, nausea, mucositis, candida infections and xerostomia. These are because of effect of irradiation on adjacent normal tissues. Despite various methods used to prevent exposure to vital organs, they are invariably exposed to radiotherapy due to their proximity to the primary or secondary site of cancer.

The effect of neck radiation on thyroid and parathyroid gland function in long term is well documented [7-9]. The present study was done to evaluate the short term effects of radiotherapy on the function of these glands by measuring the levels of thyroid and parathyroid hormones as well as calcium.

MATERIALS AND METHODS

The study was a prospective study conducted in the Department of ENT-HNS, IGMC, and Shimla over a period of one year. We included all new patients diagnosed with head and neck cancer who were treated with radiotherapy as the primary modality of treatment. Patients who underwent any form of surgical intervention (neck dissection, laryngectomy) were excluded from the study. Patients with advanced disease (T4, N3) were also excluded from the study. Patients were abstained from calcium or thyroid hormone supplementation during the study period.

Thyroid function tests (T3, T4 and TSH), serum parathormone (PTH) and serum calcium levels were measured before the start of radiotherapy, after completion of radiotherapy and 6 months after completion of the treatment. The results were analysed by using multivariate ANOVA analysis for calculation of significance.

RESULTS

Study group included 25 patients of age group 50 -76 years (mean age 58.6 years). The study population had 76% males (n=19) and 24 % females (n=6) (table 1). All patients were diagnosed with squamous cell carcinoma except one having the verrucous variety of squamous cell carcinoma. Primary site of tumor was oropharynx in 5, nasopharynx in 1, supraglottis in 9, glottis in 4 and hypopharynx in 6 patients respectively (table 2). Stage of tumor was T1 in 7, T2 in 12 and T3 in 6 patients respectively (table 3). 5 patients who expired during RT or before completion of 2nd follow up were excluded from the final statistical analysis.

We obtained significant fall in the PTH values between the pre radiotherapy (mean= 36.47) and post radiotherapy (mean=21.99) measurements (p = 0.14). However, similar findings were not obtained the values of serum calcium and thyroid hormones. Serum calcium levels were almost maintained during the study period (mean 9.16 →8.86). T3 (mean 1.35 →1.43), T4 (mean 7.23 → 5.77) and TSH (mean 2.02 →2.60) also showed variable responses with no significant fall or rise in the values.

REVIEW OF LITERATURE

Nader S *et al.*; in 1984 [9] analysed the serum calcium levels 2 to 22 years after radiotherapy in 220 patients. Hyperparathyroidism was confirmed at surgery in one patient with hypercalcemia 15 years after radiotherapy. They concluded that patients who have received neck radiation therapy for malignant disease were not at an increased risk for the development of hyperparathyroidism in the first two decades following treatment but they should continue to be screened for this development in subsequent decades.

Cannon CR in 1994 [10] conducted a clinical review of 62 head and neck cancer patients. Within the study group, 10% of patients developed abnormally low thyroxine measurements, whereas 15% developed high thyroid-stimulating hormone levels as the only evidence of early primary hypothyroidism. Hypothyroidism was not statistically related to tumor size, nodal status, clinical staging, or treatment group. He concluded that all patients diagnosed with a head and neck cancer should undergo baseline thyroid function testing, including measurement of TSH (thyroid stimulating hormone) and have serial repeat testing after treatment as hypothyroidism is common occurrence after radiotherapy.

Schneider *et al.*; in 1995 [11] studied the effect of radiation on 2555 patients who had radiotherapy for benign head and neck disease and found an association between radiation exposure and hyperparathyroidism and suggested that the calcium levels of individuals irradiated should be monitored. Mercado G *et al.*; in 2001 [7] studied the effect of radiotherapy on thyroid gland and concluded that incidence of hypothyroidism is generally higher than reported in patients who undergo radiotherapy for head and neck cancer.

Jereczek-Fossa BA *et al.*; in 2004 [12] concluded in their study that radiation induced thyroid sequelae include primary hypothyroidism, thyroiditis, Grave's disease, benign adenomas, multinodular goitre

and radiation-induced thyroid carcinoma. Primary hypothyroidism is the most common and the earliest radiation-induced thyroid dysfunction. Boehm BO *et al.*; in 2011 [13] studied the effect of radiation exposure on parathyroid gland in Chernobyl accident victims. Clinical data obtained 14 years after the accident showed that the radiation exposure had effects on levels of parathyroid hormone (PTH) and that hypercalcemia and nephrolithiasis remained evident. The risk of primary hyperparathyroidism in this cohort of workers was substantial. Elevated PTH levels were associated with stages 1 and 2 of acute radiation syndrome. They concluded that long-term follow-up should be performed in patients exposed to nuclear radiation and that follow-up should include evaluation of the parathyroid, which should be viewed as a radiation-sensitive endocrine organ.

