International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2013): 6.14 | Impact Factor (2013): 4.438

Effects of Nasopharyngeal Cancer's Patients Irradiation in Thyroid Function

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Abstract: ***Out of 80 nasopharyngeal carcinoma patients, who were received a radical radiation dose in the range of 6000 – 6500 cGy at radiation and isotopes center of Khartoum RICK and planned for conventional radiotherapy, as assessment for thyroid hormones level T4, T3 and TSH have been studied after receiving an average dose of 2036 ±702 cGy. Accordingly the analysis of the data showed that: the thyroid hormones (T4 and T3) decreases as a results of irradiation and the reduction persists following radiation dose in a linear form by a factor of 0.02 nmol/l/cGy and 0.0004 nmol/cGy respectively while the TSH increases following the radiation dose increment and the increment factor was 0.0006 umol/cGy.***

Keywords: Radiotherapy, Thyroid, Hormones, Radioimmunoassay

1. Introduction

The first studies reporting thyroid dysfunction after radiotherapy for head and neck cancer was first reported in 1960s [1]. Since then, many publications have described radiotherapy-induced thyroid disorders such as hypothyroidism, thyroiditis, Graves' disease, adenoma, and carcinoma [2-3].

In many studies, the use of radiotherapy for the treatment of malignancies involving the head and neck and for Hodgkin's disease, especially among children, has been associated with an increase in the development of secondary malignancies, including those of the thyroid [4-6]. Also thyroid dysfunction commonly develops after ionizing radiation therapy at therapeutic doses as has been obvious in histological evidence for radiation therapy of normal thyroid glands that received doses ranging from 225 - 4300 cGy during external irradiation of head & neck tumors [7]. Up to recent years of 1995-1996, the irradiation was the only demonstrated as etiological risk factor for thyroid cancers [8]. And the dose of radiation was the chief correlate for the development of hypothyroidism [9]. A higher incidence of thyroid cancer has been reported in epidemiological studies after either internal or external exposure to radiation [8]. And a pooled analysis of seven studies established that the excess relative risk ERR of thyroid cancer in subjects irradiated at a young age was very high (7.7/Gy) and the risk being significant for radiation doses as low as 0.1Gy and increasing linearly with increasing doses [8]. Also in the same realm, Bonato et al, [9] have reported that: the hypothyroidism is very common in survivors of childhood cancer treated with external beam radiation. For the significant number of patients who developed hypothyroidism following neck radiotherapy, Smit et al, [10] considered and recommended the thyroid function tests has to be as routine follow up protocol of such patients. In the study carried out by Laway et al, [11]; they showed that: the primary hypothyroidism often develops as a result of radiotherapy to the cervical region in therapeutic doses (30-70 Gy) in patients with head and neck cancer and the mean time for development of hypothyroidism was 4.5 months. The reason for such dysfunction is usually the direct radiation injury of the thyroid gland, but sometimes it is due to radiation therapy to the pituitary. There are many proposed mechanisms to explain radiation injury of the thyroid gland. For example, radiation may inhibit the active follicular epithelium and reduce the number of functional follicles; it may reduce the vascular permeability or may trigger immunologic reactions leading to several clinical events. The General objective of this study is to assess and correlate the level of thyroid hormones after nasopharyngeal carcinoma irradiation relative to received dose.

2. Methodology

The following study has been carried out on a sample consist of 80 nasopharyngeal carcinoma patients, who were received a radical radiation dose in the range of 6000 – 6500 cGy at radiation and isotopes center of Khartoum RICK. The patients were planned for two large opposed lateral fields that cover the primary tumor and the cervical lymph nodes in one volume. The field's boarders were set superiorly: at 2 cm superior to the tumor defined on the CT image, and encompass the base of skull and sphenoid sinus. The anterior boarder at 2 cm margin anterior to the tumor defined on CT and includes the posterior third of the maxillary sinus. Posterior boarder at 2 cm posterior to the mastoid process and including the involved cervical lymph nodes with 1.5 cm margin and the inferior boarder at thyroid notch as shown in Figure (1- a). Then after 40 Gy; the large fields coned down to encompass only the tumor bed i.e. the true nasopharynx and receiving a boost dose of 2000 cGy given as two opposed lateral fields, the boarders lies at: base of the skull superiorly, hard pallet inferiorly, external auditory meatus posterior, and at posterior third of the maxillary sinus as anterior boarder as shown in Figure (1 - b).

