ORIGINAL ARTICLE: ENDOMETRIOSIS

A stepped-care approach to symptomatic endometriosis management: a participatory research initiative

Paolo Vercellini, M.D.,[a,b] Agnese Donati, M.D.,[a] Federica Ottolini, M.D.,[a] Annalisa Frassineti,[c] Jessica Fiorini,[c] Vanessa Nebuloni,[c] Maria Pina Frattaruolo, M.D.,[b] Anna Roberto, Biol.Sci.D.,[d] Paola Mosconi, Biol.Sci.D.,[d] and Edgardo Somigliana, M.D.[a,b]

[a] Department of Clinical Sciences and Community Health, Università degli Studi di Milano and [b] Gynecologic Surgery and Endometriosis Departmental Unit, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Ca' Granda, Ospedale Maggiore Policlinico, Milan; [c] Associazione Progetto Endometriosi Onlus, Reggio Emilia; and [d] Department of Public Health, Research Laboratory on Citizen Engagement in Healthcare, IRCCS Mario Negri Institute for Pharmacologic Research, Milan, Italy.

Objective: To assess the proportion of patients with symptomatic endometriosis satisfied with their medical treatment 12 months after enrollment in a stepped-care management protocol.
Design: Prospective, single-arm, self-controlled study.
Setting: Academic department.
Patient(s): A cohort of 157 consecutive patients referred or self-referred to our center for symptomatic endometriosis.
Interventions(s): Systematic detailed information process on medical and surgical treatment followed by a shared decision to start a stepped-care protocol including three subsequent medical therapy steps (oral contraception [OC]; 2.5 mg/d norethindrone acetate [NETA]; 2 mg/d dienogest [DNG]) and a fourth surgical step. Stepping up was triggered by drug inefficacy/intolerance.
Main Outcome Measure(s): Satisfaction with treatment was assessed according to a five-category scale (very satisfied, satisfied, neither satisfied nor dissatisfied, dissatisfied, very dissatisfied). Variations were measured in pain symptoms with the use of a 0–10-point numeric rating scale (NRS), in quality of life with the use of the Short Form 12 questionnaire (SF-12), and in sexual functioning with the use of the Female Sexual Function Index (FSFI).
Result(s): At the end of the 12-month study period, 106 women were still using OC, 23 were using NETA, three were using DNG, and four had undergone surgery. Twenty-one participants (13%) dropped out from the study. In intention-to-treat analysis, excluding five drop-outs for pregnancy desire, the overall satisfaction rate with the stepped-care protocol was 62% (95/152; 95% CI 55%–70%). By 12-month follow-up, significant improvements were observed in all pain symptom scores and in SF-12 physical and mental component summary scores, whereas FSFI scores did not vary substantially.
Conclusion(s): Most women with endometriosis-associated pelvic pain who chose a stepped-care approach were satisfied with OC and a low-cost progestin for the treatment of their symptoms. The need to step up to an expensive progestin or surgery was marginal. (Fertil Steril® 2018;■:■–■. ©2018 by American Society for Reproductive Medicine.)
Key Words: Endometriosis, pelvic pain, medical treatment, surgery

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Reprint requests: Paolo Vercellini, M.D., Gynecologic Surgery and Endometriosis Departmental Unit, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Via Commenda, 12, 20122 Milan, Italy (E-mail: paolo.vercellini@unimi.it).

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According to the opinion of the Practice Committee of the American Society for Reproductive Medicine on treatment of endometriosis-associated pelvic pain, "endometriosis should be viewed as a chronic disease that requires a lifelong management plan with the goal of maximizing the use of medical treatment and avoiding repeated surgical procedures" (1).

In fact, surgery for endometriosis is reportedly effective for pelvic pain, but postoperative recurrence of symptoms and lesions is as high as 40%–50% at 5-year follow-up (2–4). Moreover, removal of ovarian endometriomas is associated with reduction of ovarian reserve (5, 6), and excision of deep infiltrating forms is associated with a relatively high incidence of complications, especially when rectovaginal and bowel lesions are present (3, 7, 8). Outcomes of complex surgical procedures are strictly operator dependent and therefore scarcely reproducible. Finally, surgery is expensive. For these reasons, many women would leave surgery as the second choice, only in case medications are ineffective or not tolerated (9).