Bakhshandeh M *et al.*; in 2012 [8] did a similar study and evaluated thyroid function and vascular changes during radiotherapy for patients with head and neck cancer. They concluded that radiation-induced thyroiditis is the primary damage to the thyroid gland. Thyroiditis can subsequently result in hypothyroidism or hyperthyroidism. They concluded that vessel changes can be attributed to the late effect of radiation on the thyroid gland.

Sathyapalan T *et al.*; in 2012 [14] studied the effect of radiation on pituitary gland and found that radiotherapy is the most common cause of iatrogenic hypopituitarism. It commonly involves one hypothalamic-pituitary axis; however, multiple hormonal axes deficiency starts developing at higher doses. Jahnukainen K *et al.*; in 2012 [15] conducted a study of the effect of cancer treatment on gonads and concluded that the gonads are at high risk for radiation induced damage. Radiation accelerates the disappearance of primordial follicles of ovaries in women. In men, cells responsible for sperm production are most prone to damage.

Table 1: sex distribution

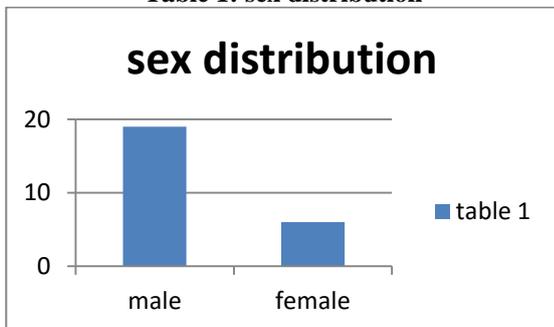


Table 2: sites on involvement

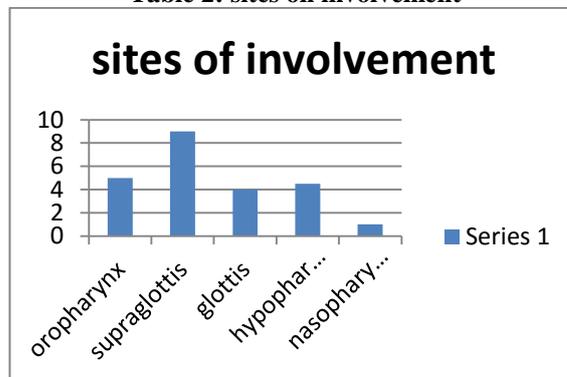


Table-3: Distribution according to T – staging

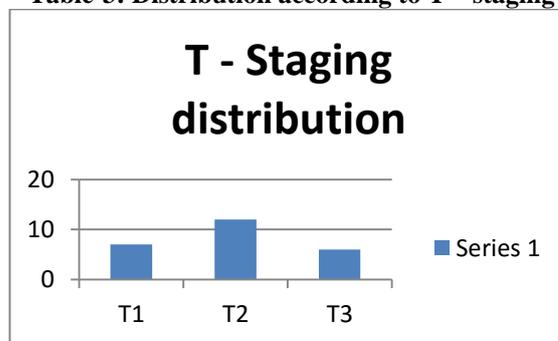


Table 4: effect of radiotherapy on PTH

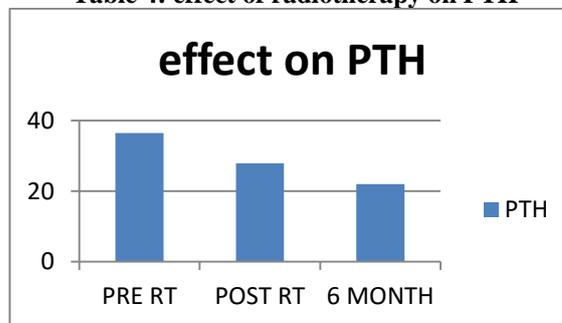


Table 5: effect of radiotherapy on calcium levels

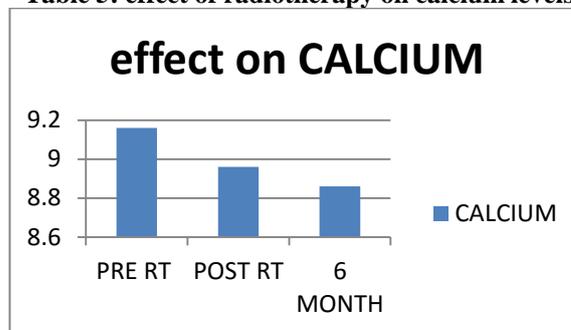


Table 6: effect on radiotherapy on T3 levels

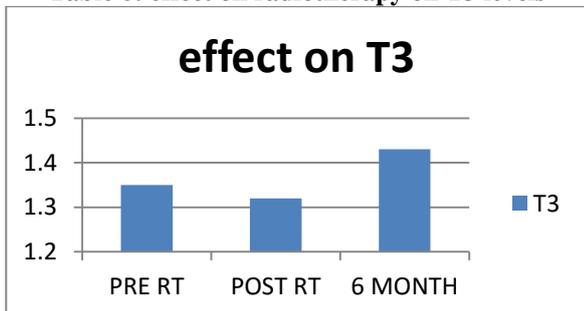


Table 7: Effect of radiotherapy on T4 levels

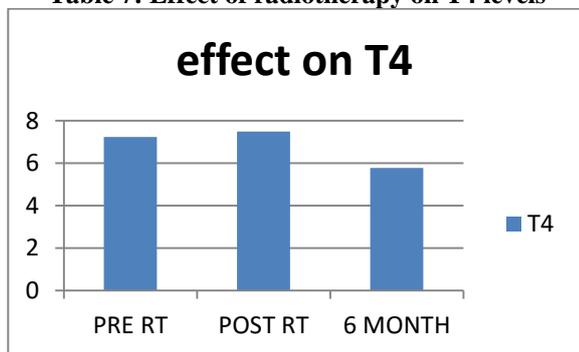


Table 8: effect of radiotherapy on TSH levels

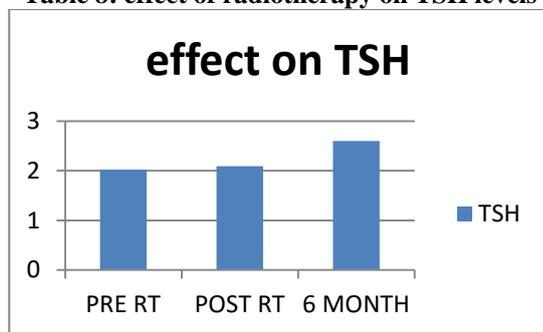
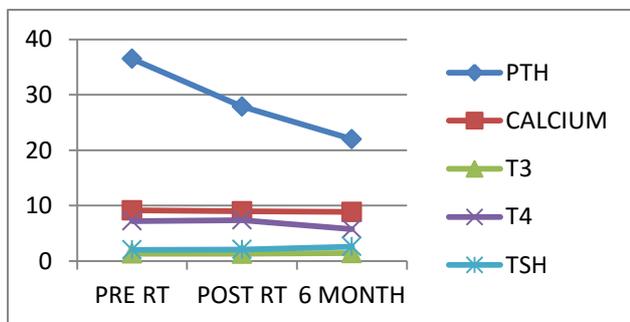


Table 9: consolidated table showing the effects on thyroid and parathyroid function



DISCUSSION

Cancer of the head and neck region is one of the most prevalent diseases in the developing countries like India [5]. Its incidence is on the rise due to consumption of tobacco in its various forms along with alcohol [6]. Early diagnosis and treatment is the key to better survival. Advancement in treatment modalities due to better understanding of the disease process has further improved the long term survival. Radiotherapy has emerged as the treatment