

Altered methylation levels of imprinting genes in children with congenital heart disease

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Abstract

Background: Congenital heart disease (CHD) is likely resulted from both genetic aberration and environmental adverse factors. Imprinting genes, which are regulated by epigenetic modifications, are essential for the normal embryonic development. However, the epigenetic role of imprinting genes in the pathogenesis of CHD remains unclear.

Objective: To examine the methylation modifications of differences imprinting genes in CHD in order to explore potential epigenetic pathogenesis of CHD.

Design: Eighteen imprinting genes associated with early embryonic development were selected to compare the methylation alternations between 27 children with CHD (ventricular septal defect in 17, atrial septal defect in 12, valvular heart disease in 7, tetralogy of Fallot in 4, patent ductus arteriosus in 4, constriction of aortic arch in 3) and 28 healthy controls by using MassArray platform.

Results: The methylation levels of 8 imprinting genes were significantly different between CHD group and Control group. Among them, the methylation levels of imprinting genes GRB10 (51.12% VS 43.42%, $P<0.001$) and MEST (56.60% VS 53.22%, $p=0.025$) were significantly higher in CHD group, while those of imprinting genes INPP5F (67.23% VS 73.17%, $P<0.001$), PEG10(45.17% VS 50.92%, $P=0.002$), NAP1L5(62.12% VS 68.86%, $P=0.007$), PLAGL1(40.97% VS 42.80%, $P=0.018$), NESP(31.31% VS 41.12%, $P<0.001$) and MEG3(39.53% VS 45.31%, $P<0.001$) were significantly lower in CHD group. However, no significant imprinting modification changes were found among different types of CHD.

Conclusions: The altered methylation levels of imprinting genes found in our study may imply an epigenetic multi-misregulation in the pathogenesis of CHD during embryogenesis. Further studies are warranted to examine potential variations in these imprinting genes in the pathogenesis of CHD.

Key words: Congenital heart disease Imprinting gene Methylation