

A Study of the Physiological Effects of the Anticancer Paclitaxel in Men

Received :12/7/2016

Accepted :2/11/2016

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ABSTRACT

The present study aims to investigate the effect of Paclitaxel drug on hematological, biochemical parameters and sex hormones of men. Adult men divided into two groups for each sex (33 for each group), the first group (control) and the second group treatment with Paclitaxel drug. Results study indicated a significant decrease ($P \leq 0.05$) in red blood cell count (RBC), packed cell volume (PCV), Total white blood cell count (WBC) and LH level in the men to second group compared with the control group. Also, it showed a significant increase ($p \leq 0.05$) in Creatinine and urea levels to second group compared with the control group. Also, the result showed non-significant in FSH levels to mean in control and second groups.

Keywords: Paclitaxel, Blood and biochemical parameters, sex hormones, Men.

Physiology Classification QP 501-801

Introduction

Cancer is the most common and wide spread diseases around the world are infect the people of different age categories, as is the second cause of death after heart disease in the world^[1]. Cancer is caused by a defect in the gene that controls cell multiplication and differentiation and death^[2].

Tumors can be malignant tumors the most dangerous and are a fast-growing, as it need for a short time to be a mass of tumor malignancy and have the ability to widespread to the other parts of the body due to tumor cell's ability to penetrate the surrounding tissue and move through the blood circulation and lymphatic system of locations arise to other locations which few differentiation or undifferentiated^[3]. Benign tumors advantage slow their growth It takes years and have no the ability to investation surrounding tissues of the body and can be differentiation^[4].

Many cancers treatments, including surgical excision, radiation therapy or chemotherapy and hormonal treatments and more depend on the type and stage of the

tumor, the patient's age and health status of the patient^[5]. In recent years drug was used with great characteristics and effectiveness in reducing tumor disease, a drug Paclitaxel (taxol) and record that this is a different side effects^[2].

Taxol is one of the active compounds in the treatment of tumors and extracted from the bark of *Taxus brevifolia*^[6]. Side effects of the drug Taxol is weight loss and hair loss of appetite, diarrhea, vomiting, severe fatigue and difficulty breathing pricking in the hands and infertility as well as causes of drug appearance effects cellular genetic include abnormalities structural and numerical chromosome^[7].

Mechanism of action Taxol It has the ability Linked to microtubules that are important in the process of cell division because it is one of the main components in the Spindle mitotic which helps to separate the chromosomes during cell division, When taxol associated micro-tubule become stable, which is impossible to division the cell with it and die as soon as the cell divides^[2].

MATERIALS AND METHODS

Collection (66) blood sample from patients in Habboubi hospital in a province Thi-Qar, Iraq. the period of study from 01/11/2015 up to 01/03/2016 The patients' ages ranged from (22-59 years) and included samples (33) a sample of men and those patients suffering from cancer and continued to take the drug taxol, while the control group included (33) men healthy.

The blood parameters were measured by using counter coltter in the laboratory of Habboubi hospital in Thi-Qar, Iraq. 4 ml of blood samples were collected and divided in to two parts the first part was 2 ml by EDTA

tubes, and analyzed to determine of hematological parameters such as a red blood cell count (RBC), the packed cell volume (PCV), hemoglobin (Hb) and the total of white blood cells (WBC) by using an automatic hematological assay analyzer (Nihon Kohden corporation, Japan), and the second part was 2ml blood was collected from each adult men into plain centrifuge tubes, at room temperature for clotting. Serum was separated by centrifugation at 3000g for 30 min and analyzed, for determination concentration of Creatinine, urea, FSH and LH level.

Statistical Analysis:

A Student's t-test was used. The data are presented as means \pm S.E. and statistically

analyzed using SPSS (version 14). Significance was set at the level of ($P \leq 0.05$).

RESULTS

The effect Taxol on hematological parameters of men exposed are presented in table (1), the results showed a significant decrease ($P \leq 0.05$) in red blood cell count

(RBC), packed cell volume (PCV), white blood cell (WBC) in second groups compared with the control group.

Table (1): Effect of Taxol on some hematological parameters of men

| Parameters groups | RBC $10^6/\text{mm}^3$ | HB % | PCV % | WBC $10^3/\text{mm}^3$ |
|------------------------------|---------------------------|--------------------|-------------------|---------------------------|
| First group (control) | 5.19 ± 0.30^a | 12.08 ± 0.32^a | 42.0 ± 0.9^a | 8.3 ± 0.23^a |
| Second group Treatment Taxol | 3.40 ± 0.12^b | 9.5 ± 0.34^b | 29.7 ± 0.99^b | 3.8 ± 0.26^b |
| LSD | 1.15 | 0.26 | 3.38 | 0.15 |

❖ Values are means \pm S.E.

