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Treatment with Lithium Prevents Serum Thyroid Hormone Increase after Thionamide Withdrawal and Radioiodine Therapy in Patients with Graves' Disease

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Serum thyroid hormone concentrations increase after radioiodine (RAI) therapy for Graves' disease. This phenomenon has been ascribed to either antithyroid drug withdrawal before RAI therapy or release of preformed thyroid hormones into the bloodstream from the RAI-damaged thyroid. Lithium blocks the release of iodine and thyroid hormones from the thyroid, thus enhancing the effectiveness of RAI therapy. Changes in serum-free thyroxine (FT4) and triiodothyronine (FT3) levels after methimazole (MMI) discontinuation and RAI therapy were evaluated in a prospective, randomized, control study of 36 patients with Graves' disease. After a 3- to 4-month course of MMI, patients were assigned to one of three groups: G1 (RAI alone); G2 (RAI plus lithium for 6 d starting on the day of RAI therapy); or G3 (RAI plus lithium for 19 d starting on the day of MMI withdrawal). G1-G2 patients had an increase in serum FT4 and FT3 levels from 13.5 ± 6.5 to 19.8 ± 9.2 pmol/liter and 5.0 ± 2.0 to 8.0 ± 4.8 pmol/liter, respectively ($P < 0.0001$), 2–5 d after MMI withdrawal, but G3 patients showed no changes. In the 30 d after RAI therapy, mean serum FT4 values increased in G1 patients ($P = 0.02$), peaking at 3–7 d ($P < 0.05$) but not in G2 and G3 patients. Serum FT3 levels decreased in G1, G2, and G3 ($P = 0.03$, $P = 0.001$, $P = 0.02$, respectively). Hyperthyroidism was cured in 8 of 12 G1 patients, 11 of 12 G2 patients, and 11 of 12 G3 patients ($P = 0.31$). Control of hyperthyroidism was prompter in G2 ($P = 0.08$) and G3 ($P < 0.05$) than in G1 patients. Patients in the three groups received a similar dose of RAI, but the committed radiation to the thyroid was higher in G3 (563 ± 174 Gray) and G2 (588 ± 347 Gray) than in G1 (429 ± 204 Gray) ($P < 0.03$). In conclusion, the results of the present study demonstrate that: 1) MMI withdrawal is associated with a slight rise in serum thyroid hormone levels; 2) a further increase occurs after RAI therapy; 3) changes in serum thyroid hormone concentrations are prevented by lithium; and 4) the increased effectiveness of RAI therapy in lithium-treated patients is related to the increased RAI retention in the thyroid gland. Accordingly, a short course of lithium therapy can be considered a useful adjunct to RAI therapy to obtain a prompter control of thyrotoxicosis and avoid its transient exacerbation because of MMI withdrawal and RAI administration. (*J Clin Endocrinol Metab* 87: 4490–4495, 2002)

RADIOIODINE (RAI) IS an established method of treatment for Graves' hyperthyroidism and achieves this effect by permanently damaging thyroid follicular cells (1, 2). However, in the short term, thyroid cell damage causes the discharge of thyroid hormones stored within the cells, leading to a rise in serum thyroid hormone levels and, possibly, to an exacerbation of thyrotoxic symptoms and signs. This may be particularly dangerous in older patients with underlying cardiovascular disorders. Antithyroid drug treatment is frequently instituted before RAI therapy to restore euthyroidism and prevent the transient rise in serum thyroid hormone levels after RAI administration. According to some studies (3–8), antithyroid drug pretreatment might impair or reduce the effectiveness of RAI therapy, but other studies (9–11) failed to show any effect of thionamide pretreatment on the final outcome of RAI therapy. The effect of antithyroid drug pretreatment might be true for propylthiouracil but not for methimazole (MMI) (12, 13). Burch *et al.* (14) proposed that the observed rise in serum thyroid hormone concentrations after RAI therapy might be due to MMI withdrawal rather than RAI therapy itself because nonpretreated patients had a progressive decrease in serum thyroid hormone levels after RAI administration. We recently reported that a short course of lithium therapy given concomitantly with RAI is associated with a prompter control of hyperthyroidism (15), possibly in relation to lithium-induced blockade of RAI release and thyroid hormone release with no concomitant effect on thyroidal RAI uptake (RAIU) (16, 17). It is unknown whether lithium administration prior to RAI might prevent the acute changes in serum thyroid hormone concentrations after RAI therapy.

