LETTERS TO THE EDITOR

Treatment with Thionamides before Radioiodine Therapy for Hyperthyroidism: Yes or No?

To the editor:

We read with great interest the paper by Bonnema et al. published in a recent issue of the Journal of Clinical Endocrinology and Metabolism (1). This randomized clinical trial showed that the efficacy of radioactive iodine (RAI) therapy for hyperthyroidism was reduced when RAI was administered after pretreatment with propylthiouracil (PTU) (1). Although the results of Bonnema et al. are convincing, this effect might be specific for PTU. In fact, two well-designed, prospective, randomized trials (2, 3) failed to show any consequence of methimazole (MMI) pretreatment on the efficacy of RAI therapy. This difference might be related to the longer radioprotective effect of PTU. Because data of the literature and our own experience indicated that MMI pretreatment does not affect successful management of hyperthyroidism by RAI therapy, we treat all hyperthyroid patients with MMI for 2–3 months before RAI administration to restore euthyroidism and to deplete intrathyroidal iodine stores (4). In our opinion, this approach is particularly important in patients who are old or have underlying nonthyroidal illness. In addition, prompt correction of hyperthyroidism is required in Graves’ patients with associated ophthalmopathy, because restoration of euthyroidism is associated with a more favorable course of eye disease (5).

In the paper by Bonnema et al. (1), as well as in a previous report by Burch et al. (6), RAI therapy was not followed by an increase in serum thyroid hormone concentrations. However, because thyroid function was not evaluated 3 wk after RAI therapy (1), early and transient changes in serum thyroid hormone levels might have been missed. In addition, the results of Bonnema et al. clearly showed that, when RAI therapy was given, serum thyroid hormone concentrations were markedly higher in nonpretreated patients than in pretreated patients (1). Thus, although the interval between randomization and RAI therapy was not specified, nonpretreated patients were presumably exposed to a longer period of uncontrolled hyperthyroidism than patients receiving thionamide pretreatment. As we mentioned earlier, we believe that this is not acceptable in patients whose hyperthyroidism represents a threatening condition and must be promptly and effectively controlled. Many thyroidologists are concerned about the consequences of subclinical hyperthyroidism; in our opinion, we should worry even more about the potential untoward effects of overt hyperthyroidism. In this regard, we recently demonstrated that lithium administration for a few days before RAI therapy and for 2 wk thereafter can effectively prevent the increase in serum thyroid hormone concentrations that follows RAI administration and/or MMI withdrawal before RAI therapy (7). Lithium adjuvant therapy was also associated with a prompter goiter shrinkage after RAI therapy (7).

In conclusion: 1) the study by Bonnema et al. (1) demonstrated that PTU pretreatment is associated with a lower efficacy of RAI therapy, but MMI does not seem to share this effect; accordingly, we support the view that MMI pretreatment should be given for a better control of hyperthyroidism before RAI therapy; 2) uncontrolled hyperthyroidism is an unacceptable and potentially dangerous situation that requires a more aggressive approach, particularly in at-risk patients; and 3) a short course of lithium adjuvant therapy, shortly before and after RAI therapy, is helpful to prevent the increase in serum thyroid hormone concentrations related to RAI therapy and/or thionamide withdrawal, to obtain a prompter control of hyperthyroidism, and to achieve a more rapid shrinkage of goiter.

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References

Authors’ Response: Treatment with Thionamides before Radioiodine Therapy for Hyperthyroidism: Yes or No?

To the editor:

We thank Bartalena et al. (1) for their comment. The main purpose of our study (2) was to clarify whether propylthiouracil impairs the efficacy of radioiodine therapy in hyperthyroid diseases. It may be true that this feature of propylthiouracil is unique among the antithyroid drugs available, perhaps due to the larger doses of propylthiouracil needed to control the hyperthyroidism. We fully agree with Bartalena et al. that untreated hyperthyroidism may have serious health consequences. The risk of developing heart arrhythmias and osteoporosis is well known. However, it is not elucidated by large controlled studies whether hyperthyroidism results in irreversible physical or mental impairment despite attainment of euthyroidism. Nevertheless, we believe, probably in agreement with most other physicians, that euthyroidism should be obtained as soon as possible when overt hyperthyroidism is detected. Treatment of hyperthyroidism can be achieved by antithyroid drugs, radioiodine, or surgery. Obviously, total thyroidectomy with subsequent T-thyroxine substitution is a very quick way to restore euthyroidism, but this method is rarely the first choice (3).