□□ Different letters refer to a significant difference ($p \leq 0.05$).

□□ Same letters refer to non a significant differences ($p \leq 0.05$).

The effect Taxol on hematological parameters of men exposed are presented in table (2), the results showed a significant increase ($P \leq 0.05$) in Creatinine concentration second group compared with

the control group. Also, the result showed a significant decrease urea concentration in first group compared with the control groups.

Table (2): Effect of Taxol on the level of serum urea and Creatinine in men

| Parameters groups | Creatinine mg/dL | Urea mg/dL |
|------------------------------|---------------------|-------------------|
| First group (control) | 0.74 ± 0.05^a | 4.08 ± 0.2^b |
| Second group Treatment Taxol | 1.50 ± 0.05^b | 6.22 ± 0.14^a |
| LSD | 0.006 | 0.06 |

❖ Values are means \pm S.E.

□□ Different letters refer to a significant difference ($p \leq 0.05$).

□□ Same letters refer to non a significant differences ($p \geq 0.05$).

The effect Taxol on hematological parameters of men exposed are presented in table (3), the results showed a significant decrease ($P \leq 0.05$) in luting hormone (LH) and testosterone

hormone in second groups compared with the control group. The results showed non-significant differences in Follicle stimulation hormone (FSH) in control and second groups

Table (3) Effect of Taxol on sex hormones of men

| Parameters groups | FSH U/L | LH U/L | TESTO U/L |
|---------------------------------|-------------------|--------------------|-------------------|
| First group (control) | 13.7 ± 1.64^a | 13.05 ± 0.92^a | 10.2 ± 0.70^a |
| Second group Treatment Taxol | 9.31 ± 2.00^a | 8.6 ± 1.21^b | 5.85 ± 0.4^b |
| LSD | 8.07 | 2.79 | 0.78 |

❖ Values are means \pm S.E.

□□ Different letters refer to a significant difference ($p \leq 0.05$).

□□ Same letters refer to non a significant differences ($p \geq 0.05$).

DISCUSSION

The results of the current study showed a reduction in blood parameters of mean treated with Taxol, Taxol have an impact on blood components. The decrease of those blood parameters may be attributed to effect of Taxol on the membranes of blood cells, the blood ones, as other cells, are surrounded by plasma membranes made of a high rate of phospholipids and the phosphatidyl choline is the most important phospholipids^[8].

A major reasons for the low standards of blood in the male is the toxicity of the drug Taxol acute on bone marrow cells generated blood cells through the occurrence of pharmacological suppression of these cells^[9],

Because The rise level of the hormone erythropoietin secreted from the kidney cell response of feed feedback in male serum treatment drug Taxol, and clear evidence of low blood standards, for his role in stimulating the bone marrow to produce blood cells to compensate for the shortage in the number of RBC and WBC in the peripheral blood^[10].

Chemotherapy drugs can tentatively affect the number of healthy blood cells within the body. Blood cells (RBC, WBC) are released by the bone marrow (the spongy material found in the hollow part of bones) to alteration those which are naturally used up within the body. Chemotherapy reduces the ability of the bone

marrow to make these cells. However, there is a reducing number of WBCs and the apparition cases of interior bleeding. Taxol attacks proteins found on surface cell membrane and as a result of this the cell dies^[11].

In the present study showed in chemical treatments the rise in serum Creatinine levels cause a decrease in Glomerular filtration rate (GFR), and since the drug Taxol causing affected and degenerated in the composition of the glomerulus, May be because significant increase in the Creatinine level of this effect, and anti-cancer drugs affect different places of Nephron, which is the basic unit functional and structural kidney especially the glomeruli and tubules proximal and distal, and cause dysfunction of the glomeruli reduction of glomerular filtration resulting in an increase in the level of Creatinine^[12].

In this study it revealed significant rise in levels of urea in the blood serum this refers

to an imbalance in renal function such as increased vascular permeability^[13].

The present study showed significant decrease in LH hormone level, an influence directly and clearly significant decrease happening in the level of testosterone, as hormone LH stimulates cells Leydig on the synthesis and secretion of the hormone, Many of chemical treatments cause histologically and functionally damage in cells Leydig and influential so negatively in the production of the hormone testosterone^[14].

In the present study showed in decreases in LH hormone by chemotherapy Taxol by affecting hypothalamus-pituitary axon and this leads to changes in gonadotropin releasing hormone (GnRH) secreted by the hypothalamus, Also causes this treatment the reduction in the number of LH receptors in cells Leydig in the testes, resulting in a decrease in LH to stimulate cells Leydig for the synthesis of testosterone hormone^[15].

