Section: Otorhinolaryngology

Original Research Article

EFFECT OF THYROXINE THERAPY ON BRAINSTEM-EVOKED RESPONSE AUDIOMETRY MEASURED AUDITORY PROCESSING IN NEWLY DETECTED PATIENTS OF HYPOTHYROIDISM

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Abstract

Background: This research focuses on evaluating the improvement of hearing functions in individuals with newly diagnosed hypothyroidism using Brainstem-Evoked Response Audiometry (BERA) based audiological status of patients before and after 6 months of thyroxine therapy. **Materials and Methods:** A prospective study was conducted on 50 newly diagnosed hypothyroid patients at the Department of Otorhinolaryngology, Vinayaka Mission's Medical College & Hospital, over 18 months. Participants aged 18-60 years underwent physical, clinical, and otorhinolaryngology examinations, alongside thyroid profile measurements before and after 6 months of thyroxine treatment. The BERA test was utilized to evaluate auditory responses. **Result:** A significant improvement in thyroid hormone levels post-thyroxine therapy, is evidenced by a decrease in TSH and an increase in free T3 and free T4 levels. BERA assessments pre and post-treatment indicated statistically significant improvements in auditory response times/latencies, particularly for waves III, V (mean differences of 0.086ms and 1.103ms and p values of <0.05 and <0.001 respectively) and interpeak latencies I-III, III-V, and I-V (mean differences of 0.155ms, 0.923 and 1.191ms respectively and all p values <0.001); which showcased enhanced neural transmission along the auditory pathway. These results were more pronounced in later stages of auditory processing, suggesting that hypothyroidism primarily impacts these stages and that thyroxine therapy significantly mitigates these effects. **Conclusion:** While conforming to various existing evidence, this study underlines the critical role of thyroxine in improving thyroid function and thus the auditory function in hypothyroid patients. It presents robust evidence of the positive impact of thyroxine on auditory processing speeds, especially in the auditory pathway's later stages. This highlights the importance of early diagnosis and thyroxine therapy in managing hypothyroidism, suggesting that BERA should be considered in the evaluation and monitoring of the central auditory pathway in newly diagnosed patients.

INTRODUCTION

The thyroid gland, with its origins in anatomical descriptions by Andreas Vesalius in the 16th century and the naming by Thomas Wharton in the 17th century, plays a pivotal role in metabolic regulation through hormone production. Weighing 20-25g and located in the neck, its basic structure, the thyroid follicle, produces thyroid hormones T3 and T4 essential for metabolic processes. Hormone synthesis involves iodide trapping and iodination of tyrosine in Thyroglobulin, regulated by the hypothalamic-pituitary-thyroid axis and transported by specific proteins. These hormones influence metabolism, impacting lipid, carbohydrate, and protein utilization and interacting with other bodily hormones. Hypothyroidism, characterized by insufficient thyroid hormone production, manifests in various symptoms across bodily systems including cardiovascular, gastrointestinal, and neurological, affecting cognitive functions and hearing (sensory neural hearing loss). The human ear, from the

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external to the inner cochlea, plays a critical role in hearing, with the central auditory pathway transmitting signals from the cochlea to the brain, illustrating the complex interplay between thyroid function and overall health.[1-4]

Brainstem Evoked Response Audiometry (BERA) is also known as Auditory Brainstem Response (ABR) or Brainstem Auditory Evoked Potentials (BAEP), is a valuable diagnostic tool for evaluating the functional integrity of the central auditory pathway. It is used for various purposes, including hearing loss screening, intraoperative monitoring, localization of brainstem dysfunction, and differentiation between peripheral and central nervous system abnormalities. To record BERA, a mixed-frequency stimulus is used, and electrodes are placed on the scalp and ears. The key components in BERA waveforms are waves I, III, and V, with inter-peak latencies (IPL) providing valuable diagnostic information. BERA is a non-invasive method for assessing the integrity of the auditory pathway.[5-9]

Need for the study: In conclusion, the thyroid gland and its hormones play a crucial role in various physiological processes. Hypothyroidism can lead to a wide range of symptoms, including neurological issues affecting the auditory system. BERA is a valuable tool for diagnosing even mild to moderate (otherwise clinically undiagnosable) auditory pathway abnormalities and understanding the impact of thyroid disorders on hearing. So our study plans to find the effects of thyroxine therapy in newly diagnosed hypothyroidism patients on their hearing capabilities and/or in improving hearing abnormalities.

Objectives: The primary objective of this study is to assess the improvement of hearing functions in individuals with newly diagnosed hypothyroidism using Brainstem-Evoked Response Audiometry (BERA) based audiological status of patients before and after 6 months of thyroxine therapy.

