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The impact of lifestyle factors on pelvic pain and quality of life in endometriosis

Doctoral (PhD) thesis

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1. Introduction

Definition, general remarks

Endometriosis is a condition or disease, when endometrial tissue (called endometrium), that normally lines the inner surface of the body of the uterus, is found elsewhere. Similarly to the eutopic endometrium, the ectopic endometrial tissue is under the influence of hormones, proliferates, changes in histological caracteristics, undergoes degeneration and then „shedding", just like in the case of menstruation. During these processes it might cause severe destruction of the surrounding tissues and organs. Endometriosis affects millions of women world wide. It can severely alter quality of life an d leads to extensive problems with fertility and loss of work time. Endometriosis might remain asymptomatic and discovered accidentally. However, it may cause symptoms, which include chronic pelvic pain, bleeding, infertility, and increases susceptibility to development of adenocarcinoma. Signs and symptoms arise from cyclic bleeding into the surrounding tissues, resulting in inflammation and formation of scarring and adhesions. It is peculiar, that symptom severity does not correlate well with the extent or progression of the lesions. The exact roles of different factors contributing to the establishment and persistence of the endometriotic lesion are still not fully understood. Despite the high associated morbidity and health care costs, the incidence, prevalence, and risk factors of endometriosis remain uncertain.

Clinical signs and symptoms

The primary symptom of endometriosis is pelvic pain, often associated with menstrual period. Although many women experience cramping during their menstrual period, women with endometriosis typically describe menstrual pain that's far worse than usual. They also tend to report that the pain has increased over time. Common signs and symptoms of endometriosis may include painful periods (dysmenorrhea). Pelvic pain and cramping may begin before and extend several days into the period and may include lower back and abdominal pain. Other pain symptoms are pain with intercourse (pain during or after sex is common with endometriosis), pain with bowel movements or urination. Most likely these symptoms are experienced during the period. Occasionally patients may experience heavy periods (menorrhagia) or bleeding between periods

(menometrorrhagia). Another important issue of endometriosis is infertility. Endometriosis is first diagnosed in some women who are seeking treatment for infertility. Other symptoms might include fatigue, diarrhea, constipation, bloating or nausea, especially during menstrual periods.

The severity of the pain is not necessarily a reliable indicator of the extent of the condition. Some women with mild endometriosis have extensive pain, while others with advanced endometriosis may have little pain or even no pain at all.

Management

Symptomatic endometriosis can be managed surgically and/or medically. The aim is pain relief and/or amelioration of infertility. Medical treatment is usually long term, and recurrence is frequent after its cessation. Classic endometriosis pharmacotherapy is represented by GnRH agonists, oral contraceptives and type II progesterone receptor ligands. All medical treatments seem to be equally effective in managing endometriosis. Although about 80-85% of patients have improvement in their symptoms, many women experience unsatisfactory results. However, little is known about factors on patient's side influencing the efficacy of generally accepted therapeutic approaches used to alleviate symptoms caused by endometriosis.

2. Aim of the study

We aimed to investigate the effectiveness of combined surgical and medical therapy of patients with histologically confirmed endometriosis with regard to pain relief and overall quality of life issues. To determine these parameters we used a questionnaire before laparoscopic surgery and upon cessation of post-surgery medical therapy. With that, we wanted to determine efficacy of therapy from the patient's point of view, with relation to several non-medical variables such as marital status, level of education smoking and sport activities.

3. Materials and methods

Study population and sample

The prospective cohort study population consisted of patients of reproductive age complaining about persistent pelvic pain and undergoing laparoscopy in our department

(Department of Obstetrics and Gynecology, Faculty of Medicine, University of Pécs, Hungary). Following laparoscopy and histological examination, a random sample of 150 patients with histologically proven endometriosis were recruited. This initial number of recruited patients was arbitrarily set and reached in a 6 month period between June and December, 2008. The refusal rate upon reaching the desired number of 150 was less than 5%, however, the drop-out rate during the entire study period was 46%. Those who were lost for follow-up did not differ in any characteristics based on the collected data comparing to those who completed both questionnaires. Final statistics were carried out using data from those 81 patients completing the study.

