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Reduction of surgery rate in endometriosis patients who take Chinese medicine: a population-based retrospective cohort study

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Summary

Objectives: Female patients have frequently utilized Chinese medicine (CM) to treat symptoms that could possibly be related to endometriosis. The objective of this population-based retrospective cohort study was to evaluate the relationship between CM use and subsequent surgery among patients with endometriosis.

Design: A total of 8,283 CM users were identified among the 22,488 endometriosis patients found in the National Health Insurance reimbursement database between 2000 and 2010. A control group was identified and consisted of 8,283 matched nonusers with the same disease. A Cox proportional regression analysis was performed in order to assess risk factors for surgery for the CM users and nonusers.

Results: When compared to nonusers, CM users were significantly less likely to undergo surgery, with a hazard ratio of 0.47 (95% CI = 0.421, 0.534) after adjusting for age, occupation, childbirth

Abbreviations: CI, confidence interval; CM, Chinese medicine; ICD-9-CM, International Classification of Diseases, 9th Revision Clinical Modification; HR, hazard ratio; IR, incidence rate; IRR, incidence rate ratio; LHID, Longitudinal Health Insurance Database; NHI, National Health Insurance.

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status, hypermenorrhea, iron-deficient anemia, dysmenorrhea, and amount of conventional medications. Among patients who had undergone surgery, the follow-up time was longer for CM users than for CM nonusers ($p < 0.001$). Moreover, the most frequently used CM single and formula were *Cyperus rotundus* and Gui-zhi-fu-ling-wan, respectively.
Conclusions: These results suggest that whatever the underlying reason, CM provides an alternative option that reduces the incidence rate of surgery in endometriosis patients.

Background

Endometriosis is an estrogen-dependent inflammatory disorder defined by the presence of active endometrial tissue outside the uterine cavity. Asian women are reported to have a higher risk of endometriosis than other races,[1] and the prevalence of endometriosis is estimated to be 2.7% in Taiwanese women.[2] The most common sites for endometriosis to occur are the ovaries, cul-de-sac, posterior broad ligaments, uterosacral ligaments, the uterus, fallopian tubes, the sigmoid colon and the appendix.[3] The implantation of endometrioid mucosa is associated with the main chronic features of the disease, including pelvic pain, severe dysmenorrhea, hypermenorrhea, dyspareunia and infertility, although it may also be asymptomatic.[4]

The management of endometriosis varies according to the individual, with a multidisciplinary approach, and with goals of pain relief and/or a successful pregnancy for infertile patients.[5] For patients with a mild form of the disease, pharmacological therapies are advisable for controlling symptoms so as to avoid side effects and the costs of surgery until menopause,[6] when endometriotic implant growth is suppressed as a result of reduced ovarian estrogen production.[7] For patients whose symptoms have failed to resolve or have worsened under medical treatment, surgical management is advisable. Conservative surgery, including fulguration, excision, cauterization, and ablation, is recommended for women who have not completed childbearing, since it preserves the uterus and as much ovarian tissue as possible.[6] On the other hand, definitive surgery, including hysterectomy, with or without the removal of fallopian tubes and ovaries, is indicated when incapacitating symptoms persist even after conservative therapy, and when pregnancy is not desired.[8] However, surgery is always associated with long lasting complications, including fistula formation, adhesion, and sexual dysfunctions, which can last well beyond menopause, sometimes resulting in a negative quality of life outcome.[9,10]

Chinese medicine (CM) is the most popular complementary alternative medicine in Asian countries and the Taiwanese Government's National Health Insurance (NHI) covers it.[11,12] Based on the NHI database, CM is commonly used by females to treat reproductive system diseases, including menstruation disorders, abnormal bleeding, as well as non-infectious disorders of female genital organs,[13–16] which can potentially be caused by endometriosis. However, no population-based evidence has been reported about the benefit of CM in women with endometriosis. Research regarding the effects of CM on subsequent endometriosis-related conventional treatment is also very limited.

This population-based retrospective cohort study followed patients diagnosed with endometriosis from 1996 to 2010, using a national insurance reimbursement database. The association between CM use and the incidence of surgery in women with endometriosis was then evaluated. The results imply the benefits of CM for endometriosis patients from a public health perspective.

Methods

Subjects

Endometriosis patients were identified according to the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) code 617 from 2000 to 2010 in the Longitudinal Health Insurance Database 2000 (LHID2000). The LHID2000 was set up by Taiwan's National Health Research Institute and it contains chronological information about one million randomly selected individuals who were beneficiaries from 1996 to 2000.

Study designs

The date of the first diagnosis was used as the entry date, and the date of surgery was used as the outcome date. The types of endometriosis-related surgery include hysterectomy, oophorectomy, fulguration, excision, and the electric cauterization of endometriosis. Subjects who had undergone surgery before the entry date were excluded. CM users were defined as subjects who had received an orally administered CM treatment for more than two consecutive weeks. The CM nonuser group consisted of randomly selected patients who had not used CM, and this was matched with the CM user group according to age and to the duration between diagnosis and CM usage at a 1:1 ratio. The endpoint date was defined as the date of surgery, death, withdrawal from the insurance program, or December 31, 2010. The follow-up time was defined as the period from CM usage to the endpoint date.

Examined variables included socio-demographic factors (age, income level, and occupation status), childbirth status, and endometriosis-related co-morbidities, including hypermenorrhea (ICD-9-CM 626.2), iron-deficiency anemia (ICD-9-CM 280), and dysmenorrhea (ICD-9-CM 625.3).

Statistical analysis

In terms of categorical and continuous variables, CM users and CM nonusers were compared using *chi*-square tests and