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The Developmental Characteristics of Mastoid Pneumatisation in Cleft Palate Children: The Genetic Influence

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A B S T R A C T

Physiologic and developmental role of mastoid pneumatisation in children with otitis media with effusion (OME) is still controversial. For measuring mastoid pneumatisation and examine developmental characteristics, we used children with orofacial malformation of high risk for long term negative pressure in the middle ear and are expected to have lower rate of size and growth of pneumatisation. Mastoid were measured on Schuller's mastoid X-ray pictures planimetrically in study group of 146 children with bilateral (BCLP), unilateral (UCLP) and isolated (ICP) cleft palate, and control group of non-cleft 52 children, both groups with confirmed otitis media with effusion and no previous otological surgery. The lowest pneumatisation found in BCLP, BCLP and UCLP showed no growth of mastoid with age and lower mastoid size than OME controls. ICP is the only cleft type with growth of mastoid with aging.OME patients has the highest size of mastoid and growth rate with aging.

***Key words**: cleft lip and palate, mastoid pneumatization, planimetry*

Introduction

Mastoid pneumatisation and middle ear are distal end of system of organs which include organ of Eustachian tube which proximal end consist of nasal septum, palate and pharynx.The mastoid process bulges put of the petrous bone after birth as part of first branchial arch which part are anatomical structures of the orofacial region and are is structurally changed in the presence of orofacial clefting. Malposition and hypoplasia of the *tensor veli* palatine and *levator veli* palatine are more pronounced in cleft lip and palate typed with more extensive structural changes[1–3]. Cleft palate children have high opening pressure and poor ventilator Eustachian tube function in early childhood with negative influence on the process of aerisation of the mastoid bone as biggest storage of gas important for equalizing of the middle ear pressure with atmospheric. Hearing disturbance and otitis media with effusion (OME) are usual findings in the cleft palate children and occur more frequently in the cleft palate patients than in the non/cleft population[4–8]. The size of mastoid air cell system is determined by the degree of pathological involvement of the middle ear during the childhood[9–11]. Long term negative middle ear pressure leads to mucosal oedema and impairment of microcirculation. Oedema leads from transudation to exudation and finally to obliteration of existing air cells what is high risk for recurrent inflammations of the middle ear[9].

Hypothesis of this study was that pathoanatomical structural differences in different cleft types and their structural defects correlate with size of mastoid pneumatisation.

Objectives of this study was to find out possible correlation between structural severity of the cleft types with size of mastoid pneumatisation according to age, and their growing rate with aging. This study is contribution to the better understanding of the phenotype of the cleft

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palates which leads to more effective research of genotype which is until now still no revealed completely.

Subjects and Methods

We examined characteristics of mastoid pneumatisation 146 cleft palate patients (median age 6.0 years, range 2–14) free of associated malformations and 52 non-cleft OME patients (median age 5.5 years, range 2–14). The age difference between the two groups was not significant. Among cleft patients, there were 14 bilateral cleft lip and palate patients (median age 6 years, range 2–10), 58 unilateral cleft and palate patients (median age 6 years, range 2–14) and 74 isolated cleft palate patients (median age 7 years, range 2–14). The age differences between the cleft groups were not statistically significant. All of the patients studied were referred to the department of otorhinolaryngology for evaluation of varying degrees of hearing loss and impedance audiometry analysis. All patients and controls presented a history, tympanic membrane, tonal audiometry and tympanogram findings typical for OME.

Mastoid pneumatization was assessed by standard computerized planimetric methods (Flisberg and Sigmond, 1965). Lateral temporal bone X-rays using Schueller views were obtained. These have been used by many investigators for years and have not been surpassed by CT. The X-rays were scanned and entered into a computer database. Scanned images were studied separately for each ear. Experienced otologist outlined projection areas of bone pneumatization using a mouse or light-pen pointing device. The areas within these outlines were measured in pixels and converted to cm^2. These areas in cm^2 were labelled as MP. Separate MP values were obtained for both left and right mastoid for every patient for each case we calculated an average MP between the left and right mastoid. Areas for the right and left sides were measured in pixels using Adobe software (1 pixel = approximately 0.28 mm^2).The same otorhinolaryngologist performed the clinical examination in all cases. All cleft palate patients had undergone primary correction of the cleft palate by the same plastic surgeon using the identical surgical method, mostly at the age of 22 months.