A standardized questionnaire adopted from the International Pelvic Pain Society (the so called „Pelvic Pain Assesement Form") was translated to hungarian and used to elicit information from women on the following groups of variables: age, marital status, education, reproductive and medical history. The questionnaire was purposefully designed to ascertain information on potential confounders, which included gravidity (number of pregnancies regardless of outcome) and parity (number of live births), knowledge of accompaniing pelvic disorders, concurrent cigarette smoking and caffein intake, since all have been reported as risk factors for endometriosis. Further variables were concurrently used medication including pain killers, as well as daily habits of excersice, type of work and general quality of life estimates including self-image. Pelvic pain was scored using a visual analogue scale from 0-10. Only patients with histologically confirmed endometriosis and with no other pelvic/abdominal alteration or disease confirmed at laparoscopy were then eligible to continue the study. Patients then received a 6 month GnRH analogue therapy and were asked to fill out the same questionnaire upon completing medical therapy.

Laparoscopies were performed by highly trained and experienced surgeons. Following the operations they completed a standardized operative report to ascertaine information on postoperative diagnosis and other pathology regardless of surgical indication. Severity of endometriosis was staged according to the American Fertility Society's revised definition. In all patients endometriosis lesions were laparoscopically removed and/or electrocauterized and histological examination confirmed diagnosis. Data obtained from patients were then statistically analyzed.

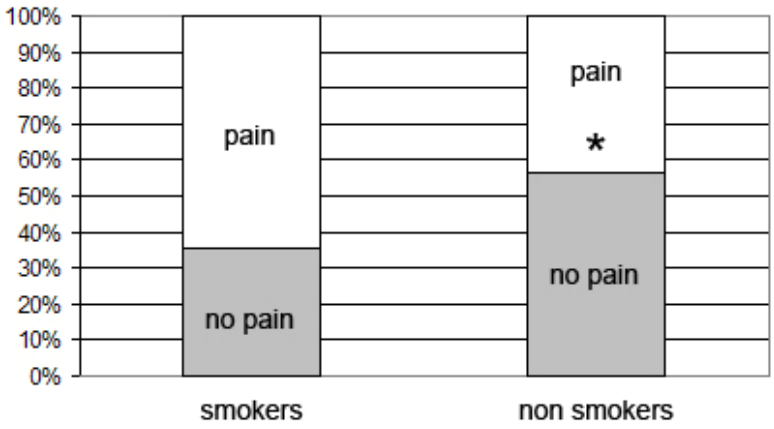
4. Results

Study groups

Mean age of participating patients was 31,2 years (21-43 years). Different stages of endometriosis were equally noted (with no statistical differences) among regular smoker and non-smoker patients, as well as among those performing regular sport activities and those being physically inactive. More than half of the patients were married, 17% of them were regular smokers and 38% of them were active in sports. Mean cigarette consumption was 9,5 pcs/day. Pain during period was reported by 82% of non-smokers, 92% by smokers, with the difference being statistically non-significant (p=0,597). Average pain score was 6,39, 6,14, 6,41 and 6,31 among the non-smoker, smoker, physically active and inactive patients, respectivelly. Pain scores were statistically non-significant among these study groups before the operation.

Outcomes in pain relief

At the end of the treatment period, 53.0% of patients reported the total absence of pain that they had specifically complained about at the beginning of the study. Among these patients, only 11.6% were smokers, corresponding to 35.7% of all smokers in the study. However, 56.7% of non-smoker participants reported a positive outcome that proved to be significantly larger than the ratio of pain-free smoker participants, as calculated by Chi-Square test (p=0.02).

