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Brainstem auditory evoked potentials features in thalassemia major

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ABSTRACT Patients with thalassemia major are at high risk for hearing impairment. The objective of the study is to determine the prevalence, grade and type of hearing impairment according to brainstem auditory evoked potentials (BAEP) investigation in thalassemia major. A descriptive cross sectional study was conducted between December 1999 until August 2000 in 72 thalassemic patients between 3 and 18 years of age. Only 65 patients were evaluated, because of time limitation. The results showed the prevalence of hearing impairment in thalassemia major was 29.2%. Most of them were moderate to severe unilateral sensorineural hearing impairments. Mild sensorienural hearing impairment occured in only 12.3%. Conductive hearing impairment was only found in 1 patient. Hearing impairment was frequently found between 7 to 12 years of age (41.5%). Conclusion: the prevalence of hearing impairment in thalassemia major according to BAEP investigation is high and BAEP examination should be done regularly in all of thalassemic patients to investigate early detection and treatment of hearing impairment. **[Paediatr Indones 2001; 41:166-170]**

Keywords: *thalassemia, brainstem evoked potentials, children.*

THALASSEMIA DISEASE IS A LIFE-LONG HEMOLYTIC disease, causing various problems for the patient. Chronic anemia caused by hemolytic process may affect various organ disorders either as a result of the disease or the treatment.[1,2] Hearing impairment is one of the disorders that may occur in thalassemic patients.[3] Hearing impairment in thalassemia is generally correlated to chronic anemia,[4] iron overload,[4-6] extramedullary hematopoiesis,[7] and the side effect of desferoxamine chelation therapy.[6,8-12]

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Various diagnostic tools are used to detect hearing impairment, one of them is brainstem auditory evoked potential (BAEP). BAEP as a neurophysiologic diagnostic tool can detect hearing impairment precisely and accurately. BAEP advantages are not requiring patient's cooperation, objective, and non invasive.[13-16]

BAEP that has been performed in thalassemic patients to detect early diagnosis and to monitor hearing impairment during the course of the disease,[17-19] are reported by Wong et al in 12% patients,[17] and Konzoglou et al in 27% patients.[18] Meanwhile Zafeiriou et al demonstrated sensorineural hearing impairment with prolonged I-V interpeak latencies in 25% patients and I-III interpeak latencies in 10% patients.[19]

In Indonesia, various studies in thalassemic patients have been done,[20] while brainstem auditory evoked potentials features in thalassemia major have not been reported. The aim of this study was to determine brainstem auditory evoked potentials (BAEP) features in thalassemia major patients.

Methods

This descriptive cross sectional study was performed at the Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta, from December 1, 1999 until August 31, 2000. The inclusion criterias were all of thalassemia major patients, age of the patients ranged between 3 to 18 years, and there was consent provided by patient or parents.

Sample size was calculated using descriptive formula for single with a = 0.05 and Z= 1.96, giving the required subject of 72 patients. BAEP examination was done in 72 thalassemic patients with Neuropack 4 mini evoked potential measuring system MB-5304K. Sedation with chloralhydrate was done in patients under 6 years of age or uncooperative ones. BAEP examination was performed twicely by staff in BAEP laboratory and was interpreted by pediatric neurologist. Patient was judged as having hearing impairment if his hearing threshold was more than 30 decibels as recommended by World Health Organization in assessing hearing status. Data were analyzed with SPSS version 9.01.

Results

Subject characteristics

During study period BAEP was performed in seventy two thalasemic patients. Seven patients were excluded. Analysis was done in 65 patients aged from 3 to 18 (mean 9.9; SD 4.5) years. Patients consisted of 35 females and 30 males. See Table 1.

TABLE 1. CHARACTERISTIC OF THALASSEMIA MAJOR PATIENTS BY SEX AND AGE

Age (years)	Sex		Total
	Male	Female	
3 - 6	10	11	21
7 - 12	13	14	27
13 - 18	7	10	17
Total	30	35	65

Nineteen patients (29.2%) showed hearing impairment by BAEP. Unilateral hearing impairment was the most frequently found in 13 (20%) patients, and bilateral hearing impairment was found in 6 (9.2%) patients as shown in Table 2.

TABLE 2. DISTRIBUTION OF HEARING IMPAIRMENT BY BAEP INVESTIGATION

Hearing threshold	n
Normal	46
Abnormal :	
Unilateral hearing impairment	13
Bilateral hearing impairment	6
Total	65

Normal hearing threshold (<30 decibels) was found in 46 (70.8%) patients, and abnormal hearing threshold (> 30 decibels) was 19 (29.2%) patients have abnormal hearing threshold as shown in Table 3.

