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Research

Valproate, thalidomide and ethyl alcohol alter the migration of HTR-8/SVneo cells

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Abstract

Background: Valproate, thalidomide and alcohol (ethanol) exposure during the first trimester of pregnancy is known to cause several developmental disorders. All these teratogens are known to pass the placental barrier and interfere directly with the normal development of the fetus. However, these teratogens also alter the formation and function of the placenta itself which may in turn affect the proper nourishment and development of the fetus. Optimum development of the placenta requires adequate invasion of trophoblast into the maternal uterine tissues. Changes in the migratory behavior of trophoblast by maternal exposure to these teratogens during placentogenesis may therefore alter the structure and function of the placenta.

Methods: In the present study, the effects of sodium valproate, thalidomide and alcohol on the migration of human first trimester trophoblast cell line (HTR-8/SVneo) were examined *in vitro*. Cells were cultured in the wells of 48-well culture plates as mono or multilayers. Circular patches of cells were removed from the center of the wells by suction, and the migration of cells into the wound was studied using microscopy. Effects of low and high concentrations of valproate, thalidomide and alcohol were examined on the healing of wounds and on the migration rate of cells by determining the wound areas at 0, 3, 6, 12, 24 and 48 h. Effects of drugs and alcohol on the proliferation and the expression levels of integrin subunits beta1 and alpha5 in cells were examined.

Results: The migration rates of trophoblast differed between wounds created in mono and multilayers of cells. Exposure to teratogens altered the migration of trophoblast into mono and multilayer wounds. The effects of valproate, thalidomide and alcohol on the proliferation of cells during the rapid migratory phase were mild. Drug exposure caused significant changes in the expression levels of beta1 and alpha5 integrin subunits.

Conclusion: Results suggest that exposure to valproate, thalidomide or alcohol during the first trimester of pregnancy may change the ultrastructure of the placenta by altering the migration of trophoblast cells and this effect may be mediated by drug- or alcohol-induced changes in the expression levels of beta1 and alpha5 integrin subunits.