MATERIALS AND METHODS

In this study, 50 newly diagnosed hypothyroid patients were examined at the Department of Otorhinolaryngology, Vinayaka Mission's Medical College & Hospital, Karaikal, over 18 months. The prospective study included patients aged 18 to 60 years with confirmed hypothyroidism. Excluded respondents were those who were already on treatment for hypothyroidism or with a history of ear surgery, hearing loss, loud noise exposure, or specific drug intake; or those who were of age extremes, unwilling to participate, or with any systemic illnesses. Ethical approval was obtained and patients' physical and clinical examination-related information and medical history were collected. All required personal details were collected, Otorhinolaryngology examinations and thyroid profile evaluations were conducted before and after 6 months of thyroxine treatment. The dosages of thyroxine were prescribed by their treating physician as per routine treatment. Brainstem Evoked Response Audiometry (BERA) was used to evaluate auditory responses, involving detailed procedures such as electrode placement, auditory stimuli delivery, and latency measurements. BERA was recorded by using "RMS medulla-201 ABR" system (already clinically validated) with installed BERA software.10 Overall, the study comprehensively assessed the audiological status of hypothyroid patients, particularly highlighting the BERA procedure.

RESULTS

In this study of 50 newly diagnosed hypothyroid patients over 18 months, the majority were females (94%), and the most common age group was 21-30 years (48%). The mean age was 31.46 ± 8.33. Thyroid hormone levels were significantly improved with thyroxine therapy, as evidenced by a decrease in TSH and an increase in fT3 and fT4 levels ($p<0.001$). The study also evaluated auditory responses using Brainstem Evoked Response Audiometry (BERA) before and after thyroxine treatment.

Interaural differences of absolute and interpeak latencies in newly diagnosed hypothyroid patients before and after thyroxine therapy:

[Table 1]. shows data on the interaural differences of absolute and interpeak latencies in newly diagnosed hypothyroid patients before and after thyroxine therapy. The data are presented for both right and left ears, with the mean and standard deviation (SD) provided for measurements pre and post-treatment, alongside the mean difference between these two time points and the associated p-values.

Key Findings

Right Ear:

- Absolute and Interpeak Latencies of sound waves (I, III, V, I-III, III-V, I-V): Statistically significant improvements ($p<0.05$) were observed in the latencies of III, V, I-III, III-V, and I-V after thyroxine therapy, indicating a reduction in latency times post-treatment. The most substantial mean difference was observed in the interpeak latency of waves I-V measurement, with a decrease of 1.312 ms ($p<0.001$).
- The latency for the initial sound wave (I) did not show a significant change ($p=0.913$), suggesting that the earliest auditory response was not significantly affected by the therapy.

Left Ear:

- Absolute and Interpeak Latencies (of Waves I, III, V, I-III, III-V, I-V): Similar to the right ear, significant improvements were observed post-treatment in the latencies V, I-III, III-V, and I-V, with the latency V showing the most considerable mean difference reduction of 1.107 ms ($p<0.001$). This indicates enhanced auditory response times after therapy.
- The latency for the initial sound wave (I) and the latency III did not show significant changes

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(p=0.561 and p=0.482, respectively), indicating that these aspects of the auditory response were not significantly altered by the treatment.

Interpretation

The data suggests that thyroxine therapy in newly diagnosed hypothyroid patients leads to significant improvements in auditory response times, particularly in the later stages of the auditory pathway (as evidenced by latencies V, III-V, and I-V). These findings imply that hypothyroidism may affect auditory processing and that thyroxine therapy helps in mitigating these effects, improving the efficiency of neural transmission in the auditory pathways.

The lack of significant change in the earliest auditory response (latency I) in both ears suggests that the initial auditory reception might not be as affected by hypothyroidism or that the improvements due to therapy are more pronounced in the later stages of auditory processing.

Overall, these results highlight the positive impact of thyroxine therapy on auditory function in hypothyroid patients, with significant improvements in the speed of neural conduction across the auditory pathway post-treatment. This could have clinical implications in the management of auditory symptoms in hypothyroid patients.

