Progesterone is a potent substance which inhibits the migration of ovarian cancer cells by reducing epithelial-mesenchymal transition via progesterone receptor-dependent pathway

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ABSTRACT

Ovarian carcinoma (OC) is the most deadly and leading cause of cancer death occurring in the female reproductive tracts. Several factors involved in ovarian carcinoma remain poorly defined and the therapy for OC is limited. Epidemiological data strongly suggest that endogenous and exogenous steroid hormones may play important roles in ovarian carcinogenesis. We predicted that progesterone would inhibit the migration of BG-1 ovarian cancer cells by reducing epithelial-mesenchymal transition (EMT) as well as the growth of cancer cells. First, we investigated the expression of progesterone receptors in ovarian cancer cells with RT-PCR. Next, we determined a proper concentration of progesterone, 17β-estradiol (E2; a positive control), and Mifepristone (anti-progesterone receptor agent) through MTT assay. We confirmed that progesterone reduced the ovarian cancer cell viability in a dose-dependent manner, which was inhibited by Mifepristone. Also, the migration of ovarian cancer cells was reduced by the treatment of progesterone in comparison with negative and positive control groups. Additionally, the alteration of EMT markers such as vimentin was examined at mRNA and protein levels by using reverse-transcription (RT)-PCR and western blot. The expression of Vimentin in was reduced in the treatment of progesterone while the expression of its reverse transition marker E-cadherin was increased. These results indicate that progesterone can inhibit the migration of BG-1 ovarian cancer cells by reducing EMT. Further studies using in vivo xenografted mouse models will be needed to predict that progesterone significantly inhibits the growth of ovarian cancer without any virulent effects on the animals. Consequently, the present results represent that progesterone is a potent substance which inhibits the growth of human ovarian cancer cells and metastasis. Therefore, this hormone therapy may be a clinically effective tool for the treatment of human ovarian cancer.

RESULTS

Figure 2. The effects of Progesterone on mRNA expression of Epithelial-mesenchymal transition related genes. BG-1 cells were treated with 0.1% DMSO as a vehicle. The effects of Progesterone (10−6 M, 10−8 M, 10−10 M) was investigated on the expression of (A) E-cadherin, (B) Vimentin in BG-1 cells by RT-PCR. The products were separated in a 1.5% agarose gel.

Figure 3. The effects of Progesterone on protein expression of Epithelial-mesenchymal transition related genes. BG-1 cells were treated with 0.1% DMSO as a vehicle and 10−6 E2 as a positive control. The effects of Progesterone (10−8 M, 10−10 M ) was investigated on the expression of E-cadherin and Vimentin in BG-1 cells by western blot.

Figure 4. The effects of Progesterone on protein expression of Epithelial-mesenchymal transition related genes in the presence of anti-Progesterone receptor (Mifepristone). BG-1 cells were treated with 0.1% DMSO as a vehicle and 10−6 E2 as a positive control. The effects of Progesterone (10−8 M, 10−10 M ), Mifepristone (10−8 M) was investigated on the expression of E-cadherin in BG-1 cells by western blot.

REFERENCES


CONCLUSION

In this study, we showed that Progesterone reduced the ovarian cancer cell viability in a dose-dependent manner, which was inhibited by Mifepristone. The expression of Vimentin was reduced in the treatment of progesterone while the expression of its reverse transition marker E-cadherin was increased. Also the wounded area of BG-1 cell monolayers healed slowly in vehicle-treated cells. On the contrary, in the presence of Progesterone, the closure of the wounded gap was significantly inhibited at 48h. These results indicate that progesterone can inhibit the migration of BG-1 ovarian cancer cells by reducing EMT. Consequently, the present results represent that progesterone is a potent substance which inhibits the growth of human ovarian cancer cells and metastasis.