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Original article

Study of Electroencephalogram changes in Hypothyroidism

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Abstract

Hypothyroidism is a common disorder with highly variable presentations; no predictable progression of symptoms is apparent. This study mainly focuses on the effect of hypothyroidism on central nervous system.

Aim - The purpose of this study is to study the changes in Electroencephalogram in hypothyroidism, to know the prevalence of background slowing of brain activity on electronencephalogram in patients with hypothyroidism and to correlate mental status changes with electroencephalpogram abnormalities.

Study setting and Design - 60 patients with hypothyroidism were examined in outpatient/inpatient in a tertiary care hospital from July 2013 to September 2015. It is a prospective type of study. Written and informed consent were taken in language respondent understand. Data collection was done with the help of detailed examination.

Data analysis – Statistical Programme for Social Sciences (SPSS) software 15 version and OpenEpi software version 2.3 were used for data analysis.

Results – Out of 60 patients with hypothyroidism, abnormal EEG finding was seen among 12 cases with hypothyroidism. MMSE score and EEG association showed that MMSE score was significantly less among the cases with abnormal EEG. Symptoms like fatigability, difficulty in concentrating, increased sleep and slowing of physical activity were significantly associated with abnormal EEG. Association between T3, T4 and TSH with EEG showed that Mean TSH was significantly raised among the cases with abnormal EEG as compared to normal EEG.

Conclusion- Our study showed significant number of Hypothyroid cases having Electroencephalogram changes. TSH was significantly raised among Hypothyroidism cases with abnormal EEG.

Key words – Hypothyroidism, Electroencephalogram, Mini-mental status examination, TSH levels.

Introduction

The thyroid gland plays an important role in tissue metabolism and development. It secretes thyroxine (3,5,3'5'-tetraiodothyronine) T4, and small amounts of (3,5,3'-triiodothyronine)T3. Abnormal thyroid hormone levels lead to hypothyroid and hyperthyroid states. The central nervous system is a major target organ. Inadequate thyroid hormone during development leads to congenital hypothyroidism (also known as cretinism) with associated irreversible brain damage.[1] The neurological manifestations occur in conjunction with the systemic features of the disease and may be noted only incidentally. However, symptoms and signs of neurologic

dysfunction may be the presenting feature in some patients and can contribute significant disability. The effects of hypothyroidism are manifested as slowness in thinking, marked latency of behavioral response and decrement in mood level. [2] Although the deleterious effects of abnormal thyroid hormone levels have been characterized, there has been little consideration of whether thyroid function is relevant to the normal regulation of brain activation and behavioral activity. Recent neurophysiologic investigations have shown direct effects of thyroid hormones on brain. [3]

The purpose of this study is to objectively study the changes in Electroencephalogram in hypothyroidism, as the effects of hypothyroidism on the central nervous system need to be studied and solidly understood by clinicians who treat patients with this disease, as early detection prompts early treatment and hence it can be reverted back to normal.

Subjects and methods –

60 patients with hypothyroidism, admitted in medicine wards were included in this study over a period from July 2013 to September 2015.

The main objective of this study was to analyze the Electroencephalogram changes in hypothyroidism, to study the prevalence of background slowing of the brain activity, to know the epileptic form on EEG in patients with hypothyroidism and to correlate mental status changes with Electroencephalogram abnormalities in patients with hypothyroidism. At the time of registration, the baseline information was taken especially with respect to socio – demographic factors, clinical findings, specific investigations for Hypothyroidism, MMSE scoring, EEG and other investigations. Hence, each and every patient was followed up in Medicine department till the time of discharge and even on outpatient department basis. The data thus collected was analyzed to study the associations and various outcome of the disease.

Inclusion criterias –

1. Age more than 15 years.
2. Overt cases of Hypothyroidism with biochemical evidence of TSH more than 10 mIU/L.
3. Subclinical Hypothyroid cases with biochemical evidence of TSH level between 4.5 – 10 mIU/L.
4. Iatrogenic Hypothyroidism – Post surgical and after radioactive iodine therapy.

