antibody production. This effect could be of potential value in influencing the autoimmune process in these conditions.

This work was supported by grants from the Medical Research Council, the North of England Cancer Campaign, the Wellcome Trust, the League of Friends of the Royal Victoria Infirmary, the Ernest and Minnie Dawson Cancer Trust, the research committee, Newcastle Area Health Authority (Teaching), and the Welsh Office Scheme for Development of Health and Social Research. We are most grateful to Miss B Sims for secretarial help.

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(*Accepted 1 September 1980*)

Thyroxine replacement therapy: prescribing patterns and problems in 2710 patients

SCOTTISH AUTOMATED FOLLOW-UP REGISTER GROUP

Summary and conclusions

The use of thyroxine replacement therapy was studied in 2710 patients with a previous diagnosis of either thyrotoxicosis or primary hypothyroidism. The patients, who were treated in five centres, were followed-up continuously using an automated register. Seventy per cent of patients had been prescribed daily doses of thyroxine of 200 μg or more. The estimated 10-year cumulative incidence of detected undertreatment was 13·2% (95% confidence limits 10·9-15·6%). The median cumulative incidence of recognised overtreatment was 6·2%.

Improved patient education and the dissemination of guidelines to doctors on the use of thyroxine replacement may reduce the incidence of undertreatment or overtreatment.

Introduction

Overt spontaneous hypothyroidism is a relatively common condition with a prevalence of up to 2% of the general population aged 18 and over.[1] To this must be added patients with congenital hypothyroidism, currently estimated at between 1 in 3000 to 1 in 9000 live births.[2] Hypothyroidism is common in patients who have been treated for thyrotoxicosis; in a recent study in four different teaching hospital centres, the prevalence of hypothyroidism ranged from 24% to 63% in a total of 1902 patients after radioiodine therapy and from 23% to 52% in 1428 patients after subtotal thyroidectomy (unpublished observations).

Many studies[3 4] have shown that patients often do not take long-term medication in the recommended dosage and sometimes stop taking it altogether either on their own initiative or because of the intervention of another doctor. The prevalence of inadequate treatment with thyroxine was as high as 75% in one study.[5] This problem was re-examined in thyroxine-treated patients who were under continuous surveillance through a follow-up register[6] and were offered an assessment of their thyroid status every 12 to 18 months over 10 years.

The Scottish Automated Follow-up Register (SAFUR) has been providing follow-up facilities for patients treated for thyroid disease since 1967, as a joint venture between hospital and primary care. The system is used by hospital doctors in five Scottish centres and 1547 general practitioners to follow-up patients treated by radioiodine, subtotal thyroidectomy, and thyroxine replacement. There are now over 6000 patients on the register. Follow-up examinations are usually carried out by general practitioners, and biochemical analyses, processing, and reporting of results are performed by a central registry with laboratory and computing facilities.

Patients and methods

Analysis of 2710 computer-held patient follow-up records produced information about 2926 prescriptions for thyroxine. Twenty-seven prescriptions (0·9%) were for less than 100 μg/day and 204 (7%) for 300-500 μg/day. Lists of these patients were sent to the centres concerned for checking for possible errors in recording and for appropriate action. In the remaining group of prescriptions only 861 (29%) were for doses in the range of 100 to 150 μg, 1714 (59%) were for 200 μg, and 120 (4%) for 250 μg.

When undertreatment was detected at the follow-up examinations[7]

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an attempt was made to determine whether it was due to inadequate prescription or irregular use of medication. Follow-up assessments consisted of an initial examination and biochemical screening test (protein bound iodine or serum thyroxine) carried out by general practitioners followed by assessment at a hospital clinic for those with results outside the reference range. Patients were eligible for recall to the clinic if the serum thyroxine concentration was below 90 nmol/l (7·0 μg/100 ml) or greater than 290 nmol/l (22·5 μg/100 ml). Reassessment was based on the procedures usually used in individual clinics for estimating adequate thyroxine replacement.

Results

A total of 217 adjustments (187 to increase or restore the original dose, 30 to decrease the dose) were made to the replacement treatment either for hypothyroidism or because of excessive thyroxine replacement. By applying a follow-up life-table analysis[8] to the data in the patient records, the 10-year cumulative incidence of undertreatment apparently due to either inadequate dosage or irregular usage, in individual patients was found to be 13·2% (95% confidence limits 10·9-15·6%) (fig 1). The median cumulative incidence of recognised excess treatment with thyroxine over six years in four teaching centres was 6·2%.

