Radioiodine therapy for women with thyroid cancer does not adversely affect subsequent pregnancies and those offspring over a 10-year follow-up period

Garsi JP, Schlumberger M, Rubino C, Ricard M, Labbe M, Ceccarelli C, Schvartz C, Henri-Amar M, Bardet S, De Vathaire F. Therapeutic administration of ^{131}I for differentiated thyroid cancer: radiation dose to ovaries and outcome of pregnancies. J Nucl Med 2008;49:845-52.

SUMMARY

BACKGROUND Ten years ago this group reported that radioiodine (^{131}I) therapy had no effects on the outcome of subsequent pregnancies and offspring in women treated for thyroid cancer, with the exception of miscarriages in a small number of women that occurred during the first year after ^{131}I therapy. The current study has twice the number of pregnancies, and updates these earlier findings.

METHODS From 1994 to 2004 the entire cohort of women treated for thyroid cancer at the Institut Gustave-Roussy and the Institut Jean Godinoit in France and at the Institute of Endocrinology in Pisa were routinely interviewed by trained data managers, who collected information regarding the following features of each pregnancy: induced abortion, miscarriage, stillbirth, prematurity, birth weight below the 10th percentile for gestational age, congenital abnormalities, and death during the child's first year of life and the development of thyroid disease in children, including tumors at other sites.

RESULTS Study subjects were 1126 women with differentiated thyroid cancer who had a total of 2078 pregnancies, of which 112 (5%) occurred before patients had undergone surgery alone for thyroid cancer and 483 (23%) after ^{131}I therapy. In the latter group, 212 (44%) were given 3700 MBq or more of ^{131}I (≥ 100 mCi) in 1 to 2 treatments that were administered a mean of 35 months (range, 0 to 243) before conception.

A total of 341 therapeutic and elective abortions were done, 221 (65%) before any treatment, 26 (8%) after thyroid cancer surgery alone, and 94 (28%) after both surgery and ^{131}I therapy. Abortions were more frequent after surgical therapy, both with and without ^{131}I therapy, than before any treatment had been done (odds ratio [OR] = 2.14, Figure 1), Higher cumulative activities of ^{131}I (370 to 3700 MBq [10 to 100 mCi]) before pregnancy were not associated with a greater probability of an induced abortion (OR = 0.83, Figure 1). Yet both the cumulative ^{131}I received during the year preceding pregnancy (P< 0.001 for trend) and smoking during pregnancy (OR = 2.15) significantly increased the probability of an induced abortion. A total of 18 induced abortions of 34 pregnancies (53%) occurred in women who had received ≥370 MBq (≥100 mCi) ^{131}I during the year before conception, which was a greater proportion of abortions than occurred in pregnancies preceded by smaller amounts of ^{131}I (16 to 25%, P<0.001). Abortions were significantly more frequent in women older than 45 years and in women who continued using alcohol or tobacco during pregnancy (OR = 3.3, P<0.001).

Miscarriages were observed in 193 of 1857 pregnancies (10%) before any thyroid cancer treatment was administered, and were more frequent (21%) in pregnancies that occurred after surgery alone, but were about the same before

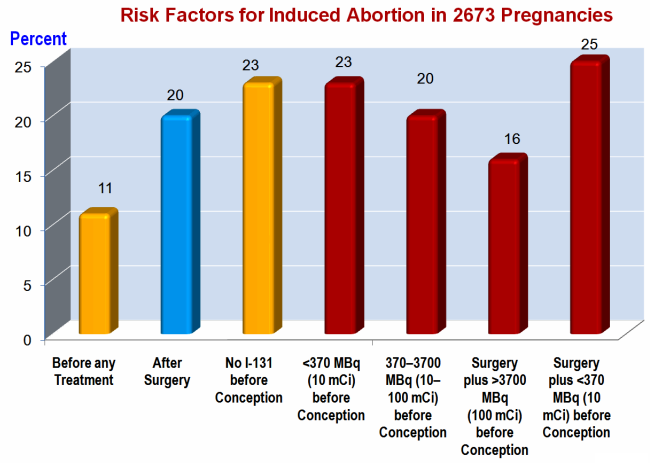

Figure 1. Risk factors for therapeutic and elective abortions are shown according to the cumulative amount of ^{131}I given to the mother before conception (rounded to nearest integer). This figure is drawn from the data in Table 1 of Garsi et al.

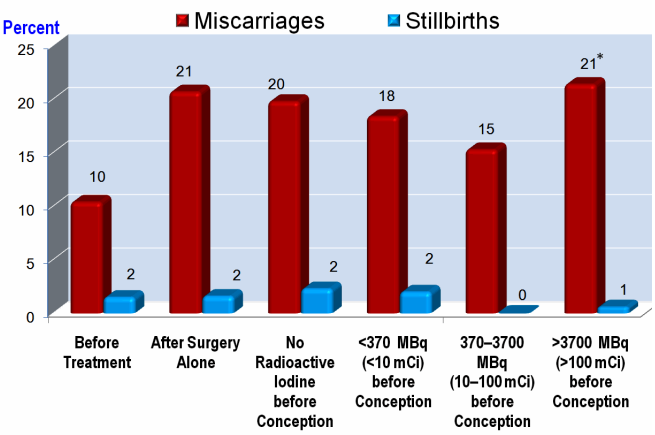

Figure 2. The risk factors for miscarriage and stillbirth in 2332 pregnancies are shown according to maternal exposure to ^{131}I prior to conception. *P = 0.05, as determined by χ^2 test for heterogeneity. This figure is drawn from the data in Table 3 of Garsi et al.

