Comparable Bioavailability of a Novel Levothyroxine Solution when Administered with Coffee

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Levothyroxine (LT4) is the treatment of choice for hypothyroidism and the second most prescribed medication in the United States. Despite its established efficacy and widespread availability, approximately 40% of patients treated with LT4 fail to achieve thyroid stimulating hormone (TSH) levels within the normal range. Current LT4 product guidelines recommend administration in the fasting state 30-60 minutes before breakfast to avoid a food interaction leading to reduced intestinal absorption of LT4. This recommendation may impact compliance, as over 50% of adult Americans drink coffee every day, 65% of which is consumed during breakfast. While the majority of patients receive LT4 tablets, there is evidence that liquid formulations that bypass the gastric dissolution phase may mitigate the interference with coffee. Thyquidity® (levothyroxine sodium) oral solution has demonstrated bioequivalence to Synthroid® under fasting conditions and allows individualized dosing flexibility in a variety of clinical scenarios. A bioavailability study was conducted to assess the rate and extent of absorption of the oral LT4 solution(100 mcg /5 mL) administered with coffee compared to administration under fasting conditions in an open label, randomized, two-period, two-treatment, two-sequence, crossover, single dose bioavailability study in 40 healthy adults. A single 600 µg oral dose of LT4 solution (Thyquidity®, 30 mL) was administered 5 minutes before drinking 8 ounces of American coffee (without milk or sweeteners) or under fasting conditions in each study period. Blood samples were collected for total (bound and free) T4 for 48 hours after drug administration. Treatment periods were separated by a 40-day wash-out period. The ratios of geometric LS means with corresponding 90% confidence intervals (CI) were calculated from the exponential of the difference between the LT4 solution administration 5 minutes prior to coffee and administration under fasting condition for AUC 0-48 and Cmax. An absence of a food effect would be concluded if the baseline corrected 90% CIs of this ratio fell within 80.00% to 125.00% for Ln-transformed AUC 0-48 and Cmax. Forty healthy adults participated in the trial. There were no serious adverse events (AE) or discontinuations due to AEs. The geometric LS mean ratio of AUC 0-48 and Cmax for baseline-adjusted LT4 were 93.98% (90.06-98.07%) and 95.99% (92.64- 99.45%) respectively. The corresponding 90% CIs were included within the FDA acceptance range for bioequivalence. This study demonstrated comparable bioavailability of a single oral 600 µg dose of Thyquidity oral solution administered, 5 minutes prior to coffee or under fasting conditions. These results are consistent with earlier evidence that liquid LT4 overcomes the interference from coffee seen with LT4 tablets and may offer additional flexibility for patients.

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