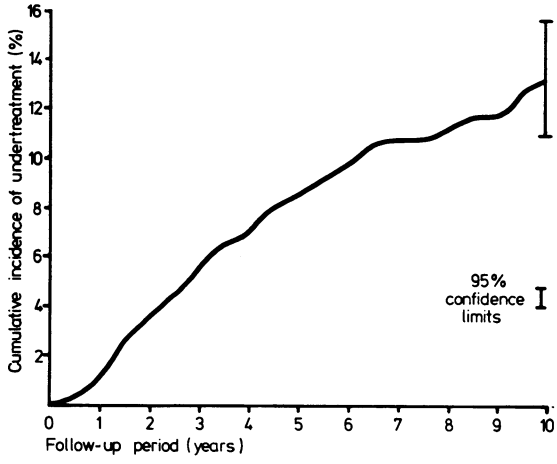

FIG 1—Thyroxine replacement therapy: cumulative incidence of undertreatment.

Discussion

This analysis of prescriptions for thyroxine shows that most patients were receiving more than the replacement dose suggested to be optimal for suppressing serum thyrotrophin concentrations in three studies from the UK,[9] USA,[10] and Sweden[11] (100 to 150 μg). Nevertheless, it remains to be shown whether all of these patients do in fact have persisting biochemical or any other evidence of hyperthyroidism and what effect "overtreatment" has on the long-term morbidity and mortality of this group. The sensitivity of the system for detecting patients who are possibly overtreated with thyroxine could be improved by lowering the upper limit of the "acceptable" range of serum thyroxine results obtained at follow-up examinations. This would, however, inevitably increase the work of reassessing patients, and our own studies have not so far produced evidence of any adverse effects—for example, on the cardiovascular system.

There are considerable discrepancies in the doses recommended for thyroxine replacement between the recent studies cited[9 10 11] and some other standard references. Obviously information in formularies and textbooks will be modified in new editions but it is equally important that guidelines issued by manufacturers are brought into line with current knowledge.[12] The demonstration and feedback of information that the recorded dose of medication was unexpectedly either very low or high enabled the management of those patients to be reviewed by the clinicians concerned.

In a continuous follow-up programme the minimum annual incidence of undertreatment with thyroxine appeared to lie between 1 and 2% of the treated population, as determined by biochemical screening tests followed by clinical examination. Information so far available indicates that inadequate patient education, poor comprehension or compliance, lack of communication, and errors in either prescribing or dispensing are responsible for many of these events. A further possibility is a change in the patient's metabolic requirements for thyroxine if the concentration of circulating thyroid stimulating immunoglobulins falls in patients who become hypothyroid after treatment with destructive therapy for thyrotoxicosis.[5]

Some important conclusions can be drawn from this study. The current moves to discard some outdated prescribing practices, such as the use of thyroid extract,[13 14] should be extended to discouraging the use of arbitrary doses of thyroxine. Many of the patients in this study were initially treated before two new facts emerged about thyroxine metabolism and its effect on the pituitary thyroid axis: firstly, that thyroxine may be a prohormone which undergoes peripheral conversion to triiodothyronine so that larger doses of thyroxine are not required to compensate for lack of endogenous triiodothyronine[15] and, secondly, that the average dose of thyroxine required to suppress concentrations of thyrotrophin is about 160 μg/day.[9] Improved dissemination of this information is now clearly required. For general practitioners this might be achieved through the available communications network of a follow-up system such as the register.

The use of explicit guidelines for starting and controlling treatment should be considered. For thyroxine replacement therapy the important criteria and procedures could be conveniently summarised in the form of a decision-tree (fig 2). Patient education at the start of treatment together with patient-held medication records and reinforcement at the time of