To address this issue, a blind, randomized, controlled study was undertaken in which the effects of lithium treatment on serum thyroid hormone levels after MMI withdrawal and after RAI therapy were evaluated. Our results indicate that lithium therapy after MMI withdrawal prevents the rise in serum thyroid hormone concentrations occurring either after MMI discontinuation or shortly after RAI therapy.

Abbreviations: AbTg, Antithyroglobulin; AbTPO, antithyroperoxidase; FT3, Serum-free T_3; FT4, serum-free T_4; MMI, methimazole; RAI, radioiodine; RAIU, radioiodine uptake; Tg, thyroglobulin; TRAb, TSH receptor antibody.

Subjects and Methods

Study groups

During yr 1999–2000, 36 consecutive patients were enrolled who had newly diagnosed, untreated Graves' disease, age older than 20 yr, recent-onset hyperthyroidism (<6 months), nonsevere or absent Graves' ophthalmopathy, and goiter volume lower than 60 ml. Patients with severe ophthalmopathy, previous treatment of hyperthyroidism with RAI or surgery, contraindications to glucocorticoid (peptic ulcer, gastritis, active infectious diseases, previous tuberculosis infection) or lithium treatment (kidney diseases), or goiter larger than 60 ml were excluded; all enrolled patients lived in the Pisa area. Patients were treated with MMI for 3–4 months to restore euthyroidism and then randomly assigned to one of the following groups by the method of random allocation: G1, treatment with RAI alone (n = 12); G2, RAI plus lithium (900 mg/d for 6 d, starting on the day of RAI administration); or G3, RAI plus lithium (900 mg/d for 19 d, starting on the day of MMI withdrawal). MMI was withdrawn 5 d before RAI therapy. The RAI dose was 7 MBq/g estimated thyroid tissue, corrected for the 24-h RAIU value. All patients received a short course of prednisone starting on 14th day after RAI therapy to prevent RAI-associated progression of Graves' ophthalmopathy (18, 19). No patient was lost from the study. The study was approved by the institutional review committee, and all patients gave their informed consent.

Study design

Baseline evaluation included ophthalmologic examination, evaluation of thyroid function, thyroid scan, 24-h RAIU determination, thyroid ultrasonography, white cell count, differential count, hematocrit, platelet count, blood urea nitrogen, creatinine, serum electrolytes, urinalysis, and electrocardiogram.

Serum-free T_4 (FT4) and T_3 (FT3), TSH, and thyroglobulin (Tg) levels were measured on the day of MMI withdrawal (T-5), at T-3, T0 (day of RAI administration), T+1, T+3, T+5, T+7, T+14, and T+30 and then every month for the entire follow-up period. Thyroid ultrasound was performed by the same operator, blinded to the treatment given to patients.

Thyroid volume was determined by ultrasound at T0, T+7, T+14, and T+30 and then every month for the entire follow-up period.

Patients were considered cured when they developed permanent hypothyroidism. Hypothyroidism or persistent hyperthyroidism after RAI treatment was corrected, within 2–3 wk, by T_4 or MMI administration, as appropriate. A second RAI dose was given to patients with persistent hyperthyroidism at the end of the follow-up period. Serum lithium level was measured on d 6 (G2 and G3) and d 14 (G3) after RAI therapy.

A questionnaire was filled out by all patients 15 d after RAI treatment to evaluate side effects of lithium and RAI therapy.

Assays

Serum FT4 and FT3 (Lisophase kits; Laboratory Bouty, Sesto S. Giovanni, Italy) and TSH (Auto-Delfia Wallac, Inc., Gaithersburg, MD) were measured by commercial kits. Normal ranges were: FT4, 8.4–23.2 pmol/liter; FT3, 3.8–8.4 pmol/liter; and TSH, 0.4–3.7 mU/liter. Serum TSH receptor antibody (TRAb) was determined by radioreceptor assay (TRAK assay; normal values, <5 U/liter; BRAHMS Diagnostica, Berlin, Germany). Serum Tg (normal values, <3–30 mg/liter; Sorin Biomedica, Saluggia, Italy), anti-Tg (AbTg) (Sorin Biomedica; undetectable in normal controls), and anti-thyroperoxidase antibodies (AbTPO) (Serodia, Tokyo, Japan; undetectable in normal controls) were also determined by commercial kits. Serum Tg was measured in Tg antibody-negative subjects. Urinary iodine excretion was measured using an autoanalyzer (Technicon, Rome, Italy). The median urinary iodine excretion in our area is 110 μg/liter. Serum lithium concentration was measured by a standard chemical method. Thyroid volume was measured by ultrasound using a 7.5-MHz linear transducer and calculated by the ellipsoid model: width × length × thickness × 0.52 for each lobe (20). Normal values ranged from 6–16 ml.

