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ASSOCIATION OF *MSX1* GENE WITH NON-SYNDROMIC ORAL CLEFT IN SOUTHERN BRAZIL

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INTRODUCTION

Oral clefts (OC) are the most common craniofacial birth defect in humans, with an average worldwide prevalence of 1/600 live births, varying according to geographical and ethnical factors. The occurrence is due to incomplete formation of the lip and (or) palate in the process of facial embryogenesis. Its etiology is complex, involving genetic and environmental factors.

Association studies suggest that multiple genes are responsible for lip and palate genesis, including growth factors, collagen and homeothic proteins. One of the develpoment homeothic genes associated with cleft lip and (or) palate (CL/P) is *MSX1*, located in 4p16 region. The homeobox gene *MSX1* functions as transcriptional regulator that control cellular proliferation and differentiation during embrionyc development. This gene has two exons and a repetition polymorphism of CA dinucleotides. Some studies suggested the interaction between *MSX1* CA polymorphim and non-syndromic oral clefts.

OBJECTIVE

Study the association between *MSX1* CA polymorphism and non-syndromic oral clefts in Southern Brazil.

METHODOLOGY

The sample included individuals with non-syndromic CL/P or cleft palate only (CPO) and their parents. Patients were recruted during visit to the Craniofacial Outpatient Clinic at Hospital de Clínicas de Porto Alegre. All the patients signed Informed Consent.

The *MSX1* CA repetition polymorphism was identified by polymerase chain reaction (PCR). The amplifications were analyzed by automatic sequencer ABI 3130X. Statistical analysis was performed with the Transmission Disequilibrium Test (TDT) using FBAT software (Family Based Association Test).

Support: FIRCA/NIH, CNPq, FIPE/HCPA

RESULTS

We studied 365 individuals from 150 nuclear families, including 65 complete case-parents triads. 54% of probands were male. CL/P was more frequent in this gender (58,1%), while CPO was more observed in females (71,4%). There was a higher rate of CL/P (129 cases) when compared to CPO (21 cases). Data are specified in Table 1:

Table 1: Cases frequency according to gender and type of Oral Cleft.

Gender	*CL/P n(%)*	*CPO n(%)*	*Total n(%)*
Male	75 (58,1)	6 (28,6)	81 (54)
Female	54 (41,9)	15 (71,4)	69 (46)
Total	129 (100)	21 (100)	

In CA repetition polymorphism analysis we identified the four alleles. TDT analysis demonstrated an overtransmission of allele 3 and allele 4 (p = 0,001), according to data shown in Table 2:

Table 2: Allele frequencies and results of Transmission Disequilibrium Test (TDT)

Allele	*Allele Frequency*	*p*
1 (175 bp)	0,045	0,796
2 (173 bp)	0,164	0,267
3 (171 bp)	0,097	0,0015
4 (169 bp)	0,694	0,0013

CONCLUSIONS

These data demonstrate a positive association between alleles 3 and 4 of *MSX1* gene CA repetition polymorphism with Oral Clefts in our population. Posterior association studies including environmental factors will be performed.