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A comparison of auditory brainstem response thresholds in infants born with or without cleft lip and/or palate and otitis media with effusion

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SUMMARY

The prevalence of otitis media with effusion (OME) is much higher in infants born with cleft lip and/or palate (CLP) than without CLP. It would be interesting to know if the related hearing thresholds are poorer in infants with CLP than without, which could have a possible impact on the early development of hearing, communication and speech. The aim of the study was therefore to investigate the early hearing thresholds in infants with OME with and without CLP. The present study investigated the hearing thresholds with auditory brainstem response (ABR) for 60 infants 30 infants with CLP and OME and 30 infants without CLP with OME in the control group. The mean age at the time of assessment for infants with CLP and OME was 10 weeks for boys and 7 weeks for girls. In the control group the mean age was 15 weeks for boys and 16 weeks for girls. The results showed no statistical difference in the ABR thresholds between the infants with CLP and OME and those with OME without CLP. There was no significant difference in ABR thresholds due to cleft type. No gender difference was found within the CLP group or within the control group. Therefore, OME seems to be the only responsible factor for the elevated ABR thresholds at the newborn hearing screening for these two groups of individuals.

Key words

Auditory brainstem response (ABR), hearing thresholds, infants, cleft lip and palate (CLP), otitis media with effusion (OME)

Abbreviations

OME otitis media with effusion

ABR auditory brainstem esponse

CLP cleft lip and palate

dBnHL decibel normal hearing level

ICP isolated cleft palate

UCLP unilateral cleft lip and palate

BCLP bilateral cleft lip and palate

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INTRODUCTION

Research aims

The aim of this study was to investigate and compare auditory brainstem response (ABR) thresholds related to otitis media with effusion (OME) in infants with and without cleft lip and/or palate (CLP). There was also an interest in investigating possible gender differnces and if there were any differences releted to cleft type. There are only a few studies to date that have looked into the difference in hearing in young children with CLP and OME and the previous studies that have used ABR as an evaluation for assessing the ABR thresholds in babies with CLP had no control group (Andrews, Chorbachi, Sirmanna, Sommerland & Hartley's, 2004, Viswanathan, Vidler & Richard, 2008). Therefore it is not clear if there is a difference in the threshold levels for children with OME with and without CLP. Thus does the presence of a cleft palate deteriorate the threshold level further?

BACKGROUND

Otitis media with effusion (OME)

Otitis media with effusion (OME) is an accumulation of fluid in the middle ear without signs or symptoms of an infection (i.e., it is different than acute otitis media, AOM). OME is very common in small children and it has been estimated that 10% of children have had one episode of otitis media by 3 months of age. The fluid in the middle ear might be a result of an earlier episode of AOM (Bull & Clark, 2007). OME occurs in about 80% of all children at some point in life from birth up to 3 years of life (Broen, Moller, Carlstrom, Doyle, Devers & Keenan, 1995). It has been reported that the peak incidence of otitis media is around 6-15 months of age in children without CLP (Klein, 1989). The prevalence of OME in children with CLP has been found to be 92% in children aged between 2 months and 2 years (Sheahan & Blayney, 2003). Dhillon (1988) found 97 of 100 ears of children with cleft palate had OME before surgical closure of the cleft. OME was present before 4 months of age. The OME might cause a conductive hearing loss with a median of 25dB (Klein, 1989).

Eustachian tube function

The Eustachian tube permits ventilation of the middle ear. The tube is normally closed and opens on swallowing due to the movement of muscles of the palate (Bull & Clark, 2007). Individuals with a cleft palate have a dysfunction of the Eustachian tube due to the lack of insertion of the tensor veli palati and levator veli palatini muscles. The Eustachian tube has also been found to have more abnormalities in the structure in patients with cleft. Eustachian

tube dysfunction may lead to a negative middle ear pressure and OME (Sheahan & Blayney, 2003).

Cleft lip and/or palate (CLP)

CLP is one of the most common congenital birth defects in Sweden. The incidence of cleft lip and palate in Sweden is approximately 2.0/1000 live births with a range of 1.2-2.3/1000 (Milred, Larson, Hagberg & Ideberg, 1997, Hagberg, Larson & Milerad, 1998). CLP is more common among males compared to females (Hagberg et al., 1998). The cleft lip and palate occurs early in the pregnancy (Lohmander, Persson & Henningsson, 2008). There are different types of CLP. The palate, lip and alveolar ridge can be involved to different degrees. Isolated Cleft Palate (ICP) affects only the soft and/or hard palate with different extension into the palate Unilateral Cleft Lip Palate (UCLP) and Bilateral Cleft Lip Palate (BCLP) also involve the alveolar ridge and lip on one or two sides. Thus ICP involves the palate only, UCLP involves the soft and hard palate and one side of the alveolus and lip and BCLP involves the soft and hard palate and both sides of the alveolus and lip (Lohmander et al., 2008).
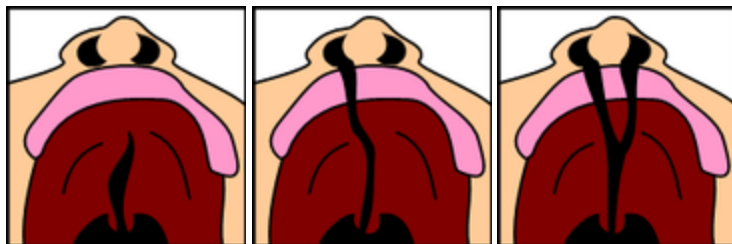
Figure 1 Showing (1) ICP, (2) UCLP and (3) BCLP. Pictures from Wikipedia with permission.

Auditory brainstem response (ABR)

The auditory brainstem response (ABR) is an objective electrophysiological assessment method that measures the electrical activity of the auditory system that occurs when an acoustic stimulus is presented. There are seven different waves in an ABR response waveform that are marked on the curve generated as a response to the acoustic stimuli. They are marked I-VII and occur within 10ms of the onset of the stimuli. Wave V may also occur with the IV wave in an IV-V wave complex. This occurrence is also considered as a normal response (Arnold, 2000).

