

RESEARCH ARTICLE

Serum Thyroid Hormone Levels in Epileptic Children Receiving Anticonvulsive Drugs

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Abstract

Objective

The aim of this study was to investigate serum thyroid hormone levels in epileptic children receiving anticonvulsive drugs.

Materials & Methods

In this case- control study, 30 epileptic children who were receiving anticonvulsive drugs (case group) were compared with 30 healthy children (control group). This study was carried out in the Qazvin Children's Hospital (Qazvin, Iran) from October to December 2007. Both groups were matched for age and sex. Thyroid hormone levels were measured using a radioimmunoassay and immunoradiometric assay. Data were analyzed using Chi-square and Student's t-tests.

Results

The mean serum T3 and T4 levels in the case group were 2.36 ± 0.73 nmol/L and 95.96 ± 27.01 nmol/L, respectively, and the corresponding values in the control group were 1.88 ± 0.93 nmol/L and 147.46 ± 35.77 nmol/L, respectively. The mean serum thyroid-stimulating hormone (TSH) levels in the case and control groups were 2.73 ± 0.73 mIU/mL and 2.49 ± 2.17 mIU/mL, respectively.

Conclusion

This study revealed that long-term consumption of anticonvulsive drugs resulted in a decline in serum T4 levels and an increase in serum T3 levels, but had no effect on TSH levels.

Keywords: Thyroid hormones; anticonvulsants; child

Introduction

Convulsion is the most common neurologic sign in children. Previous studies have shown that 10% of children have a history of convulsion during childhood (1). A variety of factors have been shown to cause convulsion in children. The most common forms of seizures are febrile seizures and epilepsy. The prevalence of febrile seizures and epilepsy in children is 3%-4% and 5.2-8.1 in 1000 children, respectively (2). Anticonvulsive drugs such as phenobarbital, carbamazepine, and sodium valproate are used in the treatment of epilepsy (1, 2). Several side effects, such as hypothyroidism, have been observed following the consumption of anticonvulsive drugs (1). A study conducted in central Iran revealed that long-term consumption of anticonvulsive drugs resulted in a decline of serum T4 levels, while serum T3 and thyroid-stimulating hormone (TSH) levels remained unchanged (3). The present study was performed to evaluate the levels of serum thyroid hormone in

epileptic children receiving anticonvulsive drugs in the Qazvin Children's Hospital, Qazvin, Iran.

Materials and Methods

In this case - control study, serum thyroid hormone levels were compared in 30 epileptic children receiving anticonvulsive drugs (case group) and 30 healthy children (control group). The study was carried out from October to December 2007 in the Qazvin Children's Hospital, which is affiliated with the Qazvin University of Medical Sciences, Qazvin (Iran). Both groups were matched for age and sex. Children were selected sequentially. The inclusion criteria for the case group were as follows: a minimum duration of 6 months of anticonvulsive drug therapy, absence of any other diseases, and receipt of standard and regular therapeutic dose. Following the collection of samples in anticoagulant-free tubes, the sera were removed and stored at -20°C . The T3, T4 and TSH levels were measured using a radioimmunoassay and immunoradiometric assay. The measurements were carried out using the Kavoshyar kit manufactured by the Iranian Atomic Energy Organization (Tehran, Iran) and the Genesys Gama counter set (USA). Intra assay coefficient of variant values of present kit for T3, T4 and TSH were $\leq 6.3\%$, $\leq 6.2\%$, and $\leq 3.7\%$, respectively and Also, these values for inter-assay coefficient of variant were $\leq 7.7\%$, $\leq 8.6\%$, and $\leq 5.7\%$, respectively. The data were analyzed by the Chi-square test and Student's t-test. Statistical significance was accepted for a $P < 0.05$.

Ethics

All parents were given clear explanations regarding the methodology of research. The present study was ethically confirmed by the ethical committee of the research department of the Qazvin University of Medical Sciences (Thesis No: 159). The children were included in the study if their parents were satisfied and signed the consent form.

Results

Of the 30 children who were receiving anticonvulsive drugs (case group), 16 were males and 14 (46.7%) were females. In the control group, the ratio of males to females was 13:17 ($P=0.606$). The minimum and maximum ages in the case group were 12 and 132 months, respectively, with a mean age of 59.30 ± 30.70 months.

