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Vitamin D Attenuates Sphingosine-1-Phosphate (S1P)-Mediated Inhibition of Extravillous Trophoblast Migration

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ABSTRACT

Introduction

Failure of trophoblast invasion and remodelling of maternal blood vessels leads to the pregnancy complication pre-eclampsia (PE). In other systems, the sphingolipid, sphingosine-1-phosphate (S1P), controls cell migration therefore this study determined its effect on extravillous trophoblast (EVT) function.

Methods

A transwell migration system was used to assess the behaviour of three trophoblast cell lines, Swan-71, SGHPL-4, and JEG3, and primary human trophoblasts in the presence or absence of S1P, S1P pathway inhibitors and $1,25(OH)_2D_3$. QPCR and immunolocalisation were used to demonstrate EVT S1P receptor expression.

Results

EVTs express S1P receptors 1, 2 and 3. S1P inhibited EVT migration. This effect was abolished in the presence of the specific S1PR2 inhibitor, JTE-013 ($p<0.05$ versus S1P alone) whereas treatment with the S1R1/3 inhibitor, FTY720, had no effect. In other cell types S1PR2 is regulated by vitamin D; here we found that treatment with $1,25(OH)_2D_3$ for 48 or 72h reduces S1PR2 (4-fold; <0.05), but not R1 and R3, expression. Moreover, S1P did not inhibit the migration of cells exposed to $1,25(OH)_2D_3$ ($p<0.05$).