Descriptive statistics were used in order to establish the main features of the data. Kolmogorov-Smirnov goodness of fit test was used to estimate the normality of data distribution in both groups. Since the shape of age and mastoid pneumatization area distribution in some groups was significantly different from the normal distribution, non-parametric tests were applied for comparison. The Kruskal-Wallis, Jonckheere-Terpstra and Mann-Whitney tests from SPSS 9.0 was applied to establish significance of pneumatization differences between independent samples, whereas Wilcox-on test was used to estimate significance for related samples. Nonparametric Spearman correlation was used to estimate relationship between age and pneumatization. All statistical calculations (except Power and Sample Size calculations) were performed within SPSS 9.0 for Windows.

Results

In the non-cleft OME patients the median mastoid pneumatization projection area (MP) at the left side was 8.35 cm^2 (range 3.99–21.26 cm^2) and 8.09 cm^2 (range 5.53–21.19 cm^2) at the right side (see Table 1). Difference between left and right side was not significant (Wilcox-on test; $p=0.44$). Within the same group, average MP values between the left and right side were also calculated for each patient and taken into account in further statistics (median 8.72 cm^2, range 4.76–20.86 cm^2).

Within total cleft palate group (all cleft types taken together) median MP at the left and right side was 7.02 cm^2 (range 3.47–13.98 cm^2) and 7.48 cm^2 (range 3.13–21.03 cm^2) respectively (median MP 7.31 cm^2, range 3.30–17.50). MP on the right side was significantly higher than those on the left side (Wilcox-on test; $p<0.001$).

Mastoid pneumatisation on the left side in the total cleft group was significantly lower than those obtained within non-cleft OME group (Mann-Whitney U-test; $p=0.001$) whereas on the right side this difference was not significant ($p=0.09$).

Table 1 shows descriptive statistics of mastoid pneumatisation size within BCLP, UCLP and ICP groups in comparison to non-cleft OME group. In all cleft types MP was lower on both left and right sides than those obtained in non-cleft OME group.

Within the BCLP group, median MP at the left was 6.27 cm^2 (range 3.47–8.42) and was significantly lower than MP at the right 6.69 cm^2 (range 3.13–11.44) (Wilcoxon $p=0.03$). Median MP was 6.85 cm^2 (range 3.30–9.93) In UCLP patients, median MP at the left was 7.23 cm^2 (range 4.95–11.94). It was also significantly lower (Wilcoxon $p<0.001$) than MP on the right (median 7.50 cm^2, range 5.85–14.78) (median MP 7.36 cm^2, range 5.50–12.84). In ICP patients MP at the left was 7.13 cm^2 (range 4.69–13.98) and at the right it was 7.29 cm^2 (range 5.14–21.03). This difference was also significant (Wilcoxon $p=0.001$). Median mastoid pneumatisation was 7.31 cm^2 (range 5.26–17.50).

It must be emphasized that within non-cleft OME group there was no significant difference between left and right MP in contrast to this significantly lower MPA values on the left side in BCLP, UCLP and ICP cleft patients.

MP on the left side was significantly higher in non-cleft OME group than those obtained in ICP (Mann-Whitney U-test; $p=0.02$); UCLP ($p=0.004$) and BCLP ($p=0.005$). MP on the right side was also somewhat higher in non-cleft OME group than those obtained within BCLP, UCLP and ICP groups, but not significantly (Figure 1).

Mastoid pneumatisation on left and right side in BCLP, UCLP, ICP and non-cleft OME group (Table 1)

Mastoid pneumatisation of left and right mastoid in BCLP, UCLP, ICP and non-cleft OME group according to 3-year age groups. Table presents descriptive statistics for MP of left and right side according to 3-year age sub-groups in BLCP, UCLP, ICP and non-cleft OME patients. Totals for BCLP, UCLP, ICP and non-cleft OME patients (all age groups together) were also presented (Table 2).

