

# LETTER TO THE EDITOR

## Thyroid Function Test Imbalance in Epileptic Children Under Anticonvulsive Therapy

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### Dear Editor,

There have been many studies regarding the impact of antiepileptic drugs (AEDs) on thyroid function. There are some challenging scopes which must be considered for conducting the study addressing the focused question. "Which one of the thyroid hormones is related to the AEDs consumption?". Some studies demonstrated that there may be alterations in all thyroid function tests (T3, T4 and TSH) after antiepileptic therapy in children (1). Some studies concluded that long-term prescription of anticonvulsive medications resulted in a decline in serum T4 levels, although it had no effect on serum TSH levels. However, changes in serum T3 level was challenging and it must be investigated further (2).

There were some confounding factors which may interfere with the conclusion. One of them is the type of the study. There are various study plans for this purpose such as cross-sectional, case-control, experimental, self-controlled cohort and double-blind randomized clinical trial studies. It seems that the proper protocol of study for this propose is a double-blind randomized clinical trial study. By using other designs, the authors cannot interpret the effect of AEDs on thyroid function; however, they can discuss the prevalence of thyroid hormone imbalance and the coordination among T3, T4 and TSH.

Moreover, one of the confounding factors is the thyroid binding globulin (TBG) effect. It has appeared that some of the AEDs may change the amount of TBG and in this way may affect the amount of thyroid hormones (3). Clonazepam and valproic acid do not have any enzyme inducing effects, but phenobarbital, carbamazepine, phenytoin and primidone may induce the hepatic enzyme (4-6). Therefore, it seems necessary to analyze each group of patients based on the type of drug which is prescribed and also by using the free amount of thyroid hormones, the researcher will be able to exclude the TBG effect. In addition, age is an important factor which should be considered. The epileptic patients show extra-thyroid adverse effects such as vitamin D and bone metabolism disorders due to antiepileptic drugs (7). Other secondary clinical disorders which interact with the thyroid metabolism should be considered and overruled in the study with the mentioned proposal, especially in the older population.

It appears that the confounding effect of the duration of AED intake must be adjusted regarding the children's age using multivariate analysis such as regression model or partial correlation test. The etiological mechanism of serum concentrations of thyroid hormone change by AEDs has not been clarified clearly and besides, patients with a personal or family history of thyroid disorders may progress to overt thyroid hormone imbalance secondary to AED consumption

(6). Therefore, it is suggested that the pure etiological mechanism of thyroid disorders due to AEDs should be studied in such cases. Previous reports suggested that return to normal of all parameters was observed after withdrawal of anticonvulsive therapy and this reversibility of the thyroid hormone imbalance may be a clue for further investigations in order to study the patho-physiologic mechanism of this disorder (6).

Recently, new pharmaceutical drugs have been successfully used for epileptic patients. It is expected that the therapeutic role of these new medications will become more prominent in these patients in the future and future studies should be focused on their adverse effects.

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