In the control group, the minimum and maximum ages were 12 and 120 months, respectively, with a mean age of 55.53 ± 28.3 months ($P=0.62$). In the case group, the minimum and maximum periods of anticonvulsive drug consumption were 6 and 72 months, respectively, with a mean period of 17.37 ± 13.61 months. Twenty-four children were receiving a single drug, 3 children were receiving 2 drugs, and the rest were receiving 3 drugs. The most commonly used drug was phenobarbital (Table 1). The most common type of seizure was tonic-clonic generalized seizure in 28 children (93.3%). None of the children receiving anticonvulsive drugs showed any clinical symptoms of hypothyroidism. The mean serum T3 levels in the case and control groups were 2.36 ± 0.73 nmol/L and 1.88 ± 0.93 nmol/L, respectively ($P=0.03$). The mean serum T4 levels in the case and control groups were 95.96 ± 27.01 nmol/L and 147.46 ± 35.77 nmol/L, respectively ($P=0.000$). The mean serum TSH levels in the case and control groups were 2.73 ± 0.73 mIU/mL and 2.49 ± 2.17 mIU/mL, respectively ($P=0.56$) (Table 2). There was no significant difference in the levels of serum thyroid hormones depending on the duration of anticonvulsive drug consumption ($P=0.56$) (Table 3).

Discussion

This study revealed that long-term consumption of anticonvulsive medications resulted in a decline in serum T4 levels and an increase in serum T3 levels, but it had no effect on serum TSH levels. Various studies have been conducted on the effect of anticonvulsive medications on thyroid hormones. Shiva reported that the consumption of anticonvulsive drugs resulted in reduction of serum T4 levels, while no detectable effect was observed on serum T3 and TSH levels (3). Kimura showed that anticonvulsive drugs lead to a decline in T4 concentration and an increment in T3 levels, with no effect on TSH levels (4). Another study showed that consuming carbamazepine and sodium valproate resulted in hypothyroidism. Therefore, it is recommended that serum thyroid hormone levels be measured following long-term consumption of these drugs (5). Isojavri reported that sodium valproate consumption had no effect on serum thyroid hormone levels, but carbamazepine consumption led to a decrease in serum T4 levels (6). Verrolti and Vainionpaa reported

that long-term consumption of carbamazepine resulted in a decrease in serum levels of thyroid hormones, but sodium valproate had no detectable effect on them. They emphasized that consumption of a combination of carbamazepine and sodium valproate caused a severe decrease in thyroid hormone levels and finally led to subclinical hypothyroidism (7, 8). Vainionpaa believes that clinical and laboratory symptoms of hypothyroidism improve following the discontinuation of anticonvulsive drugs (7). Another study carried out on animals revealed that phenobarbital led to a decrease in serum T4 levels, but had no effect on serum T3 and TSH levels (9). A study in rabbits showed that long-term consumption of phenytoin resulted in a severe decrease in T4 levels(10). Schonberger and co-workers reported that the use of primidone resulted in a decline in serum T4 and an increase in serum T3 levels, but it had no effect on TSH levels (11). Others have reported that the consumption of more than one drug resulted in a greater reduction in serum T4 levels(4, 5). However, the study byTiihonen on long_term consumption of phenytoin and carbamazepine showed that these drugs have no effect on thyroid hormones. In addition, the metabolism of patients was within the normal range (12). Researchers believe that the mechanisms underlying serum T4 level reduction are augmentation of microsomal enzyme function in the liver and inhibition

of hypothalamic gland activities. An increase in serum T3 levels is due to the conversion of T4 to T3, a process that establishes a physiologic balance (3, 6, 7, 9, 13). There are different views regarding the assessment of thyroid hormone levels in children consuming anticonvulsive drugs. While some researchers consider that in epileptic patients, the thyroid hormone levels should be checked regularly(4), Vainionpaa disagrees because such patients are known to have normal metabolism (7). Because our sample size was not large enough, it was not possible to compare separately the effect of the different drugs on thyroid levels.

This study revealed that long_term consumption of anticonvulsive drugs resulted in a decline in serum T4 levels and an increase in serum T3 levels, but had no effect on TSH levels.