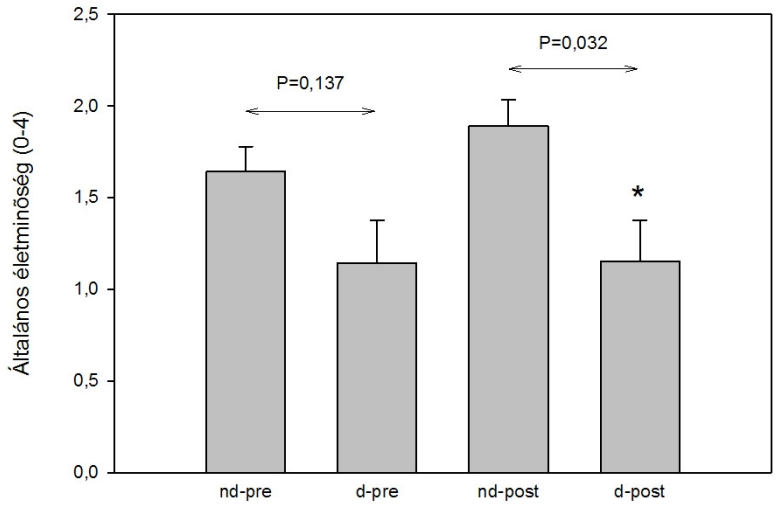


Correlation between smoker status and absence of specific pain as a basis for complaints after combined surgical and medical therapy of endometriosis patients. Data are presented as percentage values. *p=0.02; *pain*, specific pain is present; *no pain*, specific pain is absent

Outcomes in quality of life (self-image)

General quality of life estimates (0-4 scale)

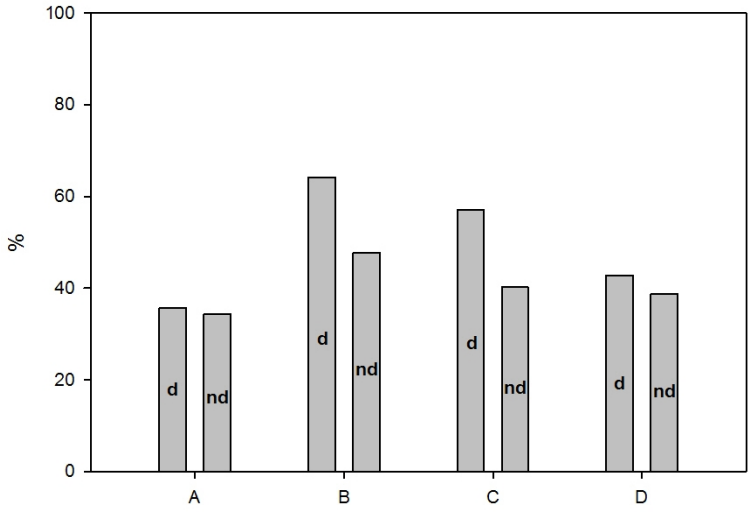
Among non-smokers, general quality of life was scored 1,642, while among smokers, that value was found to be 1,143 (the difference statistically non-significant, p=0,137, NS). By the end of the treatment period, non-smokers scored 1,889, while smoker participants scored 1,154, with the difference being significant (p=0,032).



General quality of life estimates (mean+SE) in non-smoker (nd) and smoker (d) groups, prior the operation (pre) and after the treatment (post). P: calculated significance values; *: statistical significance

Impact of health condition on daily routines prior the operation

Reduction in time of housework resulted from endometriosis related symptoms was reported by 35.7% of smoker and 34.3% of non-smoker patients, with the difference being statistically non-significant. Reduction in amount of work aimed to be completed was reported by 64,2% of smoker and 47.7% of non-smoker participants, with the difference being statistically non-significant. Blockade in performing planned tasks was as a result of endometriosis-rrelated symptoms was reported by 57.1% of smoker and 40.2% of non-smoker participants. The difference appeared to be non-significant. Problems regarding the achievements of housework was reported by 42.8% of smoker and 38.8% of non-smoker patients, with the difference being statistically non-significant.

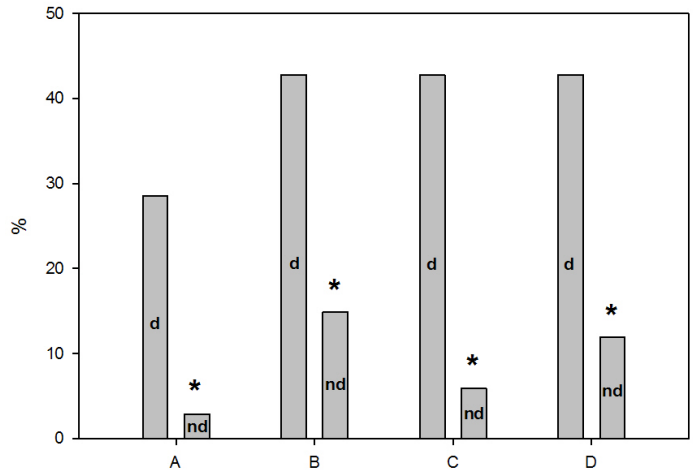


Self image prior to the operation in view of reports on impact of endometriosis-related symptoms on daily housework routines among smoker (d) and non-smoker (nd) participants. Data are presented as percentage value within one particular group. A: reduced amount of time of work; B: reduced amount of completed work tasks; C: blocked work activities; D: problems with usual daliy work routines

