Alteration in methylation pattern of GATA-4 promoter region in vitamin A-deficient offspring's heart.

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BACKGROUND: Epigenetics might explain correlations between lifestyle and risk of disease. Maternal diet has been shown to dynamically alter epigenetic regulation, including affecting DNA methylation status.

OBJECTIVE: This study was designed to test the hypothesis that GATA-4 gene methylation would lead to congenital heart defects in vitamin A-deficient offspring.

METHODS: Ten weaning female rats (VAN group) were fed with a diet which contents 4 IU vitamin A/g diet, while 20 rats (VAD group) were maintained on a diet without vitamin A. After 10 weeks of feeding, all the female rats were mated with normal male rats. The VAN group and a portion of VAD group rats were still given the same diet as before mating, while the rest of the rats from the VAD group (VADS group) were transferred to a diet with enough added vitamin A (10 IU/g diet) for the pregnancy cycle. The embryo hearts were dissected out at embryonic day 13.5 (E13.5) for observation of cardiac development, GATA-4 gene methylation status and the expression of DNA methyltransferases (DNMTs).

RESULTS: Embryos from vitamin A-deficient group exhibited a high incidence of cardiac defects. High methylation was present in the CpG loci of GATA-4 gene with a low expression of GATA-4 mRNA from vitamin A-deficient group embryos. Moreover, up-regulation of DNMT1 and down-regulation of DNMT3a and DNMT3b expression were found in this group embryo.

CONCLUSIONS: These findings show that aberrant methylation is one of key mechanisms to heart defects in vitamin A-deficient offspring. DNMTs play a critical role in this process.

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