8. Summary

Introduction: While carbamazepine (CBZ) treatment may affect serum thyroid hormone concentrations it rarely leads to clinically important hypothyroidism. This study was aimed to evaluate an early effect of CBZ on thyroid status in hypothyroid patients with thyroid hormone replacement, as compared with patients without a thyroid disorder.

Methods: Twenty-nine patients indicated for CBZ treatment were followed prospectively. Their thyrotropin (TSH), total thyroxine (TT4), free thyroxine (FT4) and antibodies against thyreoperoxidase (TPO-ab) and thyreoglobulin (TG-ab) serum levels were assayed before the start of CBZ medication (150 mg/d increasing to 450 mg/d), and then their TSH, TT4 and FT4 serum levels were assayed at week intervals for 7 weeks. Nineteen patients had no thyroid disorder before CBZ treatment (control group A), whereas 10 patients were treated with L-thyroxine (median 100μg/d) for hypothyroidism and were stable before CBZ treatment (group B). The fluctuations of thyroid status after the start of CBZ treatment were compared between the groups.

Results: In the control group, TT4 was significantly decreased by ca. 15 to 25 %, starting from the 1st week of treatment (Friedman, $p<0.001$), while FT4 was decreased by only ca. 10 to 15 %, and the significance ($p<0.001$) was delayed till the 2nd week. There was a concomitant increase in FT4/TT4 ratio ($p<0.001$) and a mild, non-significant increase in TSH ($p=0.073$) never exceeding normal range.
Conversely, in group B with hormonal replacement, a similar TT4 and FT4 decline was followed by significantly increasing TSH levels ($p = 0.011$), while the FT4/TT4 ratio was not significantly changed ($p = 0.218$). In 4 of 10 patients TSH rose over 5 mU/L and the treatment had to be modified. Looking back, these 3 patients had significantly higher pre-treatment TSH levels (median 2,63 mIU/L) than the rest of the group B (median 1.07 mIU/L; Mann-Whitney test, $P = 0.019$).

Conclusions: CBZ treatment seems to increase demand for thyroid hormones, due to their increased metabolic clearance rate. In patients with no thyroid pathology, there is a compensatory reaction, leading to new steady state, and keeping them euthyroid.
In patients supplemented with T4 for hypothyroidism, assessment of thyroid status (preferably with TSH) seems advisable in the first 3 to 4 weeks of CBZ treatment, in order to identify those prone to deterioration. If TSH after CBZ increases above normal range, T4 dose adjustment may be appropriate. Alternatively, CBZ may be replaced by an anticonvulsant without enzyme-inducing capacity.