

Overweight – a common problem among women treated for hyperthyroidism

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Summary: We sent out a questionnaire to 112 women treated for diffuse toxic goitre 2–5 years earlier to evaluate the prevalence of problems with overweight after the disease. Of 87 responders, about 50% (irrespective of surgical or radioiodine treatment) reported weight problems, and we randomly selected 40 of these women (20 with and 20 without reported weight problems) for a clinical follow-up (32 appearing).

At the follow-up examination (mean 4 years after treatment for hyperthyroidism), 27 women had a higher weight than their estimated premorbid weight. The weight gain correlated with the estimated premorbid body mass index (BMI; $P < 0.005$), indicating that excess weight gainers may have had a premorbid problem now exaggerated in the post-hyperthyroid period. However, many women with a BMI within the limits stated to be ideal (21–25 kg/m²) also showed dramatic increases in weight. In contrast, the average middle-aged woman in our region did not appear to have gained in weight during a corresponding time period as judged from a longitudinal population study. Women with reported weight problems (mean weight increase 15.6%, $n = 16$) did not differ from women without (mean weight increase 6.7%, $n = 16$) as regards pretreatment hormone levels, method of treatment, (change of) smoking habits or post-treatment levothyroxine administration, or in serum concentrations of thyroid hormones, thyrotrophin, cortisol, procollagen-III-peptide, cholesterol, HDL cholesterol or triglycerides.

Women with hyperthyroidism should be informed about the risk of gaining weight after therapy and given early support as to dietary and lifestyle change.

Introduction

Many individuals lose weight during the acute catabolic stage of hyperthyroidism. However, when summing up the final outcome of their disease, many patients tell their clinician that they have in fact gained in weight. Although in one study the mean final weight was only 2.5% above the premorbid weight,¹ a more recent study showed a final weight gain of 16% in a group of patients without dietary intervention and 9.8% in a group receiving dietary advice.² These discrepant results are not readily explained, but one factor of importance may be a sex difference, the former study from a Veterans Administration Medical Center (USA) mainly comprising men and the latter, a study from Great Britain, comprising women. In our experience single patients have even opposed treatment for hyperthyroidism because of fear of weight gain after treatment, referring to anecdotal cases of pronounced gain of weight.

Since we felt that the clinical importance of this consequence of treated hyperthyroidism has been underestimated in clinical practice, we performed a retrospective study of patients who recently received radioiodine or surgical treatment for hyperthyroidism at our hospital. We only studied women, where the prevalence of thyroid disease is high, and where weight problems may be more pronounced judging from the British study.³

Patients and methods

Clinical background

In our region, individuals with hyperthyroidism are either selected for operative treatment (subtotal thyroid resection) or radioiodine treatment (100 Gy absorbed dose to the thyroid calculated after ¹³¹I-uptake and scintigraphic and palpatory estimation of thyroid volume) according to generally accepted criteria. All patients planned for surgery are treated with anti-thyroid drugs (methimazole) until euthyroidism when levothyroxine is added for

at least 3 weeks. Preoperative iodine treatment is given if the patient develops adverse reactions against anti-thyroid drugs. Individuals planned for radioiodine are treated with methimazole in case they have pronounced symptoms. Patients awaiting operative or radioiodine treatment are, when troubled by pronounced palpitations, also treated with betablockers. In only rare cases, with no obvious goitre, long-term methimazole administration is tried as a definitive treatment. After operation or radioiodine treatment, the patient is followed closely, especially during the first year. Treatment with levothyroxine is started when the individual shows laboratory and clinical evidence of hypothyroidism, individuals receiving levothyroxine thus only having experienced a brief period of slight hypothyroidism.

Study design

In 1989 we mailed a brief questionnaire to 112 randomly selected women then aged 23–54 years who had received treatment (surgery or radioiodine) for diffuse toxic goitre in 1984–1987. Patients with other diseases were excluded. The women were asked whether they had had problems with their weight after their thyroid disease, whether their problems now were slight or pronounced, and if they received treatment with levothyroxine.

