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ORIGINAL ARTICLE

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Characteristics and outcomes of patients with hyperthyroidism attending a hospital endocrine clinic—A retrospective study

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Summary

Aims: A study looking at the distribution, management and outcomes of patients referred to a secondary care endocrine clinic with a diagnosis of hyperthyroidism.

Methods: Retrospective longitudinal study of 442 patients referred over a 15-year period (2002-2017) with a diagnosis of hyperthyroidism to a secondary care endocrine clinic. Information on demographics, diagnosis, treatments and outcomes was recorded as patients attended for clinic visits. Patients were initially treated with 1-2 courses of thionamides and subsequently referred for radioiodine or surgery in cases of relapse.

Results: Patients (75% female, age range 17-91 years) were treated with thionamides for an average of 295 days. As expected, the majority of patients had Graves Disease (GD) (80%), followed by those with multinodular goitre (MNG) (8.6%), amiodarone-induced hyperthyroidism (6.7%) and toxic nodule (3.7%). Drug-induced remission rates were best seen in patients with GD (43%), and side effects necessitating change in treatment were relatively low (2.5%). In 121 patients who received radioiodine, hypothyroidism occurred in 50% of patients and was commoner in patients with GD (65%) than in those with MNG (22%) and toxic nodule (6.3%).

Conclusions: This study is only one of a few reporting on the characteristics of patients with hyperthyroidism attending a typical secondary care endocrine clinic. Whilst we appreciate its limitations, we encourage similar methods of collecting valuable real world data to facilitate conduction of specialist peer review visits in other similar clinic settings.

KEYWORDS

diagnosis, radioiodine, thionamides, thyroid

1 | INTRODUCTION

Hyperthyroidism affects an estimated 1 in 2000 people annually in Europe. The most common causes of hyperthyroidism include Graves' disease (GD), multinodular goitre (MNG) and toxic nodule. Appropriate treatment for patients relies on correct diagnosis and is influenced by both the clinical experience of endocrinologists and patients' coexisting comorbidities and preferences. Early and appropriate treatment of hyperthyroidism is important in preventing cardiovascular and metabolic complications such as osteoporosis[1] and thyroid storm[2] and is based on recommendation by specialist bodies such as the British Thyroid Association.[3]

The mainstays of treatment include antithyroid drugs, radioiodine therapy and thyroidectomy.

1.1 | Antithyroid medications (Thionamides)

Thionamides (carbimazole [CMZ] and propylthiouracil [PTU]) are usual first choice treatments in UK and Europe and are typically used short-term with the aim of inducing remission in GD or longer term when radioiodine treatment or surgery is contraindicated or declined. The British Thyroid Association guidelines recommend a period of treatment with thionamides of 12-18 months.[3] In USA, radioiodine is generally considered early on after achieving a euthyroid state with a short course of thionamides.[4]

Although patients are often considered to be in remission if they retain a normal thyroid function test (TFT) 1 year after discontinuation of antithyroid drugs, we used a 6-month cut-off in our series. The remission rate varies considerably between geographical areas. A European study showed a 50%-60% remission rate after 5-6 years after discontinuation of treatment, whereas a US based study demonstrated only a 20%-30% remission at 18 months.[5]

Lower remission rates have been described in men, younger patients, smokers and those with large goitres or elevated TSH receptor antibodies (TRAB) at diagnosis.

In patients with toxic MNG, definitive treatment such as radioiodine or surgery is generally considered early as prolonged treatment with thionamides rarely offers cure.[6]

Thionamides are generally well tolerated and agranulocytosis occurs in <3% of patients.[7] Milder and commoner side effects include skin rashes, pruritus and hair loss (commoner with CMZ), GI symptoms, and deranged LFTs (commoner with PTU), and occur in about 10% of patients.[8]

1.2 | Radioiodine therapy

Radioiodine (usual prescribed dose range 350-600 MBq) has been used to treat hyperthyroidism for more than seven decades and works by inducing damage of DNA leading to death of thyroid cells. It is usually well tolerated and severe complications are rare. The most common complication is permanent hypothyroidism (40%-80% of subjects) and may occur from 4 to 16 weeks after treatment. Rarer side effects include sore throat and radiation thyroiditis, but there is no convincing evidence for increased cancer risk.[9] It is not recommended for patients with active thyroid eye disease (TED) and is contraindicated in pregnancy and in those in prolonged contact with children (eg, young mothers). Some patients, such as those with large goitres, may need repeated (higher dose) treatments to achieve euthyroidism.[10] In unusual cases refractory to more than three administrations of radioiodine, surgery should be considered.

