Do oxytetracycline and PGE1 have protective effect against harmful effects of hysterosalpingography on endometrium? An experimental study

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INTRODUCTION

- Radiation initiates synthesis of reactive oxygen molecules (ROS) in cells and tissues.
- ROS causes damage in DNA and membrane lipids, which is called lipid peroxidation.

Taysi et al. 2002

 Lipid peroxidation stimulates collagen synthesis in cell cultures and causes fibrosis in tissues

Lee et al. 1995

- Cells counteract against ROS with
- ✓ antioxidant enzyme systems → superoxide dismutase, glutathione peroxidase
- \checkmark antioxidant hormones \rightarrow melatonine
- ✓ antioxidant drugs → PGE-1, Vitamin E, Vitamin C, Tetracycline

Sapmaz et al. 2003, Sapmaz et al. 2002

 PGE1 is a vasodilatator prostaglandin which decreases oxygen consumption and superoxide anion production in damaged tissues. PGE1 arrests apoptosis induction

Vargas et al. 1995, Olthoff et al. 1991, Kawamura et al. 1997

Tetracyclines decreases apoptosis and represses ROS production.

Orsucci et al. 2009

- PCNA is a reliable marker for detection of endometrial cell proliferation.
- The expression of PCNA in the endometrium of the rat has been shown to increase from diestrus to pro-estrus and disappear at estrus.
- In women, the PCNA index of the glandular epithelium has been reported to increase during the follicular phase and to decrease during the luteal phase.

Chatdarong et al. 2005

Goal: To investigate whether oxytetracycline and PGE1 have protective potential for prevention of degenerative effects of hysterosalpingography on endometrium.

Materials and Methods

- Wistar Albino female, 12-14 weeks old, 190-220 g, adult, 28 rats were randomly divided into four groups.
- -Group1 (n=7): only laparotomy
- -Group2 (n=7): laparotomy + 0.1 mL Lipiodol into both of uterine horns + X ray application
- -Group3 (n=7): laparotomy+intraperitoneal 10 mg/kg oxytetracycline +15 minutes later 0.1 mL Lipiodol into both of uterine horns
- -Group4 (n=7):laparotomy+intraperitoneal 200 mcg/kg PGE1 + 15 minutes later 0.1 mL Lipiodol into both of uterine horns.

- After these procedures, whole body radiation were applicated 3 times with 2 minutes intervals in group 2,3 and 4. And closure of abdomen was done.
- Three hours later, relaparotomy and bilateral uterine horn excision were performed on all of the rats.
- Uterine horns were fixed with 10% formaldehyde.
- Cytoplasmic immune staining and TUNEL staining were scored as follows: 0=absence, 1=minimal, 2=mild and 3= severe.
- Statistical analysis were done with Kruskal Wallis test and Mann Whitney U test.

RESULTS

- Congestion, displasia and apoptosis scores in endometrial glands of group2 were significantly <u>higher</u> than of group1,
- but PCNA activation of group2 was significantly <u>lower</u> than of group1.



• Uterine horns on HSG

- Congestion and displasia scores of group 3 were significantly <u>higher</u> than of group1
- apoptosis scores of group 1 and 3 were <u>similar</u>
- PCNA immune reactivity was <u>low</u> in group 3.



• Distribution of contrast in peritoneal cavity

- Epithelial degeneration score of group 4 was significantly <u>higher</u> than of group1, but there was <u>no difference</u> for scores of congestion and apoptosis.
- PCNA reactivity of group 4 was lower than of group1.

HISTOLOGICAL FINDINGS

(Masson's trichrome staining)



G1; normal uterine tissue,
 black arrow= epithelium



 G2; increased epithelial degeneration and congestion (black arrow); red arrow= congestion





 G3; epithelial degeneration and congestion are similar with G2.

Black arrow= epithelium,

Red arrow= congestion.

• G4; decreased congestion, but epithelial degeneration is going on.

Black arrow= epithelium

IMMUNOHISTOCHEMICAL FINDINGS





- G1; PCNA staining with
 +3 intensity
- G2: severely decreased PCNA staining
- +1 intensity





• G3; decreased PCNA staining +1 intensity

• G4; decreased PCNA stainig +1 intensity

TUNEL FINDINGS





• G1; Tunel staining intensity is +1

• G2; increased Tunel staining +3 intensity





• G3; decreased tunel staining +1 intensity

• G4; decreased tunel staining +1 intensity

CONCLUSION

 Oxytetracycline and PGE1 were insufficient for prevention of endometrial degenerative effects of hysterosalpingography.

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