**SUMMARY**

**Context:** There is little consensus regarding the most appropriate dose of radioiodine ($^{131}$I) to be administered to patients with hyperthyroidism.

**Objective:** To compare the efficacy of fixed dose regimens of $^{131}$I in curing hyperthyroidism and to define simple clinical and biochemical factors that predict outcome in individual patients.

**Design & Setting:** Consecutive series of hyperthyroid subjects treated with $^{131}$I. Single Secondary/Tertiary Care Hospital Clinic.

**Participants:** A total of 1,278 patients (1,013 females & 262 males, mean age 49.7 years) presenting with hyperthyroidism between 1984 and 2006.

**Intervention & Main Outcome Measures:** Treatment with $^{131}$I using a fixed dose regimen. Probability of cure and risk of development of hypothyroidism following a single dose of $^{131}$I.

**Results:** Patients given a single dose of $^{131}$I of 600 MBq (16 mCi) ($N = 485$) had a higher cure rate (84.1%) compared with those receiving either 370 MBq (10 mCi) (74.9%, $P < 0.001$) or those given 185 MBq (5 mCi) (63%, $P < 0.001$). An increased incidence of hypothyroidism by 1 year was evident with higher doses (600 MBq: 60.4%; 370 MBq: 49.2%, $P = 0.001$; 185 MBq: 38.1%, $P < 0.001$). Binary logistic regression analysis identified a 600 MBq dose of (131)I [adjusted odds ratio, AOR: 3.33; $P <0.001$], female gender [AOR: 1.75; $P = 0.002$], lower presenting serum free T4 concentration [AOR: 1.01; $P <0.001$] and absence of a palpable goitre [AOR: 3.33; $P <0.001$] to be independent predictors of cure. Similarly, a 600 MBq dose [AOR: 3.79; $P <0.001$], female gender [AOR: 1.46; $P = 0.02$], younger age [AOR: 1.03; $P <0.001$], absence of a palpable goitre [AOR: 3.85; $P <0.001$] and presence of ophthalmopathy [AOR: 1.57; $P = 0.02$] were identified as independent factors predicting the probability of development of hypothyroidism at one year. Based on these findings, formulae to indicate probability of cure and risk of hypothyroidism for application to individual patients were derived.

**Conclusions:** Simple clinical/biochemical criteria can be used to predict outcome after $^{131}$I treatment. These factors determine that males, those with severe biochemical hyperthyroidism, and those with a palpable goitre require larger doses (600 MBq) in order to achieve cure.

**COMMENT**

This is an interesting large scale clinical retrospective study aiming at evaluating long term results of the use of radioiodine in the treatment of thyrotoxicosis. Present study encompassed over 1,200 patients and spanned more than 2 decades. In my comments, I will try to summarize a few items showing marked differences between results of this UK study and our way of handling similar patients.
A first comment concerns the etiology of thyrotoxicosis. Graves’ disease (GD) represented 43% and toxic nodular hyperthyroidism (TNA) 18% of the patients. The 2/1 ratio between GD & TNA is certainly higher than in our practice where the frequency of GD patients receiving radioiodine is smaller, because we tend to operate more often GD patients when the first line period of treatment with antithyroid drugs was not considered satisfactory. Another difference is that we would have subdivided the 2nd group of patients between toxic multinodular goiter (TMNG) and toxic solitary adenoma (TSA) because the methods we use to calculate the dose of radioiodine would be strikingly different: 250 μCi/gr tissue for TSA (in order to ablate), compared with 50-120 μCi/gr for TMNG.

A second comment concerns a 3rd ‘bizarre’ group, entitled hyperthyroidism of “indeterminate etiology”. There were 502 patients in this group, which was almost as prevalent as GD patients. The reason was explained by the authors. Since thyroid radionuclide imaging is not routinely carried out in the work up of patients with thyrotoxicosis, they are left with this rather awkward category. It is worth mentioning that obtention of a scintigraphy to refine the diagnosis would not have been too complicated since the patients received radioiodine.

Another difference in our attitudes is the approach to the administration of radioiodine. In the UK, there is a tradition to administer fixed I\(^{131}\) doses, classically 5 milli-Ci (185 MBq) for a small goiter with moderate hyperthyroidism, 10 milli-Ci (370 MBq) for a larger goiter and more severe hyperthyroidism, and finally 15 milli-Ci (555 MBq) for an even larger goiter and severe thyrotoxicosis. This modality simplifies the administration of I\(^{131}\) but it does not take into account thyroidal uptake of the radionuclide and its effective half-life, nor the etiological diagnosis of thyrotoxicosis, nor a medical decision to be more or less ablative depending upon clinical circumstances. It must, however, be admitted that there is no strong evidence-based data to indicate clearly that the method used in determining the amount of I\(^{131}\) influences the final outcome.

In a rather macro-economical analysis, present results indicate that the single administration of 5 mCi of I\(^{131}\) was less effective (cure: 63%) than 10 mCi (cure: 75%) and again than 16 mCi (cure: 84%). Since it is not possible to win on all sides, as could be expected, the gain in efficacy was counterbalanced by an inversely proportional risk of inducing hypothyroidism, which increased from 38% to 60% with increasing I\(^{131}\) doses. One weakness of the study was that ophthalmopathy (GO) changes were not assessed before versus after I\(^{131}\) treatment in GD patients. The authors then tried to delineate useful markers for ‘prediction of cure’ as well as ‘prediction of hypothyroidism’ following I\(^{131}\). Independent predictors of cure were being less thyrotoxic, having a smaller goiter, receiving a larger dose of I\(^{131}\), and being a female patient: that’s nice - and logical - but not terribly helpful, especially that the female/male ratio was 4/1. Similarly, independent predictors of development of hypothyroidism one year after I\(^{131}\) were a younger age & being a female, receiving a higher I\(^{131}\) dose, and the presence of GO. This is the reason I wrote earlier that it was unfortunate not to provide information about GO changes related to I\(^{131}\) treatment, since it is known that any hypothyroid phase that follows I\(^{131}\) administration is a strong triggering factor for GO exacerbation.

Finally, the authors derived a formula (that can be found on their website) to predict success and hypothyroidism. Based on this formula, a 25-yr old woman with GD, who does not smoke, has no ophthalmopathy and no family history, without palpable goiter and with a serum free T4 level at twice the upper limit of normality has a 93.5% probability of cure after receiving 600 MBq of I\(^{131}\), but also a 85.9%
probability of developing hypothyroidism after the treatment. In summary, does it help you, the readers, decide what to do with this typical female patient? (Daniel Glinoer, M.D.; Ph.D.)

See Figure below