Based on secondary research findings (10) and according to guidelines issued by several international gynecologic societies, hormonal compounds to treat endometriosis have similar effects on pain, but different metabolic and subjective side-effects and costs (1,11–14). Therefore, in women who prefer medical rather than surgical treatment, those drugs with the most favorable therapeutic profile and lower cost should be used first, stepping up to drugs with a less favorable therapeutic profile or higher cost selectively in those patients who do not respond or do not tolerate the first-line medications.

Despite decades of intensive clinical research, the ultimate prognosis of a woman with symptomatic endometriosis who chooses prolonged medical treatment with first-line drugs instead of surgery is currently unknown. In other words, the likelihood that a woman will succeed in successfully controlling her complaints and be satisfied with her treatment without having to step up to second-line compounds and eventually to surgery is currently undefined. The answer to this practical question seems crucial for informing patient decisions. Even women preferring medical rather than surgical treatment may choose differently in case the risk of having to resort anyway to surgery is high.

Given this unclear scenario, we deemed it of interest to assess the trajectory of an unselected cohort of consecutive endometriosis patients through a pre-planned stepwise therapeutic protocol including three subsequent medical steps (oral contraception [OC]; norethindrone acetate [NETA]; dienogest [DNG]) and a fourth, final, surgical step. The main objective of the investigation was to estimate the probability of being satisfied with this stepped medical care approach 1 year after starting the use of a low-dose OC.

MATERIALS AND METHODS

This study was conceived and designed, the results interpreted, and the report written, together with representatives of a large Italian nonprofit endometriosis patient association (Associazione Progetto Endometriosi Onlus), and it was conducted within the framework of a participatory research initiative aimed at prioritizing topics and research questions that patients consider to be important. Engaging patients in the design of a new pragmatic study model on endometriosis management was deemed to be crucial to capturing aspects of health and functioning that matter to them.

The manuscript was prepared according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for reporting observational studies (15). The investigation was performed in an academic department specializing in endometriosis management, and the relevant Institutional Review Board approved the study (Comitato di Etica Milano Area B; determination no. 903/2015). Every patient signed an informed consent form before enrollment.

Design

A prospective, single-arm, self-controlled, observational study design was adopted. The main objective was to assess the degree of satisfaction with stepped medical treatment care in a cohort of consecutive patients with symptomatic endometriosis starting therapy with an OC used continuously, and sequentially stepping up to NETA and then to DNG in case of drug inefficacy or intolerance. Secondary objectives were the evaluation of within-person variations in pain symptoms, health-related quality of life, and sexual function after 12 months, as well as of the proportion of patients eventually needing to step up to surgery. With this study design, each participant acted as her own control to avoid the potential confounding caused by differences between patients (16). In fact, variation in satisfaction with treatment was not assessed after a pre-planned shift to another drug in a general population of patients taking OC, but specifically in those patients who stepped up to a second- or third-line medication owing to dissatisfaction with, respectively, OC or NETA because of inefficacy or intolerability and who would otherwise have discontinued medical therapy.

Study Participants

We considered 18- to 40-year-old women not seeking conception with a surgical diagnosis of ovarian and/or deep endometriosis, or a current nonsurgical diagnosis of ovarian and/or deep endometriosis (17), consecutively referred or self-referred to our tertiary-care endometriosis center because of moderate or severe pelvic pain symptoms of >6 months' duration. Those patients who were already using any type of pharmacologic therapy and were satisfied with their treatment were not considered for enrollment.

Nonsurgical diagnoses were based on ultrasonographic criteria in patients with ovarian endometriomas (18, 19), on visual inspection of the posterior fornix and biopsy of vaginal lesions in those with rectovaginal endometriosis (20, 21), on ultrasonographic criteria (22), cystoscopic findings, and biopsy of vesical lesions in those with bladder detrusor endometriosis, on physical signs at rectovaginal examination and ultrasonographic criteria (23, 24) in those with deep lesions infiltrating the Douglas pouch and parametria, and on ultrasonographic criteria (24), double-contrast barium enema,