Psychosomatic disturbances, including irritability, insomnia, and anorexia, follow. Other mental disturbances may develop, such as mood swings, mania, declining intellect, apathy, and hallucinations.

Subcutaneous injection of metallic mercury is always harmful, causing local abscess and granuloma formation. Subcutaneous deposits of mercury are also systemically absorbed. Our patient as well as several patients in previously reported cases demonstrated high levels of mercury in blood and urine, without clinical signs or symptoms of a toxic reaction.

Blood and urinary mercury levels may not accurately indicate CNS accumulation and toxic reactions. Industrial workers exposed on a long-term basis to dangerous environmental levels of metallic mercury (air threshold concentration, 100 μg/cu m) experienced CNS toxic reactions, with blood and urinary levels lower than those of our patient (6 μg/dL in blood and 260 μg/L in urine corresponding to their threshold of toxicity).

Experience with occupational and industrial metallic mercury poisoning proves the effectiveness of chelation therapy for CNS toxic reactions. We did not chelate our patient, because he did not have a CNS toxic reaction or altered renal function.

Surgical excision of mercury granulomas effectively lowered serum and urinary mercury concentrations in our patient and in a previously reported case. It is especially interesting in our patient that, despite roentgenographically detectable residual mercury, his urinary and serum mercury levels dropped substantially after surgery.

Based on experience with our patient and those recorded by others, the following steps seem appropriate in the management of subcutaneously injected metallic mercury: (1) prompt excision of all readily accessible subcutaneous areas in which mercury is demonstrated, irrespective of whether there are manifestations of toxicity, (2) appropriate monitoring of CNS and renal function for evidence of mercurial toxicity, (3) chelation therapy when there is such systemic toxicity, and (4) psychiatric consultation and treatment when indicated.

References

Hormonal Content of Thyroid Replacement Preparations

Robert W. Rees-Jones, MD; Arturo R. Rolla, MD; P. Reed Larsen, MD

ACCORDING to present pharmaceutical industry estimates, there were 15 million prescriptions written in the last year for thyroid replacement in the United States. Of these, approximately 50% were for synthetic hormones, and the remainder were for preparations derived from animal sources. At present, both generic thyroid and levothyroxine preparations are available, and their use has been encouraged by recent changes in prescription regulations. Since the Food and Drug Administration still accepts the United States Pharmacopeia standard based on organic iodine content for this medication, there is no specification of the precise hormonal content of these tablets. This study reports the triiodothyronine (T3) and thyroxine (T4) content of a number of generic thyroid and T4 preparations, using a radioimmunoassay. This survey was occasioned by the experience of a patient who received a biologically ineffective thyroid tablet.

Report of a Case

A 54-year-old woman with primary hypothyroidism since age 29 years had been treated with 3 grains of thyroid a day without difficulty. In 1978 she renewed her prescription, purchasing 5,000 tablets (1 grain each) of a less expensive generic brand. After several months, the patient noted the recurrence of hypothyroid symptoms that continued despite an increase in her daily dosage to 4 grains. On physical examination, the patient was clinically hypothyroid, and the serum T4 level was 2.5 μg/dL; the T3 levels were 0.1 μg/dL and 0.2 μg/dL, respectively.

For the purpose of this study, the first patient was also treated with a generic T4 preparation, levothyroxine sodium.
Total iodine analyses of tablets were performed by Boston Medical Laboratory, Waltham, Mass. Statistical comparisons were performed by Student's t test.

Results

The Table shows the T3 and T4 content of eight generic 1-grain thyroid preparations. The Armour tablet was arbitrarily used as a standard for reference purposes, since its T3 and T4 content is constant based on our previous experience.1 The preparation purchased by the aforementioned patient is lot No. 1 of company A. These 1-grain tablets contained only 9 µg of T3 and 8 µg of T4, values that are 15% and 53%, respectively, of the quantities of these hormones in the Armour preparation. A second lot of thyroid from the same distributor had modestly less T3 and slightly more T4 than the Armour product. The remainder of the generic preparations contained from 67% to 100% of the amount of T3, and from 73% to 120% of the T4, present in the Armour preparation. Differences of greater than 10% were generally statistically significant, as indicated in the Table. The tablets from companies A (lot No. 1), C, and F were assayed for total iodine content, which were 0.19±0.01%, 0.09±0.02%, and 0.08±0.02%, respectively, by weight (mean±SE). The 2-year-old Armour thyroid tablets contained 56±1.9 µg of T3 (SD) and 15±1 µg of T4, results not significantly different from fresh tablets. The Parke-Davis preparation manufactured more than ten years ago contained 42±5 (SD) and 9±0.4 µg of T3.

The T3 content of Synthroid and Letter and two generic T4 tablets was not significantly different from the stated value. The other two contained 121±6 and 137±8 µg of T4, which was significantly greater than the 100 µg expected (P<.001). All T4 preparations tested contained less than 2% T3.

Comment

The USP requires only that desiccated thyroid contain between 0.17% and 0.23% organic iodine by weight. The present study indicates this criterion is not adequate for this animal product. There were notable variations in hormonal content among the generic thyroid preparations, with one clinically ineffective lot extremely deficient in T3 and T4, despite meeting the USP standard for iodine content. The relatively normal assayed hormonal content of the preparations manufactured two and ten years ago suggests that these variations in generic thyroid are not age related but are secondary either to manufacturing technique or to characteristics of the original animal material employed. Interestingly, two of the four generic 0.1-mg T3 preparations studied had significantly more T4 per tablet than indicated.

Biologically ineffective preparations of thyroid have been reported on previously.3 While in the past preparations from unknown or unreliable manufacturers could be avoided by specifying a brand name, this practice is discouraged by the recent emphasis on generic "equivalents." The data in the Table suggest that many of the generic preparations of thyroid are not "equivalent," at least to Armour Thyroid. The latter was taken as a standard primarily because of its uniform composition and popularity.4 Because there is no absolute standard for T3 and T4, content of thyroid, its selection is arbitrary. Arguments against the use of thyroid as replacement therapy because of its supra-physiological T3/T4 ratio compared with that of human thyroid have been presented previously and will not be reviewed here.1,5,7 However, the results of analyses of four generic T3 tablets indicate that two of these had greater than 120% of the stated hormonal content. Thus, it seems that the physician or pharmacist, in a well-intentioned attempt to reduce (albeit modestly) medication costs, may supply the patient with a generic thyroid replacement preparation with either more or less than the expected biologic activity. This undesirable situation might be avoided by the establishment of appropriate guidelines for the hormonal content of these widely prescribed medications.

This study was supported in part by Public Health Service grant AM18616.

References