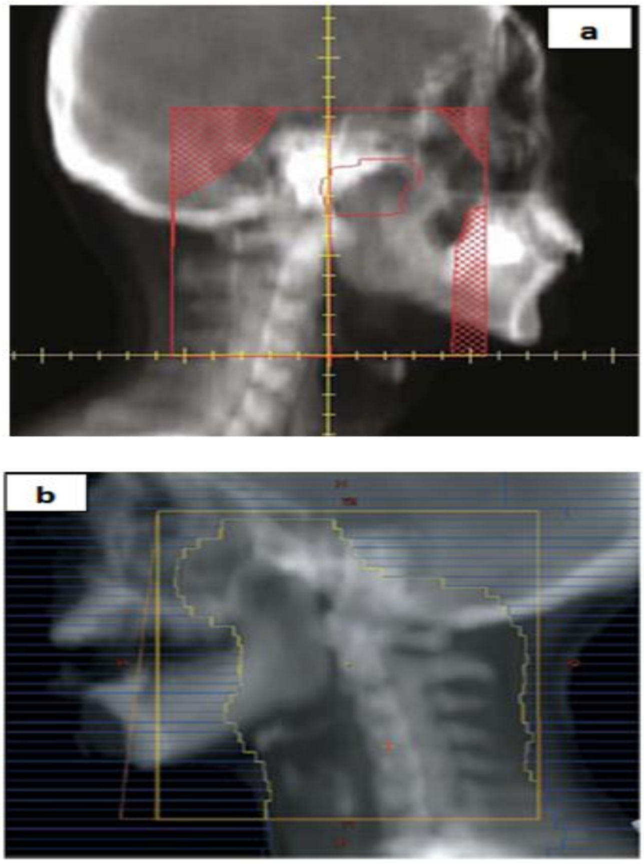

Figure 1: shows the initial simulation 2 opposed lateral fields using conventional radiotherapy with possible shielded vital area (a) and with using multi leaves collimators to protect same vital area (b) as suggested by Jiade and Luther, [12]; Ann et al, [13].

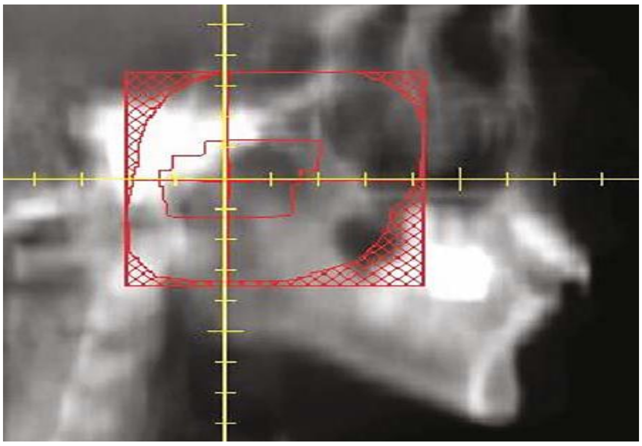

Figure 2: shows the shrinkage final boost fields to a total of 20 Gy, to satisfy the radical tumor dose with 60 Gy (simulation field proposed by Jiade and Luther, [12]).

Then a CT images have been carried out showing the location of tumor which have cent to treatment planning system for dose histogram as shown in Figure (3). For the cancer patients who received the radical radiation doses, their hormones level were assess by withdrawing 5 cc of blood sample which then collected in dry tubes and immediately centrifuged at 2000 rpm (rotation per minutes) for 5 minutes and the amount of separated sera (T3, T4 and TSH) have been assessed using Radio-immunoassay kits (DPC, USA) on Gammamatic II gammacounter (Contron, Switzerland) for each patient. The doses received by thyroid gland have been calculated using Day's method i.e. calculating of radiation dose outside of the field as off axis dose calculation [14-15].

3. Results

Figure 4 shows the dose distribution for true nasopharyngeal carcinoma boosted irradiation and relative percentage iso-dose dose lines. It reveals that: the tumor bed received 100% of the prescribed dose and the PTV received 95% of the prescribed dose which is in agree with ICRU, [16]; Mohammed et al, [17] and Zhu, [18] that the tumor dose should not exceeds ±5% variation from the prescribed radiation dose. And the doses at Optic Chiasma represented 30% (1900 cGy), and the eye lens 10% (560 cGy) which were all within the tolerance ranges 50 Gy and 10 Gy respectively with consideration that the dose per fraction was 2 Gy; as stated by Ann et al, [13].