Impact of health condition on daily routines after therapy

Reduction in time of housework resulted from endometriosis related symptoms was reported by 28.5%- of smoker and 2.9% of non-smoker patients, with the difference being statistically significant (Z value 2.763). Reduction in amount of work aimed to be

completed was reported by 42.8%- of smoker and 14.9% of non-smoker participants, with the difference being statistically significant (Z value 2.018). Blockade in performing planned tasks was as a result of endometriosis-rrelated symptoms was reported by 42.8% of smoker and 5.9% of non-smoker participants. The difference was statistically significant (Z value 3.369). Problems regarding the achievements of housework was reported by 42.8% of smoker and 11.9% of non-smoker patients, with the difference being statistically significant (Z value 2.394).



Self image prior to the operation in view of reports on impact of endometriosis-related symptoms on daily housework routines among smoker (d) and non-smoker (nd) participants. Data are presented as percentage value within one particular group. A: reduced amount of time of work; B: reduced amount of completed work tasks; C: blocked work activities; D: problems with usual daliy work routines; *significant difference

Impact of chronic pain on specific daily activities

Within this category, patients were asked to score the negative impact of pain using a 0-3 scale (0: none; 1: minimal; 2: moderate; 3: severe).

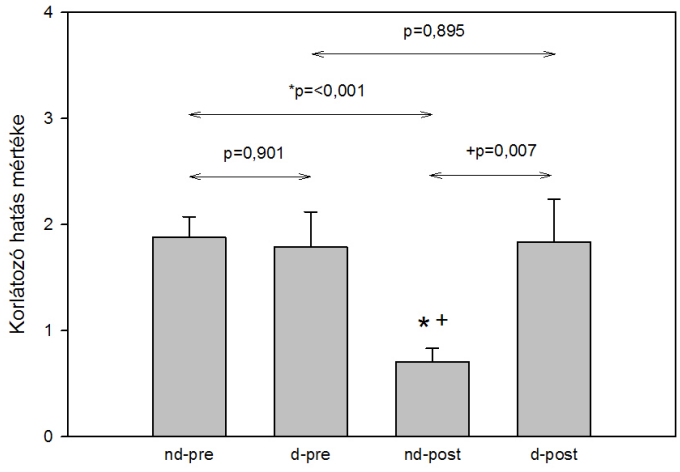
The following variables were scored in a significantly different manner following the treatment cessation among smoker and non-smoker participants. Data represent the change in scores (*prior* and *after* therapy, respectively): high energy consuming activities, non-smokers: 1,508 vs. 0,774, p= <0,001, smokers: 1,571 vs. 1,231, p=0,452. Simple activities, non-smokers: 0,969 vs. 0,508, p=0,017, smokers: 1,429 vs. 0,923,

p=0,177. Hauling, lifting, non-smokers: 1,154 vs. 0,583, p=0,007, smokers: 1,214 vs. 0,750, p=0,193. Stepping on stairs high up, non-smokers: 1,046 vs. 0,450, p=0,004, smokers: 1,214 vs. 0,917, p=0,479. Stepping on stairs not high up, non-smokers: 0,762 vs. 0,367, p=0,019, smokers: 1,000 vs. 0,667, p=0,266. Showering, clothing, non-smokers: 0,646 vs. 0,283, p=0,017, smokers: 0,429 vs. 0,500, p=0,929. Walking for short disctance, non-smokers: 0,708 vs. 0,300, p=0,013, smokers: 0,571 vs. 0,500, p=0,884. Walking for long distance, non-smokers: 0,831 vs. 0,333, p=0,032, smokers: 0,714 vs. 0,667, p=0,836.

Impact of chronic pain on daily activities in general

Within this category, patients were asked to score the negative impact of pain using a 0-4 scale (0: none; 1: minimal; 2: moderate; 3: high; 4: severe).

