SUMMARY

Background: A randomized clinical trial was performed to clarify whether the continuous use of methimazole (MMI) during radioiodine therapy (RI\(^{131}\)) influences the final outcome of this therapy.

Design: Consecutive patients with Graves’ disease (N= 30) or a toxic nodular goiter (N = 45) were rendered euthyroid by MMI and randomized to stop MMI 8 days before RI\(^{131}\) (group: ‘-MMI’; n=36) or to continue MMI until 4 weeks RI\(^{131}\) (group: ‘+MMI’; n=39). Calculation of the I\(^{131}\) activity included an assessment of the I\(^{131}\) half-life and the thyroid volume.

Results: The 24-hour thyroid I\(^{131}\) uptake was lower in the ‘+MMI’ group (44.8 ± 15.6%) than in the ‘-MMI’ group (62.1 ± 9.9%; p<0.001). At 3 weeks after therapy, no significant change in serum free T\(_4\) index was observed in the ‘+MMI’ group (109 ± 106 versus 83 ± 28 nmol/L at baseline; P = 0.26), contrasting with an increase in the ‘-MMI’ group (180 ± 110 versus 82 ± 26 nmol/L at baseline; P<0.001). The number of cured patients was 17 (44%) and 22 (61%) in the ‘+MMI’ and ‘-MMI’ groups, respectively (P = 0.17). Cured patients tended to have a lower 24-hour thyroid I\(^{131}\) uptake (50.1 ± 13.8% versus 56.4 ± 17.1%; P = 0.09). By adjusting for a possible interfactorial relationship through a regression analysis (variables analyzed: randomization; 24-h and 96-h thyroid uptake; type and duration of disease; age; gender; presence of thyroid antibodies; thyroid volume; dose of MMI), only the continuous use of MMI correlated with treatment failure (P = 0.006) whereas a low thyroid I\(^{131}\) uptake predicted a better outcome (P = 0.006).

Conclusion: Continuous use of methimazole hinders an excessive increase of the thyroid hormones during RI\(^{131}\) therapy of hyperthyroid diseases. However, such a strategy seems to reduce the final cure rate, although this adverse effect paradoxically is attenuated by the concomitant reduction of the thyroid I\(^{131}\) uptake.

COMMENT

Radioiodine (RI\(^{131}\)) therapy is widely used for the treatment of hyperthyroidism. A controversy remains regarding the ideal I\(^{131}\) dose calculation and the use of antithyroid drugs (ATD) in conjunction with RI\(^{131}\) therapy. An excellent example of the controversy concerning the I\(^{131}\) dose calculation can be found in a recent investigation carried out by Marianne Tondeur et al. among the Nuclear Medicine Centers in Belgium (see: Clinical Endocrinology 65: 206-209, 2006). Concerning the concomitant use of ATD during (or immediately before) RI\(^{131}\) administration, several retrospective studies
have indicated that ATD reduce the beneficial effects of RI\(^{131}\). However, these studies might carry the risk of having been influenced by selection biases and, furthermore, recent prospective trials have not confirmed a detrimental effect of ATD. Considering the contradictory results from earlier studies, the authors bravely undertook the present randomized clinical trial. Their results confirmed that the thyroid I\(^{131}\) uptake was decreased in patients receiving ATD. RI\(^{131}\) undergoes organification in the thyroid gland, and ATD block the organification processes, thereby reducing thyroid uptake. This implies that the half-life or I\(^{131}\) in the thyroid is altered (i.e. increased) because it is no longer (or less avidly) trapped within the thyroid, probably explaining the decreased cure rate associated with ATD administration during RI\(^{131}\) therapy. The results also confirmed a higher rate of treatment failure in patients receiving ATD. The present trial supports the concept that a greater rate of treatment failure is to be expected when ATD are continued during RI\(^{131}\) therapy. Therefore, either ATD should be withdrawn a few days before RI\(^{131}\) administration (and resumed one to two weeks later when clinically required to control thyrotoxicosis) or the calculated RI\(^{131}\) dose should be adapted in order to account for this detrimental effect of ATD.

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See Figure below

![Trial profile diagram]

**Fig. 1.** Trial profile.