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Is Normal Kidney Cells Viability Influenced by Estradiol Valerate Administration in Cell Culture?

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Abstract: *Studies have shown that sex steroids may have cytotoxic or proliferating effects on various cells. This study was exerted to assess the effects of estradiol valerate on viability of normal kidney cells (HEK cell line) in cell culture. HEK cells were exposed to 0.0001, 0.001, 0.01, 0.1, 1 and 10 mg/ml of estradiol valerate solution. MTT assay was used to determine cytotoxic effects of the estradiol valerate. Our results indicated that administration of ≤ 1 mg/ml of estradiol valerate resulted in significant decrease in viability of HEK cells compared to control cells (P<0.05). Administration of 10 mg/ml of estradiol valerate did not significantly change viability of HEK cells. According to our finding, estradiol valerate administration may have cytotoxic effects on normal kidney cells proliferation.*

Keywords: *Estradiol valerate , HEK cell line, Viability*

1. Introduction

Estradiol valerate is a synthetic ester and is also a female estrogen hormone. It works by replacing natural estrogens in a woman who can no longer produce enough estrogen. Estradiol valerate is used for treating certain symptoms of menopause (eg, hot flashes, vaginal itching, burning, or dryness). It is used to treat low levels of estrogen caused by certain conditions. It may be used to treat certain types of prostate cancer (advanced androgen-dependent) [1].

Human Embryonic Kidney 293 cells, also often referred to as HEK 293, are a specific cell line originally derived from human embryonic kidney cells grown in tissue culture. HEK 293 cells were generated in 1973 by transformation of cultures of normal human embryonic kidney cells with sheared adenovirus 5 DNA in Alex van der Eb's laboratory in Leiden, The Netherlands. HEK 293 cells are very easy to grow and transfect very readily and have been widely used in cell biology research for many years. They are also used by the biotechnology industry to produce therapeutic proteins and viruses for gene therapy [2], [3].

Some Studies show that some of sex steroids may have cytotoxic on some stem cells [4]. Also, some studies show that some of sex steroids can have impress on some of cells including HEK cell line [5]. From the other towards results of some studies show that estradiol valerate can effect on some cells, such as stem cells [6].

In contrast, Some Studies show that some of sex steroids have a protective role counteracting prostate overgrowth [7].

Since sex steroids such as estrogens are important hormonal drugs in the world [9] and also in Iran [11] and according to the side effects caused by many drugs [12] and costly treatment imposed on patients with cancer [13] and conflicting data on the effects of sex steroids on cancer cells [4],[7], this study was carried out to determine the effects of aspirin on viability of normal kidney cells in cell culture.

2. Materials and Methods

Different concentrations (0.0001, 0.001, 0.01, 0.1, 1 and 10mg/ml) of estradiol valerate were prepared and used in our study. HEK cells (normal kidney 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 75cm^2 flasks, 96-well plates or 6-well plates. Cytotoxicity of different doses of the extract was assayed using MTT method. Analyses were conducted using the SPSS 20 and ANOVA.

3. Results

Administration of ≤ 1 mg/ml of Estradiol valerate resulted in significant decrease in viability of HEK cells compared to control cells (P<0.05). However, there was no significant difference between viability of cells exposed to 0.0001, 0.001, 0.01, 0.1 and 1 mg/ml of estradiol valerate. There was not also significant difference between viability of cells exposed to 10mg/ml of estradiol valerate and control cells (Figure I).

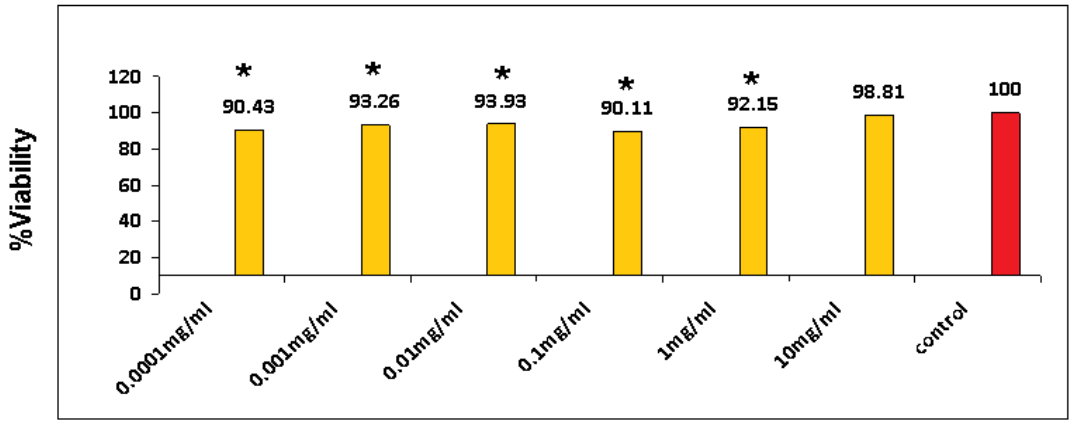

Fig. 1. Viability of HEK cells compared to control group. * indicates significant difference compared to control group (P<0.05).

