PROGESTERONE CHALLENGE TEST IN SCREENING ASYMPTOMATIC POSTMENOPAUSAL WOMEN FOR CANCER ENDOMETRIUM

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SUMMARY

The search is on for a sensitive and convenient screening test for Cancer Endometrium (Ca Endom.) in asymptomatic Post Menopausal Women. Adenomatous hyperplasia is a precursor of Ca. Endom. The Progesterone Challenge test (P.C.T.) (the presence or absence of withdrawal bleeding after medroxy progesterone acetate, 10 mg. twice daily orally for 10 days) was carried out in 70 asymptomatic, post-menopausal women, and in 25 patients with known adenomatous hyperplasia (AH) of the endometrium; and correlated with the endometrial histology. The PCT was positive in all patients with AH (100% sensitivity). It was positive in 4/70 (5.7%) post-menopausal women of whom, two (2/4) had AH (50% specificity). None of the patients with negative PCT (66/66) had AH i.e. 100% reliability of negative PCT. The PCT is a simple, in-expensive, safe and reliable test that can be used to screen asymptomatic post-menopausal women for cancer endometrium. The PCT can identify a high-risk group who need endometrial sampling to detect adenomatous hyperplasia and early endometrial cancer. A negative PCT would also abviate the need for endometrial sampling prior to hormone replacement therapy.

INTRODUCTION

Endometrial Cancer ranks as the second most common invasive genital tract malignancy and occurs most commonly in menopausal women (Davies et al 1981). Twelve (12%) adenomatous hyperplasia (A.H.) and 30% atypical

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hyperplasia progress to Ca. Endom. in 10 years. AH was found to be present in 10% asymptomatic perimenopausal women. Adenomatous hyperplasia may be symptomatic, leading to abnormal uterine bleeding to Ca. Endom. (Simsen et al 1981). Currently, there is no accepted method of screening post-menopausal women for Ca-Endom. or adenomatous hyperplasia. Vaginal Cytology identifies only half the cases and is a more time consuming method necessitating careful screening. The Novak currette and the Vabra aspirator which have a 90% and 100% diagositic accuracy respectively are not applicable as a screening procedure both from cost and patient acceptance view points (Hofmeister, 1974). Thus, the search is on for a convenient, simple, efficient method of screening and identifying women with AH, so that endometrial sampling could be used in a more selective diagnostic manner. Several authors (Hanna et al 1983; Toppozada et al 1988), have tried the Progesterone Challenge Test (PCT) as a screening test for Ca. Endomet. Our prospective study was designed to study endometrial histology of asymptomatic post-menopausal women and correlate with (PCT) result, and to test the possibility, reliability and usefulness of the PCT as a screening procedure for asymptomatic post-menopausal women for Cancer Endometrium.

MATERIAL & METHODS

Seventy asymptomic Post-Menopausal patients with intact uterus, no history of Post-menopausal bleeding and not currently on any estrogen or progesterone therapy, were studied. A thorough physical examination with note of obesity was done. Per vaginal examination to note cervix, size of uterus & ovaries was done. Blood sugar was tested and Pap smear was taken to rule out malignancy. The patients then underwent endometrial aspiration, (E.A.) and the tissues were submitted for histopathological examination (HPE). The patients were warned of slight spotting for 2-3 days after the biopsy. After 4 weeks the Progesterone Challenge Test (PCT) was done. The patients were given 10 mgm oral medroxy-progesterone acetate, twice daily for 10 days. They were called after another 10 days to note presence or absence of withdrawal bleeding.

The second group, consisting of 25 symptomatic perimenopausal women with endometrial hyperplasia on E.A. also had the PCT.

The result of PCT was correlated with the endometrial histopathology.

RESULTS & OBSERVATIONS

All 25 women with adenomatous hyperplasia had withdrawal bleeding after the progesterone challenge test. Thus the sensitivity of PCT in cases of AH is 100%.

In the 70 post-menopausal women, the Vaginal cytology was found to be atrophic in 48 cases, inflammatory in 18 cases and scanty in 4 cases.

