Effects of treatment with radioiodine (^{131}I) on the gonadal function of the hyperthyroid patients

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ABSTRACT

Introduction: Hyperthyroidism is a relatively common disorder caused by different etiologies. Graves' disease, and toxic-nodular goiter (Plummer's disease) are among the most common causes. Treatment with radioiodine is considered to be the treatment of choice in many of the patients. Higher biological half-life of ^{131}I in hyperthyroid patients as compared with patients with differentiated thyroid carcinoma who have undergone thyroidectomy, may lead to a higher frequency of complications with radioiodine at similar dosage. Therefore gonadal dysfunction in hyperthyroid patients treated with radioactive iodine is not unlikely.

Materials and Methods: Hyperthyroid patients with the clinical diagnosis of Graves' disease, toxic multinodular goiter and toxic adenoma were entered the study. Their Age distribution was 16-40 years in women and 17-60 years in men (reproductive years). Patients were euthyroid at the time of radioiodine treatment. FSH, LH, testosterone and semen analysis in men; and FSH, LH, estrogen and progesterone in women were measured before and 3 months after radioiodine therapy. All patients with previous history of radioiodine treatment, those with known sexual hormone abnormalities, women with a history of tube ligation and men with a history of vasectomy, as well as those women who were receiving OCP contraception were excluded from the study.

Results: From 104 enrolled patients, 40(38.5%) were men and 64(61.5%) were women. The cause of hyperthyroidism was Graves' disease in 66 cases (63.5%), toxic multinodular goiter in 28 cases(26.9%), and toxic adenoma in 10 others(9.6%).

Hormonal status was normal in all patients before therapy while this became abnormal in 20(19.2%) of patients after treatment.

Semen analysis became abnormal in 8/20(40%) of the patients after treatment.

Conclusion: Among different variables which were analyzed during study, meaningful correlation was found in the following situations:

FSH values in men and women were found to be increased after radioiodine treatment (p value<0.0001), sperm count decreased from 124000000 to 62000000 (p value<0.0001), the difference in semen analysis changes was also meaningful in men among two different age groups(=<35y, >35)(p value=0.003) and changes in hormonal status in women in two different age groups(=<30, >30)were found to be statistically significant(p value=.015).

Key words: *Hyperthyroidism, radioactive iodine, sexual hormones, semen analysis.*

Introduction

Hyperthyroidism is a relatively common disorder caused by different etiologies. Graves' disease, and toxic-nodular goiter (Plummer's disease) are among the most common causes. (1) Different therapeutic strategies (surgery, antithyroid drugs, and radioiodine) have acceptable efficacies, but each has its own disadvantages. Relatively high surgical complications in the hand of surgeons without the necessary experience with this delicate operation, the time and cost of hospitalization and the morbidity and possibly mortality of this surgical procedure as well as the long course of therapy with antithyroid drugs and their relatively common side effects; make radioactive iodine the first line of therapy in most of the patients (1-3). Biological half-life of ^{131}I is higher in hyperthyroid patients as compared with patients with differentiated thyroid carcinoma who have undergone thyroidectomy (1-3). This may lead to a higher frequency of complications with radioiodine at similar dosage. Therefore gonadal dysfunction in hyperthyroid patients treated with radioactive iodine is not unlikely (this complication, although transient has been reported in patients with thyroid cancer who have undergone thyroidectomy and then treated with radioactive iodine (4-7,9,10).

Materials and Methods

Hyperthyroid patients with the clinical diagnosis of Graves' disease, toxic multinodular goiter and toxic adenoma were entered the study. Their Age distribution was 16-40 years in women and 17-60 years in men(reproductive years). Patients were euthyroid at the time of radioiodine treatment. FSH, LH, testosterone and semen analysis in men; and FSH, LH, estrogen and progesterone in women were measured before and 3 months after radioiodine therapy. All patients with previous history of radioiodine treatment, those with known sexual hormone abnormalities, women with a history of tube ligation and men with a history of vasectomy, as well as those women who were receiving OCP contraception were excluded from the study.

