Clinical versus biochemical assessment in thyroxine replacement therapy: a retrospective study

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ABSTRACT – A retrospective audit of a thyroid clinic revealed that only 67% of clinical assessments of thyroid status in patients receiving thyroxine replacement therapy were correct. The identification of patients on excessive doses of thyroxine appears to be the most difficult by clinical assessment alone, only 10% of those patients with a suppressed TSH level being identified. This study emphasises the importance of thyroid function tests in the assessment of patients on thyroxine replacement.

Thyroid deficiency is a common disorder with an estimated prevalence of overt hypothyroidism between 0.8% and 1.1% [1]. The follow-up of these patients involves both hospital doctors and general practitioners, and there is disagreement about the best method of assessment. Most authors advocate the use of a combination of clinical examination and thyroid function tests, the latter including a sensitive assay of TSH using an immunoradiometric assay [2]. Others have suggested the use of clinical assessment alone [3]. This is an important issue, not only because of the financial implications in supplying outpatient appointments and/or performing thyroid function tests regularly on such a large number of patients, but also because there is at present concern over the effects of supraphysiological replacement on bone loss [4]; this is of particular significance in postmenopausal women who constitute the majority of patients receiving thyroxine replacement therapy.

Audit of medical practice has been advocated for some time, and this has been reinforced by the recent policy statement of the Royal College of Physicians [5] and the White Paper on the NHS [6].

This paper is a retrospective audit of the effect of the clinical examination and thyroid function tests on the management of patients receiving stable doses in thyroxine replacement therapy. Its purpose was to determine the value of hospital based clinical assessment and thyroid function testing in these patients and to use the results to plan an economical strategy for their future management.

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Methods

Data were collected retrospectively from the records of patients attending the thyroid clinic at St Thomas's Hospital over a period of 6 months from October 1986 to March 1987. Patients receiving thyroxine for thyroid carcinoma were specifically excluded since the aim in these patients is to suppress TSH levels. The thyroid clinic is held once a week and is staffed by doctors with varying experience in the management of thyroid disease, including a consultant, senior registrars and registrars. The patients studied had all been receiving thyroid replacement therapy at a constant dose for at least 1 year. They were identified from three sources—the clinic appointments book, the letters written to their general practitioner following their clinic attendance, and the results of thyroid function tests taken at their clinic visit. Information concerning patients on thyroxine replacement therapy was collected in the following way. Their name, age, sex and diagnosis were recorded. From the first attendance of the patient within the study period (the index visit) the thyroxine dose prescribed, the clinical assessment of the patient (hypothyroid, euthyroid, hyperthyroid), the seniority of the clinician involved (consultant, senior registrar, registrar) and the results of the thyroid function tests were recorded. Serum TSH was measured using an Amerwell immunoradiometric assay which has an intra-assay coefficient of variation of 2.5% at a TSH of 4.9 mU/litre and an inter-assay coefficient of variation of 5.2% at a TSH of 3.8 mU/l. The normal range for our laboratory is 0.3–6.5 mU/l. A TSH level below 0.3 mU/l was assumed to represent

excessive thyroxine replacement and a level above 6.5 mU/l to represent inadequate replacement, although it is to be expected that 5% of the normal population will have values outside the normal range. The effect of the result of the thyroid function tests on the subsequent clinical management of the patients was assessed by recording whether the clinical diagnosis or the patients' treatment dose was revised at their next clinic attendance.

Results

During the 6 months study, of the 622 individual patients who attended the clinic, 328 met the study criteria. Complete information was available for 314 (96%) (263 women and 51 men). The aetiology of their thyroid deficiency was as follows: primary in 184 (58.6%), subsequent to radioiodine administration in 125 (39.8%), post-thyroidectomy and chronic lithium therapy in 5 (1.6%). The age range was 23–86 years (median 59 years) and the median dose of thyroxine taken was 100 micrograms (range 25–300).

