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Original Article

Assessment of auditory brainstem response in infants in relation to type of feeding

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ABSTRACT

Background: Breast milk is important for brain development as it contains high concentration of long chain polyunsaturated fatty acids, also it contains cholesterol, amino acids as taurine and also lactose which broken to glucose and galactose, All are important nutrients for the brain and central nervous system tissues. Auditory Brainstem Response (ABR) is considered to reflect brain function of the infant and is widely used to determine/measure the brain development / maturation of the infant.

Objective: to assess auditory brainstem maturation in breast-fed and formula fed infants as part of brain maturation using ABR.

Methodology: this case-control was study carried out upon 100 apparently healthy infants; 50 infants of them were exclusively breast-fed and 50 infants were exclusively formula-fed, all of them aged 4-6 months. Each infant was subjected to detailed history, a full physical and neurological examination together with estimation of ABR.

Results: There was statistically significant prolongation of absolute latencies of wave III and wave V of ABR of right and left ear in bottle feeding infants in comparison to breast feeding infants. Also, there was statistically significant increase of mean wave interpeak latencies I-III, III-V and I-V of right and left ear in bottle feeding infants compared to breast feeding infants.

Conclusion: Better brain maturation in breast-fed infants compared to formula-fed infants evidenced by ABR.

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Keywords: Breast feeding, infants, auditory brainstem response, formula-fed infants.

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INTRODUCTION

Nutrition plays an important role in brain development from conception to 3 years of age and exclusive breastfeeding is the best way to be given to the infants, during the first two years of life, it is the most obvious nutritional strategy to sustain healthy brain development [1]. Breast milk contains all the nutrients that an infant need in the first six months of life, including fat, carbohydrates, proteins, vitamins, minerals, and water. Breast milk also contains bioactive factors that augment the infant's immature immune system, providing protection against infection, and other factors that help digestion and absorption of nutrients. Breast-milk fat contains long chain polyunsaturated fatty acids e.g. docosahexaenoic acid (DHA) and arachidonic acid (ARA) that are not available in other milks. These fatty acids are important for the neurological development of a child [2].

Development of the brain leads to auditory maturation, with the central auditory system maturing with age. The auditory system presents maturational and developmental patterns that are reflected in the possibility of recording the amplitude measured in micro-volts (Ω v) and the latency measured in milliseconds (ms) of the auditory evoked potentials (AEP). Electrophysiological studies for the auditory system have demonstrated that the maturation of the structures occurs from the periphery to the core, without following a hierarchical pattern. Auditory Brainstem Response (ABR)is one of the qualitative and quantitative measures to see the maturation processes in children, from birth to 3 years of

age which is the critical period for the development of the auditory system [3].

The ABR registers the electrical activity in the auditory system from the inner ear to the brainstem by presenting an acoustic stimulus. It is reliable, objective, and non-invasive test to assess auditory function and to localize pathologies affecting brainstem pathways. It has been widely used in the detection of hearing loss in newborns, infants, and children [4]. The ABR consists of five to seven components or peaks. They are labeled I–VII. Wave I, III and V, which originate from the cochlear nerve, cochlear nucleus, and lateral lemniscus and inferior colliculus, respectively, are the major ABR components used for analysis. Wave V is the most robust ABR parameter for detection of the hearing threshold. The decrease of absolute and interpeak latencies is influenced by degree of myelination, axonal growth, and synaptic efficacy in the auditory pathway [5]. The auditory pathway of the human brainstem from the proximal end of the cochlear nerve to the inferior colliculus undergoes myelination between week 26 and 29 of fetal life. The axon of the cochlear nerve and brainstem pathways acquire linear arrays of oligodendrocytes and myelin sheaths by week 26 of gestation. Myelination in all auditory pathways occurs in week 29. The increase of myelination density occurs in all pathways until at least 1-year postnatal age [6]. The aim of this study is to assess auditory brainstem maturation in breast-fed and formula-fed infants as part of brain maturation using ABR.

SUBJECT AND METHOD

Type, place, and duration of the study

This case-control study was carried out at paediatric department, Al-Zahraa University, Cairo, Egypt, during the period from October 2019 to March 2020. Samples were selected from pediatrics outpatient clinic whose mother came for follow up and were apparently healthy.