To facilitate the comparison and in order to have a criterion for better assessment two new variables (sex hormone status, and semen analysis status) were defined. In the case that any of the male sexual hormones (FSH, LH, testosteron) or female sexual hormones (FSH, LH, estrogen and progesterone) was deranged from the normal range; the sex hormonal status was considered abnormal. Also in the case that the sperm count was out of the normal range (60-200 millions) or whenever the sperm motility decreased from grades III or IV to grades I or II, the semen analysis was considered abnormal.

The gathered information were entered the computer and were statistically analyzed using SPSS (10) software. In order to compare the numerical values before and after treatment, paired sample t-test was used. While for comparing the variables in different age, sex, or dosage groups, Chi-square (X^2) was used as the statistical tool. P value < 0.05 was considered statistically significant.

Results

From 104 enrolled patients, 40(38.5%) were men and 64(61.5%) were women. Hormonal status was normal in all patients before therapy while this became abnormal in 20(19.2%) of patients after treatment.

Semen analysis became abnormal in 8/20(40%) of the patients after treatment.

The cause of hyperthyroidism was Graves' disease in 66 cases (63.5%), toxic multinodular goiter in 28 cases (26.9%), and toxic adenoma in 10 others (9.6%).

Figure 1)Mean FSH value in men

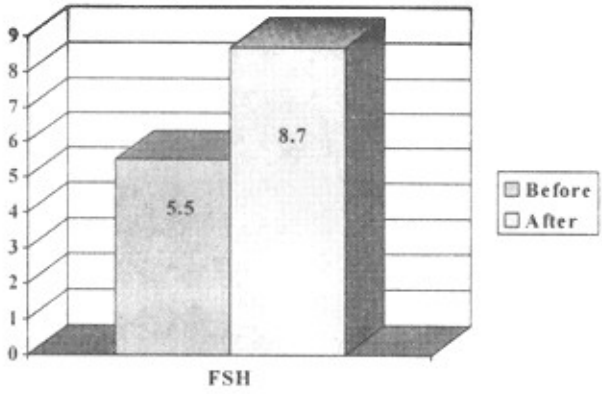
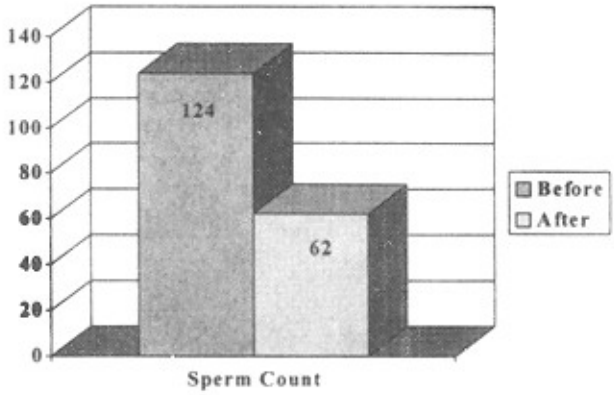


Figure 2) Sperm Count



The mean FSH value increased from 5.931 miu/l before treatment to 7.798 miu/l after treatment. These changes for other hormones were as follows: LH increased from 6.419 miu/l to 6.425 miu/l, progesterone decreased from 6.884 pg/ml to 5.984 pg/ml, and sperm count decreased from 124 millions to 62 millions.