An ABR may be recorded from a series of 4 electrodes. The non-inverting electrode may be placed at the middle of the forehead just below the hairline or it can be placed on the vertex. The ground electrode may be placed on the forehead. The two inverting electrodes, left and right, may either be placed on the earlobe or on the mastoid of the ear being tested. The stimulus is commonly presented by air conduction via headphones or insert earphones. A bone conduction stimulus may be presented via a bone conductor, placed on the mastoid. For evaluation of hearing thresholds, clicks and/or tone bursts are the most commonly used stimuli and are clinically valuable in estimating the electrophysiological hearing thresholds.

The click stimulus is an ideal stimulus as it is leads to a synchronous onset of the neurons contributing to the ABR waveform, which under normal circumstances leads to clearly defined waves. The tone-burst are more frequency-specific than the click stimuli, but still has a considerable spectral splatter. Analysis of the waveform and the detection of the wave V component are done during and after the measurement. The patient's estimated hearing level is at the lowest level were the wave V is detectable. However there is a 5-10dB difference in the estimated hearing threshold and the behavioural hearing threshold. If the wave V formation can be identified at 20dBnHL the hearing is considered normal for children and adults (Hall & Swanepoel, 2010; Arnold, 2000). The threshold level that is considered to be normal hearing may vary between studies.

The age effect on the ABR thresholds in infants is very limited when the thresholds are expressed in dBnHL. The difference in ABR threshold levels for normal hearing infants between the age of 2-4 months is 4.00±3.87dBnHL compared to 3.33±4.08dBnHL at 4-6 months of age (Marcoux, 2010).
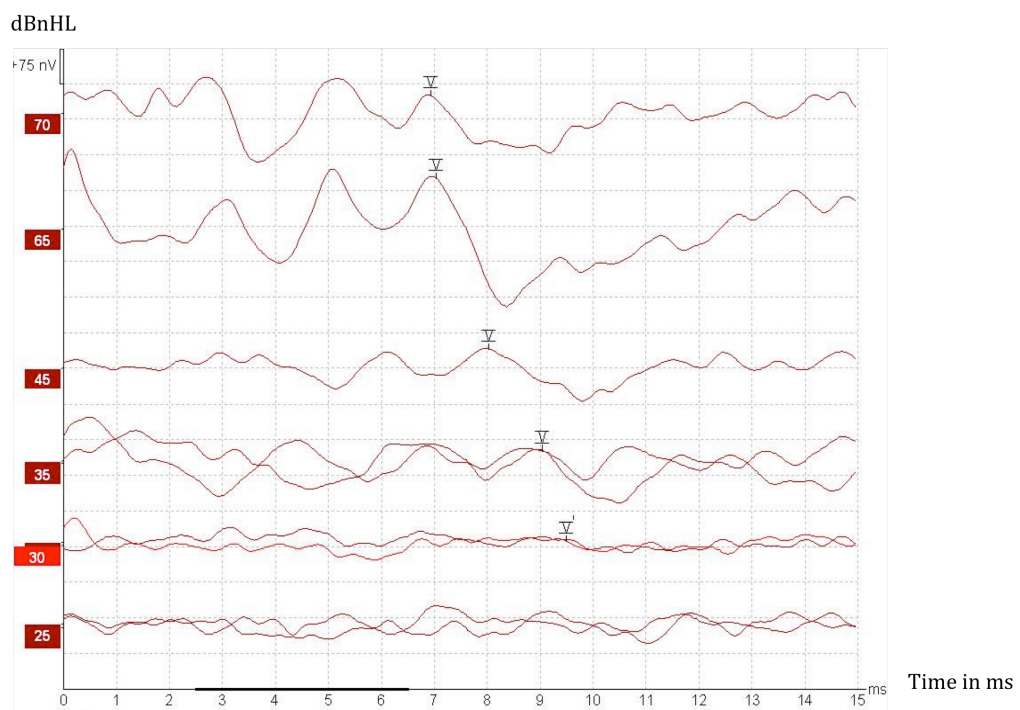
Figure 2 An ABR threshold measurement of an infant with OME. The wave V is denoted.

Literature review

No studies have previously examined hearing before 1 year of age , with CLP and OME and compared them to children with no cleft and OME Two previous studies have focused on newborn hearing screening and OME (Boone, Bower & Martin, 2004; Lok, Anteunis, Meesters, Chenault & Haggard, 2011). Boone et al. (2004) found that 64.5% of children who were referred for failing the newborn hearing screening had OME. The presence of OME was

diagnosed by an experienced otolaryngologist that used an otomicroscope to evaluate the infant's tympanic membrane. The presence of OME was diagnosed if the tympanic membrane was opaque and/ or demonstrated impaired mobility. They found that the mobility of the tympanic membrane was sometime difficult to establish as the ear canal sometimes moved more than the membrane due to the distensible nature of the ear canal. Lok et al. (2011) investigated different risk factors for failing the hearing screening. Risk factors mentioned were having siblings but this was not further specified, Gender was also found to be a risk factor as boys were found to have almost twice the odds for developing an OME related hearing loss compared to girls. They authors also found that genetic disposition for OME was a risk factor in failing the hearing screening. These studies did not examine children with CLP who were excluded from the database. Therefore, no comparison between children with OME and children with OME and CLP was done.

Earlier studies that have evaluated the newborn hearing screening program for children with CLP have focused on infants at-risk for hearing loss, including patients with CLP (Ohl, Dornier, Czajka, Chobaut & Tavernier, 2009, Chen, Messner & Curtin, 2008). Ohl, et al., (2009), found children with craniofacial anomalies (including children with CLP) to have a significantly higher risk for a conductive hearing loss compared to a group of infants with normal hearing. However, there was no difference concerning the risk of a sensorineural hearing loss between the group with craniofacial anomalies (including children with cleft palate) and the group with normal hearing (Ohl, et al., 2009). Chen et al. (2008) demonstrated that 72% of children born with CLP passed the newborn hearing screening in both ears. The study also examined hearing after the palate was surgically repaired and found that 13 (43%) of the infants who failed the newborn hearing screening had a permanent conductive or sensorineural hearing loss. Eleven of these thirteen infants were diagnosed with a syndrome (Chen, et al., 2008).

Hearing in children with CLP from 3 to 30 months of age have previously been studied by Broen et al. (1996) and by Fria, Paradise, Sabo & Elster, (1987). In the first study the hearing of children with and without CLP during 9-30 months of age, was examined at 3 months intervals. They found that children with CLP failed the hearing screening more often than the non-cleft group. The CLP group was also found to have a higher number (94.1%) of abnormal tympanograms compared to the non-cleft group (48.5%). Fria et al. (1987) used ABR as an evaluation method of hearing levels before and after the placement of ventilation tubes in 23 children between 3 and 21 months of age. They found that the hearing levels improved after the placement of ventilation tubes.