Spearman correlation coefficients between age and MP, for both left and right mastoid, as well as correlation between age and average MP in BCLP, UCLP, ICP and non-cleft OME.

The relationship between age and MP was estimated by Spearman non-parametric correlation. In the BCLP group MP on the left side significantly increases with age (Spearman r_s=0.774; p=0.002) whereas MP on the right

TABLE 1

MPA OF THE LEFT AND RIGHT MASTOID IN BCLP, UCLP, ICP AND NON-CLEFT OME GROUP ACCORDING TO 3-YEAR AGE GROUPS

			Group							
			BCLP		UCLP		ICP		non-cleftOME	
			MPA left side	MPA right side	MPA left side	MPA right side	MPA left side	MPA right side	MPA left side	MPA right side
Age	1–3yrs (N=32)	Count	2	2	4	4	10	10	16	16
		Median	3.47	3.13	7.03	7.10	6.76	6.35	6.81	6.77
		Percentile 25	3.47	3.13	6.34	5.85	6.18	6.28	5.89	5.17
		Percentile 75	3.47	3.13	7.73	8.36	7.57	7.05	10.37	7.38
		Minimum	3.47	3.13	6.34	5.85	5.48	6.06	5.53	3.99
		Maximum	3.47	3.13	7.73	8.36	7.57	7.05	13.65	13.32
	4–6 yrs (N=72)	Count	6	6	28	28	26	26	12	12
		Median	6.57	8.81	6.86	7.97	6.58	8.16	8.51	9.39
		Percentile 25	6.27	8.24	5.96	6.92	6.18	7.24	7.50	7.87
		Percentile 75	8.42	11.44	7.28	8.85	7.74	8.88	12.53	12.82
		Minimum	6.27	8.24	5.35	5.88	4.69	6.76	6.53	6.07
		Maximum	8.42	11.44	8.65	14.78	10.81	11.28	17.50	21.26
	7–9 yrs (N=58)	Count	4	4	12	12	32	32	10	10
		Median	5.18	5.92	6.90	7.48	7.38	8.62	13.53	10.40
		Percentile 25	4.87	5.15	5.44	6.15	5.90	5.68	10.60	10.24
		Percentile 75	5.48	6.69	7.40	7.52	11.26	11.52	17.30	15.45
		Minimum	4.87	5.15	4.95	6.06	5.38	5.14	7.98	8.92
		Maximum	5.48	6.69	8.41	9.86	13.98	21.03	21.19	20.53
	10–12 yrs (N=18)	Count	2	2	2	2	2	2	12	12
		Median	7.23	6.47	7.41	9.15	9.23	5.25	7.84	7.88
		Percentile 25	7.23	6.47	7.41	9.15	9.23	5.25	6.30	7.38
		Percentile 75	7.23	6.47	7.41	9.15	9.23	5.25	9.35	8.50
		Minimum	7.23	6.47	7.41	9.15	9.23	5.25	6.28	5.59
		Maximum	7.23	6.47	7.41	9.15	9.23	5.25	11.90	16.36
	13+ yrs (N=18)	Count			12	12	4	4	2	2
		Median			7.38	7.41	9.61	10.29	11.88	8.12
		Percentile 25			7.31	7.38	7.14	6.96	11.88	8.12
		Percentile 75			7.48	8.42	12.08	13.63	11.88	8.12
		Minimum			6.26	7.30	7.14	6.96	11.88	8.12
		Maximum			11.94	13.74	12.08	13.63	11.88	8.12
Group Total	(N=198)	Count	14	14	58	58	74	74	52	52
		Median	6.27	6.69	7.23	7.50	7.13	7.29	8.35	8.09
		Percentile 25	4.87	5.15	6.26	7.22	6.18	6.35	6.73	6.92
		Percentile 75	7.23	8.81	7.41	8.75	8.26	10.09	11.90	10.40
		Minimum	3.47	3.13	4.95	5.85	4.69	5.14	5.53	3.99
		Maximum	8.42	11.44	11.94	14.78	13.98	21.03	21.19	21.26