Overall Absolute and Interpeak Latencies of Waves in newly diagnosed hypothyroid patients before and after treatment:

Overall absolute latencies [Table 2] of wave III, V (3.84 ± 0.25 - before,3.76 ± 0.36 – after, 0.086 - mean difference and $p<0.05$; 6.86 ± 0.56 - before, 5.76 ± 0.66 – after, 1.103 - mean difference and $p<0.001$ respectively) and interpeak latencies of waves I-III, III- V, I-V (2.57 ± 0.44 - before, 2.42 ± 0.18 – after, 0.155086 - mean difference and $p<0.001$; 3.29 ± 0.77 – before, 2.37 ± 0.41 – after, 0.923 - mean difference and $p<0.001$; 5.50 ± 0.77 - before, 4.31 ± 0438 – after, 1.191 - mean difference and $p<0.001$ respectively) shows statistically significant differences after treatment with thyroxine.

The results outline the effects of thyroxine treatment on absolute and interpeak latencies in newly diagnosed hypothyroid patients. The data include mean and standard deviation (SD) values for each measurement both before and after treatment, along with the mean differences and p-values to assess statistical significance.

Key Observations

- Latency of Wave I: There is a slight increase in the mean latency (from 1.62 ms to 1.65 ms) after treatment, with a mean difference of 0.024 ms, which is not statistically significant (p=0.553). This indicates that the initial auditory response is not significantly affected by thyroxine treatment.
- Latency of Wave III: Shows a reduction in mean latency from 3.84 ms to 3.76 ms post-treatment, with a mean difference of 0.086 ms, which is statistically significant ($p<0.05$). This suggests that the neural transmission up to the midbrain level improves with thyroxine treatment.
- Latency of Wave V: There is a notable decrease in mean latency from 6.86 ms to 5.76 ms after treatment, with a mean difference of 1.103 ms, which is highly significant ($p<0.001$). This indicates a significant improvement in neural transmission speed to the level of the inferior colliculus and auditory cortex.
- Interpeak Latencies (I-III, III-V, I-V): All show statistically significant reductions in mean latencies after treatment:
- I-III: Decreased by 0.155 ms ($p<0.001$), indicating improved neural transmission between the auditory nerve and the midbrain.
- III-V: Decreased by 0.923 ms ($p<0.001$), suggesting faster transmission from the midbrain to the auditory cortex.
- I-V: Decreased by 1.191 ms ($p<0.001$), reflecting overall enhancement in auditory pathway efficiency from the auditory nerve to the cortex.

Interpretation

The findings from Table 2 indicate that thyroxine treatment in newly diagnosed hypothyroid patients leads to significant improvements in auditory processing speeds, particularly in the later parts of the auditory pathway. The significant reductions in latencies III, V, and interpeak latencies (I-III, III-V, I-V) post-treatment suggest that hypothyroidism may impede neural transmission in these areas, and that thyroxine treatment effectively mitigates these delays, enhancing the efficiency of neural conduction.

The initial auditory response (Latency I) was not significantly altered by treatment, indicating that the effects of hypothyroidism and the benefits of thyroxine therapy may be more pronounced in the neural transmission aspects further along the auditory pathway.

These results underscore the importance of thyroxine therapy in addressing not only the general symptoms of hypothyroidism but also in improving specific neurological functions, such as auditory processing. This has implications for the clinical management of hypothyroidism, suggesting that auditory function improvements can be an additional benefit of thyroxine therapy in affected patients.

Overall, the study indicated that thyroxine treatment had a positive impact on both thyroid hormone levels and auditory responses in newly diagnosed hypothyroid patients. These findings highlight the potential benefits of early diagnosis and treatment in managing hypothyroidism.

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Table 1: Interaural differences of absolute and interpeak latencies in newly diagnosed hypothyroid patients before and after thyroxine therapy

	Pre treatment	Post treatment		
	Mean ± SD	Mean ± SD	Mean Difference	p-Value
Right Ear				
I	1.59 ± 0.12	1.60 ± 0.13	0.045	0.913
III	3.88 ± 0.25	3.75 ± 0.25	0.128	0.004
V	6.87 ± 0.56	5.75 ± 0.47	1.098	<0.001
I - III	2.59 ± 0.48	2.42 ± 0.16	0.176	0.019
III – V	3.43 ± 0.73	2.34 ± 0.46	1.088	<0.001
I-V	5.61 ± 0.72	4.30 ± 0.50	1.312	<0.001
Left Ear	Pre-Treatment	Post Treatment	Mean Difference	p-Value
I	1.65 ± 0.18	1.70 ± 0.47	0.002	0.561
III	3.81 ± 0.24	3.77 ± 0.45	0.044	0.482
V	6.84 ± 0.56	5.74 ± 0.81	1.107	<0.001
I - III	2.55 ± 0.39	2.42 ± 0.21	0.135	0.024
III – V	3.16 ± 0.79	2.40 ± 0.35	0.758	<0.001
I-V	5.39 ± 0.80	4.32 ± 0.46	1.069	<0.001