Only two articles to date have evaluated hearing thresholds with ABR in infants with CLP (Andrews, Chorbachi, Sirmanna, Sommerland & Hartley's, 2004, Viswanathan, Vidler & Richard (2008). The aim of the study by Andrews at al. (2004) was to investigate the hearing thresholds in 40 infants with cleft palate with ABR prior to palatal repair to estimate a hearing threshold guideline for insertion of ventilation tubes. Their study included all types of clefts with or without cleft lip. They also included infants with different types of syndromes. In their study the ABR thresholds varied between 25dBnHL to 102dBnHL. The two infants with the highest thresholds were diagnosed with a syndrome. In a retrospective study by Viswanathan et al. (2008), hearing levels were estimated in 90 infants (47 males and 43 females) with different cleft types (UCLP and ICP). The results demonstrated a hearing loss in 82% of the infants participating. They also included different types of syndromes. The estimated ABR hearing threshold varied between 25dBnHL to 90dBnHL. In both studies the ABR threshold estimation was done during natural sleep and up to 3 months of age. None of the two studies had a control group and the infants middle ear status at the time of the ABR assessment was

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not mentioned. However, both studies used both air conduction and bone conduction thresholds (i.e. they were both able to estimate the type of hearing loss). Viswanathan et al. (2008) found the mean air conduction threshold for the right ear was 40dBnHL and the mean bone conduction was 18.9dBnHL for the same ear, i.e. there was a conductive hearing loss present. The left ear was also evaluated for the presence of a conductive hearing loss and was found to have a mean air conduction threshold at 39.7dBnHL and the mean bone conduction was found to be18.1dBnHL. Eighty-nine percent of the hearing losses found by Viswanathan et al. (2008) were conductive, 86% were mild (>35 ≤ 45dBnHL) in degree and 84% of the hearing losses were bilateral. Andrews et al. (2004) found a mean air conduction threshold for the right ear of 49dBnHL and for the left ear was 53dBnHL. However, only one mean value for the bone conduction threshold was calculated 26dBnHL, as they did not differentiate between the bone conduction between the left and right ears. Bone conduction was not preformed if the air conduction hearing threshold levels were better than 30dBnHL or 25dBnHL as hearing levels below this level were considered as normal hearing (Andrews et al., 2004: Viswanathan et al.,2008). Neither study examined if there was a difference in the ABR hearing threshold due to cleft type.

There have been a limited number of studies that have investigated hearing by cleft type. One recent study investigated children and adolescents with three different cleft types (ICP, UCLP and BCLP) (Flynn, Lohmander, Möller & Magnusson, 2012). They found that children with ICP had a significantly lower number of ears with abnormal middle ear status at 7 and 16 years of age as compared to children and adolescents with UCLP and BCLP. At 16 years of age adolescents with BCLP were found to have the worst high-frequency pure tone average.

Gender differences have been investigated with respect to ABR thresholds and prevalence of OME and CLP. The gender effect on ABR thresholds in neonates has been studied (Stuart & Yang, 2000). No difference existed between boys and girls regarding the threshold level of the ABR. However they found that girls presented with shorter wave V latencies compared to boys when the stimuli was conducted by air. When the stimuli were conducted by bone, no difference between boys and girls existed for the wave V latencies. Boys have been found to have twice the risk for OME as compared to girls (Lok et al., 2011) CLP is more common in boys as well (Hagberg et al., 1998). In this essay the gender difference in ABR thresholds will be investigated.

The prevalence of otitis media with effusion (OME) with effusion is much higher in babies born with cleft lip and/or palate (CLP) than without. It would be interesting to know if the related hearing thresholds are poorer in infants with CLP than without, which could have a possible impact on the early development of hearing, communication and speech. The aim of the study was therefore to investigate the early hearing thresholds in infants with OME with and without CLP.

Questions

Is there a difference in the ABR thresholds for infants with CLP and OME compared to infants with OME but without CLP?

Is there a difference in ABR thresholds within the CLP group related to type of cleft?

Is there a gender difference within the two groups that affects the level of the ABR threshold?

METHODS AND MATERIALS

Participants

The study aimed to collect data from a total of 60 infants in two groups, one group of 30 infants with CLP and OME and one group of 30 with OME but without CLP as a control group.

Inclusion criteria
All infants with a medical record containing information about ear status with a diagnose of OME, threshold levels at the ABR evaluation and who had no syndromes were included in the study. The medical records for the infants with CLP also had to contain information about type of cleft. All infants that have been assessed with an ABR between the year of 2011 and until the second week of 2013 at the Hearing and Balance Clinic and meet the inclusion criteria were included. Infants with CLP with OME were included in the CLP group and all infants with a diagnosis of OME that meet the inclusion criteria were included in the control group.

Exclusion criteria
Infants who were found to have an uncertain diagnosis or no information about ear status in the medical record were excluded. Infants that were diagnosed with a syndrome (i.e. Down syndrome) at the time or since the ABR evaluation were also excluded from this study. Infants that had been fitted with hearing aids since the ABR threshold measurement were performed due to a hearing loss caused by other factors than OME alone were also excluded from this study. The reason for the exclusion was to eliminate other contributing factors to the elevated ABR thresholds than the OME alone.