1.3 | Thyroidectomy

This would be the preferred option where drug treatments or radioiodine have been ineffective, or are contraindicated. Such scenarios include patients with active TED, young mothers unresponsive to repeated courses of thionamides, and children.

Postoperative complications include hypocalcaemia, recurrent laryngeal nerve injury, postoperative bleeding and complications of general anaesthesia.

2 | STUDY AIMS AND METHODS

The study was intended to look at the distribution, management and outcomes of patients with hyperthyroidism attending a typical secondary care endocrine clinic.

It is a retrospective longitudinal study of 442 patients who were referred over a 15-year period (2002-2017) with a diagnosis of hyperthyroidism (GD, MNG, toxic nodule, amiodarone induced hyperthyroidism) to one of two endocrinologists (DVC) at Poole General Hospital outpatient endocrine clinic. Both endocrinologists have a similar referral pattern and serve a population of 250 000 people.

We recorded live information on age and gender, treatment duration, ultrasound or nuclear imaging findings, TFT before and after drug treatment, side effects of thionamides, radioiodine therapy (including post radioiodine hypothyroidism) and thyroidectomy, as patients attended for clinic appointments.

We tabulated data into an Excel spread sheet and categorised patients into four diagnostic groups—GD, toxic MNG, toxic nodule and amiodarone-induced hyperthyroidism. The diagnosis was based on history and clinical expertise, family history, goitre appearance (clinical and U/S) and TPO antibodies (TRAB in some instances) when indicated. A "free-text" column enabled entry of any other relevant information at the time of the clinic visit.

All patients were treated with thionamides for a minimum 6-month period, and up to 2 years until normalisation of TSH was achieved. This was followed by a variable wean off period, and we defined a complete remission (or biochemical cure) as a normalised TFT for at least 6 months after complete cessation of drug treatment. A second course of treatment was offered to patients who relapsed, but this decision was often individualised, depending on circumstance, aetiology and patient preference.

Patients who subsequently still relapsed were generally referred for radioiodine therapy or much less commonly for thyroidectomy.

3 | RESULTS

Table 1 shows the distribution of patients by diagnosis, with GD patients representing the largest group within the cohort (80%). The baseline patient characteristics are presented in Table 1. A total of 442 patients were referred as new cases, although as expected

TABLE 1 Type of diagnosis (n, %)

Graves disease	347 (80)
Multinodular goitre	37 (8.6)
Amiodarone induced hyperthyroidism	29 (6.7)
Toxic nodule	16 (3.7)

with thyroid illness some patients may have received treatments in the past, prior to referral to our clinic. For the purpose of the study analysis, the duration of treatment was considered from the time of attendance to our clinic. One patient, for example, had been on long-term thionamide treatment for several years (1995) prior to referral, and this was highlighted in the free-text column.

As expected, females accounted for the majority (75%) of the population studied. The mean age at time of diagnosis was 52.6 ± 17.1 years (range 17-91 years).

The mean duration of treatment with thionamides in the cohort was 295 days. Of these, only a small proportion (2.5%) had to stop treatment due to side effects (Table 2). Remission rates with drug treatment were better in patients with GD (43%), than in those with MNG (19%) and toxic nodule (25%) (Table 3).

A total of 122 patients (28%) received radioiodine treatment. Most patients were considered for radioiodine treatment following a relapse within 6 months of cessation of a second course of thionamide treatment. Other reasons included personal preference, high TRAB or drug side effects. A total of 18 subjects (15%) required a 2nd dose of radioiodine treatment.

A total of 61 patients (50%) developed permanent hypothyroidism within 6 months of radioiodine therapy and required thyroxine replacement therapy. As shown in Table 4, subjects with GD showed a higher incidence of postradioiodine hypothyroidism than those with MNG or toxic nodule.

