مقاله تحقیقی

بررسی میزان هیپوتیروئیدی ناشی از رادیوتراپی

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چکیده

امدافت: در این مطالعه میزان اندامگاه‌های هیپوئودیدی در بیماران مبتلا به کنسرهای دندانی و سر درونی که به رادیوتراپی اکسترنال بودند و فیلد رادیوتراپی ناحیه تروئید را شامل می‌شد ارزیابی شد.

روش‌ها: در این مطالعه آینده نگر که از ماه آوریل 2004 تا ماه دسامبر 2005 انجام شده بیماران مبتلا به کنسرهای دندانی و سر درونی که به رادیوتراپی اکسترنال جهت انجام رادیوتراپی ارجاع شده بودند و فیلد رادیوتراپی ناحیه تروئید را هم شامل می‌شد تحت برسی قرار گرفتند. در این بیماران شروع دمادن و ۳ ماه بعد از اتمام رادیوتراپی ارزیابی شد.

یافته‌ها: ۲۳ بیمار تحت ارزیابی قرار گرفتند که سن میانگین ۵۳ سال (32-۶۲) بود. ۱۸ بیمار زن و ۱۶ بیمار مرد بودند. در این بیماران میانگین CGY در محدوده ۶۰۰۰-۴۰۰۰ (۴۰۰۰-۵۰۰۰) تأثیر قابل ملاحظه‌ای در دمادن نداشت. تأثیر قابل ملاحظه‌ای نداشت.

نتیجه‌گیری: براً اساس نتایج بدست‌آمده، هیچ کدام از بیماران علائم هیپوئودیدی در طول مدت شش ماه بعد از اتمام درمان مشاهده نشد. به نظر می‌رسد که مدت زمان ۶ ماه جهت ارزیابی وضعیت هیپوئودیدی در بیماران بیماری‌های هیپوئودیدی را نگیر خواهد داد اما احتمالی ممکن در بیماران معاینه‌ای ضروری می‌باشد.

کلمات کلیدی: هیپوئودیدی، تست های کارکردی تروئید، رادیوتراپی

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Incidence of Hypothyroidism after External Radiation to Thyroid Region

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ABSTRACT

Background: In this study we evaluated the incidence of hypothyroidism in patients who received external beam radiation due to cancer, when radiation portals included thyroid gland.

Methods: This prospective study was conducted from April 2004 to December 2005 among patients with head and neck or breast malignancies who referred to Radiation Oncology Department of Cancer Institute, Imam Khomeini hospital, treated with external beam radiotherapy. All patients received radiation to the thyroid gland. Thyroid function was tested at the beginning of treatment, 3 months and 6 months after the completion of radiotherapy.

Results: In all 34 patients were included in the study. The median age of patients was 53 years. Eighteen patients were female and 16 were male. All patients received external radiotherapy. They received radiation ranging from 5000 cGy (14 patients 41.2%) to 7400 cGy (1 patient 2.9%) with median of 6000 cGy. Physical examination of thyroid at the beginning of treatment was normal and all of the patients were euthyroid. The results from TSH test showed significant difference at baseline, after 3 and 6 months follow-up (P = 0.001).

Conclusion: The findings indicated that none of the patients developed hypothyroidism in a period of six months after completion of radiotherapy. However, it seems that 6 months follow-up is early for judgment about evaluation of patients for hypothyroidism state and it needs further follow up for minimum of 12 months.

Keywords: Hypothyroidism, Thyroid Function Test, Radiotherapy
INTRODUCTION

Carcinoma of head and neck is the 5th most common malignancy worldwide (1) probably because of increased consumption of alcohol and smoking. Surgery, radiotherapy with or without chemotherapy is the mainstream of management relatively radio-resistant due to their low proliferative index, hypo function of thyroid is a known side effect of radiotherapy to the head and neck malignancies over 40 years(3). After external beam radiotherapy to the neck the documented incidence of sub-clinical hypothyroidism varies widely from 0.3% to 44% (4). Addition of surgery to the neck region vastly increases the incidence of hypothyroidism, but addition of chemotherapy probably has little or no effect (5). Hypothyroidism has a significant impact on the quality of life. Thus, assessment of thyroid gland function should be included as part of routine follow-up of patients who undergo radiation to thyroid gland region, prior to expression of frank clinical hypothyroidism, especially in children and senile cases due to their greater morbidity. This study assessed the risk of developing hypothyroidism in head and neck and breast malignancies, where radiation portals included thyroid gland.

METHODS

This prospective study was conducted from April 2004 to December 2005 among a sample of head and neck or breast malignancies with confirmed histopathological diagnosis. Patients referred to Radiation Oncology Department of Cancer Institute, Imam Khomeini hospital and treated with external beam radiotherapy. Before the initiation of the radiotherapy all patients underwent detailed history and physical examination including thyroid gland examination and measurement of T3RU, T4 and TSH. All tests were carried out in the same laboratory. Patients of such malignancies, used either alone or in combination.