Thyroid dosimetry

The committed dose to the thyroid was calculated as described previously (21, 22). The kinetics of RAI was measured using with a Victoreen 660 5/DE 400 cm^3 (Elscint Apex, Milan, Italy) from 0–840 h after RAI administration, as previously reported (22). Measurements were made before RAI therapy and at T+3, T+7, T+14, T+21, and T+30 d after RAI treatment.

Statistical analysis

Baseline values were expressed as mean ± SD (or SE, as indicated) for quantitative variables and percentage for qualitative variables. The baseline characteristics of the three groups were compared by Fisher-Freeman-Halton test or ANOVA, as appropriate. Most analyses were performed after log transformation. The control of hyperthyroidism in the three groups was analyzed using survival curves at 12 months by the Kaplan-Meier method. Comparisons among nonremission curves were performed by the Mantel-Cox test; cure rate was evaluated at 12 months by the two-side Fisher's exact test. The time trend of FT4, FT3, and Tg within each treatment was evaluated by ANOVA with repeated measures. Multiple comparisons were performed by modified Dunnett's test (23). Differences in percentage of positive patients for serum TRAb, AbTg, and AbTPO between T-5 and T+30 were evaluated by McNemar test.

Results

As shown in Table 1, there were no significant differences in the baseline clinical and biochemical features of the three groups.

In G1 and G2 patients, who were considered as a single group (G1-G2) from MMI withdrawal (T-5) to RAI therapy (T0), mean serum FT4 and FT3 values rose from 13.5 ± 6.5 to 19.8 ± 9.2 pmol/liter and 5.0 ± 2.0 to 8.0 ± 4.8 pmol/liter, respectively ($P < 0.0001$), with a 32% and 38% increase, respectively, after 5 d (Fig. 1, A and B). This increase was already demonstrable 2 d after MMI withdrawal. Conversely, G3 patients (lithium treatment initiation on the day of MMI withdrawal) did not show variations in mean serum FT4 and FT3 levels before RAI therapy (Fig. 1, A and B).

G1 patients had a further rise in mean serum FT4 levels after RAI therapy, peaking at 31 pmol/liter after 5 d ($P = 0.003$ *vs.* T0) (Fig. 2A). Mean serum FT4 values increased slightly and not significantly on the day after RAI therapy from 15.7 pmol/liter to 18.6 pmol/liter (P = NS) in G3 patients, and between d 1 and d 3 in G2 patients, reaching a peak of 21.1 pmol/liter ($P = 0.09$, *vs.* T0). In the first 2 wk after RAI therapy, mean serum FT4 concentration in G1 patients, after an early increase, showed a rapid decline reaching the upper limit of the normal range values. G2 had a similar, but blunted, time trend of serum FT4, but in G3 patients it did not show any change.

Mean serum FT3 concentrations did not change during the first 3 d after RAI therapy in G1 but rose on d 5 (Fig. 2B); however, this phenomenon was essentially because of two patients with high TRAb titers; if these patients were not included, the FT3 increase was not significant. In G2 and G3, mean serum FT3 levels showed a progressive decrease (Fig. 2B). The time trend, evaluated between MMI withdrawal and RAI therapy, showed an increase in serum FT3 levels in G1-G2 ($P = 0.03$); when evaluated between RAI therapy and the following 30 d, it showed a decrease in all groups ($P = 0.03$ in G1, $P = 0.001$ in G2 and $P = 0.02$ in G3).