From the responders of this inquiry we randomly selected 40 women, 10 with pronounced and 10 without weight problems in each treatment group (surgery or radioiodine). The women were invited to a follow-up with a detailed interview, blood sampling and a physical examination. In the interview the women were asked about weight problems during the course of their thyroid disease, and the estimated figures for body mass recorded (body mass before, minimum mass during, and mass one year after treatment). Information was also obtained regarding change of size of clothes, contacts with dieticians, 'Weight-Watchers' or similar organizations, present and past smoking habits, present medication and pregnancies since the thyroid disease. The present weight, height, heart rate, systolic and diastolic blood pressures as well as waist and hip circumference were recorded, and body mass index (BMI, present and estimated pre-morbid, kg/m²) and waist/hip ratio were calculated.

Biochemical methods

In the routine thyroid function evaluation done at the time of diagnosis, serum free thyroxine (analogue method) was assayed and an additional assay of serum thyrotrophin (TSH) or total 3,5,3'-triiodothyronine (T3) as described previously.³ The recalled patients were subjected to blood sampling

after overnight fast 08.00–11.00 a.m. Serum TSH and free T4 were determined by immunochemiluminometric procedures: 'Magic Lite' TSH (reference interval 0.3–6.2 mU/l) and FT4 (reference interval 11–22 pmol/l), CIBA-Corning Diagnostics Corp., Medfield, MA, USA). The performance of these assays in our hands will be published separately. Serum total T4 (reference interval 70–160 nmol/l), total T3 (reference interval 1.5–2.7 nmol/l) and free T3 (reference interval 4.3–7.1 pmol/l) and 3,3',5'-triiodothyronine (reverse T3; reference interval 0.07–0.47 nmol/l) were analysed as described previously.⁴ Serum cortisol and procollagen-III-peptide were determined by radioimmunoassays (Cortisol [¹²⁵I] and Procollagen PIIIINP [¹²⁵I], Farnos Diagnostica, Oulunsalo, Finland). Serum cholesterol and triglycerides were determined by colorimetric methods (Monotest Cholesterol and Triglycerides GPO-PAP, Boehringer Mannheim GmbH Diagnostica, Germany). HDL cholesterol was analysed as described previously⁵ after treatment with heparin and MnCl₂. The activities of serum aspartate aminotransferase (EC 2.6.1.1), alanine aminotransferase (EC 2.6.1.2) and alkaline phosphatase (EC 3.1.3.1) were analysed according to the Scandinavian recommendations.⁶

Statistical analysis

Results are given as means (s.d.). We used Student's *t*-test for normally distributed data, for TSH concentrations after logarithmic transformation.

Results

Questionnaire

A total of 87 of 112 women returned the questionnaire. Table I summarizes the results showing that more than half of the patients – irrespective of method of treatment – considered themselves to have a problem with weight gain after having completed their treatment of hyperthyroidism.

Recall group

Of the 40 women selected from the responders of the questionnaire for a recall (20 with and 20 without weight problems; see Methods), 32 agreed to participate. The participation rate in the recall group with problems was similar to that of the group without weight problems (Table II). The range of total weight change was –1 to +26 kg for women with, and +1 to +15 kg for women without weight problems and, in all, 27 of the 32 women had gained in weight. We could not find any relation between the change in weight during

Table I Prevalence of weight problems after therapy for hyperthyroidism by questionnaire mailed to 112 women treated for hyperthyroidism

| Therapy | Response rate | Weight problem after therapy | | | On L-thyroxine (%) |
|-------------|---------------|------------------------------|--------|-----------|--------------------|
| | | Pronounced | Slight | Total (%) | |
| Surgery | 51/62 | 16 | 11 | 53 | 86 |
| Radioiodine | 36/50 | 10 | 9 | 53 | 80 |

