

Malformations in the Offspring of Women with Thyroid Cancer Treated with Radioiodine for the Ablation of Thyroid Remnants

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ABSTRACT

Rationale: Since ovarian function is only temporarily compromised by radioiodine therapy, many women with thyroid cancer treated with radioiodine can become pregnant. The present study evaluated the evolution of these pregnancies and the consequences for the offspring. **Patients and methods:** We retrospectively analyzed 78 pregnancies of 66 women submitted to total thyroidectomy, followed by radioiodine therapy (3.7–5.5 GBq ^{131}I , mean 4.64 GBq). In all patients, conception occurred one year after ablative therapy (mean of 30 months). Age ranged from 19 to 36 years (mean of 30.6 years) at the time of radioiodine treatment and from 23 to 39 years (mean of 32.8 years) at the time of conception. **Results:** Four (5.1%) of the 78 pregnancies resulted in spontaneous abortions. Three (4%) of the 74 deliveries were preterm and there was no case of stillbirth. The birthweight was > 2500 g in 94.6% of the children (mean \pm SD: 3350 \pm 450 g) and only one infant (1.3%) presented an apparent malformation at birth (intraventricular communication). No difference in the age at the time of radioiodine therapy or conception or in radioiodine dose was observed between pregnancies with an unfavorable outcome and those with a favorable outcome. **Conclusion:** We conclude that pregnancies that occur 12 months after ablative therapy are safe. (Arq Bras Endocrinol Metab 2006;50/5:930-933)

Keywords: Malformations; Radioiodine; Thyroid cancer

RESUMO

Malformações na Prole de Mulheres com Câncer de Tireóide Tratadas com Radioiodo para Ablação de Remanescentes Tiroideanos.

Arrazoado: Uma vez que a função ovariana está apenas temporariamente comprometida pela terapia com radioiodo, muitas mulheres com câncer de tireóide tratadas com radioiodo podem engravidar. O presente estudo avaliou a evolução dessas gravidezes e suas conseqüências para a prole. **Pacientes e métodos:** Analisamos retrospectivamente 78 gravidezes de 66 mulheres submetidas a tireoidectomia total seguida de radioiodoterapia (3,7–5,5 GBq ^{131}I , média 4,64 GBq). Em todas, a concepção ocorreu um ano após a terapia ablativa (média de 30 meses). A idade variou de 19 a 36 anos (média de 30,6) à época do tratamento com radioiodo e de 23 a 39 anos (média de 32,8) na época da concepção. **Resultados:** Quatro (5,1%) das 78 gravidezes resultaram em abortamento espontâneo. Três (4%) dos 74 partos foram pré-termo, mas não houve nenhum natimorto. O peso ao nascer foi >2.500 g em 94,6% das crianças (média \pm DP: 3.350 \pm 450 g) e somente uma delas (1,3%) apresentou uma malformação aparente ao nascimento (comunicação intraventricular). Nenhuma diferença quanto à idade na época da radioiodoterapia ou na concepção ou na dose de radioiodo foi observada entre as gravidezes com ou sem um desfecho favorável. **Conclusão:** Gravidezes que ocorrem 12 meses após terapia ablativa com radioiodo são seguras. (Arq Bras Endocrinol Metab 2006;50/5:930-933)

Descritores: Malformações; Radioiodo; Câncer de tireóide.

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WOMEN OF FERTILE AGE correspond to a significant portion of patients with differentiated thyroid carcinoma in whom radioiodine therapy is widely used (1). Ovarian function is only temporarily compromised by radioiodine (2-5), with permanent infertility being rare (2). Thus, many women with thyroid cancer treated with radioiodine may become pregnant, and it is therefore important to evaluate the evolution of these pregnancies and the consequences for the offspring. A higher risk of abortion has been reported for the first year after application of the ^{131}I dose (6-8) and it is recommended that conception be avoided during this period (9); however, malformations or more serious consequences for the offspring do not seem to be frequent in these cases (6-8,10-12).

We report here the outcome of pregnancies of patients with thyroid cancer treated with radioiodine at our service.

MATERIAL AND METHODS

We retrospectively evaluated 78 pregnancies of 66 women with thyroid carcinoma (50 with papillary and 16 with follicular carcinoma) submitted to total thyroidectomy followed by radioiodine therapy (single ^{131}I dose of 3.7–5.5 GBq, mean 4.64 GBq). In all patients, conception occurred one year after ablative therapy (15 to 74 months, mean 30 months) as advised at the time of treatment (9). Age ranged from 19 to 36 years (mean 30.6 years) at the time of radioiodine therapy and from 23 to 39 years (mean 32.8 years) at the time of conception. None of the patients presented important clinical co-morbidities that would affect the evolution of pregnancy and all women attended regular prenatal visits since the first trimester of pregnancy. The patients were maintained on suppressive levothyroxine therapy ($\text{TSH} < 0.3 \text{ mIU/l}$) even during pregnancy.