Serum Tg concentration in Tg antibody-negative patients

TABLE 1. Clinical and biochemical features of the study groups at baseline

	Group 1	Group 2	Group 3
No. of patients (M/F)	12 (4/8)	12 (2/10)	12 (3/9)
Mean age [(range) (yr)]	52 ± 13 (33–71)	48 ± 9 (31–69)	51 ± 9 (24–67)
Onset of hyperthyroidism (months)	5.3 ± 1.8	6.1 ± 2.4	5.7 ± 2.0
Smokers (%)	68	65	67
Ophtalmopathy (present/absent)	8/4	7/5	8/4
Mean thyroid volume (ml)	25 ± 13	19 ± 10	21 ± 11
Serum FT4 (pmol/liter)	15.5 ± 7.7	11.6 ± 3.9	15.5 ± 11.6
Serum FT3 (pmol/liter)	6.2 ± 3.0	4.6 ± 1.5	6.2 ± 4.6
Serum TSH (mU/liter)	2.3 ± 1.8	1.3 ± 1.3	1.4 ± 1.7
Positive TSH-receptor antibody (%)	10/12 (84)	11/12 (92)	11/12 (92)
Positive AbTg (%)	3/12 (25)	5/12 (42)	4/12 (33)
Positive AbTPO (%)	7/12 (58)	10/12 (83)	10/12 (83)
UIE (μg/liter) (median)	98	105	101
Hyperthyroid patients at the time of RAI (%)	4/12 (33)	2/12 (17)	2/12 (17)

Values, expressed as mean ± SD, were determined on the day of MMI withdrawal. Normal values are: FT4, 0.65–1.8 ng/dl (8.4–23.2 pmol/liter); FT3, 0.25–0.55 ng/dl (3.8–8.5 pmol/liter; TSH, 0.4–3.7 mU/liter; serum TRAb <5 U/liter); AbTg, negative; AbTPO, negative; thyroid volume was measured by ultrasound (normal range, 6–16 m). To convert serum FT4 hormone values to pg/ml, divide by 1.29. To convert serum FT3 values to pg/ml, divide by 1.54. To convert MBq to mCi, divide by 37. UIE, Urinary iodine excretion; in the Pisa area the median value is 110 μg/liter. No statistical differences were present among groups at baseline.

TABLE 2. Outcome of therapy at the end of the follow-up

	Group 1	Group 2	Group 3
Outcome of therapy[a]			
Not cured (hyperthyroid)	4	1	1
Cured (hypothyroid)	8	11	11
Cured (euthyroid)	0	0	0
Serum lithium concentration (mEq/liter)	0	0.3 ± 0.1	0.4 ± 0.3

Values are expressed as mean ± SD. Serum lithium concentration was measured by a standard chemical method; therapeutic levels for psychiatric disorders range 0.6–1.2 mEq/liter.

[a] Control of hyperthyroidism was prompter in G2 ($P = 0.08$) and G3 ($P < 0.05$) than in G1 patients; cure rate evaluated at 12 months was not different ($P = 0.31$) in the three groups, due to the small number of patients.

(n = 9 in G1, n = 7 in G2, n = 8 in G3) slightly increased in G1 and G2 between T-5 (MMI withdrawal) and T0 (RAI therapy) (P = NS), but it decreased in G3 ($P < 0.02$; Fig. 3A). Serum Tg levels increased in all groups the day after RAI therapy ($P < 0.05$ in G3) and then declined during the following 14 d (Fig. 3B).

Cure of hyperthyroidism was achieved in 8 of 12 G1 patients (67%), 11 of 12 G2 patients (92%), and 11 of 12 G3 patients (92%) ($P = 0.31$, probably because of the small number of patients). Patients treated with RAI plus lithium had a prompter control of hyperthyroidism than patients treated with RAI alone ($P < 0.05$ G3 *vs.* G1, $P = 0.08$ G2 *vs.* G1) (Table 2).

The therapeutic dose of RAI did not differ in the three groups (Table 3), but G2 and G3 retained RAI longer than G1, resulting in a larger amount of radiation committed to the thyroid gland. The adsorbed dose of RAI was 563 ± 174 gray in G3, 588 ± 347 gray in G2 and 429 ± 204 gray in G1 ($P < 0.03$); these values were higher in the lithium-treated patients also when corrected by the administered dose of RAI ($P < 0.03$) (Table 3).

Thyroid volume was similar in all groups at baseline (25 ± 13 ml in G1, 19 ± 10 ml in G2, 21 ± 11 ml in G3, P = NS; Table 1) and decreased in all groups during the study period ($P < 0.0001$).

