Ovarian function and ovarian blood supply following premenopausal abdominal hysterectomy

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Abstract

Introduction: The issue of conserving the ovaries at hysterectomy in premenopausal women with benign gynecologic disease has been the subject of considerable controversy. Some clinicians prefer prophylactic oophorectomy in premenopausal women during hysterectomy to prevent future development of malignant changes in conserved ovaries. Other clinicians prefer to conserve apparently normal ovaries, because bilateral oophorectomy in premenopausal women results in an abrupt imbalance, sudden onset of menopausal symptoms, decreased libido, increased cardiovascular risk and osteoporosis.

Material and methods: Two hundred and twenty multipara women (who had completed their families), with benign uterine pathology were included in this prospective study for abdominal hysterectomy with bilateral ovarian preservation. Pre-operative vaginal ultrasound, Doppler studies, diagnostic hysteroscopy and endometrial biopsy were done followed by laboratory studies including Anti-mullerian hormone (AMH), follicle stimulating hormone (FSH) and estradiol for all studied women. Doppler studies, AMH, FSH and estradiol were repeated 6 and 12 months post-operative for assessment of the ovarian function and ovarian blood supply after hysterectomy.

Results: Pre-operative AMH, FSH and estradiol of the studied women were statistically insignificant compared to AMH, FSH and estradiol 6 and 12 months post-operative. Twelve months post-operative right and left ovarian volumes (6.92 ± 0.18 and 6.85 ± 0.19 cm³, respectively) were significantly larger than pre-operative right and left ovarian volumes (6.19 ± 0.22 and 5.86 ± 0.23 cm³, respectively), and, 12 months post-operative right and left ovarian pulsatility indices (2.92 ± 0.15 and 2.96 ± 0.16 cm/s, respectively) were significantly lower than pre-operative right and left ovarian pulsatility indices (3.45 ± 0.19 and 3.36 ± 0.2 cm/s, respectively). Eight (3.6%) cases of the studied women developed an ovarian cyst 6 months after hysterectomy, 3 were spontaneously resolved and the remaining 5 (2.27%) cases underwent exploratory laparotomy.

Conclusions: There is no evidence of ovarian dysfunction affecting conserved ovaries one year after hysterectomy in premenopausal women as evident by AMH, FSH and estradiol. Furthermore, an increased ovarian volume and reduced ovarian pulsatility indices indicate a possible increase in ovarian blood supply, and preserved non-compromised ovarian function.

Key words: ovarian, function, blood supply, premenopausal, abdominal hysterectomy.

Introduction

The issue of conserving the ovaries at hysterectomy in premenopausal women with benign gynecologic disease has been the subject of considerable controversy [1-5]. Some clinicians prefer prophylactic oophorectomy in premenopausal women during hysterectomy to prevent future development of malignant changes in conserved ovaries [6-16].

Other clinicians prefer to conserve apparently normal ovaries, because bilateral oophorectomy in premenopausal women results in an abrupt imbalance, sudden onset of menopausal symptoms, decreased libido, increased cardiovascular risk and osteoporosis [17-23].

There is conflicting evidence regarding the effect of premenopausal hysterectomy on the conserved ovarian function. Some research indicates an increase in incidence and severity of menopausal symptoms following removal of the uterus despite the ovaries remaining in place, which may be due to reduction in ovarian blood flow and follicular atresia [6]. Animal studies (rat models) concluded that hysterectomy with ovarian conser-
transvaginal ultrasound and Doppler studies were done using Philips HD9 (Philips International; Amsterdam; Netherlands) with a two-dimensional endo-vaginal convex probe 4-9 MHz by a sonographer who was blinded to the patients’ criteria.

Baseline measures included transverse (T), anteroposterior (AP), and longitudinal (L) diameters of both ovaries and ovarian volume (V), was estimated using the formula $V (\text{cm}^3) = T \times AP \times L \times 0.52$. Left and right ovarian artery flow in the pelvic infundibulum was visualized with the color Doppler technique and the typical velocity spectrum of this vessel was determined. Blood flow impedance was expressed as the PI (cm/s). The PI values were calculated electronically according to the formula $\text{PI} = \text{peak systolic velocity} – \text{minimum diastolic velocity}/\text{mean flow velocity}$.

