ARE COL4A1 AND COL4A2 GENE POLYMORPHISMS ASSOCIATED WITH CEREBRAL PALSY ?

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Introduction:

Although, prematurity, low birth weight and hypoxic-ischaemic injury are the most recognized risk factors in Cerebral Palsy (CP), one-third of them have not any risk factor, a genetic condition may be suspected. Collagen type IV Alpha1 (COL4A1) and Alpha2 (COL4A2) are extracellular-matrix-proteins presenting in basement membranes. Recent studies reported that intracerebral hemorrhage, porencephaly, diffuse and periventricular leukoencephalopathy associated with variations in COL4A1 and COL4A2 genes.

Purpose:

To investigate the COL4A1 and COL4A2 gene polymorphisms association with susceptibility to disease and severity of CP.

Method:

Age and sex matched CP patients and healthy controls were enrolled to this study. Two polymorphisms of COL4A1(rs1961495) and COL4A2 (rs9521733) genes were investigated by PCR-RFLP. Gross motor function classification system, medical drug using, type of involvement, number of affected limbs, accompanying conditions (growth retardation, epilepsy, mental retardation, visual and hearing impairment, etc), birth weight, gestational age and MRI data were used to evaluate the disease severity. Genotype distributions and allelic frequencies were compared between the groups by Chi-square and Cochran-Armitage Trend test.

Results:

The study population consisted of 176 (75 girls, 101 boys, 71.8±37.9 months) CP and 178 (88 girls, 90 boys 69.3±55.2 months) controls (p>0.05). Both groups were in Hardy-Weinberg Equilibrium (p>0.05). There wasn't significant difference between two groups with respect to genotype distribution and allele frequency (p>0.05, table 1-2).

Only significant association was detected between COL4A2 polymorphism and growth retardation in SP. TT genotype and T allele were higher compared to CC or CT genotypes and C allele (57.1, 38.1, 4.8 %, p=0.03 and 76.2, 23.8 %, p=0.01, respectively) in CP with growth retardation

Conclusions:

These findings suggest that two polymorphisms in the COL4A1 and COL4A2 genes don't increase genetic susceptibility to CP in a group of Turkish population but, rs9521733 polymorphism may be associated with growth retardation.

Table 1. The genotype distributions of patients and controls

Gene Polymorphism	Genotype	Group		p
		Controls number (%)	Patients number (%)	
COL4 A1	C/C	124 (69.7)	133 (75.6)	0.12
	C/T	48 (27.0)	42 (23.9)	
	T/T	6 (3.3)	1 (0.6)	
COL4 A2	C/C	39 (21.9)	32 (18.2)	0.08
	C/T	95 (53.4)	85 (48.3)	
	T/T	44 (24.7)	56 (33.5)	

p: Cochran-Armitage Trend Test

Table 2. Allele frequencies of gene polymorphisms in patients and controls

Gene Polymorphism	Allele	Group		p
		Number of Controls (%)	Number of Patients (%)	
COL4 A1	C	296 (83.1)	308 (87.5)	0.10
	T	60 (16.9)	44 (12.5)	
COL4 A2	C	178 (49.0)	149 (42.3)	0.06
	T	183 (51.0)	203 (57.7)