ORIGINAL ARTICLE

ADVERSE EVENT REPORTING IN PATIENTS TREATED WITH LEVOThyROxINE:
RESULTS OF THE PHARMACOVIGILANCE TASK FORCE
SURVEY OF THE AMERICAN THYROID ASSOCIATION,
AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS,
AND THE ENDOCRINE SOCIETY

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ABSTRACT

Objective: To survey physicians to determine whether potency and consistency issues with levothyroxine sodium (LT₄) have been resolved and to assess current experience regarding safety of substituting LT₄ products.

Methods: Members of the American Association of Clinical Endocrinologists, American Thyroid Association, and The Endocrine Society collaborated to create a survey instrument that would effectively sample the clinical experience of their society members and frequent prescribers of LT₄. More than 18000 e-mailed requests for information were generated, and the Web sites of each society provided links to the data collection form. The survey provided an opportunity to collect clinical observations of adverse events or product availability problems from physicians caring for patients with thyroid disease who required use of contemporary LT₄ preparations.

Results: After adjustment for known reasons for unstable results from thyroid function tests, 199 reports of adverse events associated with changes in thyrotropin values were further analyzed. One hundred seventy-seven reports (88.9%) were associated with a change in the source of LT₄; no change was noted in 21 (10.6%). Details regarding the circumstances of the change were provided in 167 of the 177 reports (94.4%). The reporting physicians themselves or their office staff had changed the LT₄ preparation in only 1 of the 167 cases (0.6%). The remainder of changes had been made by the patient’s pharmacy, either with the physician’s knowledge (in 13 of 167 cases [7.8%]) or without his/her knowledge (in 153 of 167 cases [91.6%]). Fifty-four of 199 cases (27.1%) described serious adverse events; 52 of these (96.3%) were associated with a substitution of one LT₄ preparation for another.

Conclusions: The clinical use of contemporary LT₄ products continues to be associated with some adverse outcomes. A small number of reports were associated with continued use of the same LT₄ products. The most frequently reported adverse outcomes were associated with the approved generic substitution of LT₄ products, frequently without the prescribing physician’s knowledge.

INTRODUCTION

Precision in levothyroxine sodium (LT₄) treatment is critical in achieving optimal clinical outcomes (1,2). Many factors affect consistent achievement of therapeutic goals and safe administration of LT₄ in clinical practice (3-10). Because LT₄ is a drug with a narrow therapeutic range (11), reliable products must be available to achieve consistent and optimal clinical outcomes (1). Issues related to the stability and potency of LT₄ products available for clinical use before 1997 led the US Food and Drug Administration (FDA) to require that all products be reconsidered through new drug applications (11) to eliminate adverse clinical outcomes due to intraproduct variability. In addition to