REFERENCES

- 1- Xiong,Q.; Yang, Y.; Zhao, and Wang, Y.(2013).Diversity of endophytic fungi and screening of fungal paclitaxel producer from anglojap yew *Taxus x media* . BMC Micro . 13(71).
- 2- Wang, H.; Yang, C .; Zhao, H. and Yang,Z. (2012). The inhibition of tumor growth and metastasis by self –assembled Nano fibers of taxol . J. Biotech. V : 33. 5848 _ 5853.
- 3- Ziaja-Soltys, M. &Rzymowska, J. (2011). The determination of changes in the expression of genes for selected specific transcriptional factors in *in vitro* ductal breast cancer cells under the influence of Paclitaxel. Biol Lett 16: 610. doi:10.2478/s11658-011-0026-8.
- 4- Moisio, Anu-Liisa. (2002). Pre disposing and modifying genes in hereditary colorectal cancer syndromes. *Haartmaninkatu 8,on 8th of March 2002, at 12 noon..*
- 5- Chlebowski, R. T.; Blackburn, G. L. and Thomson, C. A. (2006). Dietary fat reduction and breast cancer outcome : interim efficacy results from the womens Intervention Nutrition study . J . Natl . cancer inst . 98(24) : 1767-76 .
- 6- Spratlin, J. and Sawyer, M. B. (2007) . pharmacogenetics of paclitaxel metabolism . Critical Review in Oncol / Hema. 61 : 222 -229 .
- 7- Muhammad, S. K.; Ingrid, J. F.; Elisabeth, Å. L.; Curt, P. (2009). The Impact of CYP3A5*3 and CYP2C8-HapC on Paclitaxel/Carboplatin-Induced Myelosuppression in Patients with Ovarian Cancer. Journal of

- Pharmaceutical Sciences, (100), 10, 4205-4209.
- 8- Unknown. (2005) . Chemotherapy : Adapted from , [http : www , dfw . Neronetwork . com ./ pant , 6 . htm # 43](http://www.dfnetwork.com/pant/6.htm#43).
- 9- Goidwein , J. (2001) . chemotherapy , for patient introductory (WWW documenty).
- 11- Samule, B. a, b.; Jacaus, B. a , b.;micheal, C. and Mackey. (2004). Bifurcations In a whit – blood – cell production model. *Comptes Rendus. Biologies*, 327: 201-210.
- 10- Skretkiewicz, J.; sekulska, K.; Danilewicz, M.; Wagrowska, D. and Polakowski, P. (1996). Effect of some anticancer drugs and combined chemotherapy on renal toxicity. *Biol Signals*. Jan-Feb;5(1):51-8.
- 12- Malik, S.; Cusido, R. M.; Mirjalili, M. H.; Moyan, E.; Palazon, J. and Bonfil, M. (2011). Production of the anticancer drug taxol in *Taxusbaccata* suspension Culture: Areview. *Process Biochem*. 46: 23 – 34.
- 13- ulkowska-ziaja, k.; Muszynnska,B. and Konska, G. (2005) . Biologically active compounds of fungal origin displaying antitumor activity. *Actapolon. Pharma – Drug Research* 62 : 153 – 160 .
- 14- Yuan, H. (1998). Studies on the chemistry of paditaxel. P. H. D. Blank. Sloury Virginia, USA, PP. 167.
- 15- Ballatori, E. and Rolia, F. (2003) . Impact of Nausea and vomiting on Quality of life in cancer patient during chemotherapy. *Health Qual Life Outcomes*. 17; 1:46.

دراسة التأثير الفسيولوجي لدواء الباكليتاكسيل المضاد للسرطان في الرجال

تاريخ القبول : 2016/11/2

تاريخ الاستلام: 2016/7/12

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الخلاصة

تهدف الدراسة الحالية لمعرفة تأثير علاج التاكسول على المعايير الدموية والكيموحيوية والهرمونات الجنسية للذكور. اذ قسمت الدراسة الحالية الى مجموعتين كل مجموعة تتكون من (33):- المجموعة الاولى (مجموعة السيطرة) والمجموعة الثانية هي لذكور مصابين بالسرطان والمعالجين بعلاج التاكسول. اوضحت نتائج الدراسة الحالية انخفاضاً معنوياً عند مستوى احتمال ($P < 0.05$) في عدد كريات الدم الحمر وحجم الدم المضغوط والعدد الكلي لكريات الدم البيض والهرمون اللوتيني في المجموعة الثانية مقارنة مع مجموعة السيطرة. كذلك اظهرت النتائج ارتفاعاً معنوياً في مستوى الكرياتينين واليوريا في المجموعة الثانية مقارنة مع مجموعة السيطرة، بينما لم يكن هناك اي فرقاً معنوياً في مستوى الهرمون المحفز للجريبات بكلا المجموعتين.

الكلمات المفتاحية : التاكسول ، الدم المضغوط ، والهرمون اللوتيني ، الهرمون المحفز للجريبات

Physiology Classification QP 501-801