The data collection began with infants who had been seen at the clinic in 2011. In order to get 60 infants, all infants examined at the clinic during 2012 and the first two weeks of 2013 were investigated as well. During this time period there were 509 (229 in 2011, 272 in 2012 and eight in the first two weeks of 2013) ABR assessments performed on infants as a part of the newborn hearing screening program in use at the Hearing and Balance Clinic at Karolinska University Hospital in Solna. Four hundred and one infants underwent one ABR assessment. Of those 401 infants 95 underwent two ABR assessments; this was done if the child did not sleep or if the ABR thresholds were found to be elevated. Of those 95 infants 13 infants underwent a third ABR assessment. Three hundred and forty-one infants were excluded from this study according to the exclusionary criteria (see figure 3).
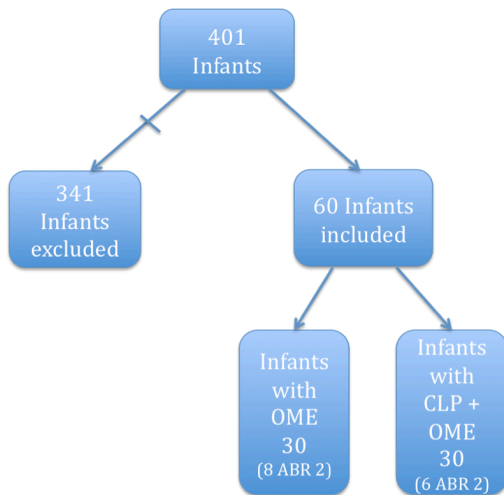
Figure 3. The infants that were examined at the clinic during the selected time period in order to reach the size of the study groups and if the were included or excluded in this study.

The final study group consisted of 30 infants (23 boys and 7 girls)with CLP with OME and the control group of 30 healthy infants with OME (22 boys and 8 girls). The mean age at the time of the assessment was for the CLP group 10 weeks for boys and 7 weeks for girls and the control group 15 weeks for boys and 16 weeks for girls (see figure 4). All data was collected consecutively.
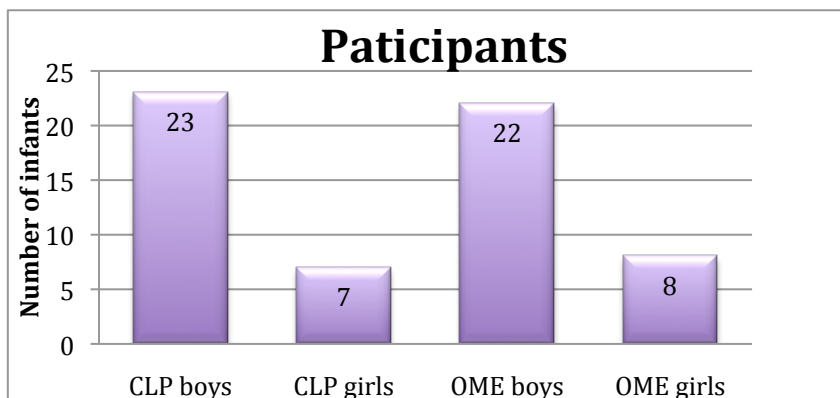
 Figure 4. The total number of infants in the study by group and gender.

The infants in the cleft group were also subdivided by cleft type. See figure 5.
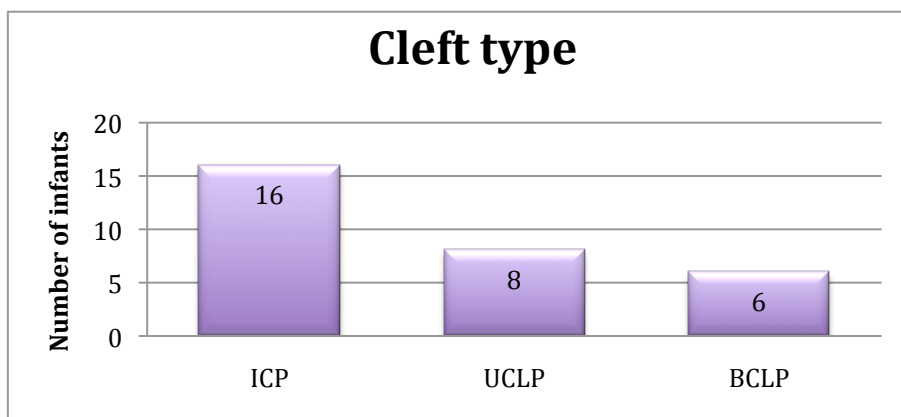
**Figure 5.** The number of infants by cleft types in the CLP group.

Table 1. The mean age, by gender, for the group of infants with CLP and OME and for the infants in the control group with OME but without CLP at time of the ABR assessment.

	Males	Females
CLP group	10 weeks	7 weeks
Control group	15 weeks	16 weeks

Procedure

A retrospective, comparative chart review was performed. All of the data, ABR thresholds, the infants age at the time of the assessment, diagnosis of OME and any hereditary for hearing loss were collected through Take Care, the medical records database in use at Karolinska University Hospital. The infants were found by searching through the appointments calendar in the Take Care system.

All infants that are seen at the clinic for ABR assessments are either: (1) referred from other clinics at the hospital due to medical reasons, including CLP (presence of a craniofacial anomaly), or (2) the infant failed three newborn hearing screening assessments with otoacoustic emissions (OAE), either unilaterally or bilaterally. The third OAE assessment is always performed at the Hearing and Balance Clinic at Karolinska University Hospital, Solna. If the infant fails on the third attempt, the infants and his or hers parents/guardian see an otolaryngologist for evaluation of ear status and information about further tests. The family is also given a time for the next assessment, which includes an estimation of the hearing thresholds completed with a clinical ABR. See figure 6.
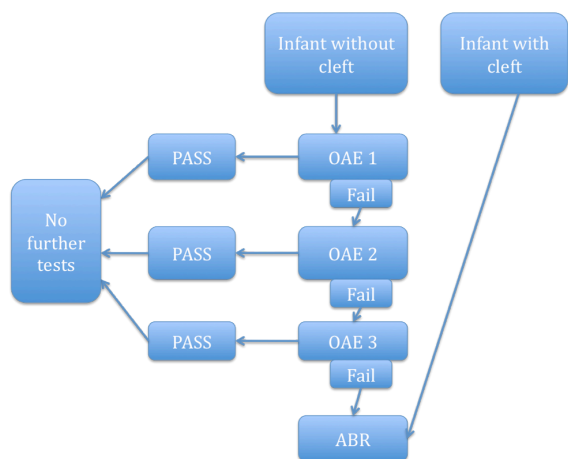
Figure 6. Illustration of the assessment route before an ABR evaluation is performed as part of the newborn hearing screening program.

