

Histopathologic findings on uterosacral ligaments in women with chronic pelvic pain and visually normal pelvis at laparoscopy

Patricia C. Nascu, MD, George A. Vilos, MD, Hellen C. Ettler, MBChB, Basim Abu-Rafea, MD, Jackie Hollet-Caines, MD, and Riad Ahmad, MD

From the Department of Obstetrics and Gynecology, St. Joseph's Health Care (Drs. Nascu, Vilos, Abu-Rafea, Hollet-Caines, and Ahmad), and the Department of Pathology, London Health Sciences Centre (Ms. Ettler), The University of Western Ontario, London, Ontario, Canada.

KEYWORDS:

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Pelvic pain;
Dysmenorrhea;
Dyspareunia;
Endometriosis;
Endosalpingiosis

Abstract

STUDY OBJECTIVE: To determine the prevalence and type of microscopic findings on laparoscopically resected uterosacral ligaments in women with chronic pelvic pain and no visible pelvic disease. The effect of this procedure on the patients' level of pain also was assessed as a secondary objective.

DESIGN: Prospective follow-up (Canadian Task Force classification II-2).

SETTING: University-affiliated hospital.

PATIENTS: Twenty-seven premenopausal women undergoing diagnostic laparoscopy for chronic pelvic pain had a normal pelvis on visual inspection. All patients underwent resection and histologic evaluation of the uterosacral ligaments. Pain relief was evaluated by use of a questionnaire administered before and at 3, 6, and 12 months after surgery.

MEASUREMENTS AND MAIN RESULTS: Microscopic examination identified endometriosis in 2 (7.4%), endosalpingiosis in 3 (11.1%), and inflammation in 14 (51.9%) patients. Laparoscopic uterosacral ligament resection was associated with a reduction in dysmenorrhea ($p \leq .001$), with 14 (52%) patients reporting improved or resolved symptoms. There was a statistically significant decrease in dyspareunia ($p \leq .01$) and in the severity of noncyclical pain ($p \leq .002$). Thirty-five percent of patients no longer required medication for pain control ($p \leq .005$). The number of days needed off work also decreased.

CONCLUSION: Despite normal laparoscopic appearance, microscopic endometriosis, endosalpingiosis, and inflammatory changes were found in uterosacral ligaments in 17 (63%) women with chronic pelvic pain. Laparoscopic resection of uterosacral ligaments improved dysmenorrhea, dyspareunia, and noncyclical pain and decreased the number of days lost from work, as well as the proportion of patients who required medication for pain control. © 2006 AAGL. All rights reserved.

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Corresponding author: Dr. Patricia C. Nascu, Department of Obstetrics and Gynecology, St. Joseph's Health Care, 268 Grosvenor Street, London, Ontario, Canada N6A 4V2.

E-mail: pnascu@uwo.ca

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Chronic pelvic pain is common in women of reproductive age. It accounts for 10% of outpatient gynecology visits, and it is the indication for up to 40% of laparoscopies and 10% to 15% of hysterectomies.¹

Laparoscopy has long been considered the gold standard in the diagnosis of chronic pelvic pain, but often it reveals no obvious abnormality. The most common findings are endometriosis (33%), adhesions (24%), and no visible disease (35%).² Absence of macroscopic disease on laparos-

copy does not exclude disease, because there are reports of microscopic disease being present in peritoneal biopsy specimens in women with an apparently normal pelvis.^{3,4}

Laparoscopic uterosacral nerve ablation is the interruption of nerve fibers that exit the uterus along the uterosacral ligaments. This procedure has been used with variable success in the treatment of chronic pelvic pain. Some authors have reported good results in terms of pain control,⁵⁻⁸ but other studies have failed to reveal a benefit.⁹ It is not yet clear whether removal of microscopic disease present on uterosacral ligaments has any effect on the patients' symptoms.