Eight patients underwent surgery, of whom six had GD and two amiodarone induced thyroid disease.

4 | DISCUSSION

Hyperthyroidism has multiple aetiologies, manifestations and treatment options. Appropriate treatment requires an accurate diagnosis and is influenced by coexisting medical comorbidities, patient preference and personal values and physician experience.

The majority of our patients were treated with thionamides in the first instance, followed by radioiodine therapy in cases of relapse despite a second course of drug treatment. Patients who had toxic MNG or toxic nodule were generally considered for radioiodine at an earlier stage than those with GD. This is supported by the better remission rates on drug treatment seen in GD compared with MNG or toxic nodule in our series (Table 3), and which are similar to those from other studies.[3] We used CMZ in preference to PTU, and we employed a dose titration method rather than a block and replace regime. The former has a more favourable side effect profile.[11] We recorded significant side effects in only 2.5% of the cohort, and these were recorded in patients in whom drug treatments had to be changed or withdrawn, explaining the relatively low incidence.

Current guidelines recommend a mean radioiodine dose of 370-555 MBq to achieve a biochemical remission. Most of our patients received a standard dose of 550 MBq as although lower fixed doses (185 MBq) are associated with a lower incidence of hypothyroidism, cure rates are extremely low.[12] In our series, postradioiodine hypothyroidism was by far commoner in patients with GD compared to MNG or toxic nodule (Table 4), encouraging early use of this treatment modality in the latter groups, whilst appropriately informing respective patients on risk of hypothyroidism. These rates are also comparable to those from a long-term study on radioiodine treatment.[9] This is very important to patients who are often worried about developing hypothyroidism and long-term weight gain and may help them make a more rational decision at the time of consent. Only a small number of our patients proceeded to thyroidectomy. Factors that mitigated the choice of surgery in our patients included surgical risk and a general preference for pharmacotherapy for thyroid illness in the UK. Our study was limited by accuracy of records and some missing data, although all record entries were made by a single observer (DVC). This can sometimes prove somewhat difficult in a busy clinic setting, but the use of electronic endocrine clinic records in our department facilitated data collection and regular updates of the study spreadsheet. The latter process was in itself a useful CPD tool as it encouraged regular case reviews and teaching and was also useful at annual consultant appraisal.

The importance and uniqueness of this study lie in comparing treatment modalities and outcomes in different subgroups within a single clinic cohort. Although the results on treatment response are similar to those from other series, our study is original in highlighting the realities of managing patients in a typical secondary care endocrine clinic.

5 | CONCLUSIONS

This is one of only a few studies to report on the characteristics of patients with hyperthyroidism in a UK population managed in an outpatient setting. We present some interesting findings showing the likely clinical response rates to various established treatment modalities. This is intended to aid clinicians counsel patients about

TABLE 2 Frequency of drug side effects (%)

Neutropaenia	1
Severe headaches	0.2
Significant rash	1.3

TABLE 3 Remission rates on thionamides (n, %)

Graves disease	150/347 (43)
Multinodular goitre	7/37 (19)
Toxic nodule	4/16 (25)

TABLE 4 Frequency of postradioiodine hypothyroidism (n, %)

Graves disease	56/85 (66)
Multinodular goitre	4/18 (22)
Toxic nodule	1/16 (6)

benefits and risks of available treatment options and to help guide patients on often difficult treatment choices. In our opinion, this study should encourage the use of accurate record keeping and collection of real world data, facilitating the conduction of now mandatory specialist peer reviews in secondary care endocrine clinics.

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CONFLICT OF INTEREST

Nothing to declare.

AUTHORS CONTRIBUTIONS

SYS is involved in data analysis and writing of manuscript. CL did the literature review. DVC instigated the idea of work, collected the data over the years and edited the manuscript in line with reviewer and editor comments. All authors approved the final version.

DATA ACCESSIBILITY

All data are provided in full in the results section of this paper.

ETHICAL STATEMENT

This was not sought as the work was part of a long-term audit programme registered with the Local audit department. Patient data were recorded on a secure hospital network and anonymised at the time of analysis.

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