The ABR assessment was performed during natural sleep on both ears. If only one ear failed three OAE screenings that ear was evaluated first with ABR and the other ear was also evaluated when possible. The ABR measurement was performed until the infants estimated hearing threshold level, in dBnHL, was found. Twenty dBnHL was the lowest stimuli used and the maximum level was 90dBnHL. The later level was only used if no thresholds were identified at any lower stimuli levels used. A rarefaction click stimuli was used and presented through ER-3A ABR insert earphones. There were minimum of 1700 sweeps for each waveform before the level of the stimuli was alternated to a lower or higher level depending on the identification of a wave V formation. There were always two or more waveforms performed at each level before it was evaluated as having a wave V formation or not. The assessment started at 50 or 60dBnHL and then decreased or increased with 10dB depending on the wave formation and the presence of wave V. If the wave V was detected, the intensity of the signal was decreased by 10dBnHL. If the wave V was not detected, the intensity of the signal was increased by 10dBnHL. The hearing level thresholds were estimated in 10dB intervals and when it was necessary, in 5dB intervals, in order to establish the hearing thresholds. The wave V was always marked when possible, wave III was marked when it was clearly identified. Other waves were not marked regardless of their presence. The presence of a wave V was identified when the waveform changed and a slope was clearly identified. If the infant was awake or woke during the assessment, the ABR measurement was not performed due to the amount of noise that is generated by muscle movement. If the infant woke during the measurement, any further collection of data was discontinued until the infant went back to sleep.

In direct connection to the ABR assessment the infant sees an otolaryngologist, the baby and his/hers parents/guardian saw the otolaryngologist at the clinic for another ear examination. This was to establish the infants present ear status, as it may have changed since the previous visit. If the infant was found to have an estimated hearing thresholds of ≥40dBnHL with no OME present or if the evaluation was incomplete (i.e. due to the lack of sleep and/or restlessness) a second ABR was scheduled.

Fourteen infants in this study underwent two ABR assessments, which were done if the evaluation was incomplete due to lack of sleep or restlessness. Out of these assessments the lowest estimated threshold of both ears was used during the analysis.

Out of the 120 ears included in the study, 119 ears were used in the data analysis. One ear was excluded due to a previous pass on the OAE screening on that ear. At the time of the ABR the infant did not sleep long enough for this ear to be evaluated with ABR.

There were two infants in each group that were found to have unilateral OME with the other ear documented as uncertain. These infants were included in the study and "matched" with each other. The infants were included to reach 30 infants in each group during the specified data collection period.

One infant in the OME group has hereditary hearing loss on the fathers' side of the family. In the medical records of four infants in the OME group there was no information about hereditary hearing loss. Two infants in the CLP group have a hereditary hearing loss in the family, one infant has a sibling with hearing loss and one infants family has given information that there are individuals with hearing loss on the mother's side of the family.

Analysis

Most data was not normally distributed according to levels of skewness and kurtosis and results of the Shapiro-Wilk test (Figures 7-9). Therefore, non-parametric tests were used in the statistical analyses. The Mann-Whitney U-test was used for test of differences between two groups, which included comparison between the cleft group and OME group, comparison related to gender in the whole group as well as within each group. When the data within the cleft group was divided by cleft type, a Kruskal-Wallis test was performed, as it was three different groups being analyzed.
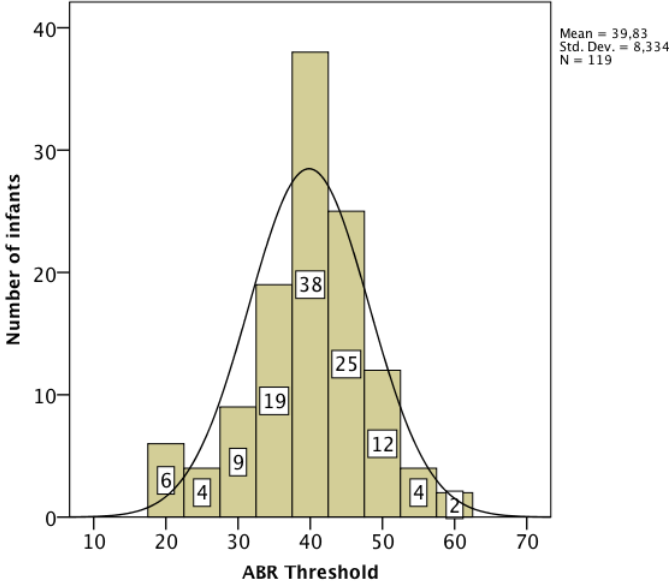
Figure 7. Histogram showing the distribution of ABR thresholds for all infants (N=60 and all ears N=119) with a normative curve (skewness: -0.359, kurtosis: 0.442 and Shapiro-Wilk test *p*=0.000).
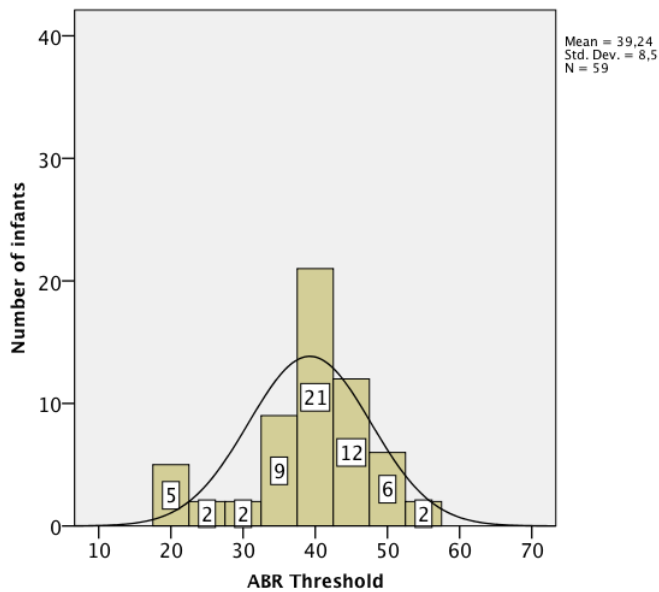
Figure 8. Histogram showing the distribution of ABR thresholds for all infants in the control group with OME (N=30 and ears N=59) with a normative curve (skewness: -0.756, kurtosis: 0.507 and Shapiro-Wilk test 0.902 $p=0.000$)
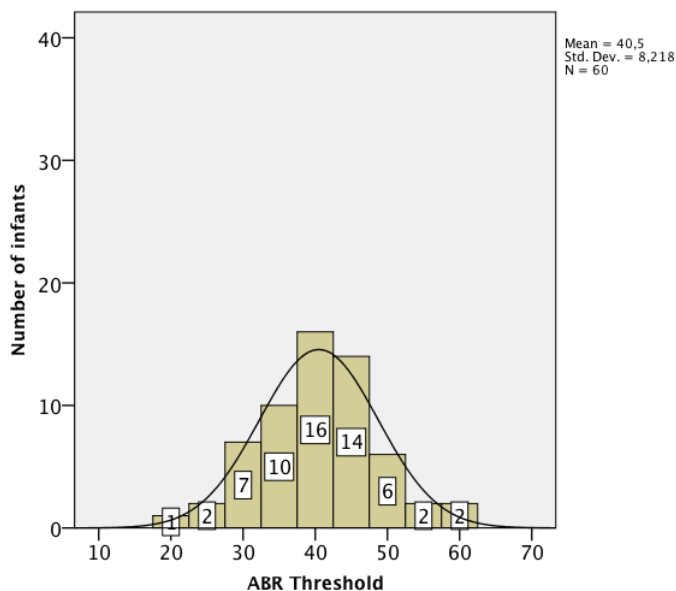
Figure 9. Histogram showing the distribution of ABR thresholds for all infants with cleft (N=30 and all ears N=60) with a normative curve (skewness 0.048, Kurtosis 0.208, Shapiro-Wilk test 0.965, $p=0.081$)