Four patients had withdrawal bleeding with progesterone (5.7% +ve PCT). In the 66 pts who had no W/B to PCT (-ve PCT) the endometrial histopathology showed mucus or blood only in 19 cases, atrophic in 41 cases, proliferative in 6 cases.

Of the 4 patients who had W/B with the PCT (+ve PCT), 2 (50%) had AH, 1 had atrophic endometrium and 1 had irregular endometrium:

Case 1. Mrs. HD 50 years, menopause

- 5 years. P O+O, 45 kg. wt. no diabetes or hypertension. Uterus N/S Fx free, Pt. came with the complaint of hot flushes. Vaginal cytology was negative for cancer. E.A. showed adenomatous hyperplasia.

Case 2. Mrs. R. 50 yrs. P4+O, menopause 3 yrs. Pt. obese Wt. 70 kg. B.P. 140/90 mg. Ut. N/S, Fx-free, Vag. Cytology - ve for Cancer. E.A. Fragmented glands with bits of squamous epithelium.

Case 3. Mrs. S. 40 yrs. menopause 2 yrs. P 1+O. No hypertension or diabetes. Ut. small Fx-free. E.A. - atrophic endometrium.

Case 4. Mrs. K.D. 61 yrs. Menopause - 15 yrs. Proplapse uterus. E.A. - Adenomatous Hyperplasia.

The PCT was always +ve (100% sensitivity) in the presence of A.H. (27/27 - 2 unsuspected, asymptomatic Post-menopausal women and 25 symptomatic patients with known AH).

In asymptomatic post-menopausal women, a +ve PCT had 50% specificity (2/4) in diagnosing adenomatous hyperplasia of endometrium.

In patients with -ve PCT, the endometrium was normal in all cases (66/66), 100% reliability of a -ve PCT.

DISCUSSION

Early detection of Ca. Endom. has been the subject of continous research. As more is known about the natural history of endometrial neoplasia, it has been brought to light that the cancer does not develop suddenly from normal tissue, but is preceeded by histopathological changes such as adenomatous and atypical endometrial hyperplasia (Novak & Woodruff 1979). If these changes are recognised early, and successfully treated, it will be possible to decrease significantly the frequency of invasive cancer.

Review of recent trends in the screening and detection of Post-menopausal women at risk for endometrial carcinoma has shown that vaginal cytology is not as effective a screening procedure as it is for cancer cervix. Routine endometrial biopsy before starting hormone replacement therapy is not cost effective and causes patient discomfort. Ultrasound has been used for the evaluation of the endometrium in post-menopausal women to select a high risk group (Kawabata et al 1989).

The progesterone challenge test (PCT) had first been suggested by Gambrell (1981) as a strategy for reducing the risk of Ca Endometrium, in pts on estrogens. In a study by Toppozoda et al (1988), 7/30 asymptomatic post menopausal women showed W/B with PCT - 5 had AH. 1 had proliferative endom and the other had atrophic endom with retrogressed cystic hyperplasia. None of the cases without W/B had AH on HPE, 100% reliability of a -ve PCT, while the +ve test was 71.4% reliable. All patients with known AH known +ve PCT.

The PCT was also studied by Hanna et al (1983). In their series, 5/30 asymptomatic post-menopausal women had W/B to PCT, (+ve PCT), 3 of whom had unsuspected AH while the other 2 had atrophic endom. No cases with -ve PCT had AH. Combining use of PCT and endometrial thickness by transvaginal ultrasound in the preventive management of post-menopausal women, Pansini et al (1993) noticed than when overt flow occurred and when spotting occurred, 100% and 22% respectively and

pathological histopathology. The ten day Progesterone Challenge test had better sensitivity than the 5 days test (Macia et al 1993).

In conclusion, the PCT may reliably screen asymptomatic post-menopausal women who may have hyperplastic endometrial changes. In the presence of AH, the PCT was always positive - 100% sensitive. If PCT was positive, 50% had endogenous estrogenic hyperplasia, of endometrium. Conversely, a -ve PCT was 100% diagnostic of normal endometrium and eliminates the need for a routine screening biopsy. The PCT can also serve as a baseline parameter before starting estrogen replacement therapy.

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