Discussion

The following changes were found to be statistically significant:

A) Mean FSH value in male patients was

Figure 3) FSH Value in Women

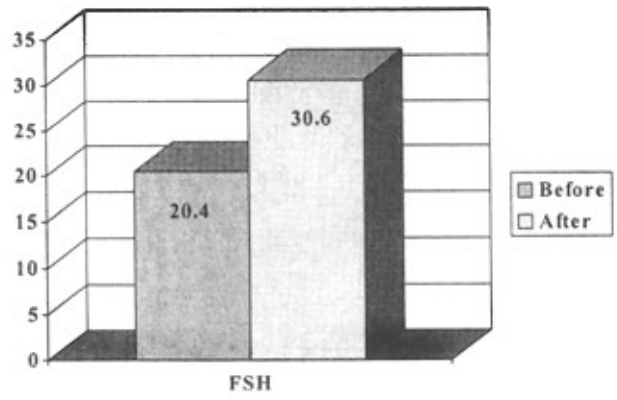


Table 1) Relationship Between Age and Semen Analysis After Treatment

		Semen analysis after treatment		Total
		Normal	Abnormal	
Age (up to 35)	count	20		20
	percent	100%		100%
Age(36 and more)	count	12	8	20
	percent	60%	40%	100%
Total	count	32	8	40
	percent	80%	20%	100%
			P value:.003	

increased from 5.500 miu/l before treatment to 8.719 miu/l after treatment(p value<0.0001) (figure 1). The increase in FSH value may be due to higher sensitivity of sertoli cells and the process of spermatogenesis to the effects of radiation. Other hormones (LH and testosterone) have shown no significant change after treatment, which is probably due to relatively higher resistancy of Leydig cells to the effects of radiation.

B) Sperm count decreased from 124 millions/ml to 62 millions/ml(p value< 0.0001)(figure 2). Again this indicates the sensitivity of spermatogenesis to radiation. Review of the literature shows that, FSH level and spermatogenesis are radiosensitive (8-11). Handelsman showed a decrease in the sperm count in patients with thyroid cancer, treated with radioiodine (^{131}I)(8). In another study on thyroid cancer patients treated with radioiodine; Pacini et al. Showed an increase in FSH level in 36.8% of patients, which was irreversible in 20% of the cases (9).

In another study, Aliyari Zenooz showed that in 246 patients with thyroid cancer (159 women and 87 men) who were treated with radioiodine (^{131}I), all men had an increase in their FSH level after treatment. This increase was proportional to the cumulative dose of radioiodine given, and this correlation was found to be statistically significant. In the same study in all of the studied populations, a decrease in the sperm count was shown after radioiodine therapy and again this was proportional to the cumulative dose. No significant change was noted in the amount of LH and testosterone values in men and FSH, LH, estrogen and progesterone values in women after radioiodine treatment (11).

C) In women as in men, a statistically significant increase in FSH values was seen after radioiodine treatment (p value < 0.0001) (figure 3). This may show that the follicular phase of menstrual cycle is more sensitive to radioiodine treatment as compared with the luteal phase. Other sex hormones in women (LH, estrogen, and progesterone) did not show any significant change after treatment with radioiodine.

D) The difference in changes of semen analysis in two age groups was statistically significant (p value=0.003)(table 1). In the first age group (<=35 y) all the semen analyses remained in the normal range after treatment, while in the second group (>35y) in 40% of cases the semen analysis became abnormal. This shows that the process of spermatogenesis is more sensitive to the effects of radiation in older men. This may be due to a decrease in spermatogenesis reserve in men.

E) The differences in the changes of hormonal status of women after treatment was also significant in two age groups (p value=0.15)(table 2). In the first age group (<= 30y) hormonal status became abnormal in 33.3% of the cases, but in the second group (> 30y) this was only 8.7%. So younger women are more sensitive to the effects of radioiodine. This may be justified by a higher FSH, and LH values in older women (who are close the menopausal age), and less significant changes of these values after radioiodine treatment.

Table 2) Relationship between age and hormonal status after treatment in women

		Hormonal status after treatment		Total
		Normal	Abnormal	
Age (up to 30)	count	12	6	18
	percent	67%	33%	100%
Age(31 and more)	count	42	4	46
	percent	91%	9%	100%
Total	count	54	10	64
	percent	84%	16%	100%
			P value:.0.015	

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