Ethical considerations

Approval to use the information in the medical records for this investigation was given by the head of the Clinical department of hearing and balance at Karolinska University Hospital, Solna. It was also been approved by the Ethics committee at the Department of speech, phonetics and audiology, Institution of clinical sciences, Lunds University, Lund, Sweden.

The medical record review did not have any negative impact on any patient as all data were already collected and no additional visits to the clinic were necessary. All data were been handled carefully and coded so the infants remained anonymous. Possible benefits for the included infants are that the additional information this study gains will be taken into account during following examinations at the clinic. The outcome of this study will also be beneficial to future patients with the same diagnosis.

RESULTS

The CLP group consisted of 60 ears with OME and the non-cleft group consisted of 59 ears with OME. Within the CLP group there were 14 ears belonging to girls and 46 ears belonging to boys. Within the non-cleft group there were 16 ears belonging to girls and 43 ears belonging to boys.

Infants with CLP and OME and infants in the control with OME

The control group had a mean threshold of 39.24dBnHL compared to the CLP group with a mean threshold of 40.42dBnHL. The standard deviation for the control group was 8.50dBnHL and 8.20dBnHL for the CLP group (See figure 10).
There was no statistical difference between the CLP group and the control group with respect to hearing thresholds estimated with ABR (Z-0.343 = (p= 0.732)).
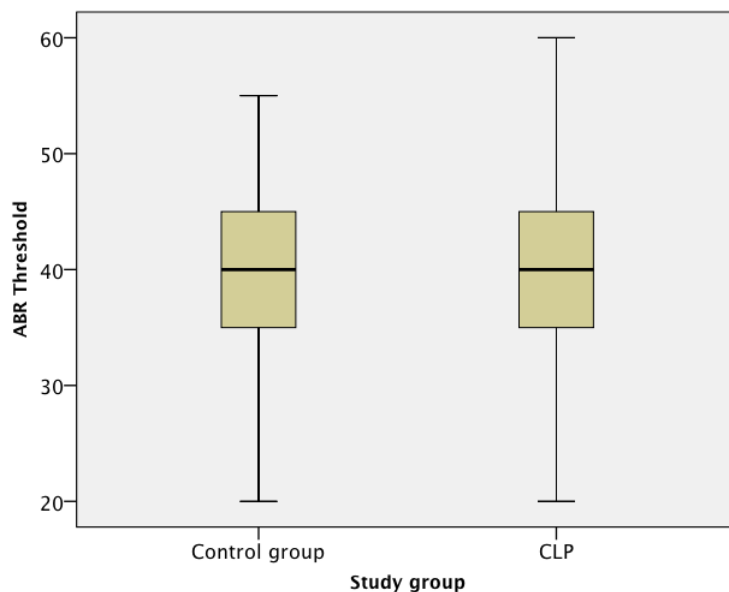
Figure 10. Boxplot showing maximum, median and minimum ABR thresholds and first and third quartile for all ears by group, (no cleft N=59 and cleft N= 60)

Infants in the control group with OME divided by gender

The mean value for boys was 38.02dBnHL and 42.50dBnHL for girls. Boys had a 15dBnHL lower minimum (20dBnHL) compared to girls (35dBnHL) however both groups had a maximum value (55dBnHL). There was no significant difference between the groups (Z=-1.740, (*p*=0.082))
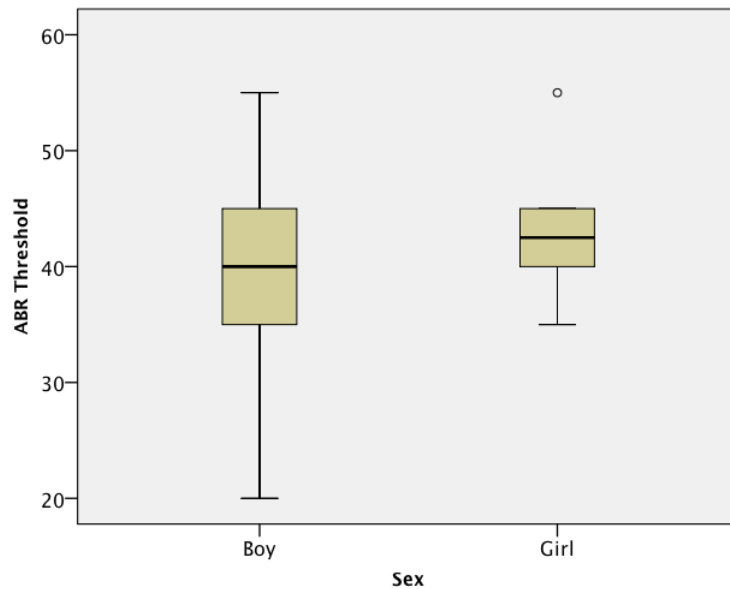
Figure 11. Boxplot showing maximum, median and minimum ABR thresholds and first and third quartile for all ears N=59 in the OME group divided by gender, (boys N=43 and girls N=16).