4. Discussion

The results showed that doses 0.0001, 0.001, 0.01, 0.1 and 1 mg/ml of estradiol valerate can inhibit viability of HEK cells in the cell culture . In this regard, Previous studies have shown that some of sex steroids effects on viability of HEK cells [5]. The results also has demonstrated that E2 down-regulates the expression of SCF/c-KIT system in prostate **cells**, which is associated with antiproliferative and proapoptotic effects. [12] Exposure to corticosteroids decreased mesenchymal **stem cells** viability in a curvilinear dose-response pattern.[13] Steroidal molecules also play an important role in determining the fate of mesenchymal **stem cells**, mainly by altering the expression of key cellular molecules.[14]

5. Conclusion

According to our finding, estradiol valerate may have cytotoxic effects on normal kidney cells proliferation.

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7. References

[1] Micks EA1, Jensen JT. Treatment of heavy menstrual bleeding with the estradiol valerate and dienogest oral contraceptive pill. Adv Ther. 2013 Jan;30(1):1-13. http://dx.doi.org/10.1007/s12325-012-0071-3

[2] Nettleship JE1, Watson PJ, Rahman-Huq N, Fairall L, Posner MG, Upadhyay A, et al". Transient expression in HEK 293 cells: an alternative to E. coli for the production of secreted and intracellular mammalian proteins. Methods Mol Biol. 2015;1258:209-22. http://dx.doi.org/10.1007/978-1-4939-2205-5_11

[3] Thomas P1, Smart TG. HEK293 cell line: a vehicle for the expression of recombinant proteins. J Pharmacol Toxicol Methods. 2005 May-Jun;51(3):187-200.
http://dx.doi.org/10.1016/j.vascn.2004.08.014

[4] Wyles CC1, Houdek MT, Wyles SP, Wagner ER, Behfar A, Sierra RJ. Differential cytotoxicity of corticosteroids on human mesenchymal stem cells. Clin Orthop Relat Res. 2015 Mar;473(3):1155-64.
http://dx.doi.org/10.1007/s11999-014-3925-y

[5] Vecchiola A1, Lagos CF, Fuentes CA, Allende F, Campino C, Valdivia C, et al" . Different effects of progesterone and estradiol on chimeric and wild type aldosterone synthase in vitro. Reprod Biol Endocrinol. 2013 Aug 13;11:76.
http://dx.doi.org/10.1186/1477-7827-11-76

[6] Frazier DE Jr1, Silverstone AE, Gasiewicz TA. 2,3,7,8-Tetrachlorodibenzo-p-dioxin-induced thymic atrophy and lymphocyte stem cell alterations by mechanisms independent of the estrogen receptor. Biochem Pharmacol. 1994 Jun 1;47(11):2039-48.
http://dx.doi.org/10.1016/0006-2952(94)90079-5

[7] Figueira MI1, Correia S1, Vaz CV1, Cardoso HJ1, Gomes IM1, Marques R1, et al" . Estrogens down-regulate the stem cell factor (SCF)/c-KIT system in prostate cells: Evidence of antiproliferative and proapoptotic effects. Biochem Pharmacol. 2016 Jan 1;99:73-87.
http://dx.doi.org/10.1016/j.bcp.2015.11.016

[8] Grandi G1, Xholli A1, Napolitano A1, Palma F1, Cagnacci A2. Pelvic pain and quality of life of women with endometriosis during quadriphasic estradiol valerate/dienogest oral contraceptive: a patient-preference prospective 24-week pilot study. Reprod Sci. 2015 May;22(5):626-32.
http://dx.doi.org/10.1177/1933719114556488

[9] Norouzi Javidan A1, Haghollahi F2, Ramezanzadeh F2, Yekaninejad MS3, Amiri Z4, Noroozi M5, et al". Effects of ethinyl estradiol plus desogestrel on premenstrual symptoms in Iranian women. Acta Med Iran. 2014;52(11):837-43.

[10] Nagis: Khodabandehloo F1, Hosseini M, Rajaei Z, Soukhtanloo M, Farrokhi E, et al". Brain tissue oxidative damage as a possible mechanism for the deleterious effect of a chronic high dose of estradiol on learning and memory in ovariectomized rats. Arq Neuropsiquiatr. 2013 May;71(5):313-9.

[11] Moskovic DJ1, Araujo AB, Lipshultz LI, Khera M. The 20-year public health impact and direct cost of testosterone deficiency in U.S. men. J Sex Med. 2013 Feb;10(2):562-9.
http://dx.doi.org/10.1111/j.1743-6109.2012.02944.x

[12] Figueira MI, Correia S, Vaz CV, Cardoso HJ, Gomes IM, Marques R, Maia CJ, Socorro S. Estrogens down-regulate the stem cell factor (SCF)/c-KIT system in prostate cells: Evidence of antiproliferative and proapoptotic effects. Biochem Pharmacol. 2016 Jan 1;99:73-87.
http://dx.doi.org/10.1016/j.bcp.2015.11.016

[13] Wyles CC, Houdek MT, Wyles SP, Wagner ER, Behfar A, Sierra RJ. Differential cytotoxicity of corticosteroids on human mesenchymal stem cells.
Clin Orthop Relat Res. 2015 Mar;473(3):1155-64.
http://dx.doi.org/10.1007/s11999-014-3925-y

[14] Salloum RH, Rubin JP, Marra KG. The role of steroids in mesenchymal stem cell differentiation: molecular and clinical perspectives. Horm Mol Biol Clin Investig. 2013 Aug;14(1):3-14.
http://dx.doi.org/10.1515/hmbci-2013-0016