Exclusion criterias –

1. Established CNS disorders –like cerebrovascular accidents.
2. Drugs - like Amiodarone, Lithium, p-amino salicylic, Interferon - α, Benzodiazepines and sedatives.
3. Critically ill patients.

Investigations –

A structured proforma was used and filled personally after interviewing and examining the patient. The following information was collected:-

Age, sex, symptoms, haemogram, renal function test, liver function test, lipid profile, blood sugar levels, thyroid function test, thyroid antibodies, USG – Neck, Mini – mental status examination, Electroencephalogram, ECG.

Results -

Table 1: Age wise distribution of cases in study group.

Age (Yrs)	No. of cases	Percentage
≤20	12	20
21 – 30	20	33.33
31 – 40	18	30
>40	10	16.67
Total	60	100

The above table shows the age distribution among 60 study subjects. The majority 20 (33%) are in the age group 21 to 30 years, followed by 30 % who are in the age group 31 to 40 years and 12 (20%) are in age group of ≤20 yrs. Only 10 are in the age group of >40 yrs.

Table 2: Sex wise distribution of cases in study group.

Sex	No. of cases	Percentage
Male	11	18.33
Female	49	81.67
Total	60	100

The above table shows the sex distribution among 60 study subjects. The majority, 49 were females and remaining 11 cases were males.

Table 3: Symptomatology wise distribution of cases in study group.

Symptomatology	No. of cases	Percentage (n=60)
Weight gain	38	63.33
Fatigability	47	78.33
Poor memory	11	18.33
Difficulty in concentrating	39	65
Increased sleep	40	66.67
Parasthesia	12	20
Slowing of physical activity	24	40

The above table shows the symptomatology wise distribution among 60 study subjects. The majority 47 cases had fatigability, 40 cases had increased sleep, 39 cases had difficulty in concentrating, 38 cases had weight gain and 24 cases had slowing physical activity. 12 and 11 cases had parasthesia and poor memory respectively.

Table 4: Motor system wise distribution of cases in study group.

Motor system	No of cases	Percentage
Delayed	5	8.33
Normal	55	91.33
Total	60	100

The above table shows the motor system wise distribution among 60 study subjects. The majority 55 cases had normal motor system and remaining 5 cases had delayed motor system in study group in the form of delayed relaxation phase of ankle reflex.

Table 5: EEG finding wise distribution of cases in study group

EEG finding	No of cases	Percentage
Abnormal	12	20
Normal	48	80
Total	60	100

The above table shows the EEG finding wise distribution among 60 study subjects. The majority 48 cases had normal EEG and remaining 12 cases had abnormal EEG in study group in the form of low amplitude of background alpha activity.

Table 6: Association between symptoms and EEG in study group.

Symptoms	EEG		Z value	P Value
	Abnormal (n=12)	Normal (n=48)		
Weight gain	10 (83.33)	28 (58.33)	1.93	>0.05
Fatigability	12 (100)	35 (72.92)	4.22	<0.0001
Poor memory	4 (33.33)	7 (14.58)	1.29	>0.05
Difficulty in concentrating	12 (100)	27 (56.25)	6.11	<0.0001
Increased sleep	11 (91.67)	29 (60.42)	2.93	<0.01
Parasthesia	5 (41.67)	7 (14.58)	1.79	>0.05
Slowing of physical activity	8 (66.67)	16 (33.33)	2.19	<0.05

The above table shows association between symptoms and EEG in study group. Among 38 cases with weight gain, 10 had abnormal EEG. Fatigability was seen among 12 cases with abnormal EEG. Among 11 cases with poor memory, 4 had abnormal EEG. All 12 cases with abnormal EEG had difficulty in concentrating. 11 cases had increased sleep with abnormal EEG. Among 24 cases with slow physical activity, 8 had abnormal EEG. To test association between symptoms and EEG Z test was applied as test of significance. Z test value was 4.22, 6.11, 2.93 and 2.19 for fatigability, difficulty in concentrating, increased sleep and slowing of physical activity respectively which are statistically significant ($p<0.001$)

Table 7: Comparison of MMSE score according to EEG in study group.

