A systematic review of the gonadal effects of therapeutic radioactive iodine in male thyroid cancer survivors


CRD summary
This review examined the gonadal effects of radioactive iodine therapy in thyroid cancer survivors and concluded that short-term abnormalities in testicular function were common, but usually resolved within 18 months of single-dose treatments. The reliability of the authors' conclusions is uncertain in light of the quality of evidence available.

Authors' objectives
To examine the gonadal effects of radioactive iodine therapy in male well-differentiated thyroid carcinoma survivors.

Searching
MEDLINE, MEDLINE in-process and non-indexed citations, Cochrane Database of Systematic Reviews, ACP Journal Club, DARE, Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, CINAHL and HealthSTAR were searched for studies published in English from inception to July 2007; search terms were reported. Reference lists were checked and experts contacted in order to identify further studies.

Study selection
Studies of radioactive iodine therapy in men with well-differentiated thyroid carcinoma that assessed at least one of the following outcomes were eligible for inclusion: sex steroid and sex-related pituitary hormone levels in men; sperm quality, quantity and motility; male fertility; pregnancy loss in partners; and birth defects. Studies had to be either cohort, cross-sectional, cancer registries, administrative data sets, meta-analyses or case series (of more than five patients) and also had to have a control group, for which there was numerical data.

In the included studies the age range of participants was six to 73 years. Initial doses of radioactive iodine therapy ranged from approximately 30mCi to 226mCi. Cumulative doses ranged from approximately 30mCi to 1335 mCi; all studies included men who received multiple radioactive iodine therapy treatments. Control groups were mostly the same patients' pre-radioactive iodine therapy measures. Sex steroid and sex-related pituitary hormone levels, and pregnancies were the most frequently reported outcomes.

Two reviewers independently selected studies for inclusion.

Assessment of study quality
The study quality assessment, done independently by two reviewers, was based on the following criteria: longitudinal or cross-sectional study design; losses to follow up; type of control group; and presence of appropriate statistical comparison.

Data extraction
Two reviewers independently extracted data.

Methods of synthesis
Results were pooled in a narrative synthesis grouped by biochemical and laboratory parameters, and clinical outcomes. Differences between studies were discussed and study details tabulated.

Results of the review
Seven studies were included in the review (it was unclear exactly how many participants were involved, but the figure appeared to be around 400). Three studies were longitudinal, two were cross-sectional, and two comprised both longitudinal and cross-sectional analyses. None of the studies used an optimal control group. Six studies appeared to have no loss to biochemical follow-up. Four studies either did not conduct or did not report statistical tests.
Rates of infertility, pregnancy loss and offspring congenital malformation showed no significant changes after radioactive iodine therapy (three studies). In all five longitudinal analyses, levels of serum follicle-stimulating hormone (FSH) increased, peaking within two to six months with normalisation in most patients at 12 to 18 months; serum testosterone levels did not significantly decrease. In the three studies that assessed levels of luteinizing hormone a rise within three to six months and normalisation at 12 to 18 months was seen. Further results were reported.

Authors' conclusions
Abnormalities in testicular function were common within several months of a single therapeutic dose of radioactive iodine therapy for men with well-differentiated thyroid carcinoma, but they normally resolved within 18 months if a single dose of <150mCi was used. The risk of persistent gonadal dysfunction was increased after repeated or high cumulative radioactive iodine activities.

CRD commentary
The review addressed a clear question and was supported by appropriate inclusion criteria. It was confusing that although Cochrane Central Register of Controlled Trials was searched, controlled trials were not listed as one of the eligible study designs. Attempts to identify relevant studies were undertaken by searching electronic databases and checking references. Because the search was limited to studies published in English, it was possible that some relevant studies were missed. Suitable methods appeared to have been used to minimise the risks of reviewer error and bias throughout the review process. Study quality was adequately assessed and was used in interpreting the results of the review. Sufficient study details were provided and an appropriate narrative synthesis of the data was undertaken. The authors' conclusions reflect the evidence presented, but their reliability is uncertain in light of the quality of evidence available.

Implications of the review for practice and research
Practice: The authors stated that sperm banking should be offered to men before multiple, or cumulative (>350mCi) doses of radioactive iodine therapy or where it was important that the timing of conception was within 18 months of therapy. The authors also stated that male patients considering radioactive iodine therapy should not be discouraged from fathering children in the future.

Research: The authors stated that research was needed into the gonadal, reproductive and offspring effects of radioactive iodine in male well-differentiated thyroid carcinoma survivors. Comparator groups would ideally comprise similar patients who chose not to have radioactive iodine therapy. Quality of life, as directly related to gonadal symptomatology, should also be studied. Research was needed to compare short- and long-term gonadal outcomes in patients treated with radioactive iodine who were pre-treated with recombinant thyrotropin compared to those who were rendered hypothyroid.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.