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Vaginal administration of oral contraceptive pill affects on vaginal cytology - a pilot study

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Objective : *To determine the effect of vaginal administration of oral contraceptive pill on vaginal cytohormonal change (onset, duration and maturation index)*

Design : *Prospective study*

Method : *Single dose of one tablet of low dose combine oral contraceptive pill (Ethinyl estradiol 30 ugm and levonorgestel 250 ugm) was applied by vaginal route in a surgical menopause 50-year-old woman. Vaginal cytohormonal assessment for maturation index by Papanicolaou technique was performed daily until 17 days after using intravaginal pill.*

Result : *The maturation index (MI) was shift to the right from 3/91/6 at the beginning to 0/85/15 on 2 days after intravaginal pill. The peak of effect was on 9 days which MI was 0/48/52. On 17 days, the MI was 0/70/30*

Conclusion : *Vaginal administration of oral contraceptive pill will affect on vaginal cytohormonal change on 2 days (onset) and persist on more than 17 days (duration). The maximal effect is on 9 day after treatment. This method may be another effective and cheaper one for the treatment of menopausal urogenital symptom. Further study to compare with estrogen cream will be published later.*

Key word : *Vaginal cytology and intravaginal oral contraceptive pill.*

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ประเสริฐ ตรีวิจิตรศิลป์, สุธนา ชมพูทวีป, กิจประมุข ตันตยาภรณ์, ทรรศนีย์ บุญยัษฐิติ.
ผลของการเปลี่ยนแปลงทางเซลล์วิทยาของเยื่อบุช่องคลอด ภายใต้หลังจากการใช้ยาเม็ด
คุมกำเนิดสอดช่องคลอด. จุฬาลงกรณ์เวชสาร 2540 ก.ย; 41(9): 659-64

วัตถุประสงค์ : เพื่อศึกษาการเปลี่ยนแปลงทางเซลล์วิทยาของเยื่อบุช่องคลอด ภายใต้
หลังจากการใช้ยาคุมกำเนิดสอดทางช่องคลอด

สถานที่ทำการศึกษา : ภาควิชาสูติศาสตร์-นรีเวชวิทยา โรงพยาบาลจุฬาลงกรณ์

รูปแบบการศึกษา : การศึกษาไปข้างหน้า

วิธีการศึกษา : ศึกษาการเปลี่ยนแปลงทางเซลล์วิทยาของเยื่อบุช่องคลอดในสตรีวัยหมด
ระดู 1 ราย โดยตรวจก่อนใช้ยาเม็ดคุมกำเนิดที่มีส่วนประกอบของ ethinyl
estradiol 30 ไมโครกรัม และ levenogestrel 250 ไมโครกรัม และตรวจ
ติดตามทุกวัน ภายใต้หลังจากสอดยาเม็ดคุมกำเนิดเพียง 1 เม็ดเข้าไปใน
ช่องคลอดครั้งเดียวจนครบ 17 วัน

ผลการศึกษา : พบว่า Maturation index (MI) จะเปลี่ยนแปลงไปทางด้านขวาจาก
3/91/6 ในวันก่อนใช้ยาเป็น 0/85/15 ในวันที่ 2 ของการใช้ยาผล
ของยาจะสูงสุด วันที่ 9 ซึ่งค่า MI เท่ากับ 0/48/52 และในวันที่ 17
หลังการใช้ยา ค่า MI ยังคงอยู่ทางด้านขวาเป็น 0/70/30

สรุปผล : การใช้ยาเม็ดคุมกำเนิดสอดทางช่องคลอด จะเริ่มมีผลในวันที่ 2
ภายใต้ การใช้ยา และจะคงอยู่นานมากกว่า 17 วัน หลังการใช้ยา
โดยจะมีผลมากที่สุดในวันที่ 9 หลังใช้ยา วิธีการนี้อาจนำมาใช้รักษา
ภาวะอาการทางระบบสืบสาวะ และอวัยวะสืบพันธุ์สตรีที่เป็นผลจาก
ภาวะขาดฮอร์โมนเพศ โดยน่าจะได้ผลดีและราคาถูกลง

In menopausal women, the prevalence of urogenital symptoms such as vaginal dryness, burning, itching, dyspareunia, dysuria and urinary frequency is high, but few of them receive adequate therapy.⁽¹⁾ All of these symptoms are associated with estrogen deficiency of urethral and vaginal epithelium where estrogen receptors have been clearly demonstrated.⁽²⁾ Vaginally administered estrogens such as via cream and the vaginal ring, and which have the advantage of avoiding the effects of the first passing through the liver as in oral estrogen, have been widely used for the treatment of these symptoms.⁽³⁻⁵⁾ However, Coutinho et al reported the efficacy and acceptability in contraception of vaginal administration of oral contraceptive pills.⁽⁶⁻⁹⁾ These pills, which are much cheaper than estrogen creams and the vaginal ring, may be benefit in the treatment of menopausal urogenital symptoms. This study was designed to determine the effect of a vaginally administered oral contraceptive pill on vaginal cyto hormonal change (onset, duration and shift of maturation index) in order to consider a continuous dosage to be studied and compared with estrogen cream.

