Effect of penicillin on uterus in mice

Muhammad - Baqir M-R. Fakhrildin and Dhuha Akram Ibrahim
High Institute for Infertility Diagnosis and Assisted Reproductive Technologies-Al-Nahrain University

Abstract:

Background:

Background: The reproductive failure is a significant public health concern. Although relatively little is known about factors affecting fertility, there is sufficient evidence to hypothesize that antibiotic may influence the fertility.

Objective:

This study was established to explore the individual impact of different doses of penicillin on some reproductive parameters.

Materials and Methods:

Forty adult female albino mice (12 -18 weeks) and weight (25- 28) gm divided into four groups. Control group (G1) was treated daily with normal saline, and other three groups that treated with different doses of penicillin G2 (2mg/kg/B.wt), G3 (3mg/kg/B.wt), G4 (4mg/kg/B.wt)for four cycles twice daily (IM) injection at proestrus phase and sacrificed at estrus phase. Parameters were assessed include, thickness of endometrium, length of epithelial cells, number and diameter of uterine gland using histological section and measurement by (motic image plus).

Results:

The results of this study demonstrate that there is significant decrease ($P<0.05$) in thickness of endometrium, height of epithelial cell, number and diameter of uterine glands of female mature mice after treatment with high doses (3mg/kg/B.wt), while, there is no significant decrease ($P>0.05$) after treatment with (2mg/kg/B.wt); (3mg/kg/B.wt) compare to control group.

Conclusion:

The result showed higher doses for long period of penicillin has impact of some reproductive parameters of mature female mice.

Key word: penicillin , reproduction , mice

Introduction

Fertility is the capacity of the women to conceive at the reproductive age , whereas, fecundity is the probability of achieving live birth in a single menstrual cycle[1].On the other hand, infertility is defined as the inability to become pregnant after 12 months of unprotected intercourse[2].The impact of lifestyle on reproductive performance may vary depending on individual etiology and circumstances. Lifestyle factors have had a dramatic impact on general health and the capacity to reproduce, including; age, weight, smoking, diet, exercise, psychological stress, caffeine consumption, alcohol consumption and exposure to environmental pollutants and antibiotics that have a role in fertility are included[3]. Antibiotic can be divided in to two groups:

1. Bactericidal drug: which kill bacteria with an efficiency of >99.9%.
2. Bacteriostatic drugs, which merely inhibit bacterial growth[4].

Antibacterial drug target interactions are predominantly fall into three classes: inhibition of DNA replication and repair,

inhibition of protein synthesis, and inhibition of cell-wall turnover[5]. The bactericidal antibiotic killing mechanisms are currently attributed to the class specific drug-target interactions[6];[7];[8];[9].

β- Lactam antibiotics are a broad class of antibiotics, consisting of all antibiotic agents that contains a β-lactam nucleus in their molecular structures. This includes penicillin, cephalosporin, monobactams, and carbapenems[10]. Most β-lactam antibiotics work by inhibiting cell wall biosynthesis in the bacterial organism and are the most widely used group of antibiotics[11]. Because the penicillins may have toxic effect in fertility, therefore, the present study was designated to investigate the effect of different doses of penicillin on the Histological changes in uterus of mice.

Materials and Methods

All experiments were performed on healthy mature females (BALB/C strain), their ages ranged between 8 -10 weeks with a body weight (B.wt.) ranged between 25 -28 g. Mice were obtained from the colony of the Animal House unit of the High Institute of Infertility Diagnosis and Assistant Reproductive Technology/Al-Nahrain University. Forty mature female mice were divided into major control (10 mice) and three treated groups. Treated groups were divided according to different doses of penicillin namely (2mg/kg/ B.wt, 3mg/kg/B.wt, and 4mg/kg/B.wt) for four cycles.