Clinical assessment indicated that the numbers of patients considered to be on excessive replacement, correct replacement or under-replacement at their initial visit were 12 (3.8%), 268 (85.4%) and 34 (10.8%) respectively. Corresponding figures based on the TSH estimation were 60 (19.1%), 190 (60.5%) and 64 (20.4%). The number of patients who had TSH levels above 10 mU/litre was 36 (11.5%). Correlation of the clinical assessment with the results of the thyroid function tests is shown in Table 1. Overall agreement was seen in 67%. This value seemed to depend on the seniority of the clinician involved—registrars scored 63%, senior registrars 69% and the consultant 74%—although this difference did not reach significance. Of the patients who received inadequate replacement on the basis of their TSH level >6.5 mU/l, 42.2% were identified by clinical examination. The corresponding value for patients who were considered to have received over-replacement (TSH <0.3 mU/l) was 10.0%.

In patients considered on clinical grounds alone to be taking the correct replacement dose the results of the thyroid function tests provoked a subsequent increase or reduction in the dose of thyroxine in 4.5% and 5.1% respectively. In four patients considered to have received inadequate replacement according to the results of their thyroid function tests the dose of thyroxine was not increased because of coexisting ischaemic heart disease. Overall the management of 27 (9.6%) patients was altered in the light of the results of thyroid function tests.

Table 1. Comparison of the results of clinical examination with TSH (IRMA) in 314 patients receiving thyroid replacement therapy

TSH (mmol/litre)	Clinical assessment: Hyperthyroid *n* (%)	Euthyroid *n* (%)	Hypothyroid *n* (%)
<0.3	6 (1.9)	53 (16.9) [a]	1 (0.3)
0.3–6.5	6 (1.9)	178 (56.7)	6 (1.9)
>6.5	0 (0)	37 (11.8) [b]	27 (8.6)

[a]Twelve of these patients had their thyroxine dose reduced at their subsequent visit.
[b]Fifteen of these patients had their thyroxine dose increased at their subsequent visit.

Discussion

Retrospective studies of this type have the disadvantage that the data may not be complete or entirely accurate. In our study this problem was minimised by identifying patients from three separate sources, and collecting simple data from the case records. These data were available for almost all the patients. For our purpose a retrospective study has the particular advantage that it audits a clinic under the usual operating conditions, whereas a prospective study might affect the way in which the patients are assessed. The introduction of the sensitive TSH assay to our hospital occurred just before the study period, so some of the results may be due in part to the learning curve associated with interpretation of the results.

The results of this study demonstrate that a substantial minority of patients receiving a stable dose of thyroxine have abnormal TSH estimations, indicating either inappropriate dosage or poor compliance. Most of these patients were not identified by clinical examination alone, even by experienced clinicians. This finding was not unexpected, as there has been a gradual reduction of the dose in thyroid replacement therapy over the past two decades since the introduction of sensitive thyroid hormone and TSH assays [7]. Evidence exists that patients with suppressed TSH levels have an accelerated rate of bone loss [4] which is most likely to cause clinical problems in the postmenopausal women who form the majority of the population surveyed. Those with elevated TSH levels may run the risk of abnormal lipid metabolism and subsequent atheroma. There is therefore a strong argument for adjusting the dose of thyroxine in all patients with abnormal TSH levels once poor compliance has been excluded. Even if alteration in dosage is confined to patients with symptoms attributable to disturbed thyroid function, regular TSH estimations appear necessary. As the study has demonstrated, clinical assessment underestimates the number of patients who are poor compliers or are receiving inappropriate doses of thyroxine.

Since thyroid function testing has an important role in the follow-up of patients receiving stable thyroxine replacement, is it necessary for all these patients to attend a thyroid clinic? A more economical approach might be to perform annual thyroid function tests on all patients, and to arrange outpatient appointments only for those who have abnormal results. This would be along similar lines to those proposed by the SAFUR group [8]. This would have reduced by half the num-

ber of clinic appointments made during the study period. The practice in our clinic now is to discharge patients who have stable thyroid function tests, with clear instructions to both the patient and the general practitioner to perform thyroid function tests on an annual basis. Any patients with abnormal results are referred back to the clinic. We are unable to set up a computer based recall system owing to financial restraints.

This study has emphasised the value of clinical audit in the planning and execution of strategies for patient management.

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