Hyperthyroidism and radio-iodine therapy in a district general hospital

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Summary

A retrospective analysis was performed of 48 patients with hyperthyroidism (41 women aged 35-80, mean 56.6 years; 7 men aged 31-77, mean 52.1 years) treated with a fixed dose of 550 MBq ^{131}I during a 12 month period May 1991-April 1992. Weight loss was common at presentation but 28.57% of women aged 35-49 years weighed over 80 kg compared to 9.98% in a standard UK population $P<0.05$. Patients treated with carbimazole (73%) prior to ^{131}I had higher FT3 levels at presentation (14.0±4.4 pmol/l) compared to those (27%) who were considered not to require such treatment (8.9±1.4 pmol/l, $P<0.001$).

Four months following radio-iodine, 67% were hypothyroid, 25% were euthyroid and 8% remained thyrotoxic and were retreated. Another patient became hypothyroid during 1 year of follow-up. Pre-treatment with carbimazole did not protect against the development of hypothyroidism (carbimazole treated 69% hypothyroid at 4 months, untreated 62% hypothyroid at 4 months). Patients with continuing thyrotoxicosis had very high FT3 levels at presentation (18.6, 21.1, 20 and in one patient reported only as >10 pmol/l). A rationalized programme of follow-up assessments at 2, 3, 4, 8 and 12 months is suggested for patients treated with this dose of radio-iodine.

Introduction

Radio-iodine treatment for thyrotoxicosis is cheap, effective, easy to administer and relatively free from serious side effects. Long regarded as the treatment of choice for patients with hyperthyroidism in the USA[1], its increased use in the UK has recently been supported[2]. The availability of radio-iodine is no longer restricted to large specialist centres and approximately 160 clinicians in the UK are licensed to prescribe it by the Administration of Radio-Active Substances Advisory Committee. Clinicians have to decide whether to administer a small dose which will in some fail to cure hyperthyroidism, but will still require some form of long-term monitoring to detect the delayed development of hypothyroidism in those rendered euthyroid, or whether to administer a large dose such that the majority of patients will become hypothyroid at an early stage. These patients can then be discharged on optimum thyroxine replacement therapy.

A recent Royal College of Physicians' (RCP) report[3] has summarized the current prescribing patterns, workloads, particular regimens, services and follow-ups for patients treated with radio-iodine in this country. Hedley and colleagues[3] found rather diverse practice and recommended use of fixed dose activities in the range 500-550 MBq. That RCP report stimulated this review of our experience of using ^{131}I in a fixed dose of 550 MBq. Treatment rates for the UK vary between 0.6-4.4/10 000 population. Pre-treatment with carbimazole is common particularly for those with severe symptoms, cardiac problems or advancing age. Half of the UK prescribers employ a fixed activity level. In Wrexham we regularly treat 2.5 per 10 000 population per year with similar indications for pre-treatment with carbimazole. All our patients are treated with 550 MBq of radio-iodine in capsule form.

Patients and methods

Forty-eight patients with hyperthyroidism (41 women aged 35-80, mean 56.6 years; 7 men, aged 31-77, mean 52.1 years) were treated with 550 MBq ^{131}I during the 12 month period May 1991-April 1992. Their case notes were reviewed retrospectively. All patients had elevated FT3 and suppressed TSH levels at presentation. None had previously been treated with radio-iodine. Details of presentation, serum FT3 levels, the decision to pre-treat with carbimazole and the outcome with respect to the development of hypothyroidism, euthyroidism or the continuation of thyrotoxicosis were collated. Pre-treatment with carbimazole in an initial dose of 20 mg twice a day depended on clinical and biochemical severity and was reduced to 10 mg twice a day on the achievement of euthyroidism. Carbimazole was discontinued 1 week prior to I^{131} and patients were reassessed at approximately 1, 2, 3, 4, 5, 6, 8, and 12 months following radio-iodine.

Analytical methods

FT3 was measured in duplicate by using the COAT-A-COUNT DPC kit (DPL Division/DPC Ltd, Gwynedd, North Wales, UK). TSH was measured in singlet assays using the NETRIA radio-immunometric TSH assay kit (NETRIA, London, UK). Thyrotoxicosis was defined as FT3 greater than 6.8 pmol/l and TSH less than 0.2 μm/l. Hypothyroidism was defined as FT3 less than 2.2 pmol/l, and TSH greater than 8 μm/l.

Statistical methods

Statistical analysis was performed with the general statistics, non-parametric statistics and multiple regression modules of the CSS Statistica package (Statsoft UK, Hertfordshire, UK).