Parameter	EEG				Z Value	P Value
	Abnormal (n=12)		Normal (n=48)			
	Mean	**SD**	**Mean**	**SD**		
MMSE score	27.50	2.97	29.46	1.69	3.04	<0.005

The above table shows comparison of MMSE score with EEG in study group. Mean MMSE score in cases with abnormal EEG was 27.50 (S.D.±2.97). Mean MMSE score among cases with normal EEG was 29.46 (S.D.±1.69) MMSE score and EEG was analyzed quantitatively. Z value worked out to be 3.04 which is statistically significant ($p<0.005$).

Table 8: Comparison of T3, T4, TSH according to EEG in study group.

Parameter	EEG				Z Value	P Value
	Abnormal (n=12)		Normal (n=48)			
	Mean	**SD**	**Mean**	**SD**		
T3	57.42	23.857	61.18	29.510	0.46	>0.05
T4	2.84	2.35	3.66	2.28	1.09	>0.05
TSH	114.5	53.8	63.1	49.9	3	<0.01

The above table shows comparison of T3, T4 and TSH with EEG in study group. Mean T3 in cases with abnormal EEG was 57.42 (S.D.±23.85). Mean T4 among cases with normal EEG was 2.84 (S.D.±2.35). Mean TSH among cases with abnormal EEG was 114.5 (S.D. ± 53.8). T3, T4 and TSH and EEG were analyzed quantitatively. Z value worked out to be 3 for TSH which is statistically significant ($p<0.01$). Z value for T3 and T4 was 0.46 and 1.09 which was statistically not significant. ($P>0.05$)

Discussion

The prospective study was carried out to study the Electroencephalogram changes in hypothyroidism. Total 60 cases with hypothyroidism were examined, based on the inclusion and exclusion criteria.

Age wise distribution showed 63% of study cases were in a group of 21 to 40 yrs, followed by 20% in age group of ≤20 yrs and remaining 10 cases were in age group of > 40 yrs. (Table no 1) Similar finding was observed in a study conducted by Naval Kishor Yadav, C. Thanpari, Mukesh Kumar Shrewastwa, Brijesh Sathian, and Rabindra Kumar Mittal (2013) assessed status of thyroid disorder in population of far western region of Nepal. The percentage of thyroid disorders was 33.66% in far western region of Nepal. High number of total thyroid dysfunction was observed in 21 to 40 years of age groups, followed by 41 to 60 years of age groups. People with age less than 40 years, were having 1.03, 0.99, 2.51 and 1.15 times risk of developing overt hyperthyroidism, subclinical hyperthyroidism, overt hypothyroidism and subclinical hypothyroidism respectively, compared to greater than 40. Female were having 0.29 times risk of developing subclinical hypothyroidism compared to male. Female were having more risk of developing hypothyroidism as compared to male.[4] Majority of cases in study were

females (81.67%) as compared to males (18.33%). (Table no 2)

Fatigability (78.33%), increased sleep (66.67%), weight gain (63.33%) and difficulty in concentrating (65%) were common symptoms among the study cases. Rests of symptoms were poor memory, paresthesia and slowing of physical activity. (Table no 3) Carlé A, Pedersen IB, Knudsen N, Perrild H, Ovesen L, Laurberg P. (2014) studied the array of symptoms as they are reported in newly diagnosed overt autoimmune hypothyroidism using a population-based case-control design. 13 symptoms were statistically overrepresented in hypothyroidism which included symptoms like tiredness (81%), dry skin (63%), and shortness of breath (51%). [5] A study conducted by Kawther.T and El-Shafie (2003) showed in their study that almost half of the patients were asymptomatic for hypothyroidism. The majority of symptoms were vague and not specific to a particular disease. The major presenting symptom was fatigue, not a specific symptom for hypothyroidism which was the only symptom in 30% of the patients. [6]