Methods

A surgical menopausal woman, 50-year-old, was assessed by history, physical examination and laboratory tests to identify any contra-indications for estrogen treatment. These included hormone dependent cancer, liver disease or thromboembolic disorders. She had history of an abdominal hysterectomy with bilateral salpingo-oophorectomy due to myoma uteri 10 years prior without any further hormonal

replacement therapy. After giving her informed consent, a vaginal cyto hormonal specimen was taken and she was then intravaginally administered one tablet of an oral contraceptive low dose combined pill containing 250 micrograms of levonorgestrel and 30 micrograms of ethinyl estradiol. The vaginal cyto hormonal assessment was done daily each working day for 2 weeks (9 times), and at 17 days after administering the pill.

The vaginal cyto hormonal specimen was taken from the upper one third portion of the left lateral vaginal wall. The smears were stained according to the Papanicolaou technique and subsequently evaluated by randomized counting and recording a total 300 of parabasal, intermediate and superficial epithelial cells. The results were expressed in terms of the maturation index.^(10,11)

Results

The vaginal cytology before treatment (Do) and on 2, 9 and 17 days after vaginally administering the combined pill (D2, D9, D17) are displayed figures 1-4, respectively. Initially, the intermediated cells were predominant with scant superficial and parabasal cells (Figure 1). After the second day the superficial cells increased proliferation and the parabasal cells disappeared (Figure 2). The maximal effect was achieved after the ninth day of treatment when the superficial and intermediated cells were about equally predominant (Figure 3). On day 17, the vaginal cyto hormonal change was still maintained with predominant intermediate cells and some superficial cells, but no parabasal cells. (Figure 4).



Figure 1. Before treatment (D_0) shows intermediate cells and amorphous dirty background on slides. Scanty superficial cell is seen.



Figure 2. Two days after administration intravaginal pill (D_2) shows more superficial cells (pyknotic nuclei and polyhedral cells).

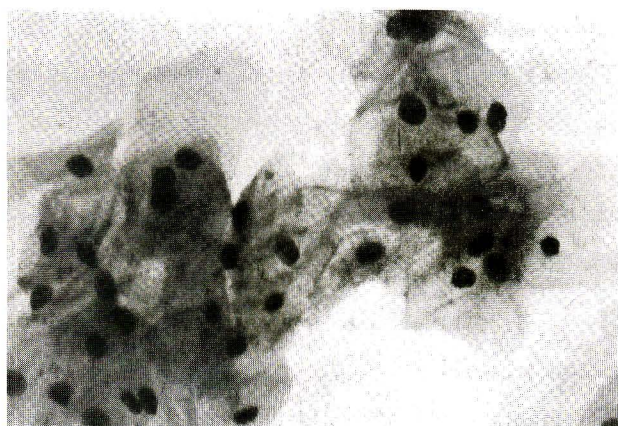


Figure 3. Nine days after treatment (D_9) show approximately equal amount of superficial cells and intermediate cells with clean background.

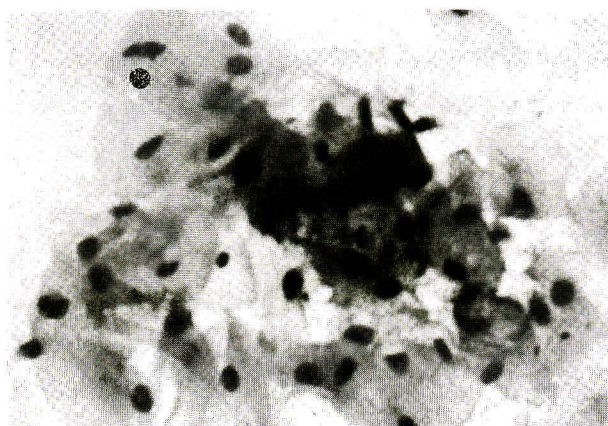


Figure 4. Seventeen days after treatment (D_{17}) shows predominantly intermediate cells, some superficial cells and rather amorphous dirty background.

A summary chart of the maturation index (MI) is shown in Figure 5. It reveals that the MI begins to shift to the right from 3/91/6 at the beginning to 0/85/15 on day 2 after administration of the

intravaginal pill. The peak effect was on day 9 when the MI was 0/48/52. On day 17 the MI was 0/70/30 with superficial cells present in two-third of the cells in the slides.

