Weight gain in patients after therapy for hyperthyroidism

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Objective. To determine the prevalence of obesity following therapy for hyperthyroidism and to assess the contributing factors associated with an undesirable weight gain.

Design. A retrospective analysis was undertaken of clinical records for 160 hyperthyroid patients attending an endocrine clinic in Bloemfontein (1994 - 2001).

Results. Of the 160 patients, 143 had Graves' disease and 17 patients had multinodular goitre. Most of our patients (*N* = 147) were treated with radioiodine, 10 patients with carbimazole and 3 patients had thyroidectomy. The median weight gain 6 months after therapy was 5.0 kg, after 12 months 9.0 kg, and after 24 months 12 kg, whereafter body mass stabilised. Before therapy 27.5% of patients had a body mass index (BMI) of < 22 kg/m^2, 29.4% were overweight (BMI > 25 kg/m^2) and 19.3% were obese (BMI > 30 kg/m^2). Two years after treatment only 8.7% of patients had a BMI of < 22 kg/m^2, 27.5% had a BMI > 25 kg/m^2, and 51.3% had become obese. The main factors associated with weight gain 24 months after therapy were poor control of thyroid function on replacement therapy, diagnosis of Graves' disease and need for thyroxine replacement.

Conclusion. This study has shown a large increase (32%) in the prevalence of obesity following treatment for hyperthyroidism. The main weight gain was during the first 2 years after therapy. The main factors contributing to excessive weight gain were need for replacement therapy and poor control of thyroid function.

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Most patients with hyperthyroidism report weight loss. The restoration of body weight is an obvious sign of normalisation of thyroid function after therapy. Previously it has been suggested that patients only normalise their body weight to premorbid levels.[1,2] In clinical practice we observed excessive weight gain in some patients after successful treatment of their hyperthyroidism.[3] The aim of our study was to determine the extent of weight gain in patients treated for hyperthyroidism and to assess the factors associated with an undesirable increase in their body mass.

Patients and methods

We investigated clinical data for 160 hyperthyroid patients referred to our endocrine clinic between 1994 and 2001 for therapy of Graves' disease (143 patients) or multinodular toxic goitre (17 patients). Gender, age at diagnosis, weight, height, body mass index (BMI), and thyroid function at diagnosis were recorded. The clinical characteristics of patients are listed in Table I. Most of the patients were treated with radioiodine (RAI) (147 patients) or with carbimazole (10 patients) and only 3 had thyroidectomy. Of the 150 patients treated with RAI or surgery, 86.7% became hypothyroid and were treated with thyroxine. The duration of follow-up ranged from 6 months to 7 years.

The measurements of weight and height were performed at our clinic, with the patients wearing light clothing without shoes. The body weight and BMI of patients were recorded before the treatment and after the treatment at 6 months, 12 months and then annually. The clinical features, thyroid function and therapy were also recorded at the same times. A history of premorbid weight loss was given by 150/160 patients but the extent of weight loss could not be ascertained accurately. For that reason we used the weight at presentation as a baseline. The patients with co-morbidity predisposing to weight changes (malignancy, known HIV positivity) and pregnant women were not included in the study.

The reference range for free T4 was 11.5 - 23.2 pmol/l, and thyroid stimulating hormone (TSH) 0.35 - 5.5 mU/l (SimulTrac Free T4 (57Co)/TSH (125I); ICN Pharmaceuticals, Diagnostic Division).

Table I. Clinical and biochemical characteristics of 160 hyperthyroid patients (136 female, 24 male)

	Mean	SD
Age (years)	47.3	13.5
Weight (kg)	65.3	14.6
BMI (kg/m^2)	25.1	5.4
Free thyroxine (pmol/l)	82.5	39.6

BMI = body mass index; SD = standard deviation.

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Statistical evaluation

Numerical variables were summarised using means and standard deviations, or medians in the case of skew distributions. Subgroup comparisons were made using Mann-Whitney tests and 95% confidence intervals (CIs) for differences between medians.

Results

The median BMI of patients before therapy was 24.8 kg/m² and the median weight 63.0 kg. The median weight gain after 6 months was 5.0 kg, after 12 months 9.0 kg, and after 24 months 12 kg, whereafter the weight decreased slightly and reached a plateau (Fig. 1). The median increase in BMI after 6 months was 1.77 kg/m², after 12 months 3.56 kg/m², and after 24 months 4.25 kg/m² (Fig. 2). Before therapy 27.5% of patients had a BMI < 22 kg/m², 29.4% were overweight (BMI > 25 kg/m²) and 19.3% were obese (BMI > 30 kg/m²). Two years after treatment only 8.7% of patients had a BMI < 22 kg/m², 27.5% had a BMI > 25 kg/m² and 51.3% had become obese (Fig. 3). There was a 32% increase in the prevalence of obesity 2 years after therapy. As indicated in

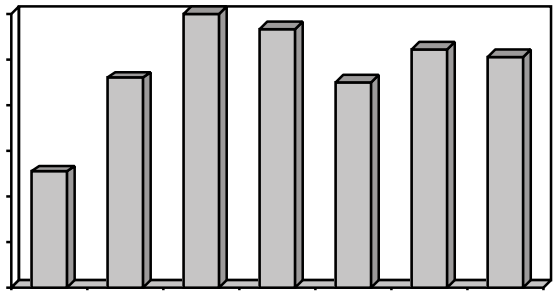

Fig. 1. Weight gain following therapy for hyperthyroidism.