The aim of this study was to determine the prevalence and type of disease in laparoscopically resected uterosacral ligaments in women with chronic pelvic pain and an otherwise normal pelvis. As a secondary outcome we assessed the effect of the procedure on patients' level of pain.

Materials and methods

From September 1998 through March 2003 a total of 108 patients with chronic pelvic pain were evaluated and underwent laparoscopy. Inclusion criteria were chronic pelvic pain for at least 6 months duration, no or minimal relief with hormonal therapy and nonsteroidal anti-inflammatory drugs, no other medical condition that could account for the pain, and visually normal pelvis at laparoscopy. Eighty-one of them had macroscopic disease and were excluded. In 27 women, the pelvis was found to be visually normal, and they were included in the study.

After informed consent, all patients underwent laparoscopy by the senior surgeon (G.A.V.). A careful visual inspection of the entire abdomen and pelvis was performed in a systematic fashion. If no abnormality was detected on inspection, laparoscopic resection of uterosacral ligaments was carried out. First, the course of the ureters was identified, and both uterosacral ligaments were divided with the CO₂ laser (Lumenis, Santa Clara, CA), near the point of their attachment to the cervix and approximately 2 cm proximally from the first division. The portion in between, 1 to 2 cm in length, was resected and sent for histopathologic examination.

The same pathologist examined all specimens. The presence of nerve fibers and any histologic abnormality were recorded. Endometriosis was considered to be present if both endometrial glands and stroma were detected on microscopic examination. Endosalpingiosis was characterized by the presence of cuboidal or columnar tubal epithelium in the absence of endometrial stroma. If present, chronic (lymphocytic) inflammation was graded as grade 1 or 2, depending on the number of inflammatory cells seen: grade 1 was defined as rare inflammatory cells, and grade 2 as moderate amount of inflammatory cells seen at low power.

Pain relief was evaluated with a questionnaire administered before surgery and at 3, 6, and 12 months. Patients

were asked to rate their pain on a 10-point numerical scale (1-3 mild pain, 4-7 moderate pain, 8-10 severe pain). Quality of life was assessed by inquiring about the number of days lost from work because of pain and the impact of pain on patient's sexual function. The current use of medication for pain control also was evaluated.

Results

The median age for all patients was 24 years (range 17-35 years). Seventeen women (63%) were nulliparous. At the time of the preoperative evaluation, 24 women (88%) were using hormonal therapy in the form of either oral contraceptives or medroxyprogesterone acetate. Twenty-five (92%) women had used nonsteroidal antiinflammatory drugs or oral opioids in the 6 months preceding the surgery with incomplete relief of pain.

Before laparoscopy, all patients reported pain and tenderness during pelvic examination. However, because there was no induration felt along the uterosacral ligaments, it was difficult to discern whether the tenderness was related to the uterosacral ligaments or the rest of the cul-de-sac. Bilateral uterosacral ligament resection was performed in all but one patient, in whom only the left uterosacral ligament could be safely resected because of the proximity of the ureter to the ligament.

The histopathologic examination revealed nerve tissue in all specimens. Endometriosis was identified in two patients (7.4%) and endosalpingiosis in another three women (11.1%). Chronic inflammation, characterized by lymphocytic infiltrate, was detected in 14 patients (51.9%). The inflammation was graded as 1 in 12 women and as 2 in 2 women. Inflammation was concurrent with endometriosis in one woman and with endosalpingiosis in two other women. Psammoma bodies were noted in two women. This finding was associated with endosalpingiosis in one woman, but was an isolated finding in the other. In nine other patients focal mesothelial hyperplasia was seen.

Twenty-three patients completed the pain questionnaire, and four were lost to follow-up. Before surgery, all of them reported dysmenorrhea, 15 (65%) had dyspareunia, and 21 (91%) had noncyclical pelvic pain. A change in pain score was considered clinically significant if it reached 2 or more on the 10-point numerical pain scale.