Table II Clinical and laboratory data mean(s.d.) at follow-up of patients previously treated for hyperthyroidism

| | Present problem with weight* | No problems with weight* |
|---|--------------------------------|--------------------------------|
| Recall participation rate, surgery | 8/10 | 6/10 |
| Recall participation rate, radioiodine | 8/10 | 10/10 |
| Number of individuals studied | 16 | 16 |
| Weight problems before disease | 5 | 0 |
| Reported weight before disease (kg) | 63.4 (9.8) | 56.8 (7.0) |
| Estimated body mass index before disease (kg/m ²) | 23.4 (3.3) | 20.6 (1.9) |
| Reported minimum weight during disease (kg) | 62.5 (12.1) | 53.5 (8.5) |
| Reported weight 1 year after disease (kg) | 70.3 (12.6) | 58.7 (8.8) |
| Smoker before thyroid disease | 9 | 7 |
| Smoker after thyroid disease | 8 | 6 |
| Dietician, 'Weight Watchers', etc. after disease | 5 | 1 |
| Increased size of clothes after disease | 13 | 10 |
| Present weight (kg) | 73.3 (14.0) | 60.6 (10.1) |
| Present body mass index (kg/m ²) | 27.2 (5.1) | 22.1 (3.0) |
| Present waist/hip ratio | 0.78 (0.07) | 0.74 (0.05) |
| Years between treatment and follow-up | 3.5 (1.4) | 4.1 (1.3) |
| Age at treatment (years) | 41 (8.5) | 41 (9.0) |
| Serum T3 concentration at diagnosis (nmol/l) | 6.3 (1.6) | 7.0 (4.2) |
| Serum free T4 at diagnosis (pmol/l) | 50.1 (14.1) | 48.8 (20.4) |
| Number with L-thyroxine | 15 | 12 |
| Dose of L-thyroxine (mg) | 0.96 (0.41) | 0.95 (0.56) |
| <i>Present laboratory data</i> | | |
| Free T4 (pmol/l) | 19.9 (3.5) | 18.0 (4.3) |
| Free T3 (pmol/l) | 4.7 (1.8) | 4.8 (0.8) |
| Reverse T3/T4 | 0.33 (0.12) × 10 ⁻² | 0.28 (0.06) × 10 ⁻² |
| Free T3/Free T4 | 0.23 (0.07) | 0.27 (0.08) |
| Thyrotropin (mU/l) | 1.4 | 2.7 |
| Cortisol (μmol/l) | 323 (92) | 334 (153) |
| Cholesterol (mmol/l) | 5.9 (1.3) | 5.6 (1.2) |
| HDL cholesterol (mmol/l) | 1.7 (0.4) | 1.6 (0.3) |
| Triglycerides (mmol/l) | 0.82 (0.66) | 0.77 (0.45) |
| Procollagen-III-peptide (μg/l) | 3.3 (0.8) | 3.0 (0.6) |

*As recorded by the patient.

the hyperthyroid phase and later weight increase. No individuals experienced any period with pronounced hypothyroidism before levothyroxine substitution. There was a significant correlation

between the final weight increase (weight at time of recall minus pre-morbid weight) for the whole group of women and estimated body mass index before thyroid disease ($r = 0.54$; $P < 0.005$, see Figure 1).

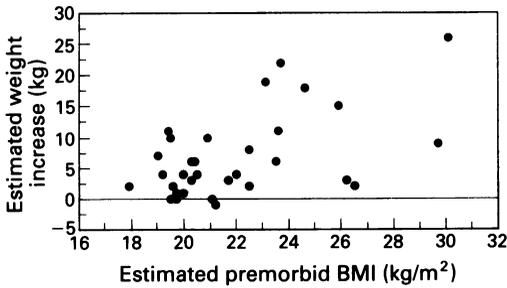


Figure 1 Relationship between estimated weight gain and estimated body mass index in 32 women treated for hyperthyroidism after a mean follow-up of 4 years.