In conclusion: 1) the study by Bonnema et al. (1) demonstrated that PTU pretreatment is associated with a lower efficacy of RAI therapy, but MMI does not seem to share this effect; accordingly, we support the view that MMI pretreatment should be given for a better control of hyperthyroidism before RAI therapy; 2) uncontrolled hyperthyroidism is an unacceptable and potentially dangerous situation that requires a more aggressive approach, particularly in at-risk patients; and 3) a short course of lithium adjuvant therapy, shortly before and after RAI therapy, is helpful to prevent the increase in serum thyroid hormone concentrations related to RAI therapy and/or thionamide withdrawal, to obtain a prompter control of hyperthyroidism, and to achieve a more rapid shrinkage of goiter.
that use of lithium in conjunction with radioiodine may be beneficial in antithyroid drug is discontinued before radioiodine administration, a should therefore be monitored relatively closely in this period. If the also show a highly variable and unpredictable course, and the patients diseases. Such patients should preferably be pretreated with antithyroid respectively in elderly patients or in cases with known cardiovascular heart the risk of a hyperthyroid exacerbation should be minimized, particu-
al approach, using methimazole, results in a stable euthyroid state later. We have recently proved by a randomized trial (10) that such an antithyroid drug or radioiodine is most effective in terms of the shortest time interval to obtain euthyroidism. Other important issues in this context are side effects and patient satisfaction. At present, the choice between antithyroid drugs and radioiodine is based on individual factors, including patient preference and local traditions.

We agree with Bartalena et al. (1) that overtly hyperthyroid patients should not go untreated. Therefore, as discussed in our paper (2), there is no doubt that patients should be offered an antithyroid drug, if rapid access to radioiodine is impossible. If radioiodine is given to untreated hyperthyroid patients, the risk of a radioiodine-induced hyperthyroid crisis is very low. In fact, the thyroid hormone levels steadily decline after radioiodine therapy of hyperthyroid patients (2, 6, 7). In the studies by Burch et al. (6) and Andrade et al. (7), the thyroid function was closely monitored after radioiodine administration. Nevertheless, we agree that the risk of a hyperthyroid exacerbation should be minimized, particu-
larly in elderly patients or in cases with known cardiovascular heart diseases. Such patients should preferably be pretreated with antithyroid drugs before radioiodine. The thyroid function after radioiodine may also show a highly variable and unpredictable course, and the patients should therefore be monitored relatively closely in this period. If the antithyroid drug is discontinued before radioiodine administration, a transient hyperthyroid relapse follows the treatment (2, 6). We recognize that use of lithium in conjunction with radioiodine may be beneficial in this setting (8), as outlined by Bartalena et al. (1). Although lithium seems to increase the thyroid iodine retention, the final cure rate is not in-
creased by the adjuvant use of lithium 900 mg/d for 3 wk, as demon-
strated by a large randomized study (9). We do not use lithium, but we recommend that the antithyroid drug, used initially to render the patient euthyroid, is paused 4 d before and resumed 1 wk after radioiodine, with final discontinuation of the drug if euthyroidism is verified 1 month later. We have recently proved by a randomized trial (10) that such an approach, using methimazole, results in a stable euthyroid state throughout this early period after radioiodine and without adversely affecting the final outcome.

The ideal management of hyperthyroid disorders as well as the most favorable radioiodine regimen still remains to be established. Indeed, recognizing that lack of consensus prevails among centers handling thyroid disorders, future well-designed studies should address these issues.

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doi: 10.1210/jc.2004-2189