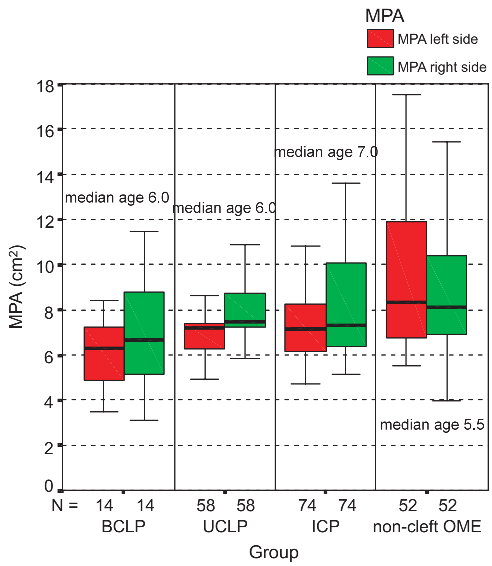

Fig. 1. Median mastoid pneumatization area (MPA) on both left and right side in cleft patients and non-cleft SOM patients according to age (in form of a box-plot – median, 25th and 75th percentile, minimum and maximum are showed).

side was not significantly correlated with age (r_s=0.456; p=0.116). Within UCLP group, we found that MP on the left side has increasing tendency with age (Spearman r_s=0.318; p=0.016) but MP on the right was not correlated with age (Spearman r_s=–0.01; p=0.911). In the ICP group, MP on both left (r_s=0.379; p=0.001) and right (r_s=0.350; p=0.002) side significantly increases with age. Within non-cleft OME group, MP on both left (r_s=0.323; p=0.021) and right (r_s=0.388; p=0.005) side significantly increases with age (Table 2). Spearman correlation coefficients between age and MP on both left and right side, and AMP are presented in order to estimate increase or decrease of MP with age for BCLP, UCLP, ICP and non-cleft OME groups. The highest positive correlation between MP and age (i.e. increase) was obtained within non-cleft OME group on the right side (r_s=0.329), whereas correlation on the left side was somewhat lower and only borderline significant. In contrast to non-cleft OME, isolated cleft palate (ICP) patients had significant increase on the left side (r_s=0.324), whereas correlation on the right was positive but not significant. Within the UCLP group MP on the left side significantly increases with age (r_s=0.272) whereas MP on the right was not correlated with age. In the BCLP group, MP correlation with age on the left side was positive therefore we obtained MP increase with age, but this was not significant in our sample. MP on the right was not correlated with age. Generally, in cleft patients MP increase with age was positive and significant or »almost significant« on the left. In non-cleft OME group MP increase was positive on both sides. It was significant on the right side and »almost significant« on the left (Table 3).

Table presents significance of obtained MP and average MP differences between non-cleft OME and total

TABLE 2
SPEARMAN CORRELATION COEFFICIENTS BETWEEN AGE AND MP A, FOR BOTH LEFT AND RIGHT MASTOID, AS WELL AS CORRELATION BETWEEN AGE AND AMPAIN BCLP, UCLP, ICP AND NON-CLEFT OME

Group				Age (years)
BCLP	Spearman's rho	MPA left side	Correlation Coefficient	0.259
			Sig. (2-tailed)	0.370
			N	14
		MPA right side	Correlation Coefficient	–0.074
			Sig. (2-tailed)	0.801
			N	14
		AMPA	Correlation Coefficient	–0.037
			Sig. (2-tailed)	0.900
			N	14
UCLP	Spearman's rho	MPA left side	Correlation Coefficient	0.272*
			Sig. (2-tailed)	0.039
			N	5
		MPA right side	Correlation Coefficient	–0.013
			Sig. (2-tailed)	0.922
			N	5
		AMPA	Correlation Coefficient	0.051
			Sig. (2-tailed)	0.703
			N	5
ICP	Spearman's rho	MPA left side	Correlation Coefficient	0.324*
			Sig. (2-tailed)	0.005
			N	74
		MPA right side	Correlation Coefficient	0.16
			Sig. (2-tailed)	0.151
			N	74
		AMPA	Correlation Coefficient	0.247*
			Sig. (2-tailed)	0.034
			N	74
non-cleft OME	Spearman's rho	MPA left side	Correlation Coefficient	0.252
			Sig. (2-tailed)	0.072
			N	52
		MPA right side	Correlation Coefficient	0.329*
			Sig. (2-tailed)	0.017
			N	52
		AMPA	Correlation Coefficient	0.343*
			Sig. (2-tailed)	0.013
			N	52