At the time of ablative therapy, all patients had received vigorous oral hydration and in cases of intestinal constipation, laxatives were administered for the adequate elimination of I^{131} in order to reduce ovarian exposure to radiation (13).

Spontaneous abortions, preterm deliveries, stillbirths, infant birthweight, and the presence of congenital malformations apparent at birth or during the first year of life were considered for analysis.

The study was approved by the Research Ethics Committee of our Institution and all patients signed an informed consent form to participate.

Differences in continuous variables between the patients with unfavorable outcome and those with

favorable outcome were estimated using a nonparametric Mann-Whitney U test. For dichotomous variables, Fisher's exact test was used.

RESULTS

None of the patients had iodine-accumulating distant metastases and uptake in the thyroid bed was $< 10\%$ on post-treatment scans in all women.

Four (5.1%) of the 78 pregnancies resulted in spontaneous abortions without apparent cause. Three (4%) of the 74 deliveries were preterm, two at 32 and one at 33 weeks of gestation, and there was no case of stillbirth. The birthweight was $> 2500 \text{ g}$ in 94.6% of the children (mean \pm SD: $3350 \pm 450 \text{ g}$). Only one infant (1.3%) presented an apparent malformation at birth (intraventricular communication), while no anomaly was diagnosed during the first year of life in the other children. These rates were not higher than those found in the general population of the municipality where the patients were living (Belo Horizonte, MG) (14). No difference was observed in age at the time of radioiodine therapy or conception, interval between treatment and conception, histological type or radioiodine dose between pregnancies with an unfavorable outcome (abortion, prematurity and malformation) and those with a favorable outcome (table 1).

The characteristics of patients with pregnancies presenting an unfavorable outcome are shown in table 2.

DISCUSSION

Radioiodine therapy may temporarily compromise ovarian function, but recovery of the menstrual cycles and normalization of FSH levels generally occur within 12 months (3-5), with permanent infertility being rare and occurring only in cases in which high doses (29 GBq or more) are applied (2). Thus, pregnancy is possible after radioiodine therapy, and knowledge about the effect of ablative therapy on the evolution of these gestations becomes important.

In the present study, all patients were advised to avoid conception during the first year after ablative therapy (9), a period during which the risk of abortions is known to be higher (6-8). With conception occurring 12 months after therapy, no increase in the abortion and prematurity rates, birthweight or malformations of the offspring was observed when compared to the general population. These data agree with various studies clearly demonstrating that pregnancy is

Table 1. Comparison of the characteristics (means) of patients with pregnancies that showed a favorable or an unfavorable outcome.

Characteristic / outcome	Unfavorable	Favorable	p-value
Age at the time of ¹³¹ I therapy (years)	29.1	30.8	Ns
Age at the time of conception (years)	33.1	32.7	Ns
Interval between therapy and conception (months)	40	29	Ns
Histological type (papillary/follicular)	6/2	44/14	Ns
¹³¹ I dose (GBq)	4.6	4.65	Ns

Table 2. Patients with pregnancies that showed an unfavorable outcome (abortion, prematurity or malformation).

Patient	Outcome	Histology	Age at ¹³¹ I therapy (years)	¹³¹ I dose (GBq)	Age at conception (years)
1	Abortion	Papillary	28	3.7	31
2	Abortion	Papillary	29	5.5	34
3	Abortion	Follicular	32	5.5	36
4	Abortion	Papillary	33	3.7	36
5	Prematurity (delivery at 32 weeks)	Papillary	26	3.7	31
6	Prematurity (delivery at 32 weeks)	Follicular	24	3.7	29
7	Prematurity (delivery at 33 weeks)	Papillary	30	5.5	35
8	Malformation (IVC)	Papillary	31	5.5	33

safe in patients when the interval between radioiodine treatment and conception is longer than one year (6-8,10-12). However, we did not evaluate patients who received high radioiodine doses or those with iodine-accumulating pelvic metastases, situations in which the ovaries are exposed to higher radiation (13).

We conclude that pregnancies starting 12 months after ablative therapy are safe in patients who received a mean dose of 4.6 GBq and who do not present iodine-accumulating pelvic metastases.

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