Inclusion criteria

It included 100 apparently healthy infants; 50 infants of them were exclusively breast-fed and 50 were exclusively formula-fed. Infants aged from 4 to 6 months of both sex and full term at delivery (35 infants were delivered by normal vaginal delivery,
and 65 infants were delivered by cesarean sections) were included into the study.

Exclusion criteria

Infants with any risk factor that can affect hearing in infancy including prematurity, drugs that affect hearing as aminoglycosides and loop diuretics, congenital infection, significant hyperbilirubinemia that required treatment, perinatal asphyxia, infants need mechanical ventilation at birth, history of CNS infection, major congenital anomalies and infants of diabetic mothers were excluded from the study. All this information was obtained by history.

Ethical consideration

The study protocol was approved by ethical review committee of Faculty of Medicine for Girls, Cairo, Al-Azhar University, Egypt. Informed consent was obtained from his/her parent before enrolment into the study. Data were unnamed and coded to guarantee privacy of the participants.

The studied groups were subjected to:

I. Full history taking including type of feeding either breast-fed or formula-fed and past history of medical conditions that may affect hearing.
II. All infants were subjected to physical examination.
III. Evaluation of ABR: The infants were tested during quiet sleep after feeding. No sedatives were used. ABR recording (a non-invasive technique) was carried out in quiet, dimly lit and electrically shielded room with Eclipse Ep 25 intercoustic machine, Denmark. Absolute wave latencies and interpeak latencies of ABR of both groups were recorded. Electrode montage of the recording was a vertical montage where, positive electrode at high forehead, the negative electrode ware placed over the mastoids (right or left according to which ear was tested) and finally the ground electrode was placed on the low forehead. The skin of the forehead as well as the mastoid area was prepared to make sure that the Impedance does not exceed 5kΩ and there is no inter electrode difference. We used band pass filter equal to 30-1500Hz bandwidth. Time window: 20ms. High sampling rate technique of 20 kHz was used. The intensity: started at 70dBnHL down to the threshold. Stimulus type: click (100 us long). The repetition rate: 21.1. Amplification: 100-150K. Number of sweeps: 1500. Polarity: rarefaction click. Transducer type: insert phones **[7].**

Statistical analysis

Statistical analyses were performed using the SPSS statistics version 16. Differences in Parametric variables were presented as mean± standard deviation (SD). Qualitative variables were presented as numbers and percentages. The Independent-samples t-test was used to compare between two means (for normally distributed data). Chi-square test was used to compare qualitative data. Probability was determined as: P-value < 0.05 was considered significant, P-value < 0.001 was considered highly significant, and P-value > 0.05 was considered in-significant (95% confidence interval).

RESULTS

The demographic data of our infants showed that the study was carried out on 100 apparently healthy infants, 50 infants of them were exclusively breast-fed and 50 were exclusively formula-fed. The frequency of feeding was on demand in both groups so, it could not be assessed. The study included 54 males and 46 females

(table1). As regard anthropometric measurement there was statistically insignificant difference of anthropometric measurements between breast-fed group and formula-fed group (table 2).

As regard hearing threshold there was statistically insignificant difference in distribution of infants with abnormal hearing threshold between breast-fed and formula-fed groups (P.>0.05) as there were only 3 cases among breastfeeding infants and 4 cases in bottle feeding infants show abnormal hearing threshold (table 3).

As regard ABR estimation there was statistically significant prolongation of the absolute latencies of wave III and wave V in the formula-fed group in comparison to the breast-fed group (P < 0.05) (table 4). Additionally, there was statistically significant increase of mean wave interpeak latencies I-III, III- V and I-V of right and left ear in bottle feeding infants in comparison to breast feeding infants(P.< 0.05) (table 5).

Within breast feeding cases, there was statistically insignificant difference of mean ABR waves I, III and V(P.>0.05) and mean wave interpeak latency I -III, III - V and I - V of right and left ear between males and females(P.>0.05) (table 6).Within bottle feeding cases, there was statistically insignificant difference of mean ABR waves I, III and V(P.>0.05) and mean wave interpeak latency I -III, III -V and I – V of right and left ear between males and females(P.>0.05) (table 7).