of choice in early head and neck cancer due to its role as organ preserving modality. However, its potential for collateral damage has limited its use to a small extent. The effects of radiotherapy on non- tumor cells is a well-researched topic for the same reason. Early signs of mucositis, trismus, dysphagia, xerostomia etc are proven to be due to the damage by the radiation to the non - tumor cells which happen to be in the field of radiation. Thyroid and parathyroid glands also come in the zone of cross fire during the radiation therapy to treat the cancer in head and neck regions.

Previous studies on the parathyroid have demonstrated a long term effect on the gland function by the causation of parathyroid adenomas leading to hyperparathyroidism [9, 11, 13]. However, short term effects of radiation have not been described. In our study, we found a significant fall the levels of parathyroid hormone in the 6 months of follow up after radiation therapy. We suggest the possibility of vascular compromise to the glands due to the effect of radiation to the tissues in the neck. The blood levels of calcium however, did not show any significant fall or rise in the study period despite the fall in PTH levels. This is explained by the calcium homeostasis that is maintained by the hormonal levels of calcitonin and vitamin D which regulate the levels of calcium.

The thyroid hormones showed variable results as has been mentioned in the literature [7, 8, 10, 12]. They can either rise or fall in the early period after radiotherapy depending upon weather the radiation induces decreased vascularity leading to hypothyroidism, or thyroiditis leading to hyperthyroid state. It is regulated by the hypothalamus – pituitary axis.

CONCLUSION:

To conclude, there is a potential for damage to the thyroid and parathyroid gland in the patients undergoing radiation therapy for the treatment of the head and neck cancer as they come within the same radiation field. Thus, the PTH and Thyroid hormone levels must be monitored in the patients undergoing

treatment. Considering the short term follow up and the small study group of this study, further evaluation needs to be done with larger study groups and longer follow ups to conclusively know the effects and formulate a protocol for the same.

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