Sample size justification

The required sample size was calculated using G*Power software version 3.17 for sample size calculation (*Heinrich Heine Universität, Düsseldorf, Germany), setting $\alpha$-error probability at 0.05, power (1 – $\beta$ error probability) at 0.95 and effective sample size ($w$) at 0.3. The effective size ($w$) was calculated as follows: $w = \chi^2/N$, where $\chi^2$ is the chi-square test and $N$ is the total sample size. The number of participants needed to produce a statistically acceptable figure was 220 women.

Statistical analysis

Data were collected, tabulated, then statistically analyzed using the Statistical Package for Social Sciences (SPSS) computer software version 18. Numerical variables were presented as mean and standard deviation (± SD), while categorical variables were presented as a number and percentage. Student t-test was used for comparison between groups as regards quantitative variables. A difference with a $p$ value < 0.05 was considered statistically significant.

Results

Mean age of premenopausal women included in this study for hysterectomy was 42.3 ± 8.7 years, parity was 4.9 ± 1.6 and body mass index (BMI) was 32.1 ± 2.07 kg/m². Hysterectomy was indicated for studied women due to fibroid uterus 131 (59.6%) cases (causing pelvic-abdominal mass 51 [23.2%] cases, menorrhagia 47 [21.4%] cases, pelvic pain or pressure 33 [15%] cases), heavy menstrual bleeding (HMB) with failed medical and hormonal treatment 52 (23.6%) cases and poly-menorrhrea 37 (16.8%) cases. The pre-operative histology of endometrium samples showed secretory endometrium in 87 (39.5%) cases, proliferative endometrium in
69 (31.4%) cases, simple endometrial hyperplasia in 36 (16.4%) cases and complex hyperplasia without atypia in 28 (12.7%) cases (Table I).

Pre-operative AMH (1.75 ± 4.61 ng/ml) of the studied women was statistically insignificant compared to AMH 6 and 12 months post-operative (1.78 ± 2.45 and 1.81 ± 2.19 ng/ml, respectively) and pre-operative FSH (7.98 ± 5.7 IU/ml) was statistically insignificant compared to FSH 6 and 12 months post-operative (8.26 ± 5.4 and 8.55 ± 6.2 IU/ml, respectively), also, pre-operative estradiol (129 ± 57.3 pg/ml) was statistically insignificant compared to estradiol 6 and 12 months post-operative (134.5 ± 66.2 and 139.3 ± 77.1 pg/ml, respectively) (Table II).

Pre-operative right and left ovarian volumes (6.19 ± 0.22 and 5.86 ± 0.23 cm³, respectively) were statistically insignificant compared to 6 months post-operative right and left ovarian volumes (6.75 ± 0.25 and 6.57 ± 1.12 cm³, respectively), and were significantly smaller compared to 12 months post-operative right and left ovarian volumes (6.92 ± 0.18 and 6.85 ± 0.19 cm³, respectively) (Table II).

Pre-operative right and left ovarian pulsatility indices (3.45 ± 0.19 and 3.36 ± 0.2 cm/s, respectively) were statistically insignificant compared to 6 months post-operative right and left ovarian pulsatility indices (3.12 ± 0.21 and 3.07 ± 0.21 cm/s, respectively), and were significantly higher compared to 12 months post-operative right and left ovarian pulsatility indices (2.92 ± 0.15 and 2.96 ± 0.16 cm/s, respectively) (Table II).

Eight (3.6%) cases of the studied women developed an ovarian cyst 6 months after hysterectomy, 3 were spontaneously resolved and the remaining 5 (2.27%) cases underwent exploratory laparotomy which revealed 3 cases of serous cystadenoma and 2 cases of a paraovarian cyst.

Discussion

In this study, there is no evidence of ovarian dysfunction affecting conserved ovaries one year after abdominal hysterectomy in premenopausal women as evident by AMH, FSH and estradiol.