Table (1): Demographic data of the study group participants

Demographic data		Study group (n=100)
Age (months)	Mean ±SD	2.25±0.78
Males Females	No. (%) No. (%)	54 (54 %) 46 (46%)
Breast feeding Bottle feeding	No. (%) No. (%)	50 (50 %) 50 (50%)

Table (2): Anthropometric measurements in the study group

Anthropometric Measurements		Breast-fed group No.=50	Bottle-fed group No.=50	P value
Weight (kg)	**Mean ± SD**	6.16 ± 0.72	6.39 ± 0.84	0.14
	Range	4.7-7.5	4.7-8.5	
Weight percentile (th) No. (%)	**10^{th} -25^{th}**	17 (34%)	10 (20%)	0.17
	25^{th} -50^{th}	18 (36%)	17 (34%)	0.86
	50^{th} -75^{th}	11 (22%)	19 (38%)	0.14
	75^{th} -90^{th}	4 (8%)	4 (8%)	1
Weight (Z score)	**Mean ±SD**	-0.14± 0.91	0.14± 1.07	0.14
	Range	-1.9- 1.5	-1.9-2.8	
Length (cm)	**Mean ± SD**	64.98±3.10	64.84±2.99	0.81
	Range	58-71	59-72	
Length (percentile) No. (%)	**10^{th} -25^{th}**	14 (28%)	11 (22%)	0.54
	25^{th} -50^{th}	24 (48%)	27 (54%)	0.67
	50^{th} -75^{th}	9 (18%)	11 (22%)	0.65
	75^{th} -90^{th}	3 (6%)	1 (2%)	0.31
Length (Z score)	**Mean ±SD**	0.02±1.02	-0.02±0.98	0.82
	Range	-2.27-2	-1.94- 2.33	
Head circumference (cm)	**Mean ± SD**	41.75±1.06	41.69±1.03	0.79
	Range	39-44	39-44	
Head circumference Percentile (th) No. (%)	**10^{th} -25^{th}**	15 (30%)	17 (34%)	0.72
	25^{th} -50^{th}	22 (44%)	23 (46%)	0.88
	50^{th} -75^{th}	12 (24%)	10 (20%)	0.66
	75^{th} -90^{th}	1 (2%)	0 (0%)	0.80
Head circumference (Z score)	**Mean ±SD**	0.03±1.01	-0.02±0.99	0.79
	Range	-2.61-2.19	-2.61-2.19	

Table (3): Distribution of impaired hearing threshold (ABR) in breast-fed group and formula-fed group

Type of feeding	Breast-fed group No.=50	Formula-fed group No.=50	Test of significant	P value
Impaired hearing threshold (ABR) N (%)	3 (6)	4 (8)	X^2- 0.0108	0.69

Table (4): Comparing between breast-fed group and formula-fed group as regard the absolute latencies of the ABR waves

ABR waves (ms)		Type of feeding		P Value
		Breast-fed group No.=50	Formula-fed group No.=50	
		Mean ± SD	Mean ± SD	
Right ear	Wave 1	1.69 ± 0.15	1.80 ± 0.36	0.097
	Wave III	3.66 ± 0.12	4.01 ± 0.25	0.031*
	Wave V	5.40 ± 0.17	6.03 ± 0.63	0.001*
Left ear	Wave 1	1.73 ± 0.13	1.78 ± 0.35	0.203
	Wave III	3.70 ± 0.13	4.01 ± 0.22	0.001*
	Wave V	5. 40 ± 0.19	6.03 ± 0.15	0.001*

* P < 0.05 is considered significant

Table (5): Comparing wave interpeak latency between breast-fed group and formula-fed group

Interpeak latency (ms)		Type of feeding		P Value
		Breast-fed group No.=50	Formula-fed group No.=50	
		Mean ± SD	Mean ± SD	
Right ear	Wave I –III	1.97 ± 0.13	2.21 ± 0.14	0.001*
	Wave III –V	1.74 ± 0.25	2.02± 0.18	0.012*
	Wave I - V	3.71± 0.22	4.23 ± 0.23	0.001*
Left ear	Wave I –III	1.97± 0.071	2.23 ± 0.14	0.001*
	Wave III –V	1.70±0.15	2.02 ± 0.17	0.011*
	Wave I - V	3.67± 0.22	4.25 ± 0.31	0.001*

* P < 0.05 is considered significant

Table (6): Comparing ABR wave's absolute latencies and interpeak latencies according to gender in breast-fed group