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Table 1: Distribution Frequency of Different Types of Anticonvulsive Drugs in Epileptic Children

	Patients, No.(%)	Dose of Drugs, mg/kg
Phenobarbital	13 (43.3)	5
Carbamazepine	4 (13.3)	10
Primidone	3 (10)	16
Phenytoin	3 (10)	5
Phenobarbital + Phenytoin	2 (6.6)	5 + 5
Phenobarbital+Sodium Valproate+Clonazepam	2 (6.6)	5 + 15 + 0.5
Primidone+ Sodium Valproate+ Clonazepam	1 (3.3)	15 + 15 + 0.5
Phenobarbital+Sodium Valproate	1 (3.3)	5 + 15
Sodium Valproate	1 (3.3)	15
Total	30 (100)	-

Table 2: Comparison of Serum Thyroid Hormone Levels in Afflicted Children Receiving Anticonvulsive Drugs (Case Group) and Healthy Children (Control Group)

	Case, Mean ± SD	Control, Mean ± SD	P value
T3, nmol/L	2.36± 0.73	1.88± 0.93	0.03
T4, nmol/L	95.96± 27	147.46±35.77	0.000
TSH, mIU/mL	2.73± 0.73	2.49± 2.17	0.56

Table 3: Serum Thyroid Hormone Levels in Children Receiving Anticonvulsive Drugs Depending on the Duration of Drug Consumption

	Time, mo, Mean ± SD		P value
	< 24	> 24	
T3, nmol/L	2.5±0.73	1.96±0.6	0.072
T4, nmol/L	95.5±26.3	97±30.7	0.902
TSH, mIU/mL	2.88±0.66	2.3±0.86	0.059

References

- Johnston M. Neurodegenerative disorders of childhood; Spingolipidoses. Nelson textbook of pediatrics, 17th ed Philadelphia: Saunders; 2004.P.2031-2.
- Sankar R, Koh S, Wu J, Menkes J. Paroxysmal disorders. In(eds): Menkes JH, Sarnat HB, Maria BL. Child Neurology. 2006.P.857-942.
- Shiva S, Ashrafi M, Mostafavi F, Abasi F, Rahbari A, Shabani R. Effects of anticonvulsant drugs on thyroid function tests. Iranian Journal of pediatrics 2003;13(02):101-106.
- Kimura M, Yoshino K, Suzuki N, Maeoka Y. Effect of antiepileptic drugs on thyroid function. Psychiatry and clinical neurosciences. 1995;49(4):227-9.
- Eris Pural J, Delrio-Garma M, Delrio - Castro – Gago M. Long Term treatment of children with epilepsy with valprovats or carbamazepin, may cause subclinical hypothyroidism. Epilepsia 1999;40(12):1961-6.
- Isojärvi JI, Turkka J, Pakarinen AJ, Kotila M, Rättyä J, Myllylä VV. Thyroid function in men taking carbamazepine, oxcarbazepine, or valproate for epilepsy. Epilepsia 2001;42(7):930-4.
- Vainionpää LK, Mikkonen K, Rättyä J, Knip M, Pakarinen AJ, Myllylä VV, et al. Thyroid function in girls with epilepsy with carbamazepine, oxcarbazepine, or valproate monotherapy and after withdrawal of medication. Epilepsia 2004;45(3):197-203.
- Verrotti A, Basciani F, Morresi S, Morgese G, Chiarelli F. Thyroid hormones in epileptic children receiving carbamazepine and valproic acid. Pediatric neurology 2001;25(1):43-6.
- Kantrowitz L, Peterson M, Trepanier L, Melian C, Nichols R. Serum total thyroxine, total triiodothyronine, free thyroxine, and thyrotropin concentrations in epileptic dogs treated with anticonvulsants. Journal of the American Veterinary Medical Association 1999;214(12):1804-8.
- Schröder-van der Elst J, Van der Heide D, Van der Bent C, Kaptein E, Visser T, DiStefano J. Effects of 5, 5 - diphenylhydantoin on the thyroid status in rats. European journal of endocrinology 1996;134(2):221-4.
- Schonberger W, Grimm W, Schonberger G, Sinterhauf K, Scheidt E, Ziegler R. [The influence of primidone on thyroid function (author's transl)]. Dtsch Med Wochenschr 1979;104(25):915-7.
- Tiihonen M, Liewendahl K, Waltimo O, Ojala M, Valimaki M. Thyroid status of patients receiving long-term anticonvulsant therapy assessed by peripheral parameters: a placebo-controlled thyroxine therapy trial. Epilepsia 1995;36(11):1118-25.
- Benedetti MS, Whomsley R, Baltus E, Tonner F. Alteration of thyroid hormone homeostasis by antiepileptic drugs in humans: involvement of glucuronosyltransferase induction. Eur J Clin Pharmacol 2005;61(12):863-72.