There is conflicting evidence regarding the effect of premenopausal hysterectomy on the ovarian function. Some research indicates an increase in incidence and severity of menopausal symptoms and ovarian failure following removal of the uterus, despite the ovaries

Tab. I. Indications of hysterectomy for the studied population and preoperative histology of endometrial samples

| Variables | Number (%) |
|-----------|------------|
| Indication of hysterectomy | |
| Fibroid uterus | 131 (59.6%) |
| Pelvic-abdominal mass | 51 (23.2%) |
| Menorrhagia | 47 (21.4%) |
| Pelvic pain or pressure symptoms | 33 (15%) |
| Heavy menstrual bleeding (HMB) | 52 (23.6%) |
| Polymenorrhea | 37 (16.8%) |
| Pre-operative histology of endometrium samples | |
| Secretary endometrium | 87 (39.5%) |
| Proliferative endometrium | 69 (31.4%) |
| Simple hyperplasia | 36 (16.4%) |
| Complex hyperplasia without atypia | 28 (12.7%) |

Tab. II. Preoperative and postoperative Anti-mullerian hormone (AMH), follicle stimulating hormone (FSH), estradiol, ovarian volume, ovarian Pulsatility Index (P) of the studied population

| Variables | Preoperative | 6 months postoperative | 12 months postoperative | P value (95% CI) test used |
|-----------|-------------|-------------------------|-------------------------|--------------------------|
| AMH (ng/ml), mean ± SD | 1.75 ± 4.61 | 1.78 ± 2.45 | 1.81 ± 2.19 | P1 = 0** (Cl: –0.71; –0.03; 0.65), t test P2 = 0** (Cl: –0.73; –0.06; 0.61), t test |
| FSH (IU/ml), mean ± SD | 7.98 ± 5.7 | 8.26 ± 5.4 | 8.55 ± 6.2 | P1 = 0.21** (Cl: –1.31; –0.28; 0.75), t test P2 = 0.89** (Cl: –1.68; –0.57; 0.54), t test |
| Estradiol (pg/ml), mean ± SD | 129.0 ± 57.3 | 134.5 ± 66.2 | 139.3 ± 77.1 | P1 = 0.98** (Cl: –17.0; –5.5; 0.06), t test P2 = 0.99** (Cl: –22.9; –10.3; 2.39), t test |
| Right ovarian volume (cm³), mean ± SD | 6.19 ± 0.22 | 6.75 ± 0.25 | 6.92 ± 0.18 | P1 = 0.97** (Cl: –0.66; –0.56; –0.51), t test P2 = 0.001* (Cl: –0.82; –0.79; –0.75), t test |
| Left ovarian volume (cm³), mean ± SD | 5.86 ± 0.23 | 6.57 ± 1.12 | 6.85 ± 0.19 | P1 = 1** (Cl: –0.86; –0.71; –0.53), t test P2 = 0.002* (Cl: –1.02; –0.99; 0.95), t test |
| Right ovary Pulsatility Index (cm/s), mean ± SD | 3.45 ± 0.19 | 3.12 ± 0.21 | 2.92 ± 0.15 | P1 = 0.9** (Cl: 0.29; 0.33; 0.36), t test P2 = 0.002* (Cl: 0.48; 0.51; 0.56), t test |
| Left ovary Pulsatility Index (cm/s), mean ± SD | 3.36 ± 0.2 | 3.07 ± 0.21 | 2.96 ± 0.16 | P1 = 0.9** (Cl: 0.25; 0.2; 0.32), t test P2 = 0.0005* (Cl: 0.36; 0.4; 0.43), t test |

**Non-significant, *Significant
P1 – p for preoperative values compared to 6 months postoperative values, P2 – p for preoperative values compared to 12 months postoperative values, t test – Student t-test, cm/s – cm/second
remaining in place [26], whereas others report no decrease in ovarian function [26].