Correlation is significant at the 0.05 level (2-tailed). * Correlation is significant at the 0.01 level (2-tailed).

cleft palate group estimated by non-parametric Mann-Whitney U-test.

Significant differences between non-cleft OME and cleft palate (all cleft types taken together) patients were obtained within age groups 4–6 and 7–9 years (Figure 2).

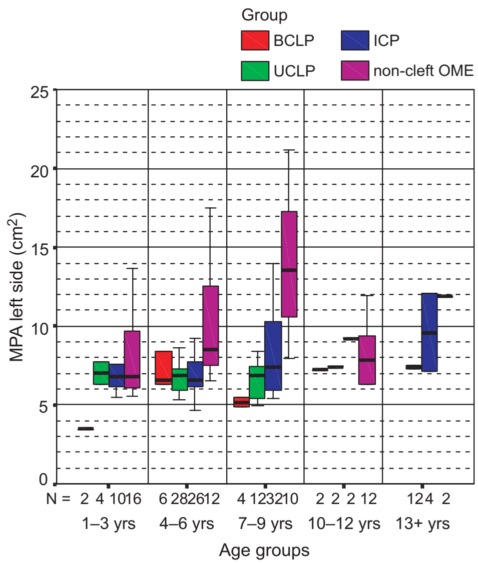

Fig. 2. MPA on the right side (right temporal bone) within cleft groups and non-cleft OME group according to 3-year age groups, in form of box-plots. Median values, quartiles and min/max values are presented.

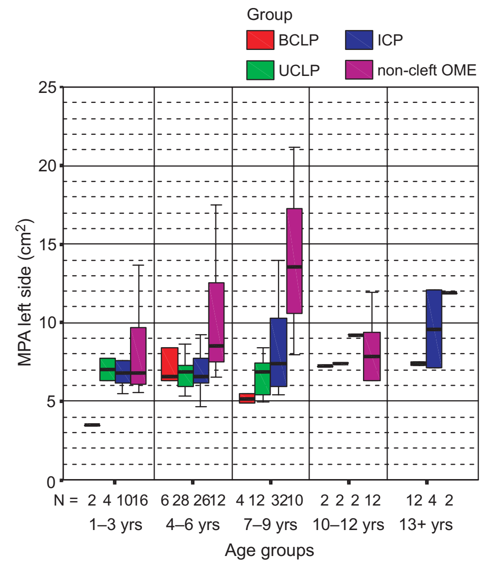

Fig. 3. MPA on the left side within cleft groups and non-cleft OME group according to 3-year age groups in form of box-plots. Median values, quartiles and min/max values are presented.

TABLE 3
SIGNIFICANCE OF OBTAINED MPA AND AMPA DIFFERENCES BETWEEN NON-CLEFT OME AND TOTAL CLEFT PALATE GROUP ESTIMATED BY NON-PARAMETRIC MANN-WHITNEY U-TEST