Preparation and administration of Procaine benzyl penicillin

Penicillin solution was prepared by dissolving completely of benzyl penicillin powder in 10 mL of normal saline to optian different doses of penicillin (2,3,4 mg/kg/B.wt.). Each dose administrated to a limited group of mice. The female mice were divided into 4 groups, one as control (injected with normal saline) and 3 treated groups (injected with different doses of penicillin). All females were intramuscular route of administration was used for treatment with penicillin 16 days period when the mice reach estrus cycle. After that each of them was sacrificed and the abdominal cavity was opened then uterus was taken out and the histological examination was done as described Bancroft and Stevens[12][13] to measure histological changes in uterus for each group.

Statistical analysis

Statistical analysis was performed by using SPSS (Statistical Package of Social Science; version 17). Crude data analysis was done using student's t-test so called paired sample t-test for tables with mean and standard error of mean (S.E.M.) to compare between pre-and post treatment for all groups. As well as, ANOVA test was applied to compare among mean groups of different penicillin concentration doses in the experimental study. Significance level was set at ($P<0.05$)[14].

Results

1. The effect of procaine benzyl penicillin on endometrial thickness

Figure (1) presented the result of endometrial thickness after 16 days of treatment for the control and treated groups. Non significant differences ($P>0.05$) in the endometrial thickness were assessed after 16 days treatment with low dose penicillin (2 mg/Kg/B.wt.) and (3 mg/Kg/B.wt.) when compared to the control group. Significant reduction ($P<0.05$) in the endometrial thickness were assessed after 16 days treatment with high doses penicillin (4mg/Kg/B.wt.) when compared to the control group. Furthermore, non significant differences ($P>0.05$) in the diameter of endometrium thickness were assessed after 16 days treatment among different groups treated with penicillin doses.

2. The effect of procaine benzyl penicillin in the number and diameter of uterine gland

Non significant differences ($P>0.05$) in the number of uterine glands were assessed after 16 days treatment with low dose penicillin (2 mg/Kg/B.wt.) and (3 mg/Kg/B.wt.) when compared to the control group. Significant decrease ($P<0.05$) in the number of uterine glands were assessed after 16 days treatment with high doses penicillin (4 mg/Kg/B.wt.) when compared to the control group. Also, non significant differences ($P>0.05$) in the number of uterine glands were assessed after 16 days of treatment with different penicillin doses as presented in the figure (2).

Non significant differences ($P>0.05$) in the diameter of uterine glands were assessed after 16 days treatment with low dose penicillin (2 mg/Kg/B.wt.) and (3 mg/Kg/B.wt.) when compared to the control group. However, significant decreased ($P<0.05$) in the diameter of uterine glands were assessed after 16 days treatment with high doses penicillin (4 mg/Kg/B.wt.) when compared to the control group. Also, non significant differences ($P>0.05$) in the diameter of uterine glands were assessed after 16 days of treatment with different penicillin doses as presented in the figure (3).

3. The effect of procaine benzyl penicillin on height of epithelial cell layer

Figure (4) showed the result of height of epithelial cell layer at 16 days treatment for control and treated groups. Non significant differences ($P>0.05$) in the height of epithelial cell layer were assessed after 16 day of treatment with low dose penicillin (2mg/Kg/B.wt.) and (3 mg/Kg/B.wt.) when compared to the control group. Significant decrease ($P<0.05$) in the height of epithelial cell layer were recorded after 16 day of treatment with high doses penicillin (4 mg/Kg/B.wt.) when compared to the control group.