The advance of menopause age after hysterectomy is related to an increased rate of follicular atresia (surgical removal of uterus will increase follicular atresia in conserved ovaries) [27]. The presence of uterus would inhibit follicle depletion or atresia and its surgical removal at reproductive age would accelerate follicular loss, atresia and subsequent accelerated menopause [27].

Other hypothesis, the increased prevalence of ovarian failure after hysterecmy, is due to stretch and thrombosis of ovarian blood vessels with a subsequent reduction in ovarian blood supply [17, 27, 28].

Deng et al. concluded that hysterecmy with the conservation of bilateral/unilateral ovaries may have some influence on the ovarian function [17], also, Ahn et al. concluded that total abdominal hysterecmy accelerates ovarian dysfunction and women treated with total abdominal hysterectomy are at risk of early menopause [6].

On the contrary, Ylikorkala and Viinikka studied pituitary-ovarian function in 2 women with congenital absence of the uterus and vagina (Mayer-Rokitansky-Kuster-Hauser syndrome) and concluded that presence or absence of the uterus does not affect the ovarian function [29].

In this study, pre-operative AMH, FSH and estradiol were statistically insignificant compared to AMH, FSH and estradiol 6 and 12 months after abdominal hysterecmy, also, Chalmers et al., concluded that there is no evidence of compromise of the ovarian function, as reflected in FSH levels, within 2 years of hysterecmy [19].

Findley et al. concluded that laparoscopic hysterecmy ± salpingectomy with ovarian preservation does not appear to have any short-term deleterious effects on ovarian reserve, as measured by the AMH level [30].

Morelli et al. compared women treated with total laparoscopic hysterecmy (TLH) plus bilateral salpingectomy, with women treated by TLH without adnexectomy and they found no significant difference between two groups regarding AMH, FSH, antral follicle count (AFC), mean ovarian diameters and peak systolic velocity [31].

Recently, Venturella et al. has concluded that OvAge is one of the first reliable attempts to create a new method able to identify ovarian reserve [32, 33].

Although, Ishii et al. found that fifteen of 33 patients became climacteric after premenopausal radical hysterectomy for stage IB and II cervical cancer with ovarian preservation, they also found a significant correlation between ovarian dysfunction after radical hysterecmy and age [34]. Petri Naháš et al. found that ovarian volumes were greater 6 and 12 months after total abdominal hysterecmy compared to controls and they found reduced PI of ovarian vessels of hysterectomized women compared to controls [18].

They concluded that the reduced PI of ovarian vessels of hysterectomized women indicates decreased resistance with a subsequent increased ovarian blood flow in hysterectomized women compared to controls, also, in this study, 12 months post-operative right and left ovarian volumes (6.92 ± 0.18 and 6.85 ± 0.19 cm³, respectively) were significantly larger than pre-operative right and left ovarian volumes (6.19 ± 0.22 and 5.86 ± 0.23 cm³, respectively), and, 12 months post-operative right and left ovary pulsatility indices (2.92 ± 0.15 and 2.96 ± 0.16 cm/s, respectively) were significantly lower than pre-operative right and left ovarian pulsatility indices (3.45 ± 0.19 and 3.36 ± 0.2 cm/s, respectively) [18].

Five to eight percent of hysterectomized women require subsequent surgeries for benign ovarian diseases [5]. The post-hysterecmy ovarian cysts appear within the first post-operative year and spontaneously resolved in more than 50% of cases, and most of these cysts are functional cysts [35]. Zalel et al. found ovarian cysts in 50.7% of hysterectomized women (37/73) and Pete et al. found ovarian cysts in 9.2% of hysterectomized women (6/65) [36, 37].

Four women were lost during follow up (excluded from the study) and short duration of post-operative follow up (one year) were the two limitations faced during this study.

Conclusions

There is no evidence of ovarian dysfunction affecting conserved ovaries one year after hysterecmy in premenopausal women as evident by AMH, FSH and estradiol. Furthermore, an increased ovarian volume and reduced ovarian PI indicates a possible increase in ovarian blood supply, and preserved, non-compromised ovarian function.

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Disclosure

Authors declare no conflict of interest.

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