Apoptotic Effect of Progesterone on CRC Cells

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***Abstract*—** Various studies have shown that sex steroids affect on cancer cells at cellular and molecular level. The aim of this study was to investigate the apoptotic effects of progesterone on colorectal cancer (CRC) (HT29) cells in cell culture. HT29 cells were exposed to cytotoxic dose (0.1 mg/ml) of progesterone solution. Real time PCR was used to measure Bax gene expression level. Our results indicated that exposure to 0.1 mg/ml of progesterone led to significant increase in BAX gene relative expression level (P<0.01). Our findings indicated that cytotoxic dose of progesterone induces BAX gene expression in HT29 cells.

***Index Terms*—** Progesterone , CRC, Apoptosis.

I. Introduction

There is a growing body of evidence for the importance of gonadal hormone action in the function of the reproductive and other systems, including bone , cardiovascular and other systems. Sex hormones (androgenic, estrogenic, and progestinic) are produced by both sexes, though the quantity and mode differ by sex and age. [1]

Colorectal cancer (CRC), also known as bowel cancer and colon cancer, is the development of cancer from the colon or rectum. Colorectal cancer is the abnormal growth of cells in colon that have the ability to invade or spread to other parts of the body. Colorectal cancer localized only at the primary site is generally curable by surgical resection, but if the tumor has spread to distant sites, the patient five-year survival rate declines quickly.[2][3] However, the male-to-female ratio peaks between 50 to 54 years and then decreases suggesting an androgenic effect and perhaps estrogenic protection. Additionally, established risk factors that vary in prevalence by sex, such as smoking and obesity, cannot fully explain the male predominance. Thus, sex steroid hormones have been proposed as a possible explanation of the sex disparity. This hypothesis is supported by sex steroid hormone involvement in the inflammatory process, including associations between testosterone and inflammatory markers sex steroid hormone receptor protein expression—specifically estrogen receptor β—in esophageal cancer tissue and lower rates of EA among men with prostate cancer, who are likely to receive anti-androgen therapies. [4] Interestingly, women have been observed to be 60% less at risk than men to develop inflammation-associated colon cancer, suggesting that female hormones may play a role in the prevention of this disease. A number of experimental models have demonstrated that estrogens have anti-inflammatory properties in tissues other than the intestine and one way in which estradiol (E2), the most biologically active form of estrogen in the human body, may be protecting against inflammation-associated colon carcinogenesis is through the suppression of intestinal inflammation[5],[6]. Previous studies mainly have focused on association between estrogens and androgens –not progesterone- and colorectal cancer. The aim of this study was to investigate the apoptotic effects of progesterone on colorectal adenocarcinoma (HT29) in cell culture.

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II. Material And Methods

HT29 cells (colorectal adenocarcinoma cell line) were purchased from National Cell Bank of Iran (Pasteur Institute, Tehran, Iran). Cells were grown and incubated in standard situation. Then, cells were sub-cultured into 75cm2 flasks, 96-well plates or 6-well plates. Cytotoxicity of different doses of the estradiol was assayed using MTT method. Real time PCR was used to measure Bax gene expression level. Analyses were conducted using the SPSS20 and ANOVA.

III. Results

MTT assay showed that 0.1 mg/ml of progesterone has cytotoxic effects on HT29 cells. Exposure to 0.1 mg/ml of progesterone led to significant increase in BAX gene expression level in HT29 cells compared to control cells (P<0.01) (Figure I).

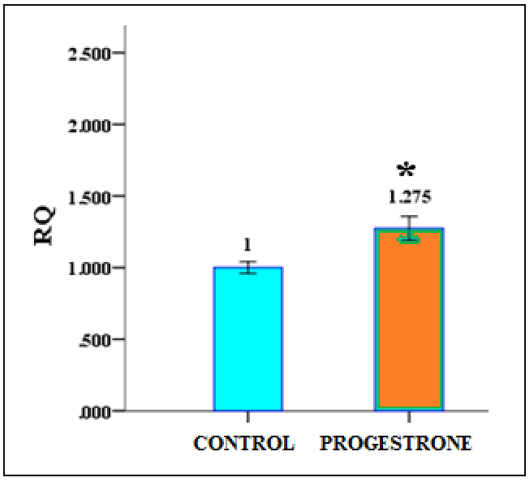

Fig. 1: Bax gene expression level in HT29 cells exposed to cytotoxic dose of progesterone compared to control group. * indicates significant difference compared to control group at P<0.01.

IV. Discussion

In this study we have shown that progesterone can kill the colon cancer cells using BAX dependent apoptosis. Previous studies have shown that sex steroid hormones have anticancer effects. Sex steroid can induce apoptosis as a rational strategy to treat anti-hormone resistant breast and prostate cancer. [7],[8]. It has also been shown that decreased estrogen and progesterone receptor has a role in endometrial cancer cells apoptosis. [9]

Studies show that estradiol might be associated with a positive pattern and high estradiol and low progesterone levels increase duration of survival in cervical cancer. [10]

Evidences also show that progesterone is protective and preventative of certain cancers including breast cancer. [11] Progesterone receptors were detected in normal and colon cancer tissues, suggesting the role played by progesterone in colon cancer development; however, eventual role of progesterone receptor in colon cancer remains to be elucidated. [12] In line with our findings observational epidemiological studies and randomized trials also have reported a protective effect of estrogen and progestin therapy (EPT) on the risk of colorectal cancer. [13]

V. Conclusion

It can be concluded that cytotoxic dose of progesterone induces BAX gene dependent apoptosis in HT29 in cell culture.

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