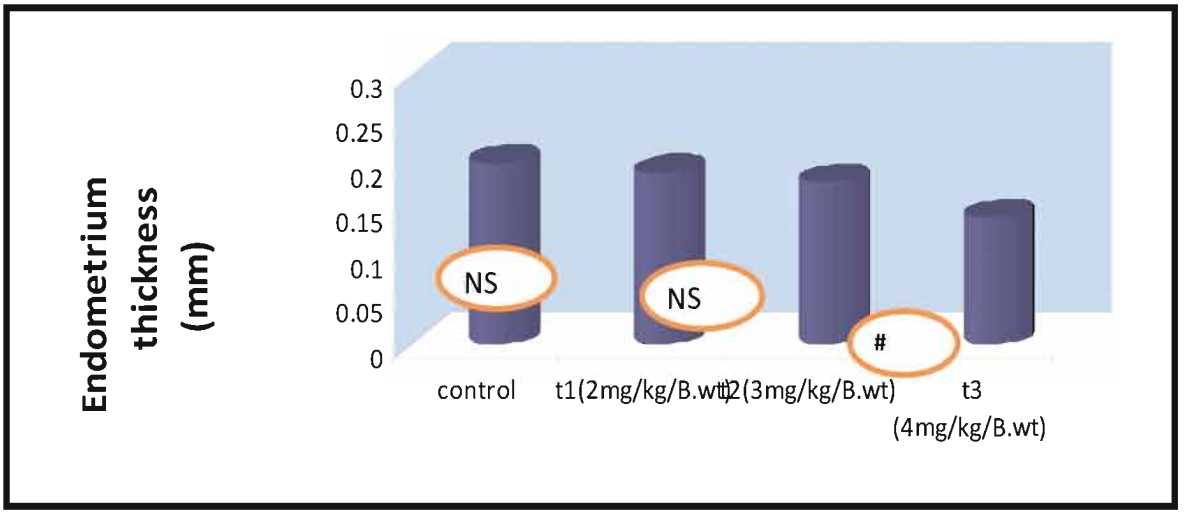

Figure (1): The effect of different doses of penicillin injected for 16 days on thickness of endometrium (mm) of mature female mice.

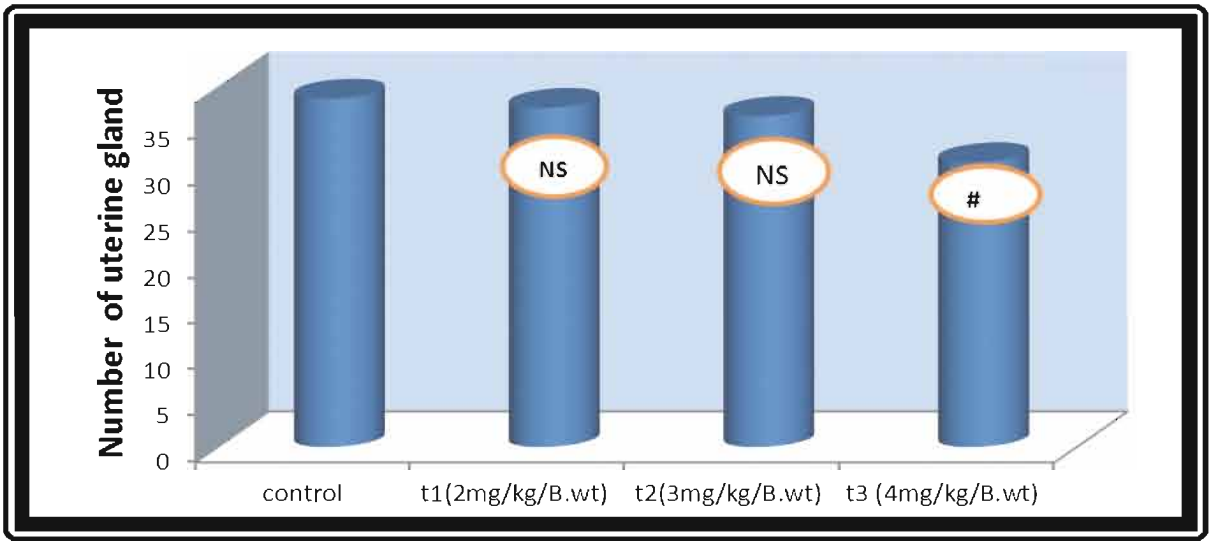

Figure (2): The effect of different doses of penicillin injected for 16 days on diameter of uterine glands of mature female mice.