Age		MPA left side	MPA right side	AMPA
1–3 yrs	Z	–1.360	–1.453	–1.209
	Asymp. Sig. (2-tailed)	0.174	0.650	0.227
	ExactSig. [2*(1-tailed Sig.)]	0.184[3]	0.669[a]	0.239
4–6 yrs	Z	–3.265	–1.693	–2.781
	Asymp. Sig. (2-tailed)	0.001	0.090	0.005
7–9 yrs	Z	–3.954	–2.883	–3.542
	Asymp. Sig. (2-tailed)	0.000	0.004	0.000
10–12 yrs	Z	0.000	–1.129	–0.753
	Asymp. Sig. (2-tailed)	1.000	0.259	0.452
	ExactSig. [2*(1-tailed Sig.)]	1.000[a]	0.291[a]	0.494[a]
13+ yrs	Z	–1.129	–1.565	–1.129
	Asymp. Sig. (2-tailed)	0.259	0.572	0.259
	ExactSig. [2*(1-tailed Sig.)]	327[a]	641[a]	327[a]

a. Not corrected for ties. b. Grouping Variable: Group (Cleft palate or non-cleft OME)

MPA on the right side within cleft groups and non-cleft OME group according to 3-year age groups was presented in form of box-plots. Median values, quartiles and min/max values are presented (Figure 3).

MP on the left side within cleft groups and non-cleft OME group according to 3-year age groups was presented in form of box-plots. Median values, quartiles and min/max values are presented (Table 4).

MPA differences between four observed groups, BCLP, UCLP, ICP and non-cleft OME were estimated by Jonckheere-Terpstra test statistics.

Tests were pefrormed separately for average MP, MP on the left side and for MP on the right. Significant differences were found at the ages of 7–9.

Discussion

Previous studies described changes of the length and angulations of cranial base, more backward and upward position of the maxilla and smaller sphenopalatine angle as additional etiological factor to high frequency of OME in cleft palate patients if compared with non-cleft palate[6,7]. Previous studies also showed that cleft palate is not isolated local defect but part of sequence of malformations including retarded mastoid in severe cleft palate, which are generated from first branchial arch[6].

This study was designed retrospectively based on clinical X-ray material which was used in past but can be useful particularly for retarded, non developed or sclerotic mastoid. CT scan is not suitable method for small conductive hearing loss in otitis media with effusion for big number of children in routine clinical work because of exposure of child to the radioactivity and because it is too expensive. Controversy about genetic or environmental factor as dominant in aetiology of »small mastoid« is still open. That was the reason why we choose model of cleft palate patient who have long-lasting dysfunction of Eustachian tube which started prenatally and consequence of universality of otitis media with effusion during the end of adolescence or adult age. Presence of huge

TABLE 4
JONCKHEERE-TERPSTRA TEST

Age group		MPA left side	MPA right side	AMPA
1–3 yrs	Number of Levels in Group	4	4	4
	N	16	16	16
	Observed J-T Statistic	51.000	47.000	51.000
	Mean J-T Statistic	40.500	40.500	40.500
	Std. Deviation of J-T Statistic	10.120	10.120	10.120
	Std. J-T Statistic	1.038	0.642	1.038
	Asymp. Sig. (2-tailed)	0.299	0.521	0.299
4–6 yrs	Number of Levels in Group	4	4	4
	N	36	36	36
	Observed J-T Statistic	278.000	234.500	264.000
	Mean J-T Statistic	221.500	221.500	221.500
	Std. Deviation of J-T Statistic	34.481	34.478	34.481
	Std. J-T Statistic	1.639	0.377	1.233
	Asymp. Sig. (2-tailed)	0.101	0.706	0.218
7–9 yrs	Number of Levels in Group	4	4	4
	N	29	29	29
	Observed J-T Statistic	210.000	184.000	198.000
	Mean J-T Statistic	130.000	130.000	130.000
	Std. Deviation of J-T Statistic	23.993	23.993	23.993
	Std. J-T Statistic	3.334	2.251	2.834
	Asymp. Sig. (2-tailed)	0.001	0.024	0.005
10–12 yrs	Number of Levels in Group	4	4	4
	N	9	9	9
	Observed J-T Statistic	12.000	13.000	13.000
	Mean J-T Statistic	10.500	10.500	10.500
	Std. Deviation of J-T Statistic	3.990	3.990	3.990
	Std. J-T Statistic	0.376	0.627	0.627
	Asymp. Sig. (2-tailed)	0.707	0.531	0.531
13+yrs	Number of Levels in Group	3	3	3
	N	9	9	9
	Observed J-T Statistic	13.000	10.000	13.000
	Mean J-T Statistic	10.000	10.000	10.000
	Std. Deviation of J-T Statistic	3.958	3.958	3.958
	Std. J-T Statistic	0.758	0.000	0.758
	Asymp. Sig. (2-tailed)	0.448	1.000	0.448