Mean serum lithium concentrations were 0.3 ± 0.1 mEq/liter in G2 and 0.4 ± 0.3 mEq/liter in G3 (P = NS), below the therapeutic levels for psychiatric (range 0.6 to 1.2 mEq/liter).

No relevant side effects of lithium or RAI were reported by the patients, with the exception of a slightly (and nonsignificantly) higher incidence of nausea and neck tenderness in G3 (Table 4).

Discussion

RAI therapy for Graves' hyperthyroidism is usually associated with a transient increase in serum thyroid hormone concentrations, which may cause a moderate to severe exacerbation of thyrotoxic features; exceptionally, thyroid storm has been reported, even complicated by encephalopathy (24). These effects have been attributed to either RAI therapy itself or antithyroid drug withdrawal before RAI administration (25, 26). Antithyroid drugs are frequently given for few months before RAI therapy to restore euthyroidism and reduce the degree of thyroid hormone rise after RAI administration. The use of propylthiouracil pretreatment has been associated with a higher rate of failure of RAI therapy, but MMI may not affect the cure rate (8, 11–13). Indeed, the large majority of our patients (all pretreated with MMI) had their hyperthyroidism cured by RAI. In our previous work (15), we showed that goiter size is an important feature for the cure of hyperthyroidism by RAI; furthermore, the addition of lithium to RAI was associated with a prompter control of hyperthyroidism and a more rapid shrinkage of goiter (15).

We also reported that lithium prevented the increase in serum thyroid hormone levels observed 1 wk after RAI therapy (15). Studies have shown that patients pretreated with antithyroid drugs have lower serum thyroid hormone levels after RAI therapy than patients given RAI without medical pretreatment (14, 27). On the other hand, antithyroid drug withdrawal was associated with a rise in both FT4 and FT3 serum concentrations, which did not occur in patients who were not pretreated with thionamides (14). It should be noted, however, that the rise in serum FT4 and FT3 concentrations in thionamide-treated patients was rather modest,

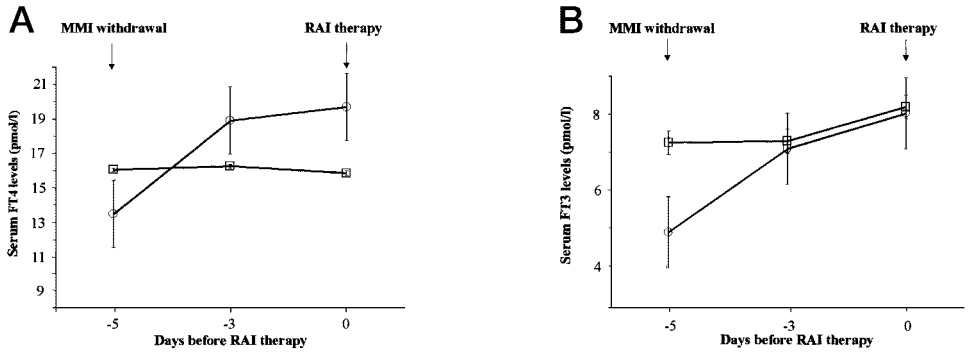

FIG. 1. Mean changes in serum FT4-A and FT3-B levels after MMI withdrawal and before RAI therapy. *Bars* indicate SE. G1 and G2 were considered as a single group (G1-G2, ○) from T-5 (the day of MMI withdrawal) to T0 (the day of RAI therapy); G3 is indicated by □. $P < 0.0001$ in G1-G2 group; P = NS in group G3.