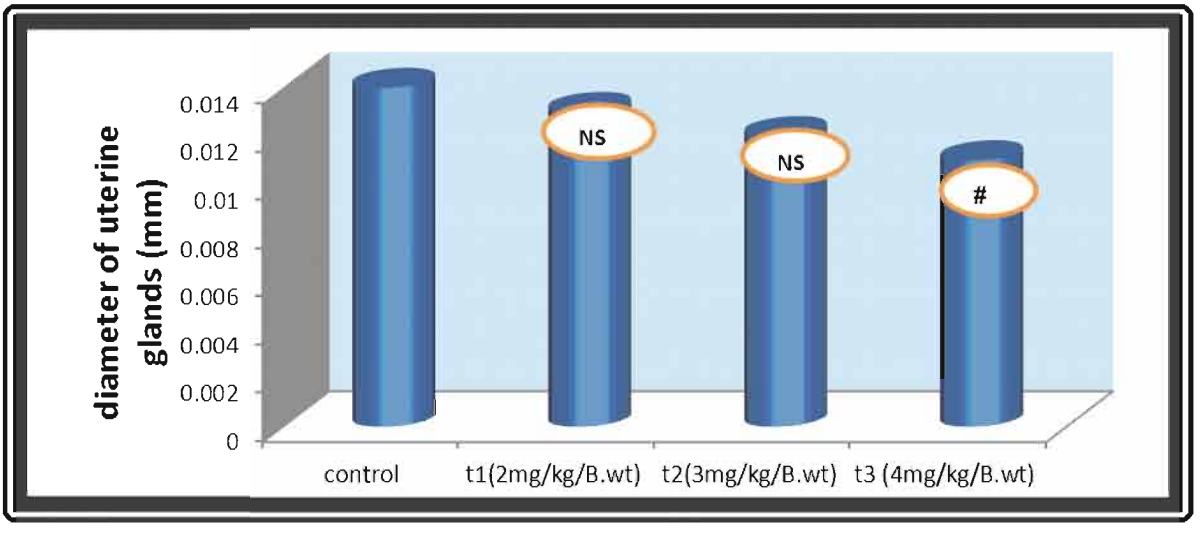

Figure (3): The effect of different doses of penicillin injected for 16 days on diameter of uterine glands of mature female mice.

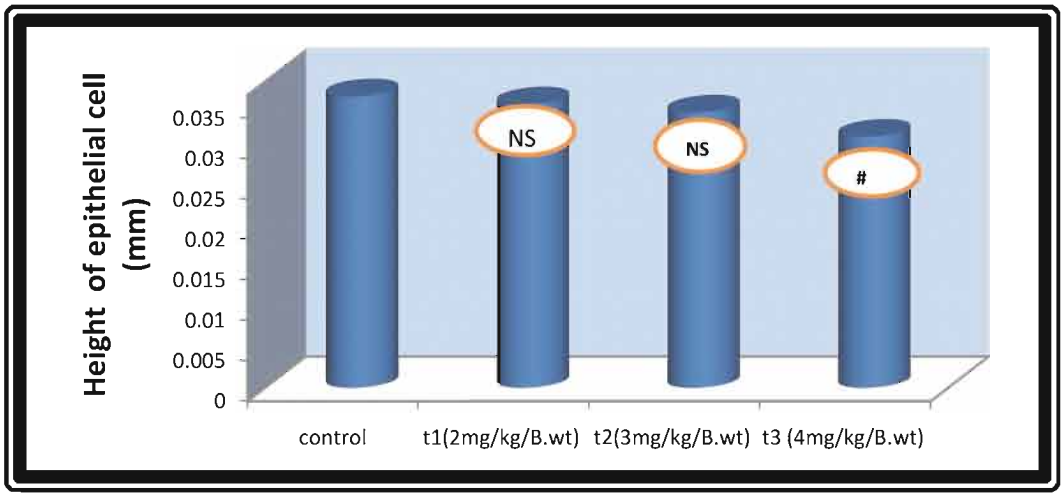

Figure (4): The effect of different doses of penicillin injected for 16 days on height of epithelial cell layer (mm) of mature female mice.
Ns: Non significant differences s (P>0.05).
≠: Significant decreased (P>0.05).

Discussion

The endometrium is the site of embryo implantation and its preparation for embryo reception is dependent on the estrogen and progesterone. These hormones cause some molecular and cellular events during uterine receptivity and the balance between them is important for cyclical changes of endometrium[15].

