SUMMARY

Purpose: Thyroid dysfunction is common, particularly among older women. The safety of thyroid hormone use and long-term prognosis of hyperthyroidism remain controversial. The authors performed a prospective cohort study to examine the relationship among thyroid hormone use, previous hyperthyroidism, abnormal thyroid function, and mortality.

Methods: Study of 9,449 community-dwelling white women aged ≥ 65 years followed for 12 years. For analyses of thyroid function, a nested case-cohort study was carried out in 487 women using a third-generation TSH assay. Causes of death were adjudicated based on death certificates and hospital records.

Results: Twelve percent of the 9,449 women took thyroid hormone at baseline, and the mean duration of thyroid hormone use was 15.8 years; 9.4% of participants reported a history of hyperthyroidism. During 12 years of follow-up, 3,159 women died (33%). In multivariate analysis, mortality among users of thyroid hormone was similar to that observed for non-users (relative hazard – RH –: 1.11; 95% CI: 0.98-1.24; P = 0.09). Previous hyperthyroidism was associated with a higher risk of all-cause mortality (RH: 1.20; 95% CI: 1.06-1.36), particularly cardiovascular mortality (RH: 1.46; 95% CI: 1.20-1.77). Low (<0.5 mU/L) or high (>5 mU/L) TSH levels were not associated with excess total or cause-specific mortality, but the power to detect these relationships was limited.

Conclusions: Among older women, thyroid hormone use is not associated significantly with excess mortality, but previous hyperthyroidism may be associated with a small increase in all-cause and cardiovascular mortality. Additional long-term studies of hyperthyroidism and its treatment should further explore these findings.

COMMENT

From a clinical epidemiological standpoint, two features are striking in this study, the high frequency of thyroid hormone use in a population of elderly women (12%), and the almost equally high frequency of previous hyperthyroidism (close to 10%). The latter results are not surprising since in our country, for instance, thyroid hormone appears to be the number “4” (or “5”) on the list of the most frequently used pharmaceutical agents, and hyperthyroidism is known to be more frequent in aging female populations. The main finding of the study was a small increase in mortality, specifically cardiovascular, that was not associated with thyroid hormone use but well with a history of previous hyperthyroidism. Is it surprising to find an association between hyperthyroidism and increased
mortality? The answer is clearly ‘no’ since the pioneering study of Clark Sawin et al. (fifteen years ago), who showed an association between ‘low’ and/or ‘high’ TSH levels with an increased risk of atrial fibrillation. Another interesting study in this field was performed by Jane Franklyn et al. (in 1998), who showed increased mortality associated with hyperthyroidism treated with radioactive iodine. Obviously, it is not radioactive iodine or thyroid hormone administration *per se* that should be suspected of increasing the mortality rate, but rather hyperthyroidism *per se* and/or the inadequate use of thyroid hormone after patients have been treated for hyperthyroidism.

One of the weaknesses of the present study is that we were not told why these women took chronically thyroid hormone, but it can be presumed that it was as a replacement therapy after radioiodine ablation for their hyperthyroidism. One reassuring finding was the evidence that the large number of postmenopausal women who take thyroid hormone do not face an excess risk of mortality.

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