Original Research

A study to analyze characteristics of primary hypothyroid patients not achieving target TSH values despite being prescribed adequate thyroxine dose

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Abstract

Background: Hypothyroidism is a common endocrine disorder in India. The aim of therapy in hypothyroidism is to achieve euthyroid state, assessed by measuring serum TSH levels. Despite the fact that treatment of hypothyroidism should be straight forward, a significant percentage of hypothyroid patients treated with thyroxine have TSH values outside the normal range.

Objective: To assess the percentage of primary hypothyroid patients with abnormal thyroid functions despite being prescribed levothyroxine for at least 2 months prior to enrolment.

Materials and Methods: This was an observational, cross sectional study which included adult patients with primary hypothyroidism, who were on treatment with stable dose of levothyroxine for at least 2 months. A total of 500 subjects,who came for routine visit, were included in the study after fulfilling inclusion criteria. A comprehensive Statistical Analysis Plan (SAP) version 11 was used for the data analysis.

Result: A total of 500 patients with primary hypothyroidism were enrolled in the study. Average daily dose of levothyroxine was found to be 1.24 μg/kg/day. The majority of patients (80%) were compliant to treatment. Twelve percent patients were moderately compliant while 8% patients were non-compliant to treatment. Among the 500 patients, 280 (56%) patients were found to have abnormal thyroid function, out of 280 patients, 198 (39.6%) were under-treated and 82 (16.4%) patients were over-treated.

Conclusion: This study revealed that although being largely compliant to treatment, a significant number of Indian patients with primary hypothyroidism have abnormal serum TSH values, despite being prescribed a stable dose of levothyroxine for at least 2 months.

KEY WORDS: Hypothyroidism, Compliance, Thyroxine, TSH

Introduction

Thyroid problems are on the rise among Indians: Over 4.2 crore people in the country are estimated to suffer from such disorders, making it increasingly important for people to pay attention to this often overlooked health problem.[1,2] Hypothyroidism is a common endocrine disorder in India. The treatment of choice for hypothyroidism is levothyroxine sodium. The aim of therapy in hypothyroidism is to achieve euthyroid state, assessed by measuring serum TSH levels. Many factors such as age, underlying etiology, concomitant medications, and comorbid illnesses are known to alter serum TSH, fuelling the need for dosage individualization.

Despite the fact that treatment of hypothyroidism should be straight forward, a significant percentage of hypothyroid patients treated with thyroxine have TSH values outside the normal range. This concern highlights the need for monitoring thyroxine therapy by regular estimation of serum TSH levels so that they remain within the normal range. Hence

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the objective of this study was to determine the percentage of primary hypothyroid patients having out of abnormal serum TSH values, despite having been prescribed thyroxine. The reasons for out of range values were assessed.

Aims and objectives

- To assess the percentage of primary hypothyroid patients with abnormal thyroid functions despite being prescribed levothyroxine for at least 2 months prior to enrolment.
- To assess the reasons for abnormal serum TSH values.

Materials and methods

This was an observational, cross sectional study which included adult patients with primary hypothyroidism those were on treatment with stable dose of levothyroxine for at least 2 months. Hundred subjects,who came for routine visit, were included in the study after fulfilling inclusion criteria. Following consent, data pertaining to the patient's demography, etiology of hypothyroidism, and thyroxine use was documented.

Inclusion Criteria: Patient of either gender, aged ≥18 years, diagnosed with primary hypothyroidism and currently on treatment with any brand of levothyroxine for at least 2 months.

Exclusion Criteria: Patients with central hypothyroidism, mental retardation, females with pregnancy or lactation phase were excluded from the study.

For the purpose of the study following definitions are used

Abnormal TSH values: Number of patients who had out of range TSH values.

Adequately treated patients: Patients whose TSH value was between 0.4 and 4 mIU/L.

Over-treated patients: Patients whose TSH value was less than 0.4 mIU/L.

Under-treated patients: Patients whose TSH value was more than 4 mIU/L.

Assessment of Compliance: Compliance was assessed by asking the patients the number of doses missed in the last one month.

Compliant to treatment: Missed <5% dose in the last 1 month.

Moderately compliant to treatment: Missed >5% but <15% dose in the last 1 month.

Non-compliant to treatment: Missed >15% dose in the last 1 month.

A comprehensive Statistical Analysis Plan (SAP) version 11 was used for the data analysis.

Result

A total of 500 patients with primary hypothyroidism were enrolled in the study. Out of these, 380 were females (76%) and 120 were males (24%). Mean age of patients was 43.2 (± 12.6) years. Average daily dose of levothyroxine was found to be 1.24 μg/kg/day. The majority of patients (80%) were compliant to treatment. Twelve percent patients were moderately compliant while 8% patients were non-compliant to treatment. Among the 500 patients, 280 (56%) patients were found to have abnormal thyroid function, out of 280 patients, 198 (39.6%) were under treated and 82 (16.4%) patients were over-treated.

Discussion

The primary objective of this study was to assess the percentage of primary hypothyroid patients in the Indian population with abnormal TSH values despite being prescribed levothyroxine. According to the normal reference range of TSH, 280 (56%) patients were found to have abnormal thyroid function, out of 280 patients, 198 (39.6%) were under-treated and 82 (16.4%) patients were over-treated.

Primary hypothyroidism is one of the most common endocrine disorders. The prevalence of hypothyroidism in general population ranges from 3.8% to 4.6%.[3] Benign thyroid diseases, including hypothyroidism, are more prevalent in women than in men.[4,5] A similar pattern was observed in our study. Several studies have found that a considerable number of patients taking medication for hypothyroidism have TSH levels outside the reference range. In the US National Health and Nutrition Examination Study, about one-third of 820 participants had TSH levels outside the reference range.[6] In the Colorado thyroid disease prevalence study, 40% of 1525 subjects had either elevated or decreased TSH levels.[7] A thyroxine treatment study in the UK revealed that serum TSH was outside the reference range in almost half of the cases (47%), with approximately one quarter (27%) having results above normal and one-fifth below normal.[8]

A significant number of hypothyroid patients having abnormal TSH values despite being treated with levothyroxine indicates either the presence of confounding factors, failure to adjust the dose as per these confounders, or poor compliance on the part of the patient.[9] While a raised TSH level might have adverse consequences in terms of an increased risk of ischemic heart disease and dyslipidemia[10], the suppression of TSH levels might have an impact on bone mineral density to osteoporosis and also an increased risk of cardiac arrhythmias and a hyperthyroid state.[11]

The limitations of present study are that, study was limited to one tertiary centre.

Conclusion

This study revealed that although being largely compliant to treatment, a significant number of Indian patients with primary hypothyroidism have abnormal serum TSH values, despite being prescribed a stable dose of levothyroxine for

at least 2 months. A failure to adjust the dose of levothyroxine based on the confounding factors like age, etiology of hypothyroidism, concomitant illness or medicines may have resulted in abnormal TSH values.

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