Infants with CLP and OME divided by gender

The mean value for boys was 40.00dBnHL with a standard derivation of 8.23 and 42.14dBnHL with a standard deviation of 8.25 for girls. Boys had a 10dBnHL lower minimum (20dBnHL) value compared to girls (30dBnHL) however both groups have the same maximum value (60dBnHL). There was no significant difference between the groups (Z=-0.784, (*p*=0.433))
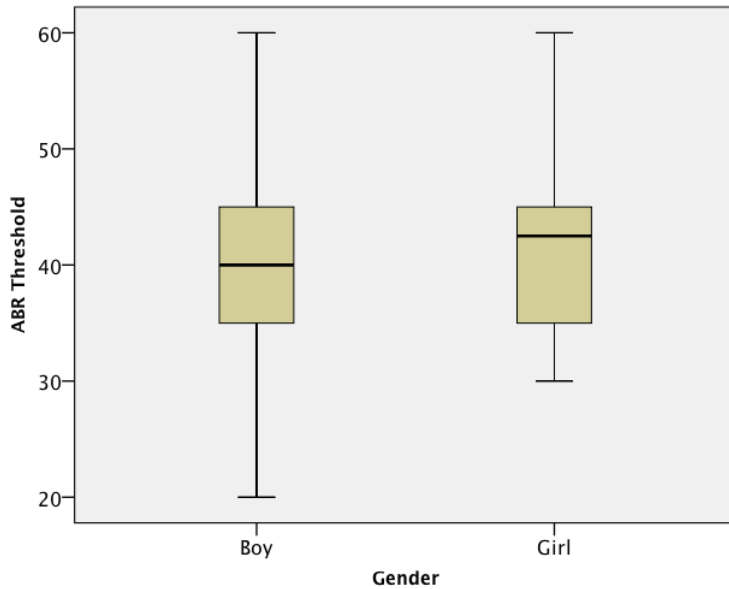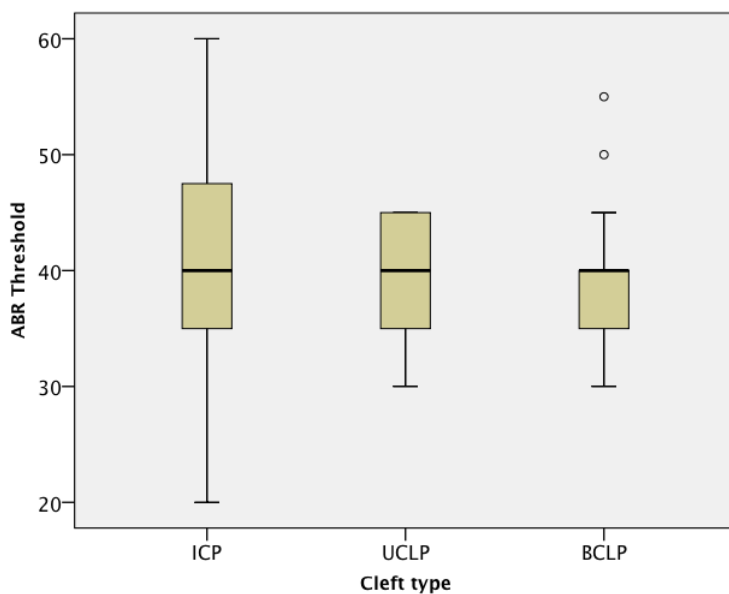
Figure 12. Boxplot showing maximum, median and minimum ABR thresholds and first and third quartile for all ears N=60 in the cleft group by gender, (boys N=46 and girls N=14).

Infants with CLP and OME divided by cleft type

The mean ABR threshold value for infants with ICP was 41.41dBnHL with a standard deviation of 9.52dBnHL. For infants with UCLP the mean threshold value was 39.29dBnHL with a standard deviation of 6,16dBnHL. Infants in the BCLP group had a mean threshold value of 39.34dBnHL and the standard deviation was 6.93dBnHL. No statistical difference was found between types of cleft within the CLP group on the ABR thresholds $(x2(2,N60)=1.122, (p=0.571))$

Figure 13. Boxplot showing maximum, median and minimum ABR thresholds and first and third quartile for all ears by group, ICP (N=16), UCLP (N=8) and BCLP (N=6).

DISCUSSION

During the years of 2011, 2012 and the first two weeks of 2013 a total number of 401 infants were assessed by ABR, 341 infants (94.32%) were not included in this study, due to no diagnosis of OME, fitting of hearing aids since the ABR evaluation, or they were diagnosed with a syndrome. The remaining 60 infants included in the study were all diagnosed with OME. This gives the material in the study validity, as the group was homogenous and therefore the results found in the study should transfer to other groups of the same population as in this study.

No significant evidence was found in this study that the presence of a CLP further elevates the ABR thresholds as compared to children with no CLP. All children in this study had a diagnosis of OME either bilaterally (N=56) or unilaterally (N=4). The study focused on the ABR thresholds: (1) between the two groups, cleft or no cleft but with a diagnosis of OME, (2) gender difference with in the groups and (3) the thresholds within the cleft group divided by cleft type.

As Boone et al. (2004) found OME is one of the risk factors for failing the hearing screening, 64.5% of the children referred after failing the OAE screening were found to have OME when diagnosed by an experienced otolaryngologist. Lok et al. (2011) investigated the risk factors for developing OME, as OME was the reason for the infant failing the hearing screening. As infants with CLP have a high risk for developing OME (Sheahan & Blayney, 2003, Dhillon, 1988) and therefore are more likely to fail the hearing screening a comparison between infants with and without CLP with OME were of interest.

The present results are consistent with the findings in one of the previously performed studies that used ABR as an assessment method for estimating the hearing thresholds for infants with CLP (Viswanathan et al., 2008). Viswanathan et al. (2008) found a mean ABR threshold value 40dBnHL for the right ear and 39.7dBnHL for the left ear, which is similar to the present study with a mean value of 40.42dBnHL for the cleft group an 39.24dBnHL for the non-cleft group. However, these studies are inconsistent with Andrews et al. (2004) who found a higher mean ABR threshold value of 49dBnHL for the right ear and 53dBnHL for the left ear. This difference might be due to inclusion of infants with syndromes. In the study by Andrews et al. (2004) 12 out of 40 infants (30%) had a syndrome. Those infants' thresholds were among the highest in the groups up to 102dBnHL. Two infants presented with a hearing threshold of 102dBnHL, both in the left ear. One of these infants had a hearing threshold of 80dBnHL in the right ear and the other infant were found to have a hearing threshold of 35dB for the right ear. The syndromes were not further specified. In the study by Viswanathan et al. (2008) 20 out of 90 children (22%) had a syndrome, but the infants' thresholds did not extend 90dBnHL. There were two infants that presented with a 90dBnHL hearing threshold. There is no information if threshold was at 90dBnHL in both ears or not. This difference in ABR thresholds between the present study and Viswanathan et al. (2008) compared to Andrews et al. (2004) might be due two the two outliners at102dBnHL found by Andrews et al.