Mean values are presented as ±standard deviation. Differences between means were tested by t-test and

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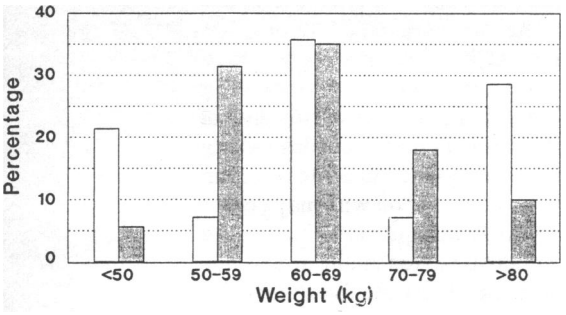

Figure 1. Weight at presentation of women with hyperthyroidism in age range 35-49 years compared with a standard UK population. □ =Patients; ■ =reference group

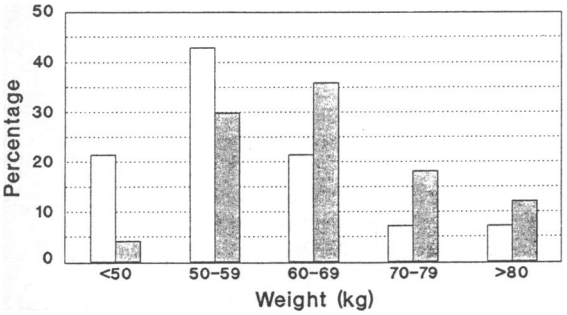

Figure 2. Weight at presentation of women with hyperthyroidism in age range 50-64 years compared with a standard UK population. □ =Patients; ■ =reference group

differences between proportions by χ^2 analysis of 2×2 tables.

Results

Clinical features

Weight loss of more than 6 kg occurred in 45% of patients, but in spite of this, many were obese at presentation with 19.5% of women weighing over 80 kg. This was particularly so in the age range 35-49 years where 28.57% women weighed over 80 kg compared to a UK standard population[4] 9.98% ($P<0.05$). Possibly reflecting weight loss, in this age range there was in addition a greater proportion of women who weighed less than 50 kg (21.43%) than in the standard population (5.6%, $P<0.05$; Figure 1). In the 50-64 years age range there was again a greater proportion of women who weighed less than 50 kg (21.43%) than in the standard population (4.13%, $P<0.005$; Figure 2). Goitre was present in 20 patients (42%), but in the majority the gland was small and diffuse. Dysthyroid eye disease, in the form of lid bulge (four patients), or exophthalmus (two patients) was present in 12.5%. Atrial fibrillation occurred in five patients, one of whom had coexistent mitral valve disease. Linear regression analysis showed a significant negative correlation between serum FT3 at presentation and age ($r=-0.50$, $P<0.0001$; Figure 3). This effect persisted when bodyweight was added as a further independent variable, and gender and carbimazole treatment were added as dummy variables.

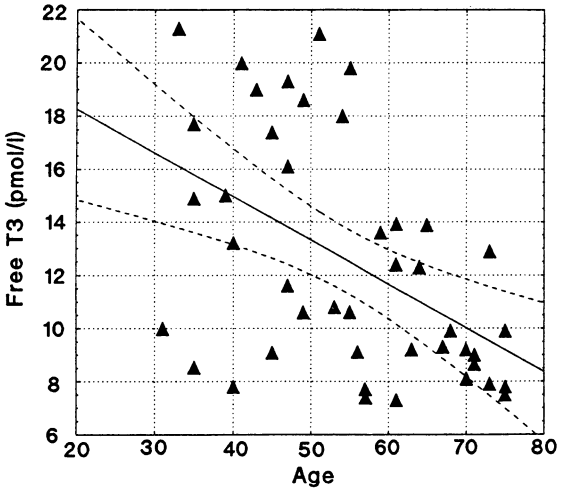

Figure 3. Correlation between age and serum free T_3 levels at presentation of hyperthyroidism. Regression equation: FT3=21.060-0.130×age. Dashed lines indicate 95% confidence interval of regression time

Seventy-three per cent of patients were pre-treated with carbimazole prior to radio-iodine. The other 27% did not receive antithyroid drugs. The patients pretreated with carbimazole had higher FT3 levels at presentation (14.0±4.4 pmol/l) compared with those who were considered not to require such treatment (8.9±1.4 pmol/l, $P<0.001$).

All patients with dysthyroid eye disease were treated with carbimazole, as were 83% of those with goitre.

Effects of ^{131}I therapy

Post-treatment hypothyroidism was first documented at 2 months, when 29% had become hypothyroid. At 3 months 52% had become hypothyroid and 4 months after treatment 67% were hypothyroid. At 4 months 25% were euthyroid but 8% remained thyrotoxic and were retreated. One euthyroid patient became hypothyroid at 12 months, and the rest remained euthyroid during the follow-up period of 8-18 months. Pretreatment with carbimazole did not protect against the development of hypothyroidism with 69% of the pretreated patients becoming hypothyroid at 4 months, compared with 62% of the patients who were not pretreated with carbimazole (not significant). Patients with continuing thyrotoxicosis tended to be those with high FT3 levels at presentation (18.6, 21.1 and 20.0, and in one patient FT3 was reported only as greater than 10 pmol/l).

