POSTSURGERY SERUM THYROGLOBULIN DISAPPEARANCE KINETIC IN PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA

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Abstract: Background. Knowing the postsurgery thyroglobulin (Tg) kinetic would enable its rationale for use in patients with differentiated thyroid cancer (DTC). Heterogeneous results were previously reported, then we aimed to evaluate the postsurgery Tg kinetic in a large group of patients with DTC.

Methods. Enrolled were 96 patients with DTC. Serum Tg was measured first at 5 minutes, then at 24, 48, 72, 96, and 120 hours after thyroidectomy. The Tg half-life (Tg[1/2]) was estimated in a 1-compartment model. A simplified 2-point formula (24 and 120 hours) was also used.

Results. The mean Tg(1/2) was 28.53 to 30.22 hours in 1-compartment model and 27.39 hours when estimated by a simplified formula. A strong inter-methods relationship was found (p < .001).

Conclusions. A reliable Tg(1/2) estimation could be obtained by a simplified formula requiring only 2 postsurgery Tg measurements (24 and 120 hours, respectively). © 2009 Wiley Periodicals, Inc. Head Neck 32: 568–571, 2010

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Serum thyroglobulin (Tg) measurement plays a critical role in the monitoring of patients with differentiated thyroid carcinoma (DTC).4 Knowing the Tg kinetic would enable rationale timing of measuring Tg after surgery to evaluate the persistence of differentiated thyroid tissue (ie, thyroid remnant or metastases).2 Heterogeneous results, generally obtained from few patients, were previously reported.3,5 Differences in circulating Tg protein in benign and malignant thyroid diseases exist, and Tg measurement is still technically and biologically challenging.6,7 Additionally, the surgical intervention may amplify the shedding of markers into the circulation, thus the method used to calculate the kinetics is critical.8 As a consequence, differences in patient selection, sampling sequence, assays, and kinetic models largely impact on the dynamic evaluation of serum Tg. The present work was then undertaken to evaluate the postsurgical Tg dynamic under strictly standardized conditions by using a high-sensitive Tg assay and a validated kinetic model in a large group of patients with DTC.
MATERIALS AND METHODS

Patients. Enrolled were 100 of 114 patients with histologically proven DTC. Exclusion criteria were: preoperative detection of lymph node metastases by neck ultrasound and fine-needle aspiration cytology (n = 5) and increased anti-Tg antibodies (n = 9). Total extracapsular thyroidectomy was performed and serum thyroglobulin was measured at 5 minutes and then 24, 48, 72, 96, and 120 hours after thyroid removal. Four patients were retrospectively excluded due to postoperative detection of metastases by histology (n = 2) or postablative 131I-whole body scan (n = 2) (Table 1).

Thyroglobulin Assay. Serum Tg was assayed in duplicate by a high-sensitive IRMA assay (DYNOtest Tg-plus). Quality control was ensured by assaying 2 different control sera with differing Tg concentrations in each series, by reassessing all sera showing a coefficient of variation exceeding 10%, and by a bimonthly participation in the European interlaboratory control Oncocheck.

Screening for Interfering Antibodies. The presence of antithyroglobulin antibodies (AbTg) was screened by a specific radioimmunoassay (DYNOtest Tg plus) and by a recovery test with a specific Tg-recovery buffer provided by the producer, as previously described. The serum rheumatoid factor (RF) was measured and the presence of heterophile antibodies (HAb) was assessed by repeating the Tg measurement after treating serum samples in a heterophilic blocking tube (HBT; Scantibodies Laboratory). Sera showing AbTg levels of more than 60 U/mL and/or recover less than 80%, or those with positive RF or HAb were excluded from the study.