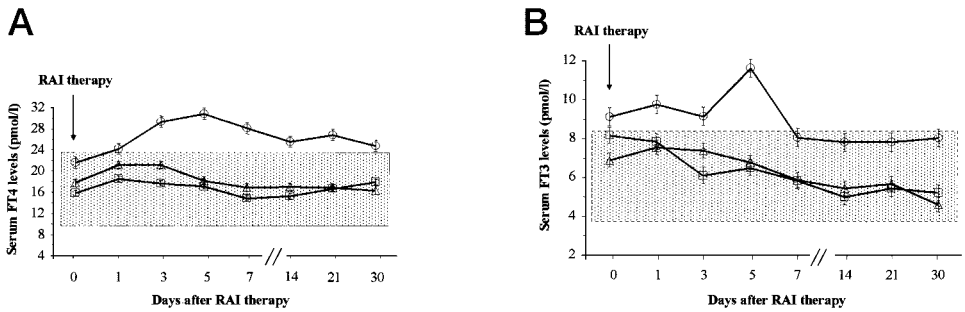

FIG. 2. Mean changes in serum FT4-A and FT3-B levels after RAI therapy. *Bars* indicate SE. Normal range for FT4 and FT3 is shown by *shaded area*. ○, G1; △, G2; □, G3. FT4: $P = 0.02$ for G1; P = NS for G2 and G3. In particular, $P = 0.008$ (T+3 *vs.* T0); $P = 0.003$ (T+5); $P = 0.04$ (T+7 for G1); $P = 0.08$ (T+3 *vs.* T0) for G2. FT3: $P = 0.02$ for G1; $P = 0.001$ for G2; $P = 0.02$ for G3.

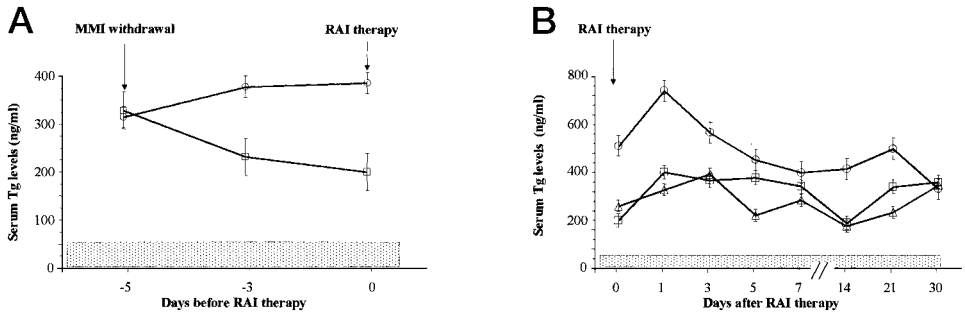

FIG. 3. Mean changes in serum Tg levels after MMI discontinuation (A; ○, G1-G2; □, G3) and after RAI therapy (B; ○, G1; △, G2; □, G3); serum Tg values were measured in AbTg-negative patients; *bars* indicate the SE.

TABLE 3. Thyroid dosimetry

	Group 1	Group 2	Group 3	*P*
24-h RAIU (%)	77.0 ± 14.0	73.0 ± 20.3	67.0 ± 21.2	0.54
Dose of RAI (MBq)	550 ± 70	510 ± 48	497 ± 78	0.33
Committed radiation to the thyroid (G)	429 ± 204	588 ± 347	563 ± 174	<0.03
Radiation to the thyroid/dose of RAI (G/MBq)	0.72 ± 0.4	1.25 ± 0.3	1.24 ± 0.4	<0.03

Values are expressed as mean ± SD. RAIU, Thyroidal RAI uptake, normal range 30–45%; to convert MBq to mCi, divide by 37. The committed dose to the thyroid was calculated as described previously (21, 22). The kinetics of RAI was measured using with a Victoreen 660 5/DE 400 cm^3 from 0–840 h after RAI administration as previously reported (22). Measurements were made before therapy administration and at T+3, T+7, T+14, T+21, T+30 d after RAI treatment.

and, in absolute terms, serum FT4 and FT3 levels were lower than those in nonpretreated patients, both at the moment RAI was given and throughout the follow-up period (14). Even though Burch *et al.* (14) reported an exacerbation of thyrotoxic features in only 12% of patients, a condition of poorly controlled hyperthyroidism, either in the pre-RAI period or in the weeks to months needed for a full RAI effect, can be dangerous, especially for older patients with cardiovascular problems. Moreover, it has been reported that the outcome of RAI therapy is negatively affected by simultaneous thyrostatic drugs, resulting in a failure rate greater than 50% in Graves' disease (28) or toxic nodular goiter (29).