Discussion

Our policy has been to treat older thyrotoxic patients with radio-iodine. Patients under the age of 20, women desirous of an early pregnancy, parents with young children, and the elderly with incontinence were excluded. Patients with active dysthyroid eye disease were also excluded. Very few patients in these categories were seen during the study period. Access to the nuclear pharmacy department records allowed complete ascertainment of the results of all treatments given during the study period. The cohort of patients treated are, therefore, a representative sample of thyrotoxic patients over the age of 30 and the data reflects the results of treatment with 550 MBq of radio-iodine in such a group.

Hyperthyroidism is now often diagnosed at an early phase of illness and weight loss is often accepted happily when other symptoms may be minimum. Thus, weight gain is often a concern in successful treatment and obese patients require dietetic advice when treatment is commenced. In this review, height was not recorded so body mass index has not been calculated; nevertheless, the weight of over 80 kg can be regarded as significant obesity and we were surprised by the number of women aged 35-49 years who fell into this category.

The negative correlation between serum FT3 and age is not easily explained. Other disease processes may have contributed to impaired deiodination in some. Impaired deiodination is a well recognized non-specific effect of disease in normal individuals and has been suggested to occur in thyrotoxicosis also[5]. Increased contact with physicians and a high index of suspicion may have resulted in the detection of more early cases of thyrotoxicosis amongst the elderly.

Three other studies have looked at the effects of ablative radio-iodine treatment of thyrotoxicosis. Wise *et al.*[6] gave 370 to 444 MBq for small or impalpable thyroids and 550 MBq for larger goitres in 50 patients with diffuse goitre in Australia. Seventy-six per cent were hypothyroid at 2-3 months, and 92% at 6 months. The greater incidence of hypothyroidism compared with our study may be due to the fact that these patients were not rendered euthyroid prior to radio-iodine. Of the four who were euthyroid at 6 months none became hypothyroid during 12 to 18 months' follow-up. Kendall-Taylor and colleagues[7] treated 225 patients, most of whom had Graves' disease, with 550 MBq. Fifty-eight per cent were hypothyroid by 6 months, which increased to 64% at 1 year. In this series also, carbimazole was not given, although some received propranolol.

Ratcliffe *et al.*[8], gave 550 MBq to 93 patients. Only patients with Graves' disease (confirmed by uptake scan) were included. There was a lower incidence of hypothyroidism: 48% at follow-up after 1-9 years, mean 37 months. However, 72% of their patients were on carbimazole or propylthiouracil which was only stopped 3 days before radio-iodine treatment. Radio-iodine uptake was therefore probably suppressed to some extent, accounting for a lower incidence of hypothyroidism. Pretreatment with carbimazole stopped 7 days prior to radioiodine treatment made no difference to the incidence of hypothyroidism in our study, although patients were not randomized to receive carbimazole, and the patients who received carbimazole had initially more active thyrotoxicosis.

Our data therefore suggests that in patients with less severe thyrotoxicosis the incidence of hypothyroidism following 550 MBq I^{131} without carbimazole pretreatment is no different to the incidence in patients first made euthyroid with carbimazole. Use of this dose of radio-iodine maximizes the benefits of close early follow up and reduces the number of patients in whom long-term supervision is required and who may be lost to follow up with untoward consequences. During the first year following radioiodine treatment, it was our practice to see patients monthly for the first 6 months, then at 9 months and then at 12 months. The above data suggests that during the first year attendances can be limited to 2, 3, 4, 8, and 12 months after radio-iodine treatment.

References

1 McDougall IR. *Thyroid Disease In Clinical Practice.* London: Chapman & Hall, 1992:117-18
2 Franklyn JA, Sheppard MC. Radioiodine for hyperthyroidism - perhaps the best option? *BMJ* 1992;**305**: 727-8
3 Hedley AJ, Lazarus JH, McGee SM, Jones RB, Sharp PF, Naven LM, *et al.* Treatment of hyperthyroidism by radioactive iodine. *J R Coll Phys* 1992;**26**:348-59
4 Gregory J, Foster K, Tyler H, Wiseman M. The dietary and nutritional survey of British adults. OPCS Social Survey. London: HMSO, 1990;**12**:41
5 Joassoo A. T_4 Thyrotoxicosis with normal or low serum T_3 concentration. *Aust N Z J Med* 1975;**5**:432-4
6 Wise PH, Burnet RB, Ahmad A, Harding PE. Intentional radioiodine ablation in Graves' disease. *Lancet* 1975; **ii**:1231-2
7 Kendall-Taylor P, Keir MJ, Ross WM. Ablative radio-iodine therapy for hyperthyroidism: longterm follow up study. *BMJ* 1984;**289**:361-3
8 Ratcliffe GE, Fogelman I, Maisey MN. The evaluation of radioiodine therapy for thyroid patients using a fixed dose regime. *Br J Radiol* 1986;**59**:1105-7

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