ABR waves (ms)		Gender		P Value	Interpeak latency (ms)		Gender		P Value
		Males	Females				Male	Female	
		Mean ±SD	Mean ±SD				Mean ±SD	Mean ±SD	
Right ear	Wave 1	1.75±0.16	1.61±0.11	0.13	Right ear	Wave I-III	1.86±0.09	1.92±0.15	0.10
	Wave III	3.57±0.12	3.55±0.13	0.49		Wave III-V	1.80±0.11	1.87±0.18	0.08
	Wave V	5.37±0.14	5.42±0.20	0.33		Wave I- V	3. 76±0.15	3.81±0.24	0.11
Left ear	Wave 1	1.76±0.11	1.72±0.13	0.12	Left ear	Wave I-III	1.87±0.05	1.89± 0.10	0.26
	Wave III	3.65±0.09	3.60±0.15	0.06		Wave III-V	1.80±0.13	1.86± 0.19	0.19
	Wave V	5.45±0.14	5.44±0.23	0.81		Wave I- V	3.69±0.17	3.76± 0.23	0.22

* P < 0.05 is considered significant

Table (7): Comparing ABR wave's absolute latencies and interpeak latencies according to Gender in formula-fed group

ABR waves (ms)		Gender		P Value	Interpeak latency (ms)		Gender		P Value
		Males Mean ±SD	Females Mean ±SD				Males Mean ±SD	Females Mean ±SD	
Right ear	Wave 1	2.06 ±0.33	2.01±0.38	0.66	Right ear	Wave I -III	2.09 ±0.13	2.03 ±0.15	0.148
	Wave III	4.16 ±0.41	4.05±0.48	0.40		Wave III-V	2.09 ±0.25	2.05 ±0.20	0.516
	Wave V	6.29 ±0.60	6.10±0.66	0.29		Wave I -V	4.23 ±0.33	4.09 ±0.33	0.123
Left ear	Wave 1	2.06 ±0.34	2.01±0.37	0.58	Left ear	Wave I -III	2.10 ±0.17	2.04 ±0.16	0.234
	Wave III	4.16 ±0.46	4.05 ±0.49	0.41		Wave III-V	2.04 ±0.21	2.03 ±0.18	0.734
	Wave V	6.22 ±0.66	6.08 ±0.65	0.46		Wave I -V	4.15 ±0.35	4.07 ±0.32	0.391

* P < 0.05 is considered significant

DISCUSSION

Our result revealed that6% of breast-fed infants had abnormal hearing threshold compared to 8% of formula-fed infants with insignificant difference. Although, the difference was insignificant but abnormal hearing threshold more in formula-fed than breast-fed infants. It may be due to maturation of the auditory brainstem is delayed in formula-fed than breast-fed infants which may impair hearing threshold. No similar study was found about that.

In the current study we found that there was statistically significant prolongation of wave III and wave V absolute latencies of ABR in formula-fed infants compared to breast-fed infants, which indicated that brainstem maturation is less in formula-fed than breast-fed infants. This is in agreement with study done by Khedr et al.[8], Ünay et al.[9] and Amin et al. [10]. This result could be due to early auditory brainstem maturation in breast-fed than formula-fed infants as breast milk contains a full complement of poly unsaturated fatty acids including docosahexaenoic acid and arachidonic acid which enhance the brain and auditory brainstem maturation as brain development including central auditory system is associated with an increase in the incorporation of long chain poly unsaturated fatty acids. While formula milk contains only the precursor's linolenic acid and linoleic acid so, formula-fed infants must synthesize their owndocosahexaenoic acid and arachidonic acid [11]. Human milk contains a wide variety of other factors including hormones and growth factors, such as (e.g. thyroxin, nerve growth factor), and several amino acid as taurine, all could affect brain biochemistry and functional development [12]. Across infants and young child development there is rapid change in the latency of auditory responses as there is progressive decrease of absolute and interpeak latencies with age. The key factor for decrease in ABR II - V latency is increase in myelin density. ABR latency changes occur because of the rapid increase in axonal myelin density in the cochlear nerve and brainstem pathways [13].

Our study showed that the absolute latency of wave I is slightly similar in both breast-fed and formula-fed infants. This was also concluded by Amorim et al. [14] in a study about the maturational process of the auditory system in the first year of life that done for 86 infants in three periods. The 1st period from 0 to29 days, the 2nd period from 30 days to 5 months 29 days and the 3rd period above 6 months. That study showed that the absolute latency of the wave I was similar to that of adults, as a complete maturation of the auditory nerve occurs in the 1st month of life. In contrast to a study done by Khedr et al.[8] and Ünay et al.[9]which showed that there was statistically significant difference in wave I absolute latency in both groups and concluded that the maturation of the auditory nerve not completed in the 1st month of life.