TABLE 3. DISTRIBUTION OF HEARING THRESHOLD BY AGE GROUP

Age group (Yr)	Hearing threshold				
	30 dB (normal)	31-40 dB (mild)	41-60 dB (moderate)	> 60 dB (severe)	Total
3 - 6	15	3	3	0	21
7 - 12	18	4	5	0	27
13 - 18	13	1	2	1	17
Total	46	8	10	1	65

Hearing impairment was frequently found in patients between 7 to 12 years of age group. According to the grade of hearing impairment, moderate hearing impairment was the most frequently found in 10 patients. The youngest patient with hearing impairment was 3 years of age.

TABLE 4. DISTRIBUTION OF HEARING THRESHOLD BY SEX.

Sex	Hearing threshold				
	<30 dB (normal)	31-40 dB (mild)	41-60 dB (moderate)	> 60 dB (severe)	Total
Male	21	4	5	0	30
Female	25	4	5	1	35
Total	46	8	10	1	65

According to sex, as shown in Table 4 there was no sex difference in the patients.

TABLE 5. DISTRIBUTION OF HEARING IMPAIRMENT TYPE BY AGE GROUP

Age group (yr)	Type of hearing impairment		
	Conductive	Sensorineural	Total
3 - 6	0	6	6
7 - 12	1	8	9
13 - 18	0	4	4
Total	1	18	19

Table 5 shows that in the 19 patients with hearing impairment, one patient showed conductive hearing impairment, and 18 patients with sensorineural hearing impairment while mixed hearing impairment was not found.

TABLE 6. DISTRIBUTION OF HEARING IMPAIRMENT TYPE BY GRADE OF HEARING IMPAIRMENT

Grade	Type of hearing impairment		
	Conductive	Sensorineural	Total
Mild	0	8	8
Moderate	1	9	10
Severe	0	1	1
Total	1	18	19

Table 6 shows that moderate hearing impairment was more frequently found in sensorineural hearing impairment.

Discussion

Study limitations

The current investigation had several limitations including incomplete BAEPs results and limitated time to complete the sample data.

Subject characteristics

During study period, only 65 patients with thalassemia major could be analyzed. Most of the patients are 7 to 12 years found in 27 patients (41.5%), 3 to 6 years (32.3 %), and 13 to 18 years (26.2%), respectively. Patients consisted of 30 males (46.2%) and 35 females (53.8%), ranged between 3 to 18 years with the means age of 9.9 (SD 4.5) years.

The features of hearing impairment in thalassemia major

Regarding the BAEP examination in 65 thalassemia major patients, hearing impairment was found in 19 patients (29.2%), consisted of 10 females (15.4%) and 9 males (13.9%). This result was lower than DeVirgilis study,[4] but higher than Zafeiriou's.[19] DeVirgilis et al demonstrated 45 patients (73%) with hearing impairment in 75 thalassemia major patients.[4] Other studies reported between 2 to 47% patients with conventional audiometry.[3,6,8,9,12] BAEP study in thalassemia major patients was first reported by Amabile et al, who studied 24 thalassemic patients but did not found any patient with hearing impairment.[21] Other BAEP studies reported between 12% to 36.6% patients.[17-19,22] This difference results were probably as the result of the difference in methods.

Argiolu et al studied 309 thalassemia major patients who received blood transfusion since age of 5 months and found the youngest age with hearing impairment was 3 years.[6] Logothetis et al, investigated in 138 thalassemia major patients ranged between 2 to 28 years, demonstrated hearing impairment in 2 patients with the youngest age of 12 years.[3] DeVirgilis et al, reported the youngest age was 3 years in 2 patients with sensorineural hearing impairment.[4] In this study, the youngest of age can not be determine because we limited the age of patient between 3 to 18 years.

We also found unilateral hearing impairment (20%) was more frequent compared to bilateral hearing impairment (9.23%). This result was in inverse ratio compared with DeVirgilis study, which showed 12% patients with conductive hearing impairment were all bilateral. From 57.33% patients with sensorineural hearing impairment, bilateral hearing impairment was found in 41.33% patients and unilateral hearing impairment in 16% patients.[4]

Hearing impairment was mostly found in age group between 7 to 12 years, nine patients (13.9%), with means 9.9 (SD 4.5) years. Argioulu et al found hearing impairment in 15.5% patients with mean 11.5 (SD 3) years,[6] Kontzoglou et al demonstrated mean 9.66 (SD 3.1) years,[18] and Gallant demonstrated mean 12 years.[8] Whereas Zafeiriou found mean 16.2 (SD 18) years, and suggested that there were a significant correlation between the age of patients over 15 years of age with the involvement of auditory pathways.[19] Several investigators reported that hearing impairment in thalassemia major patients as a result of chronic anemia,[4,11] iron

overload,[4,6,9-11,15,19,22] extramedullary hematopoiesis,[4,7] desferoxamine (DFO) neurotoxicity,[6,8-12,15,17-19,22] and blood transfusion.[4,19] In the current study, the causal factor of hearing impairment was not investigated.