Table 2: Absolute and Interpeak latencies in newly diagnosed hypothyroid patients before and after thyroxine treatment

	Pre-treatment	Post treatment		
	Mean ± SD	Mean ± SD	Mean Difference	p-Value
I	1.62 ± 0.16	1.65 ± 0.35	0.024	0.553
III	3.84 ± 0.25	3.76 ± 0.36	0.086	<0.05*
V	6.86 ± 0.56	5.76 ± 0.66	1.103	<0.001*
I - III	2.57 ± 0.44	2.42 ± 0.18	0.155	<0.001*
III – V	3.29 ± 0.77	2.37 ± 0.41	0.923	<0.001*
I-V	5.50 ± 0.77	4.31 ± 0438	1.191	<0.001*

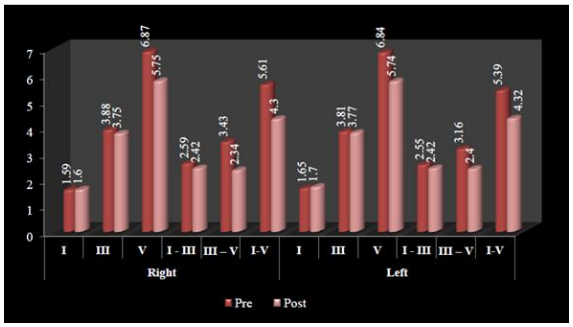

Figure 1: Interaural differences of absolute and interpeak latencies in newly diagnosed hypothyroid patients before and after thyroxine therapy

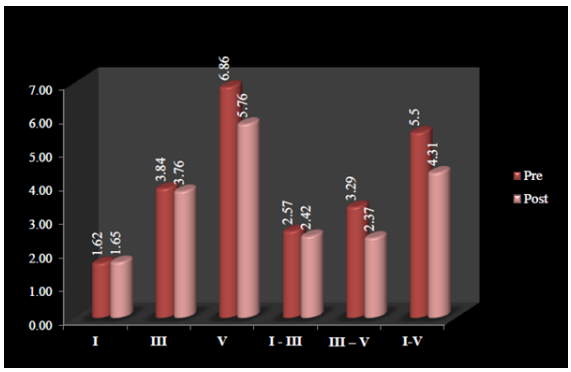

Figure 2: Overall Absolute and Interpeak Latencies in newly diagnosed hypothyroid patients before and after treatment

DISCUSSION

In a study of 50 newly diagnosed hypothyroid patients, predominantly female (94%) and within the 21-30 age group (48%), significant improvements in thyroid hormone levels and auditory processing were observed post-thyroxine therapy. The study utilized BERA to measure auditory responses, revealing significant enhancements in latencies III, V, and interpeak latencies (I-III, III-V, I-V) post-treatment, indicating improved neural transmission along the auditory pathway. These findings align with previous research indicating hypothyroidism's impact on auditory processing and the effectiveness of thyroxine therapy in mitigating these effects (Thornton et al., 2008 and Santos et al., 2010).[11,12] The unchanged latency I suggests early auditory responses may be less affected by hypothyroidism, with thyroxine's benefits more pronounced in later auditory processing stages. This complements studies by Santos et al. (2010) and Anjana et al. (2006), highlighting the specific auditory pathway improvements with thyroxine therapy.[12,13] The results corroborate evidence that thyroxine can improve sensorineural hearing loss (SNHL) and enhance auditory pathway function (Aggarwal et al., 2013 and Karakus et al., 2015), emphasizing the critical role of thyroid hormones in neurotransmitter synthesis, release, and receptor sensitivity.[14,15]

CONCLUSION

This study underscores thyroxine's role in improving thyroid hormone levels and auditory function in hypothyroid patients. By demonstrating significant reductions in latencies III, V, and interpeak latencies post-thyroxine treatment, it provides strong evidence for the beneficial effects of thyroxine on auditory processing speeds, particularly in the later stages of

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the auditory pathway. These findings contribute to a growing body of evidence suggesting the potential of thyroxine therapy not only to normalize thyroid function but also to enhance neurological and auditory functions in hypothyroid patients, highlighting the importance of early diagnosis and treatment. The study supports the inclusion of BERA in the assessment of newly diagnosed hypothyroid patients to evaluate and monitor the status of the central auditory pathway, aligning with existing evidence on the neurological impacts of thyroid dysfunction and the therapeutic potential of thyroxine (Santos et al., 2010 and Kowsalya V et al., 2014).12,16

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