There was a difference in age between the CLP and control group in this study. This is most likely due to the hearing screening routine. Infants with CLP are referred directly for ABR, while the infants without CLP had to fail three OAE before being referred for the ABR. Therefore, the infants with CLP are younger at the time of the ABR compared to infants without CLP that previously have failed the OAE screening three times. The age difference

might also explain why there were more infants with no cleft (N=8) that have performed two ABR evaluations compared to infants with cleft (N=6).

One infant with a BCLP presented with bilateral thresholds outside the range as seen in figure 8. It is also interesting to note that the group with the largest minimum and maximum values is the ICP group and the group with the least variance is the UCLP group. The mean threshold values in this study between the three cleft types, ICP 41.41dBnHL, UCLP 39.29dBnHL, BCLP 39.34dBnHL are not consistent with the findings by Flynn et al. (2012). Flynn et al., (2012) demonstrated that the BCLP group had the highest dB value for higher frequencies. This difference in the results might be due to age, as the infants in this study have not had a repeated number of OME infections. As Flynn et al. (2012) hypothesize the elevated hearing thresholds were due to repeated number of OME episodes.

There was also no significant gender difference in the ABR threshold levels between boys and girls within the CLP group or within the OME group. Boys in the CLP group had a mean hearing threshold of 40,00dBnHL compared to girls 42.14dBnHL. Boys in the OME group had a mean hearing threshold of 38.02dBnHL compared to girls 42.50dBnHL.This is consistent with previous research, which found no gender difference in neonates regarding ABR thresholds (Stuart & Yang, 2000). However, they found shorter wave V latencies in girls as compared to boys. The latencies of the wave V were not examined in the present study, as the focus was hearing thresholds between the infants with and without CLP with OME. There were more than twice as many boys in this study as compared to girls. This would be expected as boys have a much higher risk for both OME and CLP (Lok et al., 2011 & Hagberg et al., 1998).

The ABR is a well-established method for evaluating hearing thresholds in the newborn population. The values of infants with CLP have not been compared to infants without CLP. Both the non-cleft group and the CLP group had to have a diagnosis of OME to be included in the present study. OME is very common in children especially with CLP (Sheahan & Blayney, 2003). However, it is a difficult diagnosis to make in infants due to the small ear canal and a good visualization of the eardrum might be difficult to obtain. Therefore the diagnosis of OME for the included infants may be a confounding factor as some of the infants may have been given the diagnosis without presenting with OME. Some infants that were excluded from this study due to no OME diagnosis may actually have presented with OME. Limitations of the study is the diagnosis of OME as it is difficult to obtain a correct diagnosis with other methods than a otomicroscopey evaluation performed by an experienced otolaryngologist. The movement of the ear canal might be better then the movement of the tympanic membrane when testing this during otomicroscopey (Boone et al. 2004). Even though we did the best we could, in this review we could even have been more specific/sensitive with the use of a bone ABR.

The Hearing and Balance Clinic at Karolinska University Hospital would benefit from better routines for performing bone conduction thresholds at the time of the ABR evaluation. Bone conduction thresholds would better establish if the infants elevated ABR thresholds are conductive or sensorineural. This would provide the audiologist, the otolaryngologist as well as the parent/ guardian with valuable information, which would allow better management and treatment for each individual. Bone conducted ABR is currently not part of the routine in the newborn hearing screening diagnostic program. The lack of bone conduction ABR thresholds in newborn hearing screening diagnostic protocols is widespread. Only 10 out of 34 clinics, in the state of Kentucky, USA, used bone conduction ABR for follow-up assessments in the newborn hearing screening program (Windmill & Windmill, 2006). Both Viswanathan et al.

(2008) and Andrews et al. (2004) used bone conduction measurements. Therefore they were able to estimate if the elevated hearing thresholds were conductive or sensorineural. This was not possible in the present study.

Flynn, Möller, Jönsson and Lohmander (2009) studied the prevalence of OME in a group of children with CLP and a group of control children. They found that the children with CLP had a higher prevalence of OME during the first 5 years of life. The authors also found that with OME children in both groups, those with CLP demonstrated higher hearing thresholds compared to children in the control group. This was not found in the present study. No difference in ABR thresholds between the CLP group and control group was found. This difference in finding might be due to the fact that all infants in the present study were diagnosed with OME at the time of the ABR assessment. It may also depend on the age as the infants in the present study were younger than the children in the Flynn et al. (2009) study. Further research about the hearing in this population is necessary to establish at what age the difference in hearing between the two groups develops. Flynn et al. (2009) examined only four ages within the first 5 years of life, therefore further investigation into the hearing at different ages in this population is necessary to establish at what specific age the difference in hearing between the two groups develops. Flynn et al. (2009) found the hearing threshold for the children with OME but without CLP to be 26.41dBnHL compared 39.24dBnHL for the infants in the control group in the present study. Flynn et al. (2009) found the mean hearing threshold for children with CLP to be 35.71dBnHL compared to 40.42dBnHL for infants with CLP in the present study. Therefore, it seems to be a growing hearing threshold difference between the two groups over the first 5 years of life. This difference between the two groups at different ages should not be affected by the difference in hearing thresholds measured by an ABR assessment and behavioural audiometry.

CONCLUSION

No differences in ABR thresholds were found between infants in the CLP group and infants in the control group. Therefore the CLP does not seem to further increase the ABR threshold than the OME alone. As expected, no gender differences were found. As long as the cleft includes a cleft palate there is no difference in ABR threshold levels related to type of cleft.

Further studies are needed in order to investigate at what age the differences in hearing between the CLP and control group develops. Further studies are also necessary to find out when the difference in hearing between different CLP types develops.

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