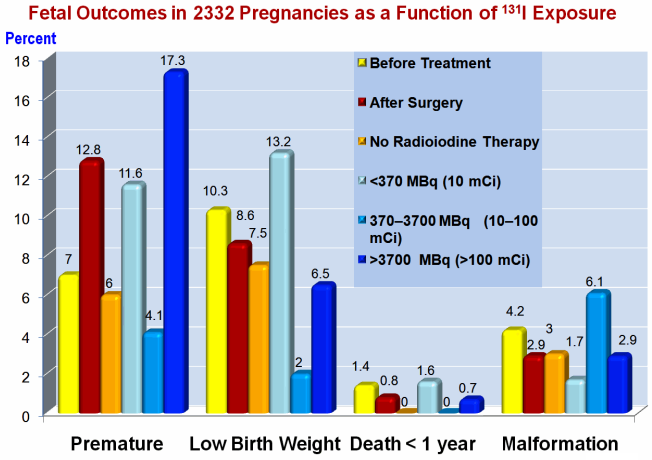

Figure 3. Fetal outcomes in 2332 pregnancies shown as a function of maternal exposure to ^{131}I. This figure is drawn from the data in Table 5 of Garsi et al.

(20%) and after (19%) ^{131}I therapy (Figure 2). There was no correlation between the cumulative ^{131}I activity and the occurrence of miscarriage. The only significant factors that predicted miscarriage, with and without ^{131}I therapy, were pregnancy after a diagnosis thyroid cancer (OR = 1.59), the mother's age >35 years at the time of pregnancy (OR = 2.12) and low birth weight, which was more common in the low-socioeconomic-status group (P<0.05). Women who took medications during pregnancy had a slightly increased risk of miscarriage (10% vs. 12%, OR = 1.04, P = 0.06), and their babies had a significantly greater risk of prematurity (10.4% vs. 5.5%, OR = 2.10).

Among the 2009 live births, none of the following appeared to be modified by mother's previous surgery or ^{131}I exposure: prematurity, low birth weight, death before 1 year, malformation, thyroid disease, and cancers. In all, 25 of 1633 children (1.3%) died less than 37 weeks after birth, 22 (1.4%) before mothers were given treatment, and 3 (0.8%) after the mother's surgery for thyroid cancer (Figure 3).

CONCLUSION The rates of therapeutic or elective abortions and miscarriages are increased in women before any treatment of thyroid cancer has been done, and are even higher after surgery but are the same before and after ^{131}I therapy. However, the risk of spontaneous miscarriage is not elevated by ^{131}I and children of mothers treated with ^{131}I have no measureable adverse effects.

COMMENTARY

This is the largest study of the outcomes of pregnancy in women treated with ^{131}I. In a 1996 study (1) of 2113 pregnancies in women previously exposed to ^{131}I for the treatment of thyroid cancer, Schlumberger et al. reported that miscarriages were more frequent (40%) in 10 women who were treated with ^{131}I (mean dose, 3.8 MBq [108 mCi]) during the year preceding conception. However, with the exception of this finding, there was no evidence that maternal exposure to ^{131}I affected the outcome of subsequent pregnancies and offspring. The current study confirms all of the results in the previous study, with the major exception that the risk of miscarriage is not elevated by increasing ^{131}I activity.

The authors were able to document the reason for abortion in only a few (45 of 341) abortions, which were for therapeutic purposes such as concern regarding ^{131}I exposure, ongoing treatment, and suspicion of fetal malformation. Still, the greatest problem in this group of patients is the high rate of induced abortions, regardless of the reason.

Although ^{131}I therapy for thyroid cancer causes transient alterations in ovarian function, even in younger women after a mean activity of 4.2 MBq (115 mCi) (2), the risk of permanent ovarian damage after ^{131}I appears to be low (3, 4). However, one of the major uncertainties is the amount of radiation necessary to induce ovarian damage. Based on an assumption that the doubling dose is 1 Gy—the amount of radiation required to produce genetic damage equal to the spontaneous mutation rate—the authors of this study found that only a few women had received an ovarian dose of sufficient magnitude to produce damage and that 139 women had received more than 140 mGy (mean dose, 305 mGy) As a result, they concluded that the study was not sufficiently powered to answer this question.

It is likely that subtle birth malformations will not be detected without large population studies. Still, this study provides strong support for the notion that maternal exposure to ^{131}I is not likely to cause significant problems during subsequent pregnancies.

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References

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