Abstract

BACKGROUND: Unpredictable endometrial bleeding disturbances due to depot-medroxyprogesterone acetate (DMPA) may be caused by endometrial matrix metalloproteinase (MMP) release and decreased tissue inhibitors (TIMP). Doxycycline is a potent inhibitor of MMP. This study aimed to study the effect of doxycycline on DMPA induced endometrial breakthrough bleeding. METHODS: Two hundred and fifty DMPA users who had frequent or prolonged endometrial bleeding were randomized into 5 groups. Group A was taken 50 mg. of doxycycline per day for 28 days. Group B was taken 200 mg. of doxycycline per day for 28 days. Group C was taken 50 mg. of doxycycline per day for 7 days and placebo for 21 days. Group D was taken 200 mg. of doxycycline per day for 7 days and placebo for 21 days. Group E was taken only placebo for 28 days. Numbers of bleeding days before and after treatment were compared. Endometrial biopsies were collected before and after treatment for immunohistochemical study of MMP-9, TIMP-1, TIMP-2 and TIMP-3 expression. RESULTS: 250 DMPA users were recruited, 5 DMPA users were loss follow up and 133 DMPA users had adequate endometrial tissue for immunohistochemical study. The number of bleeding days during 28 days of treatment and 30 days after treatment were

significantly decreased after treatment. The endometrial MMP-9 expression was significantly decreased and TIMP-3 expression was significantly increased after treatment. CONCLUSIONS: Doxycycline decreased the numbers of bleeding days, decreased MMP-9 expression and increased TIMP-3 expression in bleeding DMPA users. Further study should be required to study longer duration, more than 28 days, of doxycycline for treatment of endometrial bleeding in DMPA users.

Keywords: depot medroxyprogesterone acetate/ DMPA/ endometrial bleeding/ matrix metalloproteinase/ doxycycline.