When comparing clinical and laboratory data of the two groups (Table II), it is seen that women with weight problems after hyperthyroidism had a higher body mass prior to the disease ($P < 0.05$), and had experienced problems with weight before the disease. The two groups of individuals did not differ as regards their age at the time of diagnosis of the thyroid illness, severity of hyperthyroidism as judged from thyroid hormone concentrations during disease, (change in) smoking habits, levothyroxine treatment or present serum concentrations of thyroid hormones or procollagen-III-peptide, the latter being an indicator of the peripheral effects of thyroid hormones.⁷ The women with weight problems did not have a higher serum concentration of thyrotrophin or lower concentration of free thyroxine. The groups did not differ in blood pressure, pulse rate or blood glucose concentration (data not shown in table). No pregnancies had occurred in the two study groups since the disease. As expected, the weights before disease and at follow-up in the group of women who regarded themselves as having weight problems differ significantly ($P = 0.0001$, mean weight increase 15.6%), but a significant difference ($P < 0.005$, mean weight increase 6.7%) was also recorded in the women who had declared they had not experienced such problems.

Discussion

The results of our study show that many women increase considerably in weight as a final outcome of hyperthyroidism. We chose to emphasize the opinion of the women themselves of this problem, since a mere record of weight gain would not detect an increased, but successfully combated, tendency to gain weight. The results from the questionnaire indicate that about every second woman exper-

iences a weight problem after successful treatment of their thyroid disease as judged from a mean follow-up time of 4 years.

This retrospective study lacks a control group. We therefore compared the weight behaviour of our study group with that of the general population. A longitudinal population study of random samples of middle-aged women in our region⁸ revealed that the mean weights of women aged 44 years ($n = 336$) and 52 years ($n = 387$) were 68.0 kg and 64.5 kg, respectively, in 1974–1975 and 66.3 kg and 65.4 kg, respectively, in 1980–1981 (Dr Leif Lapidus, personal communication). Thus, in contrast to our group of women treated for hyperthyroidism, these women did not increase in weight during a corresponding time period. A cross-sectional study would not be appropriate to use as a control; in fact a recently published study of middle-aged women in 1980–1981 showed that women 5 years older had a 5% higher body weight.⁹

It might be argued that the weight increase might be associated with the therapeutic methods used here, surgery or radioiodine being much preferred to thyrostatic treatment. However, as indicated by the study reported by Alton and O'Malley,² patients treated with thyrostatic drugs do also present with problems with weight.

We thus conclude that many and maybe even the majority of women experience a troublesome or alarming increase in weight after being treated for hyperthyroidism, and that this problem in some way is related to their thyroid disease. Our study shows that the problem does not seem to be related to method of treatment, severity of disease as judged by pretreatment thyroid hormone concentrations, change in smoking habits, treatment with levothyroxine or difference in peripheral conversion of thyroxine to triiodothyronine. We could, however, not obtain reliable information as regards the duration of the hyperthyroid phase. The fact that the weight gain of the 32 women correlated with the estimated premorbid BMI indicates that excess weight gainers may have had a premorbid weight problem exaggerated after the thyroid disease. However, many women with BMI within limits generally stated to be ideal (21–25 kg/m²) also showed dramatic increases in weight (Figure 1).

It is therefore possible that after thyrotoxicosis there is a long-term disturbance in the neurochemical regulation of appetite and weight.¹⁰ Another possibility is that the individual will have a diminished metabolic rate or rate of energy metabolism,¹¹ due to a reduction during the thyrotoxic phase of lean body mass, which is not reversed after therapy. This is a possible mechanism in obese individuals with 'weight cycling'¹² and for adolescent wrestlers with repeated weight loss and regain.¹³ Many individuals in these groups

are known to have pronounced problems in keeping their weight. All patients with hyperthyroidism should be given dietary advice. However, as indicated by the British study² and also our study, in many cases such advice is of limited help, which might indicate that more profound lifestyle changes are needed.

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