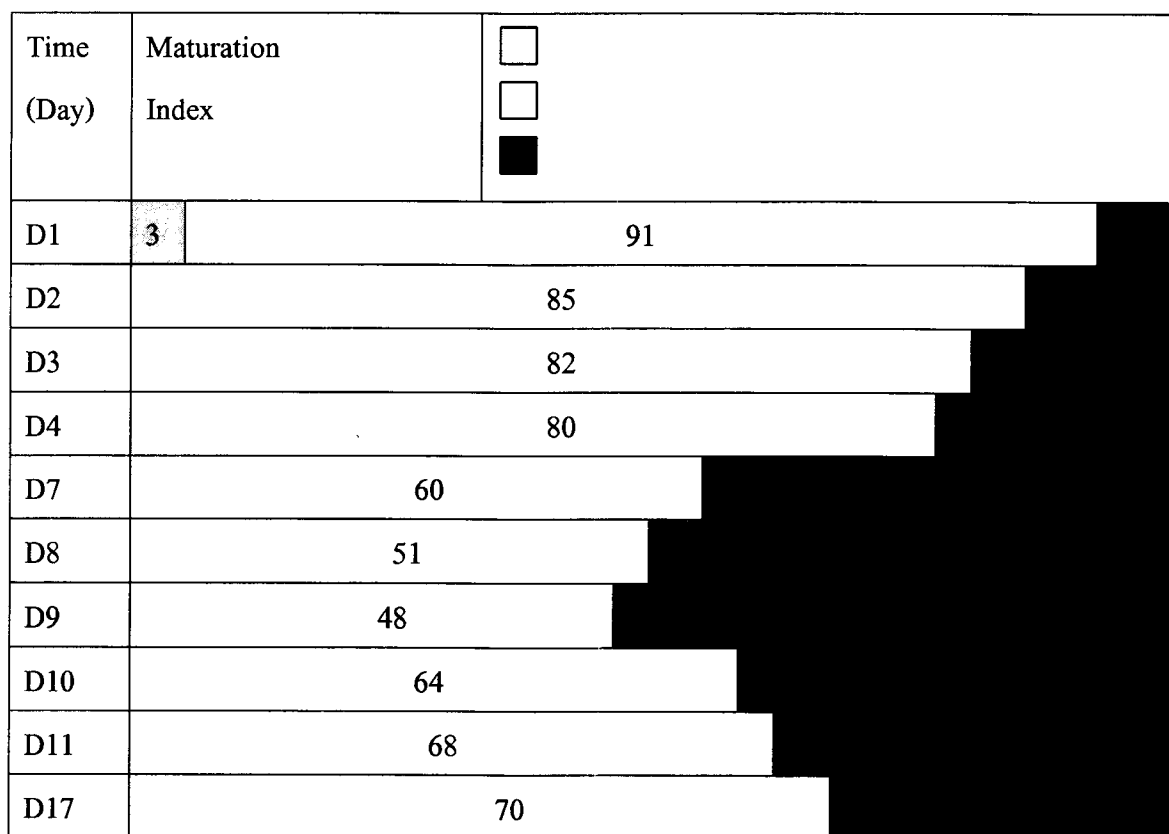


Figure 5. Maturation index (percentage of parabasal, intermediate and superficial cells) in vaginal smears of the menopausal woman before (D0) and 2-17 days after intravaginally administration of the combined pill (D2-D17).

Discussion

Urogenital symptoms are a comparatively late manifestation of estrogen deficiency in menopausal women aged around 60-65 years who are not prepared to accept withdrawal bleeding. In these cases, the vaginal and urethral mucosa a highly sensitive to endogenous and exogenous estrogens and only very low doses are required to promote proliferations.⁽¹²⁾ It has previously been reported that 7-50 micrograms of estradiol (E2) per day in a vaginal ring or pessary is effective for the treatment of menopausal urogenital symptoms and without any systemic metabolic side effects.^(12,13) Also, the vaginal administration of combined contraceptive pills is claimed to be as acceptable and efficacious as the oral route.⁽⁹⁾ This intravaginal combined contra-

ceptive pill, which is cheaper than the vaginal ring and pessary, may be a more effective method for the treatment of menopausal urogenital symptoms. In this study, single dose of a low -dose combined pill containing 250 micrograms of levonogestrel and only 30 micrograms of ethinyl estradiol was administered intravaginally and shown to induce significant proliferation and maturation of vaginal epithelium as expressed in term of the maturation index (MI).

The onset of the effect of intravaginal contraceptive pills is only 2 days when the MI shifting from 3/91/6 to 0/85/15. The peak effect is on day 9 of treatment when superficial cells become predominant in the vaginal smear. The effect was maintained thereafter throughout the 17 day after treatment period, and we can conclude that the duration may persist for more than 17 days. This means that intravaginal administration of the contraceptive pill

can be used once per 1-2 week.

In conclusion, the onset and duration of the effect of an intravaginal contraceptive pill on vaginal epithelium is only 2 days and more than 17 days, respectively. The results of this study indicate that this method may be advocated for the alleviation of urogenital symptoms in post-menopausal women. However, this method must still be compared to estrogen cream for reasons of cost, benefit and efficacy in the treatment of these symptoms. This further study will be conducted and later published.

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