In central nervous system examination, normal motor system was observed in majority i.e. 55 cases in the study group only 5 cases had delayed motor system in form of delayed relaxation phase of ankle reflex (Table no 4). Henryk Zulewski, Beat Müller, Pascale Exer, André R, Miserez, and Jean-Jacques Staub stated in his study that besides TSH and thyroid hormones, measurement of parameters known to reflect tissue manifestations of hypothyroidism, such as ankle reflex relaxation time and total cholesterol, play an important role in assessment of thyroid failure and the monitoring of treatment. In overt hypothyroid patients, there was an excellent correlation with ankle reflex relaxation time and total cholesterol. [7]

Abnormal EEG finding was seen among 12 cases with hypothyroidism in study remaining 48 cases had normal EEG study. (Table no 5) Similar finding was seen in a study conducted by Pohunková D, Sulc J, Vána S. (1989) studied influence of thyroid hormone supply on EEG frequency spectrum. Results showed that in hypothyroid state, the most remarkable finding on EEG was the increase in percentage representation of fast frequencies in beta 1 and beta 2 bands, while such values in alpha band including a dominant frequency in that band were reciprocally decreased. The EEG signs of brain hypothyroidism continued even after achieving clinical euthyroidism and normal peripheral parameters under increased serum T3 and low T4 level. [8] Khedr EM, El Toony LF, Tarkhan MN, Abdella G. (2000) evaluated objectively the functional changes in the nervous system in hypothyroidism by different electrophysiological parameters and to determine the frequencies of these changes in patients with hypothyroidism. Eight patients (35%) had EEG changes. Diffuse slowing of background activity was the commonest. No significant correlation was observed between hormonal levels and the different electrophysiological parameters. Authors concluded that CNS is more vulnerable to the effect of hypothyroidism than the PNS. [9]

Symptoms like fatigability, difficulty in concentrating, increased sleep and slowing of physical activity were significantly associated with abnormal EEG in the study group. Remaining symptoms like weight gain, poor memory and paresthesia were not significant with EEG result in the study (Table no 6). In a study by Haupt.M and Kurz.A (1993) stated when neuropsychological

testing was performed, deficits may be most pronounced in tests of attention and executive function. Memory retrieval, learning, verbal fluency, and motor speed are also often particularly impaired. Electroencephalography (EEG) may show generalized background slowing. [10]

MMSE score and EEG association showed that MMSE score was significantly less among the cases with abnormal EEG as compared to normal EEG in the study group. Mean MMSE score among abnormal EEG was 27.50 and among normal EEG was 29.46. (Table no 7)

Association between T3, T4 and TSH with EEG showed that Mean TSH was significantly raised among the cases with abnormal EEG as compared to normal EEG. Mean TSH was 114 among abnormal EEG and 63 among normal EEG. Remaining T3 and T4 were not significant wit EEG in the study group. (Table no 8)

Conclusion

Our study showed significant number of Hypothyroid cases having Electroencephalogram changes. Abnormal EEG pattern was observed in 20% of subjects in hypothyroidism. Fatigability, difficulty in concentrating, increased sleep and slowing of physical activity were common symptoms with abnormal EEG among hypothyroidism. Reduced MMSE score was associated with all the symptoms of hypothyroidism. TSH was significantly raised among Hypothyroidism cases with abnormal EEG. Hence, Central nervous system is more vulnerable to the effect of Hypothyroidism. Therefore, Electrophysiological studies like EEG, should be performed in Hypothyroid patients, early in the course of disease in order to detect the nervous system involvement. Hence, this study shows importance of early detection of neurological involvement in Hypothyroidism, as with early detection, early treatment can be started before irreversible neuronal damage occurs. EEG is not a routine investigation for Hypothyroidism, but if we add this investigation in early course of disease, that could help to evaluate early CNS involvement in Hypothyroidism.

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