One major aspect of estrogen action on the uterus is the influence on proliferative processes. It is well known that estrogen strongly increases proliferative activity in all uterine tissues[16][17]. Another important result of (especially chronic) estrogen action on the uterus is morphogenetic alterations that include changes in the types of luminal and glandular epithelia, the number and shape of glands, the glandular to stromal ratio, and the morphology of epithelial cells[18].

The results of this study showed that there is a significant decrease (P0.05) in the thickness of endometrium, height of epithelial cell, number and diameter of uterine glands after administration of high dose penicillin (4mg/kg/B.wt), which may be attributed to the decrease in the levels of those ovarian sex hormones. Whereas, there is no significant decrease in these parameters after administration of (2mg/kg/B.wt.) and (3mg/kg/B.wt.) doses of penicillin, which may be due to no effect of penicillin as well as normal

References

1. Wood JW. Oxford Reviews of Reproductive Biology. Oxford University. NewYork.1989. Pp.2 -9.
2. Healy DL, Trounson AO and Andersen AN. Female infertility: causes and treatment. Lancet. 1994. Pp: 1539–1544.
3. Homan GF, Davies M and Norman R. The impact of lifestyle factors on reproductive performance in the general population and those undergoing infertility treatment. Human Reproduction Update. 2007; 13 (3): 209–223.
4. Pankey GA and Sabath LD. Clinical relevance of bacteriostatic versus bactericidal mechanisms of action in the treatment of Gram-positive bacterial infections. Clinical Infectious Diseases J.2004; 38: 864–870.
5. Walsh C. Molecular mechanisms that confer antibacterial drug resistance. Nature J.2000; 406:775–781.
6. Davis BD. Mechanism of bactericidal action of aminoglycosides Microbiology Review J.1987; 51: 341–350.
7. Drlica K and Zhao X. DNA gyrase, topoisomerase IV, and the quinolones. Microbiology Molicular Biolology Review J.1997; 61: 377–392.
8. Lewis K. Programmed death in bacteria. Microbiology Molecular Biology Review J .2000; 64: 503–514.
9. Tomasz A. The mechanism of the irreversible antimicrobial effects of penicillin: how the beta-lactam antibiotics kill and lyse bacteria. Annual ReviewMicrobiologyJ.1979; 33: 13–137.
10. Holten KB, Onusko EM. Appropriate prescribing of oral beta-lactam antibiotics. American Family Physician J.2000; 62(3): 611–20.
11. Elander RP. Industrial production of beta-lactam antibiotics. Applied microbiology and biotechnology J. 2003; 61 (5–6):385–392.
12. Bancroft JD and Stevens A. Tissue processing. In: Theory and practice of histology techniques. Bancroft JD. Editor. 2nd edition. Edinburgh: Churchill Livingstone; 1982.Pp.41- 60.
13. Bancroft JD and Stevens A. The Haematoxylin. In: Theory and practice of histology techniques. Stevens A .Editor. 2nd edition. Churchill Livingstone: Edinburgh. 1982. Pp.109 -121.
14. Sorlie DG. Medical biostatic and epidemiology: examination and broad review.1st edition. Aplleton and lang Norwalk. Editors. Connecticut. 1995. Pp. 47- 88.
15. Fatemeh,Mojdehs, Mehdi M., *et al*. The changes in morphology and morph metrical indices of endometrium of ovariectomized mice in response to exogenous ovarian hormones. Iranian Journal of Reproductive Medicine.2008; 6(3): 125- 131.
16. Couse JF and Korach KS. Estrogen receptor null mice: what have we learned and where will they lead us?. Endocrine Reviews J. 1999; 20: 358–417.
17. Zhang Z, Laping J, Glasser S, *et al*. Mediators of estradiol-stimulated mitosis in the rat uterine luminal epithelium. Endocrinology J.1998; 139: 961–966.
18. Silverberg SG. Problems in the differential diagnosis of endometrial hyperplasia and carcinoma. Modern Pathology J. 2000; 13:309–327.