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Levothyroxine replacement dosage determination after thyroidectomy

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Abstract

BACKGROUND: The goal of this study was to identify a simple and effective way of calculating levothyroxine doses for postsurgical hypothyroidism.

METHODS: Levothyroxine dosage was calculated using a weight (μg/kg)-based formula for patients who underwent thyroidectomy for benign disease from 2001 to 2011. Other formulas using age, sex, ideal body weight, body mass index, and body surface area were also evaluated.

RESULTS: Four hundred four patients were included; 85% were women. The mean initial levothyroxine dosage was 1.4 μg/kg, which resulted in thyroid-stimulating hormone normalization in 59%, suppression in 23%, and elevation in 18% of patients. After dose adjustments, the mean therapeutic levothyroxine doses after total thyroidectomy and lobectomy were 1.5 and 1.3 μg/kg, respectively. A regression model incorporating other patient factors did not produce a more reliable dosing regimen.

CONCLUSION: A 1.5- and 1.3-μg/kg dosage calculation based on actual weight is currently the best estimation for levothyroxine replacement therapy after thyroidectomy.

Thyroid hormone replacement therapy in patients undergoing thyroidectomy for benign disease has traditionally been calculated based on actual body weight (μg/kg), a method that was initially derived from patients who were treated for primary hypothyroidism.[1,2] After the initiation of replacement therapy postoperatively, serum thyroid-stimulating hormone (TSH) levels are measured, and levothyroxine dosages are titrated until a normal serum TSH level is achieved. It has been common practice to start patients on a 1.6-μg/kg dose of levothyroxine after total thyroidectomy, a standard dose for thyroid hormone replacement in patients with primary hypothyroidism.[1,2] Although this may provide a simple estimation, the efficacy of achieving a euthyroid state with this method has not been validated in patients who have undergone thyroidectomy. Using actual body weight as a basis for dosage calculation has been questioned given the widespread prevalence of obesity and the effect of body fat composition on drug distribution. As a result, it has been suggested that body mass index (BMI), ideal body weight (IBW), or body surface area (BSA) may be a more accurate predictor of levothyroxine doses than actual body weight.[3,4] Other factors including patient age and sex may affect requirements for thyroid hormone and may be relevant for initial dosage determination.[5,6]

In this study, we sought to evaluate how accurately a 1.6-μg/kg calculation was able to predict the appropriate replacement or "final" levothyroxine dose in patients who underwent thyroidectomy for benign disease. In addition, alternative calculations using patient age, sex, BMI, IBW,

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or BSA were studied, and their accuracy of levothyroxine dosage prediction was compared with the simple 1.6-μg/kg calculation.

Methods

The electronic medical records of all patients who underwent thyroidectomy for benign disease between 2001 and 2011 were reviewed. Patients who underwent total thyroidectomy and patients who developed postsurgical hypothyroidism after thyroid lobectomy were included in the study. Patients were excluded if they did not have their initial thyroidectomy performed at MetroHealth Medical Center, Cleveland, OH, or if they failed to follow up postoperativley. Patients with thyroid cancer were excluded because they were treated with TSH-suppressive rather than replacement doses of thyroid hormone. This study was reviewed and approved by the Institutional Review Board at MetroHealth Medical Center.

Preoperative patient demographics including age, sex, body weight (kg), height (m), BMI (kg/m^2), IBW (kg), and BSA (m^2) were collected. IBW was calculated using the Miller formula as follows: for men over 5 feet, 55.7 kg plus 1.39 kg for each additional inch; for women over 5 feet, 53 kg plus 1.33 kg for each additional inch. The extent of thyroidectomy and final pathology of the surgical specimen were obtained. On postoperative day 1, patients who underwent total thyroidectomy were started on levothyroxine with a weight-based calculation of 1.6 μg/kg. Patients were instructed to take their levothyroxine after awakening in the morning and to wait at least 30 to 60 minutes before eating or drinking.