The results of our present study confirm that MMI discontinuation before RAI therapy is associated with a rapid increase in serum FT4 and FT3 levels after 2 d, approaching a plateau after 5 d. This increase in serum thyroid hormone concentration can be prevented by the administration of lithium carbonate concomitantly to MMI withdrawal. RAI therapy was associated with a further increase in serum FT4 levels in G1 patients on d 1 after RAI administration, peaking on d 5. Patients treated with lithium (G2 and G3) had a slight rise in serum thyroid hormone levels on d 1 after RAI therapy, with a rapid decline during the following 3–5 d. The increase in serum FT4 levels occurred with a similar trend in the three groups on d 1 after RAI therapy, suggesting that it likely is due to discharge of preformed thyroid hormone

TABLE 4. Side effects of RAI and/or lithium therapy

	Group 1	Group 2	Group 3
Diarrhea	1/12	0/12	1/12
Nausea	1/12	2/12	5/12
Vomiting	0/12	0/12	0/12
Polyuria	0/12	0/12	0/12
Tremor	2/12	2/12	1/12
Electrocardiogram changes	0/12	0/12	0/12
Pain in the neck region	1/12	1/12	3/12
Tachycardia	1/12	1/12	1/12
Ophthalmopathy progression[a]	0/12	0/12	0/12

All patients filled out a questionnaire 15 d after RAI therapy.
[a] Ophthalmopathy was evaluated during the study period and at the end of the follow-up (12 months).

following RAI-associated radiolysis of thyroid follicular cells. Support to this concept is provided by the observed increase in serum FT4 levels in G3 patients whose FT4 values had not changed during the 5 d preceding RAI therapy; in addition, the abrupt increase in serum Tg levels in the three groups 1–3 d after RAI therapy is also in keeping with this pathogenic mechanism. However, radiolysis is unlikely to constitute the only mechanism leading to the increase in serum FT4 and Tg levels, observed in lithium-treated patients. This should imply that lithium might somehow interfere with RAI-induced follicular disruption. This would be a novel and yet unrecognized mechanism of action of lithium, which would also contrast with the putative, more pronounced radiolytic effect related to the longer stay of RAI within the thyroid during lithium therapy. This remains speculation that our experimental data do not allow support.

Because the increase in serum thyroid hormone after MMI withdrawal continues for the first 1–3 d after 131-I therapy (14, 27), an alternative explanation might be that the effect of lithium might represent a continued reversal of the ill effect of thionamide withdrawal. Our present observation on serum Tg changes is somehow in contrast with what we reported in our previous study (15), in which we observed a rise in serum Tg levels 7–14 d after RAI therapy only in the patients treated with RAI alone but not in those concomitantly treated with lithium. To reconcile this discrepancy, it should be mentioned that in our previous study, about 50% of patients were hyperthyroid when treated with RAI, but in the present study we were particularly careful to achieve a strict control of thyroid hyperfunction: indeed, only 20% of patients were slightly hyperthyroid when receiving RAI therapy. This might affect the degree of Tg released from the RAI-damaged thyroid cells (30) and account for some of the time-related changes in serum thyroid hormone levels. The fact that serum thyroid hormone concentrations after RAI did not differ in G2 and G3 suggests that lithium therapy could be withdrawn 1 wk after RAI administration. Patients treated with lithium had a slightly higher incidence of thyroid tenderness after RAI therapy, which did not require specific treatments; lithium therapy for a short period did not cause any other relevant side effect, at variance with chronic treatment (31, 32).

In conclusion, our study demonstrates that lithium administration before RAI therapy is a useful tool to prevent the increase in serum thyroid hormone concentrations, which occurs after MMI withdrawal and RAI administration. This finding, combined with our previous study showing a prompter control of thyrotoxicosis in patients receiving lithium therapy concomitantly with RAI therapy (15), suggests that a short course of therapy with lithium carbonate is a useful adjunct to RAI therapy, to be exploited especially in patients with underlying cardiovascular disorders for whom even a transient exacerbation of thyrotoxicosis may be deleterious.

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Erratum

In the article "Growth differentiation factor-9 inhibits 3′5′-adenosine monophosphate-stimulated steroidogenesis in human granulosa and theca cells" by Noriko Yamamoto, Lane K. Christenson, Jan M. McAllister, and Jerome F. Strauss III (*The Journal of Clinical Endocrinology & Metabolism* **87:**2849–2856), an error appears in Fig. 2. The units for the steroid concentrations for the y-axis of panels A, B, and C should read (ng/10^6 cells) instead of (ng/ml). The authors regret the error.