The time difference between the onsets of each wave of ABR is called range or interpeak latency [15]. Interpeak latency differences followed the same developmental time period as wave V and were also used as an indicator of brainstem maturation[3].The current study found that there was statistically significant increase of mean wave interpeak latencies I –III, III -V and I - V of right and left ear in bottle feeding in comparison to breast feeding infants. This could be explained by that there was some sort of delay in the conduction of the auditory signals in the lower brainstem most probably due to delayed maturation of the brainstem in formula-fed than breast-fed infants. This also noted by Ünay et al. [9] a study done on 82 infants at 16 weeks of age using ABR inter-wave intervals (I-III, III-V) and concluded that interpeak latency used as an indicator of brain stem maturation.

As regard gender, there was statistically insignificant difference of mean ABR waves I, III and V of right and left ear between males and females. This was also concluded by Stuart and Yang [16] and Sliefer et al. [17]. While the study done by Li et al. [18] showed that males had longer absolute and interpeak latencies than females and they explained that it may be due to more rapid weight gain in males. In our study both groups have average weight, and the difference between them is insignificant so, it may explain our results.

CONCLUSION

We can conclude that the nervous systems of breast-fed infants mature better and earlier than formula fed infants in the first six months of life as evidenced by better early auditory brainstem maturation. Therefore, we recommend use of auditory brainstem response to assess early auditory brain stem maturation. Encouragement of breast feeding due to its important role in brain maturation is recommended.

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الملخص العربي

تقييم الاستجابة الذهنية السمعية عند الرضع مقارنه بنوع التغذية

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ملخص البحث

الخلفية: حليب الام مهم لنمو الدماغ لأنه يحتوي على تركيز عالٍ من الأحماض الدهنية المتعددة غير المشبعة طويلة السلسلة ، كما أنه يحتوي على الكوليسترول والأحماض الأمينية مثل التورين وكذلك اللاكتوز الذي يتحول إلى الجلوكوز والجلاكتوز ، وكلها عناصر غذائية مهمة للدماغ وانسجه الجهاز العصبي المركزي . تعتبر استجابة جذع الدماغ السمعية انعكاس لوظائف المخ عند الرضيع وتستخدم علي نطاق واسع لتحديد/قياس نمو/نضج الدماغ

الهدف: تقييم نضج جذع الدماغ السمعي عند الرضع الذين يرضعون رضاعة طبيعية والزين يرضعون رضاعه صناعيه كجزء من نضج الدماغ باستخدام استجابة الجذعية الدماغ السمعية

الطرق: أجريت دراسة الحالات والشواهد على مائه رضيع يبدو أنهم يتمتعون بصحة جيد, خمسون رضيعا يرضعون رضاعه طبيعية فقط وخمسون يرضعون رضاعه صناعيه فقط, وجميعهم تتراوح أعمارهم بين اربعه وسته اشهر.

خضع كل رضيع إلى تاريخ مفصل، وفحص جسدي و عصبي كامل مع تقدير الاستجابة السمعية لجذع الدماغ.

النتائج: بمقارنه نتائج البحث بالنتائج المسجلة عالميا وجد انها تتفق مع معظمها حيث انه كان هناك تمديد إحصائي كبير لوقت الاستجابة السمعية لجذع الدماغ في الرضع بالرضاعة الصناعية مقارنه بالرضع بالرضاعة الطبيعية وأيضا هناك زيادة ذات دلالة إحصائية لمتوسط زمن الوصول بين الموجات الخامسة والاولي , الخامسة والثالثة ,الثالثة والاولي للاذن اليمني واليسرى في حالات الرضاعة الصناعية مقارنه بحالات الرضاعة الطبيعية.

الاستنتاجات: نضج أفضل للدماغ عند الرضع الذين يرضعون رضاعة طبيعية مقارنة بالرضع الذين يرضعون رضاعه صناعي كما يتضح من تقدير الاستجابة السمعية لجذع الدماغ.

الكلمات المفتاحية: الرضاعة الطبيعية, الرضع, الاستجابة السمعية لجذع الدماغ, الرضاعة الصناعية

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