Figure 4: shows the dose distribution for true nasopharyngeal carcinoma boosted irradiation and relative percentage iso-dose dose lines.

Figure 5 shows the correlation between the doses received by the thyroid gland in nasopharyngeal carcinoma irradiation and relative hormonal effect in logarithmic scale. It reveals that the thyroid hormones as T4 and T3 decrease in a linear form following the radiation dose increment and the correlation could be fitted in the following equations: y = -0.024x + 174.0 and y = -0.0004x + 1.4379 respectively where *x* refers to radiation dose in cGy and *y* refers to the level of T4 and T3 in nmol/l, such correlation is so significant as R^2 = 0.7 and 0.8 respectively which indicating that the hormones decreased by 0.02 nmol/l/cGy and 0.0004 nmol/cGy respectively. The reduction of hormones could be ascribed to damage or inhibition of the active follicular epithelium and reduce the number of functional follicles; or it

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may reduce the vascular permeability or may trigger immunologic reactions leading to several clinical events including the histological changes, however such histological change within the irradiated thyroid have been reported by Mizukami et al, [19] which appeared as microscopic changes pattern of multiple adenomatous nodules with cystic changes, marked oxyphilic cell changes with nuclear atypism and various degrees of chronic thyroiditis. Also Jung et al, [20] have showed that: greater numbers of abnormal and unusually small follicles were observed in the thyroid tissues of rats subjected to radiation, such as surrounding of thyroid Follicles by cuboidal or columnar epithelium on days 4 and 7 after irradiation and inflammatory cells were observed in the inter-follicular areas. Regarding the thyroid hormones influence after irradiation, some authors reported that the thyroid hormones decrease significantly due to irradiation, as Arun et al, [21], found that the mean serum of T3 & T4 levels were found to be decreased during EBRT significantly ($p<0.001$, $p<0.005$ and Garcia et al, [22] stated that the head and neck irradiation results in biochemical hypothyroidism in at least 50% of patients as well as have been reported by Irvin et al, [23] and Khoo et al, [24]. Also TSH has been noted to be increases following the radiation dose increment in a linear correlation for that could be fitted in the following equation: $y = 0.0006x - 0.5281$, where x refers to received dose by thyroid in cGy and y refers to logarithmic of TSH level in um/l, such correlation is so significant as $R^2 = 0.8$ and the increment factor was 0.0006 per cGy. The increment of TSH could be ascribed to a reduced level of T4 and T3 in the circulating blood that triggers the production of TSH by the pituitary gland. Same result also been reported by Louis et al, [25].

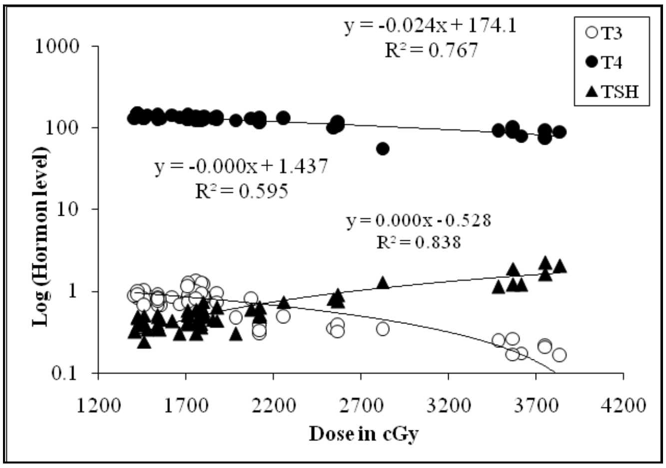

Figure 5: shows the correlation between the doses received by the thyroid gland in nasopharyngeal carcinoma irradiation and relative hormonal effect.

4. Conclusion

Radiotherapy of head and neck cancer have accompanied with serious complication in the vital organs structure and the physiological state, in this view the thyroid hormones (T4 and T3) have been reduced and the TSH increases due to irradiation of head and neck radiotherapy, and such consequences have been commonly with conventional radiation therapy.

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