Grade of hearing impairment

In this study, hearing threshold (=30 decibels) was found in 46 patients (70.8%), mild hearing impairment (31-40 decibels) in 8 patients (12.3%), whereas moderate to severe (>40 decibels) in 11 patients (16.9%). Gallant et al demonstrated mild hearing impairment in 7.86% patients and moderate hearing impairment in 16.85% patients,[8] whereas other investigator demonstrated moderate hearing impairment in all of their patients.[4] Regarding to sex proportion, males were close to females in proportion (DeVirgilis[4] and Bentur).[9]

Type of hearing impairment

In audiology, BAEP is used to determine hearing threshold, type and grade of hearing impairment. Of waves occur on the nerve nuclei along the auditory pathways, waveform and latency that is required from the onset of sound stimulus to reach nucleus can be determine. Any delayed on time to reach each nerve nuclei can give clinical values on auditory nerves condition, and around brainstem pathways. Celesia et al, suggest that BAEP latencies value can not be interpreted without considering the patient's hearing status.[16]

Conductive/sensorineural hearing impairment

Conductive hearing impairment in thalassemia major patients were reported by several investigators, such as De Virgilis et al, who performed study in thalassemia major patients and found 16% cases of 75 patients.[4] Whereas Argiolu et al, did not find any case of conductive hearing impairment in 309 patients.[6] The studies above using conventional audiometry. Triantafyllou, et al performed BAEP investigation and found 15% patients with conductive hearing impairment,[22] whereas other investigators did not find it.[17-19] In the current study, conductive hearing impairment was found in 1 patient (1.54%).

Sensorineural hearing impairment was reported by Triantafyllou,et al. in 12 patients (36.66%) from 44 patients,[22] whereas other studies reported sensorineural hearing impairment in all of patients with hearing impairment by BAEPs examination.[17-19] Previous studies by conventional audiometry, demonstrated sensorineural hearing impairment was higher compared to conductive hearing impairment [4,6,8-12] Sensorineural hearing impairment in the current study was demonstrated in 94.74% patients from all of hearing impairment as well as the previous studies. The low prevalence of conductive hearing impairment compared to sensorineural hearing impairment in this study and other BAEP studies, probably as the result of high transfusion regimen that was performed in patients study. Muhidin demonstrated 60 patients with mean post transfusion Hb level was 12.43 (SD 0.99) g/dl.[23] Iskandar suggested that with high transfusion regimen, the bone marrow would not became hyperactive and the bone marrow disorders would not be found.[24]

Conductive/sensorineural hearing impairment according to grade of hearing impairment

Regarding the grade of hearing impairment as shown on Table 7, moderate sensorineural hearing impairment is more frequent and found in 47.39% from all hearing impairments. These results are similar with the previous studies.[4,8] Whereas conductive hearing impairment is only found in 1 patient as moderate conductive hearing impairment.

Regarding to the BAEP, prolonged I-III interpeak latency is demonstrated in 1 patient with moderate bilateral sensorineural hearing impairment, whereas prolonged I-III and I-V interpeak latencies are demonstrated in 1 (1.54%) patient, with moderate unilateral sensorineural. Prolonged I-III interpeak latency demonstrates defect in brainstem auditory conduction system between N.VIII close to the cochlea and lower portion of the pons.[14,25-27] Whereas prolonged I-III and III-V interpeak latencies demonstrates diffused lesion in brainstem auditory pathways.[27] This findings are different with Zafeiriou et al, that found prolonged I-V interpeak latency in 25% patient and prolonged I-III in 10% patient with sensorineural hearing impairment that estimated as a result of ototoxic effect of DFO.[19] Prolonged I -V interpeak latency demonstrates several dysfunction of acoustic nerve or brainstem, but the localization of the lesion could not be specified.[25]

To sum up the study, we have shown that the prevalence of hearing impairment in thalassemia major was 29.2%. There is no sex difference in patient's hearing impairment and it is mostly found in age group between 7 to 12 years. Moderate to severe unilateral sensorineural hearing impairment are more frequently

found. Prolonged interpeak latency is found in 2 patients, indicating dysfunction in brainstem auditory pathways. All of the patients were without symptoms of hearing impairment. Following this study result, BAEP is expected to be applied every six months in thalassemic patient without hearing problems and more frequently in those with problems.

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