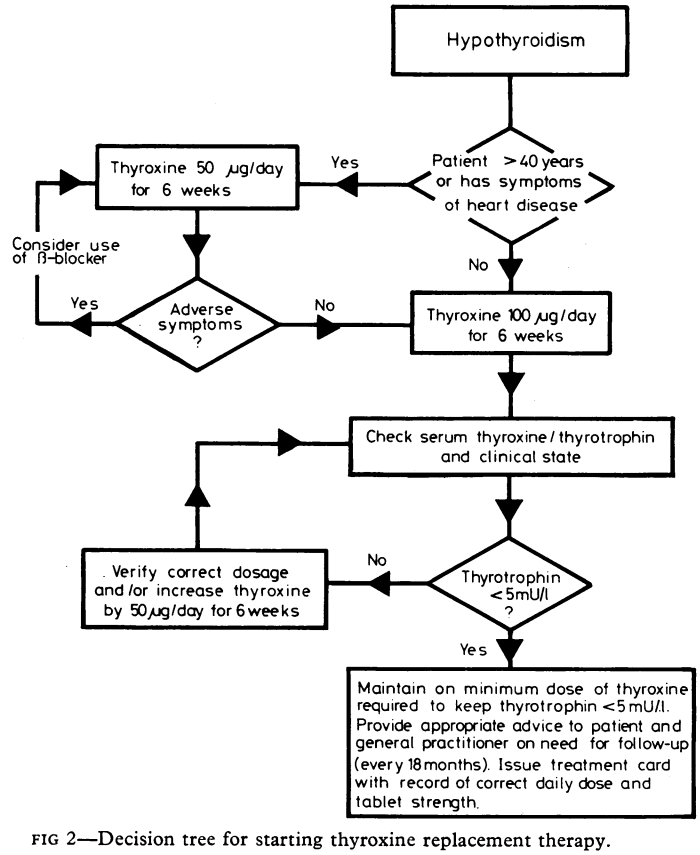

FIG 2—Decision tree for starting thyroxine replacement therapy.

follow-up may lead to measurable improvements in understanding and compliance which would be reflected in the slope of the incidence curve for undertreatment in fig 1, but the current evidence about the value of this kind of approach is incomplete or conflicting and requires further evaluation. Finally, the evidence from this study suggests that thyroxine medication, its prescribing and control, would be simpler and safer with a single tablet strength of 50 μg.

The methods used in the follow-up system for detecting undertreatment now require modification, including the use of serum thyrotrophin estimations to improve both sensitivity and specificity of the follow-up screening tests. The follow-up system offers opportunities for more detailed studies of those at particular risk of undertreatment or overtreatment.

This work was supported by a grant from the Scottish Home and Health Department. We gratefully acknowledge the work of our registry secretaries, in particular Helen Thomson, Maureen Whittet, Vivienne Nunn, and Sheena Ogilvy.

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(*Accepted 27 August 1980*)

Relevance of colour vision and diabetic retinopathy to self-monitoring of blood glucose

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Summary and conclusions

A study was performed to determine the effect of colour vision defects and diabetic retinopathy on diabetic patients' ability to use a visual method of measuring their own blood glucose concentrations. Forty-eight diabetics whose colour vision and retinal status was assessed by an ophthalmologist carried out 311 blood glucose estimations using oxidase-peroxidase test strips which were then compared with laboratory values. There was a trend towards poor performance with advancing age but neither colour vision nor diabetic retinopathy had a significant effect on patients' ability to use this visual method of estimating blood glucose concentrations.

The vast majority of diabetics who will benefit from being able to monitor their own blood glucose control should have no difficulty in using a visual method of testing, even if they do have defects of colour vision.

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Introduction

A major aim in treating diabetics is preventing the serious long-term complications. Watkins[1] has reviewed the recent experimental and clinical evidence which increasingly implicates poor metabolic control as a major factor contributing to diabetic small blood vessel disease. The widely used estimation of urinary glucose excretion is always unreliable when the renal threshold is abnormal, may correlate poorly with blood glucose concentrations even when the renal threshold is apparently normal,[2 3] and fails to detect hypoglycaemia. Measurement of glycosylated haemoglobin reflects blood glucose control in the previous few weeks but is of little use for the day-to-day adjustment of insulin therapy.[4] Self-monitoring of blood glucose concentrations by diabetics using reflectance meters has been shown to be practical,[5 6] but the accuracy of the instruments has been questioned[7] and their use does mean a capital outlay.

Experienced observers can now measure blood glucose accurately without a meter using BM Test Glycaemie 20-800 strips.[8] These glucose oxidase-peroxidase strips simultaneously develop two colours which are matched by eye on a colour comparison scale ranging from 1·1-44·4 mmol/l (19·8-799 mg/100 ml). Colour vision defects of all types are more common in diabetics, however, and patients with retinopathy are particularly liable to defects in blue-yellow discrimination.[9-11] We therefore evaluated the colour vision of 48 diabetics before assessing their ability to use these test strips for blood glucose self-monitoring.