In treatment of head and neck cancers target volume of irradiation always includes whole volume of thyroid gland and in breast cancer supraclavicular field always contains a part of thyroid gland. Thyroid gland is one of the major human’s endocrine glands with the average weight of 12-20 grams (2). Although adult thyroid cells are with thyroid metastasis, positive history of thyroid disease and thyroid surgery were excluded. All patients treated with CO 60 with radiation to the primary site and neck including the thyroid gland. Total dose of radiotherapy ranged from 5000 cGY to 7400 cGY in 20 to 37 fractions which was delivered by parallel opposed, mantel, anterior and posterior fields. Those patients who had TSH serum level higher than 4.5 m U/I were considered as sub-clinical hypothyroidism state. Thyroid function tests were repeated at 3 and 6 months follow-up.

RESULTS

In all 34 patients were included in the study. The median age of patients was 53 years, ranging from 22 to 83. Eighteen patients were female and 16 were male.

Patients histopathological characteristics were: adenoid cystic carcinoma (n = 2, 5.8%), adenocarcinoma (n = 5, 14.7%), basal cell carcinoma (n = 1, 2.9%), invasive ductal carcinoma (n = 7, 20.6%), mucin scin carcinoma (n = 1, 2.9%), poorly differentiated carcinoma (n = 1, 2.9%), sarcoma (n =1, 2.9%), squamous cell carcinoma (n = 12, 35.3%) and undifferentiated carcinoma (n =4, 11.8%).

Sites of primary tumor were: breast (n = 13, 38.2%), hypo pharynx (n = 2, 5.9%), larynx (n = 8, 23.5%), nasopharynx (n = 2, 5.9%), neck (n = 4, 11.8%), parotid (n = 1, 2.9%), skin (n = 2, 5.9%), sub mandibular gland (n = 1, 2.9%) and tongue (n = 1, 2.9%).

All of patients received external radiotherapy.
They received radiation ranging from 5000 cGY (14 patients 41.2%) to 7400 cGY (1 patient 2.9%) with median of 6000 cGY. The number of fractions was from 20 to 37 fractions with median of 29. Dose per fraction was 200 cGY in 23 patients (67.6%) and 250 CGY in 8 patients (23.5%) with median of 200 CGY. They treated with different fields such as: Mantel in 3 patients (8.8%), anteroposterior in 3 patients (8.8%), anterior in 9 patients (26.5%), bilateral in 9 patients (26.5%), and lateral in 16 patients (47.1%).

Physical examination of thyroid at the beginning of treatment was normal and all of the patients were euthyroid. According to our data: T3RUP test which was done at the beginning of radiotherapy, after 3 and 6 months did not show any significant difference (P = 0.37). Also T4 test which was done at the beginning of radiotherapy, after 3 and 6 months did not show any significant difference (P = 0.50). However, the results from TSH test at the beginning of radiotherapy (0.5912), after 3 months (0.7481) and 6 months (0.7908) follow-up showed significant difference (P = 0.001). There was no sign of hypothyroid state because TSH in none of patients was higher than 4.5 (cutting edge).

**DISCUSSION**

In addition to surgical intervention, radiotherapy is the only known curative management of patients with head and neck malignancies. It may be used either alone or in combination with surgery and/or radiotherapy.

In 1961 Felix et al. (3) first reported a case of hypothyroidism six years after treatment with external radiotherapy in a patient with laryngeal carcinoma. Since then, several other investigators have reported the occurrence of hypothyroidism in patients who have received radiotherapy in the neck region. Despite these reports, tests for thyroid functions are not yet included in the follow-up protocols of patients with head and neck malignancies (6).

There is a general agreement that hypothyroidism is a much more common complication following radio therapeutic management of head and neck cancers with a frequency ranging from 43 to 66% and sometimes up to 80% and more often depending upon duration of the follow-up (5, 6, 7).

Since radiation-induced hypothyroidism is a late effect, it is expected that as time passes the incidence will increase and some patients with sub-clinical hypothyroidism will progress to clinical hypothyroidism.

Dose of radiation required for producing hypothyroidism is also confusing. Degrot (8) and Hancock et al. (9) suggested that radiation doses in range of 3000 to 8000 rad are required to produce hypothyroidism. At the same time Hancock et al. reviewed 1787 patients of Hodgkin’s disease treated with Mantle field irradiation at the dose of 3500-4500 cGY and estimated a 43% actuarial risk of developing hypothyroidism in more than 50% of cases at a long time follow-up.

The way in which radiotherapy produces hypothyroidism is also incompletely understood. This may be due to direct follicular destruction or prevention of cell division or vascular damage to the thyroid gland or immunologically mediated damage to the thyroid gland or a various combinations of factors. Histological examination of thyroid gland after external irradiation has documented follicular cell damage following doses as low as 225 cGY (10). Most common signs and symptoms of hypothyroidism e.g. depression, lethargy, skin changes, constipation, weight gain (> 10% of original body weight) etc. are ill defined and can be easily overlooked in cancer patients. Since there is a high rate of comorbidity in these patients and the disease and its treatment may have nutritional, physical and psychological consequences, there is always a risk for masking the clinical features of hypothyroidism. Thus, clinical examination of the cancer patients for hypothyroidism alone is not enough.

We have found no effect of age, gender, cancer site, neck node status or radiation dose on the incidence of hypothyroidism. Similar findings were reported by other investigators (11, 12).

In conclusion, the findings from this study indicated that none of the patients developed
hypothyroidism in a period of six months after completion of radiotherapy. However, it seems that 6 months follow-up is early for judgment about evaluation of patients for hypothyroidism state and it needs further follow up for minimum of 12 months.
REFERENCES