Six weeks after surgery, all patients who underwent total thyroidectomy and lobectomy with isthmusectomy had their serum TSH measured. The levothyroxine dose was adjusted if the TSH level was not within the normal reference range for the patients (TSH 0.4–5.5 μU/mL). For patients who underwent thyroid lobectomy and isthmusectomy and who were not on levothyroxine before surgery, if the serum TSH level was elevated above the normal range at 6 weeks, levothyroxine therapy was initiated for the treatment of postsurgical hypothyroidism. The starting dosage was determined at the discretion of the surgeon who used a 1.6-μg/kg estimate as a rough guide to help determine what levothyroxine dosage preparation to begin. For lobectomy patients who were on levothyroxine preoperatively, the dose was continued postoperatively until their serum TSH levels were measured 6 weeks later, and adjustments were made if necessary. The final or therapeutic levothyroxine dose was defined as the dose that produced a serum TSH level that was maintained in the normal reference range (TSH 0.4–5.5 μU/mL). The final microgram dose of levothyroxine per kilogram of actual body weight was determined for each patient, and a mean value was calculated for patients who underwent total thyroidectomy and thyroid lobectomy and isthmusectomy respectively.

The final weight-based levothyroxine dosage was compard in patients based on their sex (male vs female), age ($<$55 years vs $\geq$55 years), BMI ($<$30 mg/kg^2 vs $\geq$30 kg/m^2), and extent of surgery (total thyroidectomy vs partial thyroidectomy). Multivariate logistic regression analysis using backward elimination was performed to identify the model that would best predict the final levothyroxine dosage by incorporating patient age, sex, actual body weight, BMI, IBW, and BSA.

Statistical analysis was performed using JMP software (JMP, Cary, NC). The Student *t* test was used for the comparison of continuous variables, whereas the chi-square test was used for the comparison of categoric variables. A P value $<$.05 was considered statistically significant.

Results

Four hundred thirty-four patients were identified during the study period; 30 patients were excluded from the study for either not having had their surgery at MetroHealth or not following up after surgery at all. Eighty-five percent of patients were women, and the mean age was 49 years (range 15–84 years). The average weight, IBW, BMI, and BSA of the group was 85 ± 23 kg, 60 ± 5 kg, 31 ± 8 kg/m^2, and 2.0 ± 0.5 m^2, respectively. Three hundred forty-five patients underwent total thyroidectomy. Fifty-nine of 104 patients underwent thyroid lobectomy and required levothyroxine postoperatively; this included 20 patients who were on levothyroxine before undergoing thyroid lobectomy. The mean initial levothyroxine replacement dose in patients who underwent thyroidectomy was 1.4 μg/kg.

Two hundred eighty patients (70%) were able to achieve a euthyroid state (TSH 0.4–5.5 μU/mL) during the follow-up period; 124 patients failed to follow up after their first blood draw at 6 weeks after surgery when an adjustment was made in their levothyroxine dosage. Of the 280 patients who underwent either total thyroidectomy or lobectomy, 164 (59%) did not require any adjustment from their initial levothyroxine dosage, 63 (23%) patients had initial levothyroxine dosages that were too high, and 53 (18%) patients had initial dosages that were too low. Of the 116 patients who required an adjustment in their levothyroxine dose, 53 (46%) had a normal serum TSH level after a single dosage adjustment. Subanalysis for patients who underwent lobectomy and required levothyroxine replacement showed that this subset had a higher proportion (72%) of achieving euthyroidism after 6 weeks when compared with the total thyroidectomy patients (56%, P = not significant).

The mean final weight-based levothyroxine dosage that was required to achieve a euthyroid state in patients after total thyroidectomy was 1.5 μg/kg and 1.3 μg/kg in patients after thyroid lobectomy and isthmusectomy, respectively. On univariate analysis, patient age, BMI, and extent of surgery were found to be significantly correlated with the final levothyroxine dosage (Table 1). Older patients ($\geq$55 years), obese patients (BMI $\geq$30 kg/m^2), and patients