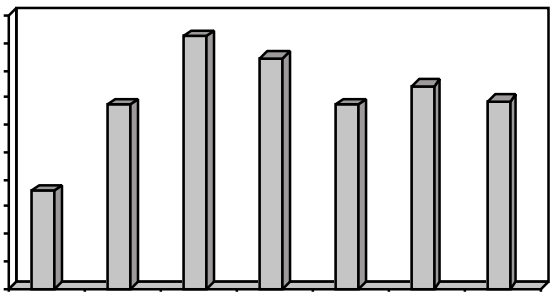

Fig. 2. Increase in BMI following therapy for hyperthyroidism.

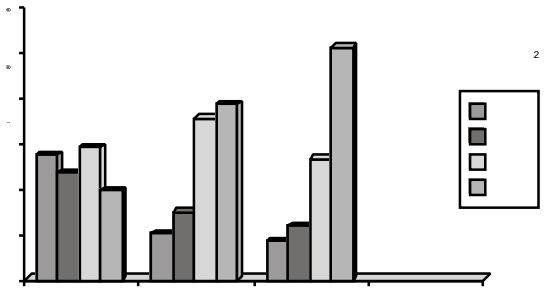

Fig. 3. Prevalence of obesity (before and after therapy).

Table II the main factors associated with an increased weight gain were quality of thyroid function after the therapy, the presence of Graves' disease versus toxic nodular goitre, and the need for thyroxine replacement therapy. The pre-treatment free thyroxine level correlated significantly with weight after the first 6 months ($p < 0.01$) and 24 months ($p = 0.05$) after therapy.

Discussion

In our study of 160 patients treated for hyperthyroidism we demonstrated significant increases in weight gain and prevalence of obesity. Obesity is an increasing problem worldwide, with the incidence of obesity having doubled in the last 30 years.[4] The estimated adult UK population prevalence of obesity (BMI > 30 kg/m²) is now 17%.[5] The prevalence of obesity among patients in our study was already high (19.4%) at presentation, and this increased after therapy.

Table II. Factors associated with increase in BMI and weight gain 24 months after therapy

Factors	Median increase in BMI (kg/m²)	Median increase in weight (kg)
Control		
Poor (*N* = 5)	6.0	15
Good (*N* = 53)	3.65	10
p-value	0.12	0.01
95% CI for difference	–0.54, 5.49	–1, 14
Diagnosis		
Graves's disease (*N* = 71)	4.78	12
Multinodular goitre (*N* = 9)	2.80	7
p-value	0.06	0.06
95% CI for difference	–0.08, 3.83	0; 10
Thyroxine		
Yes (*N* = 73)	4.63	12
No (*N* = 7)	2.40	6
p-value	0.05	0.05
95% CI for difference	–0.01, 4.17	0, 10

In the South African population obesity is frequent; 32 - 55% of the middle-aged female population is obese.[6] Two years after therapy for hyperthyroidism 51.3% of patients were obese and in total 78.7% of patients were overweight. Weight gain in our study was high (12 kg) compared with a similar study,[7] where it was only 5.5 kg. The increase in prevalence of obesity in treated patients was also much higher (32%) than in the study by Dale *et al.*[7] (8.5%). Our patients continued to gain weight for 2 years after therapy; this observation is similar to findings of other long-term studies, which suggest that weight stabilises after 2 - 5 years.[7,8] Weight gain after normalisation of thyroid function is desirable in underweight patients — so-called catch-up weight — but not in patients with normal weight or those who are overweight. We did not find any significant differences in degree of weight gain among these weight groups. This can be explained by the long-term disturbance in the neurochemical regulation of appetite and weight during the period of dietary freedom granted by hyperthyroidism.[9] The metabolic rate reduces with a decrease in serum thyroid hormone concentration[2] and this may lead to continuous weight gain if food intake is excessive. After successful antithyroid therapy patients should be advised to modify their food intake once the normal BMI is restored. We also observed that patients requiring thyroxine replacement following RAI or surgical therapy gained more weight than patients who remained euthyroid. There is still some controversy about dose and form of thyroid hormone replacement therapy. Some authors suggest that restoration of serum TSH to the reference range by thyroxine alone may constitute inadequate hormone replacement.[10]

We find that poor control of thyroid function is a significant risk factor for excessive weight gain. Even patients with subclinical hypothyroidism (normal free thyroxine level, increased TSH level) gained more weight over a 2-year period than euthyroid patients. According to our protocol, the thyroid function status of patients after antithyroid therapy is followed up monthly until euthyroidism is achieved to avoid any long period of hypothyroidism. The poor control of thyroid function in some of our patients was due to non-compliance on thyroxine therapy. The weight gain and increased adiposity in hypothyroid patients have been shown to be proportional to circulating leptin levels,[11,12] but regulation of food intake is probably not mediated through leptin.[13] Because the control of thyroid function is a modifiable risk factor for excessive weight gain replacement with thyroxine therapy should be started in due time and maintained well.

Conclusion

We demonstrated a large increase (32%) in the prevalence of obesity in previously hyperthyroid patients following antithyroid therapy. Most weight was gained during the first 2 years after therapy. These findings concur with the hypothesis that therapy for hyperthyroidism is a risk factor for obesity. Poor control of thyroid function with replacement therapy is a significant factor contributing to weight gain.

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