Laparoscopy: Desirable for most hysterectomy patients

Garry R, Fountain J, Mason S, et al. The eVALuate study: two parallel randomised trials, one comparing laparoscopic with abdominal hysterectomy, the other comparing laparoscopic with vaginal hysterectomy. *BMJ*. 2004;328:129–135.

OBJECTIVE To compare laparoscopic, abdominal, and vaginal hysterectomy, with major and minor complications as the primary endpoints.

RESULTS The laparoscopic group had less pain, quicker recovery, and better short-term quality of life than the abdominal group, but a significantly greater rate of major complications and operating time. Complication rates were similar for laparoscopic and vaginal hysterectomy, though that arm was underpowered.

EXPERT COMMENTARY This is one of only a few randomized, controlled trials comparing the 3 hysterectomy techniques. Women were randomized to laparoscopic (n = 391) versus abdominal (n = 172) hysterectomy (abdominal arm) or to laparoscopic (n = 198) versus vaginal (n = 105) hysterectomy (vaginal arm).

Study strengths and findings. Design was excellent, and investigators reported results of both trial arms, though insufficient numbers were recruited in the vaginal arm. Thus, we can draw reasonable conclusions from the large number of women involved:

- *Operating time*. Longer with laparoscopic than with abdominal or vaginal hysterectomy.
- *Quality of life*. Significantly improved with laparoscopic hysterectomy up to 1 year.
- *Minor complications*. Similar in all groups.
- *Detection of additional pathology*. Greater with laparoscopy. Surprisingly, in the abdominal arm, additional pathology was reported in 12.7% of patients versus 22.6% for the laparoscopic approach. In the vaginal arm, additional pathology was detected in 4.8% of cases versus 16.4% for the laparoscopic approach.
- *Pain*. Less with laparoscopy in the abdominal arm, but comparable in the vaginal arm.

Weaknesses. Some shortcomings in study design were largely unavoidable. For example, by excluding patients with prolapse or with a uterus larger than 12 weeks' gestation, researchers limited generalizability, as these conditions are common indications for hysterectomy in a typical clinical practice, and frequently are determinants of the approach.

The incidence of major hemorrhage (abdominal arm: 2.4%, versus 4.6% for laparoscopy; vaginal arm: 2.9%, versus 5.1% for laparoscopy) may have been related to the method of utero-ovarian vessel ligation and sealing, but no description or standardization was offered. Thus, it is unclear whether a simple alteration in technique could have eliminated this as a factor in morbidity.

Unintended laparotomy was considered a major complication in this study, but only in the laparoscopy groups. Excluding this, major complications would have been lower in the laparoscopy group compared with the abdominal group. It seems inappropriate to consider a procedure that is standard for 1 group as a major complication in another.

BOTTOM LINE Taken with existing literature, this study supports the premise that laparoscopy is desirable for most women undergoing hysterectomy. It also confirms the superiority of laparoscopic hysterectomy in recognizing and treating other pathology while ensuring a shorter recovery and hospital stay and improved quality of life.

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Controlled-release paroxetine reduces hot flashes

Stearns V, Beebe KL, Iyengar M, Dube E. Paroxetine controlled release in the treatment of menopausal hot flashes. A randomized controlled trial. *JAMA*. 2003;289:2827–2834.

OBJECTIVE To assess the effectiveness of paroxetine controlled release (CR), a selective serotonin reuptake inhibitor (SSRI), in relieving hot flashes among a general cross section of menopausal women.

RESULTS After 6 weeks, mean daily hot flash frequency decreased from 7.1 to 3.8 for women receiving 12.5 mg/day paroxetine CR, from 6.4 to 3.2 for those taking 25 mg/day, and from 6.6 to 4.8 for women taking placebo.

EXPERT COMMENTARY The vasomotor flush is the hallmark of the female climacteric, experienced to some degree by up to 85% of postmenopausal women.[1] Hormone therapy is the treatment of choice for these symptoms, but many women cannot or will not take it.

Until results of larger and longer trials are available, SSRIs are the best choices after hormone therapy for vasomotor symptoms.

Alternatives such as transdermal clonidine or oral clonidine, naloxone, or bromocriptine produce only modest relief. Natural remedies such as vitamin E and isoflavones barely outperform placebo. Medroxyprogesterone acetate (10 to 20 mg daily) and megestrol acetate (20 mg twice daily) are effective,[2,3] but concerns about exogenous steroids apply—especially in breast cancer survivors.

Study design and results. In this randomized, double-blind, placebo-controlled, parallel group study, 56 women were randomized to placebo, 51 to 12.5 mg/day paroxetine CR, and 58 to 25 mg/day paroxetine CR. At baseline, subjects experienced a minimum of 2 to 3 hot flashes daily, or at least 14 hot flashes per week.

Mean placebo-adjusted reductions in hot flash composite scores were –4.7 (95% confidence interval, –8.1 to –1.3; $P = .007$) comparing 12.5 mg/day paroxetine CR with placebo; and –3.6 (95% confidence interval, –6.8 to –0.4; $P = .03$) comparing 25 mg/day paroxetine CR with placebo. This corresponds to median reductions of 62.2% for women taking 12.5 mg/day paroxetine CR, 64.6% for those taking 25 mg/day, and 37.8% for those taking placebo.

After 6 weeks, 61% of the treated group (including 12 breast cancer survivors) had a reduction of at least 50% in the frequency and severity of flushing. At the higher dose, this effect was about 2.5 times better than with placebo, but the lower dose was better tolerated.

It is important to note that women with clinically significant mood disorders were excluded.

Unanswered questions. Key issues remain unresolved. For example, would a longer trial find the same efficacy? What about SSRIs in comparison with hormone therapy? No comparative trial has been reported. What is the lowest effective dose of paroxetine CR?

BOTTOM LINE With larger and longer clinical trials of SSRIs under way, answers to these questions may emerge. Until then, SSRIs such as paroxetine CR, fluoxetine, and venlafaxine are the best choices after hormone therapy to ease vasomotor symptoms (see "Managing menopause-related depression and low libido," page 29).

It is worth trying to titrate the dose to its lowest effective level because of a small but bothersome incidence of decreased libido. Added advantages with SSRIs are improvements in depression, anxiety, and sleep. ■

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