[a] – Grouping Variable: Group

defect of malformed bone and cleft palate muscles in severe cleft palate types with associated nasal deformation decrease gas pressure in nose and nasopharyngeal space. Pressure which is not sufficient to provide entering of the gas bolus in to the Eustachian tube, failure to open and support sculpturing of the mastoid air space. Our results showed lower mastoid pneumatisation in all tested cleft types both for left and right side if compared with non-cleft OME group. Mastoid pneumatisation of left side was smaller in group of BCLP, UCLP and ICP children than mastoid pneumatisation of the right side. Pneumatisation of the left side in those groups increase faster than of the right side and significantly with aging. Our results showed that side of the cleft has no influence on the size of the mastoid pneumatisation. Mastoid pneumatisation of left side is always smaller doesn't matter on which side cleft is situated. Those results correlate with previous results[6] about more severe hearing loss on the left ears for severe cleft types, with slower or no normalisation of the hearing threshold for moderate and severe hearing loss with aging. ICP children have bigger size of mastoid pneumatisation than other clefts, with no differences between left and right side and have the biggest increase of mastoid pneumatisation with aging. Those results correlate WITH previous results which showed that ICP children have in average smaller hearing loss than other clefts, higher rate of ears with normalised hearing level with aging, but still higher rate of tympanogram of B type across the adolescence[6,7]. Those results support genetically determined mastoid pneumatisation in the same developmental sequence as orofacial clefts. Mastoid pneumatisation in severe cleft palate is not absent primarily because of otitis media with effusion.It is undeveloped and retarded what proved no ability for growth with aging.

Control group which also had OME, developed normal mastoids, it is very doubtful that OME *per se* has any influence on the growth of mastoid pneumatization.

Conclusions

Mastoid pneumatisation size and growing rate in orofacial clefts are in dependence with severity of the cleft. Small mastoid in orofacial clefts is primary genetically determined on different pattern for group of cleft lip and palate clefts and isolated cleft palate. Small mastoid in orofacial clefts is additional etiological factor for the high rate of frequent episodas of the OME. Sum of such changes are reason for more frequent insertion of ventilation tubes and slower rate of hearing loss improvement.

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RAZVOJNE KARAKTERISTIKE PNEUMATIZACIJE MASTOIDA KOD DJECE SA RASCJEPOM USNE I NEPCA-GENETSKI UTJECAJ

SAŽETAK

Fiziološke i razvojne karakteristike pneumatizacije mastoida još su uvijek kontroverzne.Mjerenje pneumatizacije mastoida i razvojnih karakteristika primjenjeno je na djeci sa orofacijalnim rascjepima, koja imaju povećan rizik od dugotrajnog negativog tlaka srednjeg uha i posljedično smanjene mogućnosti rasta i razvoja pneumatizacije mastoida.Pneumatizacija je mjerena planimetrijski na rentgenskim slikama učinjenim metodom po Schulleru kod 146 djeteta sa sekretornim otitisom bez prethodnih otoloških operacija, podijeljenih u grupe sa obostranim (BCLP), jednostranim usne i nepca (UCLP) te izoliranim rascjepom nepca (ICP) i kontrolne grupe od 52 djeteta sa sekretornim otitisom (OME) bez malformacija.Najmanja površina pneumatizacije nađena je u grupi BCLP, kod kojih kao i kod djece sa UCLP nije bilo rasta sa porastom životne dobi a pneumatizacija djece sa rascjepom usne i nepca je imala manju površinu od OME grupe.ICP grupa je jedina imala rast mastoida sa porastom životne dobi.Najveća površina i rast pneumatizacije sa porastom životne dobi izmjerena je kod OME grupe.