Kinetic Analysis and Statistics. The Tg kinetic was analyzed in a 1-compartment model and the Tg(t1/2) estimated by linear regression analysis after logarithmic transformation of the mean values of the Tg measurement at each interval (method A). The Tg(t1/2) was also calculated by excluding the Tg value measured at 5 minutes after surgery (method B). Finally, the simplified formula $Tg(t_{1/2}) = 0.693x_{d}/ln(Tg_1/Tg_2)$ was applied, by computing Tg concentrations measured 24 ($Tg_1$) and 120 ($Tg_2$) hours after thyroidectomy. To compare the 3 estimation methods, the Tg(t1/2) value was obtained for each subject using the methods previously described for the overall population. The single factor repeated measures of a 1-way analysis of variance test which was applied to test overall homogeneity, and the Newman–Keuls test was applied to compare multiple pairs. For each statistical test, a $p$ value < .05 was considered statistically significant. The analysis was performed by using the Winks SDA, Texasoft (6.0.4 version) statistical program.

RESULTS

As shown in Figures 1 and 2, the mean Tg(t1/2) was 30.22 hours (SEM 3.05) by method A and 28.53 hours (SEM 3.45 hours) by method B. A total of 27.39 hours Tg(t1/2) was estimated by the simplified formula (method C). A strong
relationship was found between all methods (multiple regression F-ratio 1099.2297, \( p < .001 \)). The Tg\((t_{1/2})\) estimated by method A was significantly longer than those estimated by methods B and C \( (p < .01) \), whereas no differences were demonstrated between them \( (p = .54) \). The main absolute difference between method A and methods B and C was 1.69 and 2.83 hours, respectively.

Interestingly, the Tg\((t_{1/2})\) was higher in 4 patients with metastases detected by histology or post-treatment whole body scan (PT-WBS) \( (p < .001) \). Surgery induces either cytolysis and transient markers shedding, and, for example, the prostate-specific antigen (PSA) concentration is higher and the \( t_{1/2} \) shorter if the \( t_0 \) is measured 2 days rather than 5 minutes after surgery in patients with prostate cancer.\(^{13}\) Accordingly, large differences in \( t_{1/2} \) estimation from 9 to 96 hours, were previously reported for serum Tg. Here we selected patients with non-metastatic DTC and excluded both benign thyroid diseases and metastatic DTC to eliminate heterogeneity in Tg-producing tissues and multiple Tg sources, respectively. A standardized surgical procedure was done and Tg was measured by a highly sensitive and specific method after a careful screening for interfering antibody.

CONCLUSIONS

Differences in tumor markers kinetic estimation were reported and are probably related to differences in patient selection, assays, interferences, and data analysis.\(^{11,12}\) Surgery induces either cytolysis and transient markers shedding, and, for example, the prostate-specific antigen (PSA) concentration is higher and the \( t_{1/2} \) shorter if the \( t_0 \) is measured 2 days rather than 5 minutes after surgery in patients with prostate cancer.\(^{13}\) Accordingly, large differences in \( t_{1/2} \) estimation from 9 to 96 hours, were previously reported for serum Tg. Here we selected patients with non-metastatic DTC and excluded both benign thyroid diseases and metastatic DTC to eliminate heterogeneity in Tg-producing tissues and multiple Tg sources, respectively. A standardized surgical procedure was done and Tg was measured by a highly sensitive and specific method after a careful screening for interfering antibody.

Under these conditions, a Tg\((t_{1/2})\) estimation ranging from 27.39 to 30.22 hours was obtained. The Tg\((t_{1/2})\) was significantly longer by considering the Tg value measured 5 minutes after thyroid removal as the origin of the slope \( (t_0) \) even if absolute differences were limited and clinically negligible. Taking the 1-compartment model as a reference, a reliable Tg\((t_{1/2})\) estimation could be obtained by a simplified formula requiring 2 Tg measurements only. Radioiodine ablation is questioned in patients with low-risk DTC, and thyroxine is started immediately after surgery in many patients.\(^{14}\) We preliminarily showed here that the Tg\((t_{1/2})\) is higher in patients with DTC metastases than in those without. Consequently the Tg\((t_{1/2})\) should be useful early to select low-risk patients for adjuvant ablative radioiodine treatment. Our data provide a simple method for the estimation of Tg kinetics as a platform to further evaluate this hypothesis in large groups of patients with DTC.

REFERENCES


