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The Challenge of Thyroid Hormone Replacement in Primary Care

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Abstract

Seemingly, the treatment of hypothyroidism is very straightforward. A single oral dose of levothyroxine is taken once daily in the morning before breakfast. Moreover, the monitoring of thyroid function is uncomplicated and requires a simple blood test. Yet, in spite of this, a significant proportion of patients on long term treatment have not had thyroid tests performed in the last 12 months and of those who have, many are found to be out of range, with potentially serious health implications. We describe our experience and refer to the published literature.

Introduction

Both over- and under-replacement of thyroid hormone are associated with adverse health consequences. Potential effects of over-replacement include reduced bone mineral density [1] and increased fracture risk particularly in the elderly [2,3]. A low or suppressed TSH is also associated with an increased risk of atrial fibrillation [4]. By contrast, suboptimal replacement may result in reduced quality of life, weight gain, poor memory, depression, or psychosis [5,6]. Severe under-treated hypothyroidism could lead to dementia and even coma [7]. In addition, women with elevated TSH at the time of conception have an increased risk of adverse pregnancy outcomes with potential negative effects on the child's cognitive development [8]. TSH monitoring is crucial in ensuring patients with primary hypothyroidism on thyroid hormone replacement are optimally treated in order to minimise the risk of these complications [9].

We were interested to look at our local population and assess the prevalence of optimum thyroid hormone replacement. In particular, we investigated the proportion of patients on long term levothyroxine who had had their TSH tested in the last 12 months and in whom the result was in range. We further investigated the proportions with high or low TSH. Because older populations may be particularly susceptible to the effects of over-replacement, we analysed the prevalence rates in those over 65 years of age.

Method

We audited four local Surrey practices with a total patient population of 63, 534 patients. These Practices were directly recruited due to their close proximity to the author's Practice, and their GP's were happy to share anonymised patient data with us. All practices were using EMIS software to support their electronic patient record systems. The results were combined to build up a picture of local prevalence. EMIS inquiries using population reporting manager were entered to ascertain the prevalence of treated hypothyroidism. From this cohort, we analysed the proportion where the TSH had been checked within the last 12 months and from the results, the proportion with TSH falling within the local laboratory reference range (0.35 -5.0 mU/L). We further assessed the results in the subgroup aged over 65 years.

Results

The prevalence of patients with hypothyroidism treated with levothyroxine was 3.07% (1953/ 63,534). Data was obtained for these 1953 patients. Of these, 18 patients had no TSH on record. In 1474 patients (representing 75.5%), there was a record of a patient's TSH result within the last 12 months; 1019 of these results (representing 69%) were found to be in the local reference range. Thus approximately half (52%) of all treated hypothyroid patients in these practices (1019/1953) had evidence of both TSH testing and the latest result in range within the last 12 months.

Further analysis of patients with treated primary hypothyroidism with a TSH on record revealed 589 patients with latest TSH (regardless of date) not within local range. Amongst these patients, the latest TSH was >5mU/L (30%) and >10mU/L (7.8%). By contrast, 414 of the 589 patients (70%) had latest TSH<0.35mU/L. Excluding patients currently pregnant or coded with thyroid cancer, 44% (177/406) were aged more than 65

years. 54% (221/406] had TSH <0.1mU/L representing 11% of total population with treated primary hypothyroidism.

Discussion

Treatment of hypothyroidism aims to restore TSH into the normal range avoiding the hazards of over- or under-replacement. Similar to other prevalence studies [10,11], we found a worryingly high proportion of patients to be sub-optimally treated. In a general population study of more than 58, 000 patients, inadequate thyroid hormone replacement was present in 37% comprising just fewer than 20% with over-replacement and 17% under-replaced [11]. Under-replacement was associated with male gender and younger age whilst long duration of treatment correlated with over-replacement. In that study, 12% had not had a thyroid test in the preceding 12 months. In another study of over 65 year-olds taking levothyroxine, 41% had suppressed TSH and 16% had raised values indicating over- and under-replacement respectively [12]. We observed that a quarter of patients in our locality were not receiving annual TSH monitoring, and a third were not achieving TSH within local reference range.

The commonest factor leading to failure of oral thyroid hormone replacement is non-adherence to treatment [13]. Patients may miss medication doses because of memory deficits resulting from their hypothyroidism [14], or due to co-existing dementia / memory impairment. Depression or other psychiatric disorders may also be relevant. Surprisingly despite its uncomplicated administration, non-adherence to thyroid hormone replacement is similar to other long term conditions that require far more complex treatment schedules [15]. It is important to exclude conditions that might interfere with the absorption of thyroid hormones. Our local endocrine unit has a standard protocol to assess levothyroxine absorption which includes testing for coeliac disease, atrophic gastritis, and H. pylori infection. Patients receive a directly observed single weekly dose of levothyroxine calculated as [1.6 × weight (kg) × 7] µg. The rationale for weekly dosing is the long half-life of levothyroxine which is in the range of 7 days [16].

FT4 and TSH are then measured two hours after the dose to ensure adequate gastrointestinal absorption and thereafter measure TSH at weekly intervals. If the TSH is still not in range, the weekly dose is increased to [2 x weight (kg)x7]µg for 2 weeks and if still elevated, the same dose is given divided as twice weekly for a further 2 weeks [17]. In this way we are able to assess if there is evidence of poor absorption whilst simultaneously offering the option of once or twice weekly dosing for those patients who show a good response. Interference in the absorption of thyroid hormones may also be due to concomitant food, soya or coffee [18]. Drugs such as antacids, ferrous salts, and calcium carbonate can also reduce thyroid hormone absorption [19] and the GP will need to check that the patient is taking the levothyroxine on its own before eating. The risk of under-replacement of levothyroxine in the elderly is more controversial since there is evidence that a slightly raised TSH is associated with a lower mortality [20]. Age-specific TSH reference ranges have been advocated particularly in the very elderly [21].

Conclusion

Nearly a quarter of patients in this study on long term thyroid hormone replacement were not receiving regular TSH monitoring. In 21% of patients, results suggested over-replacement particularly in the 11% with very low TSH. Under-replacement was less common occurring in about 9% of patients. Systems of recall for patients who fail to attend for annual thyroid blood tests or collect prescriptions, alerts to remind GP's to check thyroid function, patient and GP education, having national standardized guidelines and once or twice weekly dosing may all potentially help in addressing this challenging issue. Further studies will be needed to show whether any of these measures improve outcome.

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