P-087 Relationship between gene polymorphisms of folate and one carbon metabolism with foetal viability

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Introduction: Folate is a methyl donor that plays an essential role in DNA synthesis and biological methylation reactions, including DNA methylation. Folate deficiency may be implicated in the development of genomic DNA hypomethylation, which can be an essential factor of foetal viability. Some polymorphisms of the genes implicated in folate cycle have been related to pregnancy loss. Two polymorphisms of the MTHFR gene are commonly accepted to be involved on foetal viability. We studied several polymorphisms of the folate cycle on samples from spontaneous abortions (SA) of unknown origin.

Material and Methods: A Group of 29 samples from spontaneous abortion of unknown etiology and a control Group (n = 154) were genotyped for DHFR (19 ins/del), TYMS (rs2853542, rs34489327, rs34743033) CBS (rs5742905, 844ins68) and MTHFR (rs1801131, rs1801133) gene polymorphisms. DNA was isolated from parafine embedded tissues and blood samples by salting-out method. Genotyping was performed by multiplex minisequencing (Snapshot?, Applied Biosystem) preceded by multiplex PCR.

Results: Only CBS844 ins68del shown statistical differences on genotype frequencies between SA and controls (SA: del/del = 0.62, del/ins = 0.38, ins/ins = 0; controls: del/del = 0.82, del/ins = 0.16 and ins/ins = 0.02; $p < 0.05$). Unlike other authors, polymorphisms of MTHFR gene (C677T and A1298C) did not show statistical differences between SA and control. Further analysis with higher number of SA samples should be done.
The high allelic frequency of CBS insertion in SA group can be interpreted as a risk factor of pregnancy loss (OR: 2.75; 95% CI: 1.17–6.464). Although the CBS insertion does not result in enzyme activity impairment, mRNA data provided evidences that the insertion carrier allele is poorly transcribed. It should be mentioned the low number of homozygous (ins/ins) in whole populations studied that could mean a strong negative role on survival in carrier subjects of this mutation. Only one study on male fertility with no statistical significance of the CBS844ins mutation has been found, and there are no studies on foetal tissues.

Conclusions: The high frequency of mutation found in abortions samples allows us to speculate that CBS844ins variant plays a role on foetal viability, perhaps in combination with other genetic or nutritional factors. Supported by Grants SAF2008-03314 and PTQ 09-01-00496.

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