Laparoscopic uterosacral ligament resection was associated with statistically significant reduction in dysmenorrhea. More than half of the patients (52.2%) reported symptom resolution or improvement, with a mean reduction in pain score of 2.4 ($p \leq .001$). At 1 year, 10 patients (43.5%) reported no change compared with the preoperative period, and 1 (4.3%) had worsening of the symptoms.

Noncyclical pain was less severe in 13 of 21 women (62%). The mean score reduction was 2.9, which was statistically significant ($p \leq .002$). The severity of dyspareunia was lower in 6 of 15 patients (40%), with a mean score

reduction of 2.5. No woman experienced an increase in dyspareunia. Of the 21 patients who required preoperative pain medication, 8 (38%) no longer needed it after the procedure ($p \leq .005$). We also noted a decrease in the number of days lost from work because of pain: before surgery 12 patients (52%) reported missing work, but this number dropped to 2 (8.7%) at 1-year follow-up.

Discussion

In this study, we found a significant prevalence of microscopic findings on resected uterosacral ligaments of patients with chronic pelvic pain and visually normal pelvis. The major finding was the presence of inflammation, but endometriosis and endosalpingiosis were also encountered. Laparoscopic resection of uterosacral ligaments was associated with improved symptoms in more than half of the patients.

In patients with no macroscopic disease, the current literature indicates that laparoscopic uterosacral nerve ablation improves pelvic pain in approximately 50% of patients up to 12 months after surgery.^{5,9} We chose to perform laparoscopic resection rather than division of uterosacral ligaments to physically remove nerve tissue and obtain samples for histologic examination.

Several studies have demonstrated existence of microscopic disease in the visually normal peritoneum of women with pelvic pain. Most of these reports included women with known endometriosis elsewhere in the pelvis.^{10,11} One study reported endometriosis in two (6%) biopsy specimens taken from uterosacral ligaments of 32 infertile women without macroscopic lesions.³ Another study confirmed that endometriosis was present in normal peritoneum in three (6%) of 53 women without visible endometriosis at laparoscopy.⁴ Our findings correlate well with the ones reported in the literature.

The role of endosalpingiosis in chronic pelvic pain is controversial. A prospective study of 1107 women undergoing laparoscopy for a variety of indications found that the frequency of endosalpingiosis in women with or without pain was not significantly different (7.9% vs 7.3%).¹² In another study, 13 patients with endosalpingiosis presented with a variety of symptoms, including pelvic pain (5 women). Additional pelvic pathology was detected in all women. The authors concluded that endosalpingiosis seems to be an incidental finding associated with other pelvic disease rather than a frequent cause of pelvic pain.¹³ On the other hand, some authors believe that endosalpingiosis may be often overlooked as a cause of pelvic pain,¹⁴ and that it may be misdiagnosed as endometriosis in up to 16.2% of cases.¹⁵

More than half of our patients had documented chronic inflammation present on the uterosacral ligaments. To our knowledge, there are no reports in the literature of inflammation of the uterosacral ligaments as an isolated finding in

women with chronic pelvic pain. One study¹⁶ reported that 108 (15.7%) of 689 patients with chronic pelvic pain had histologic evidence of chronic peritoneal inflammation in the absence of endometriosis during laparoscopy. However, it is a common belief that endometriosis-related pain is due to inflammation. Histologic studies have hypothesized that entrapment of nerve fibers by fibrosis may represent one of the mechanisms of pelvic pain.¹⁷ If this is the case, then presence of inflammation in the uterosacral ligaments could also lead to irritation of afferent nerve fibers leading to the perception of pain. However, only prospective randomized clinical trials involving resection or division of the uterosacral ligaments versus sham controls will be able to validate the safety, efficacy, and durability of this procedure in the management of chronic pelvic pain.

Conclusions

Microscopic disease, including endometriosis, endosalpingiosis and chronic inflammation, is present in the uterosacral ligaments in 63% of women with chronic pelvic pain despite a visually normal pelvis. Laparoscopic resection of uterosacral ligaments improved pain, which led to a decrease in the number of days lost from work and the need for medication.

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