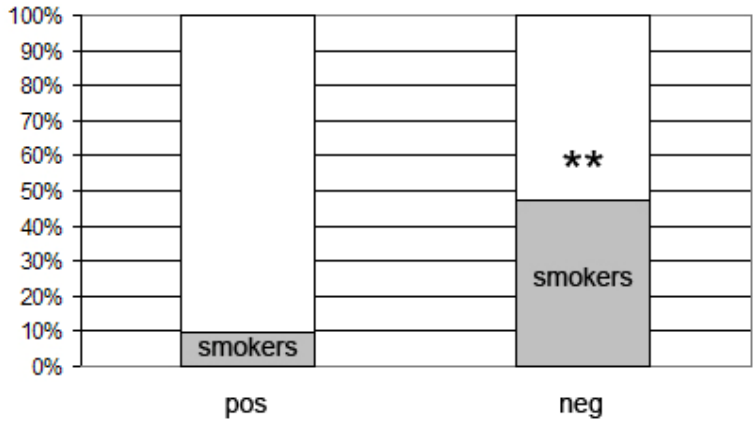
Prior the operation, non-smoker patients scored the negative impact of pain 1,877, smokers scored 1,786 (p=0,901, non-significant). Following treatment, non-smoker patients scored the negative impact of pain 0,707, while smokers scored it 1,833 (p=0,007, statistically significant). Decrease in scores from non-smokers proved to be statistically significant (1,877 vs. 0,707, p=<0,001), while that of smokers was statistically non-significant (1,786 vs. 1,833, p=0,895).



Impact of chronic pain on dail activities in general, among non-smoker (nd) and smoker (d) patients, prior the operation (pre) and following the cessation of treatment (post). Data are presented as mean + standard error. p: value of significance; *,+: statistically significant difference

Overall quality of life estimates

Patients reported improvement in their general quality of life in 73.7%, while no improvement or even deterioration was reported by 26.3% of all participants. Among those with improved quality of life only 9.4% were smokers, corresponding to 35.7% of all smoker participants. However, 47.3% were smokers among patients reporting no change or even worsening in their quality of life, that corresponded to 64.3% of all smoker participants. The correlation between smoker status and negativ quality of life outcome proved to be significant, as calculated by the Pearson's correlation test (2-tailed, $p< 0.01$).



Ratio of smokers among endometriosis patients with regard to positive or negative outcome in self-image at the end of combined surgical and medical therapy. Data are presented as percentage values. **p<0.01; *pos*, positive change in general quality of life; *neg*, no or negative change in general quality of life

Effectiveness of painkillers

Comparing subgroups of those regularly performing sport with patients without physical activity, the effectiveness of painkillers for pelvic pain was reported by 14 patients (45,1%) and 33 patients (66%), respectively ($p<0.05$).

Other cofounders

Detailed analyses revealed no significant differences in pain relief and quality of life measures at the end of therapy with relation to marital status, level of education, number of previous pregnancies regardless of outcome and parity (number of live births).

Furthermore, analyzing the data concerning the extent of the disease (i.e. the stage of endometriosis recorded at laparoscopy) and pain scores and quality of life values at the beginning and the end of the study revealed no significant correlations.

5. Summary

The present work deals with change in pelvic pain and quality of life outcomes during combined surgical and medical treatment period in endometriosis patients, in relation to certain individual factors that might influence the effectiveness of therapy. The overall rate of improvement in quality of life was identified in almost three quarters of the final study cohort (73.7%). We could not find any correlation between the revealed extent of the disease and its impact on personal quality of life and pain scores. Moreover, no significant relation could be identified between these study end points and sociodemographic variables, such as marital status, level of education, number of previous pregnancies and births.

However, we demostrated a striking relation between smoker status and pain relief, as well as overall improvement of quality of life. Those who were regular smokers reported significantly less improvement in these fields. An explanation to this finding could be provided by a relatively new hypothesis raising, that, dioxin, the most toxic of the organochlorines, is associated with an observed increase in endometriosis in the developed world. Recent investigations demonstrated that cigarette smoke contains high levels of agonists for dioxin receptors and markedly activates the dioxin signaling pathway. The an inverse relation between regular sport activity and effectiveness of painkillers for pelvic pain in endometriosis patients might be the result of regular exercise or sport that increase the circulating level beta-endorphins. We conclude, that regular smoking might have a disadvantageous impact on the success rate of combined surgical and medical therapy for endometriosis related pelvic pain.

6. Summary of novel results

1. Smoking might have a *disadvantageous effect* on the success rate of combined surgical and conservative therapy in patients with chronic pelvic pain due to endometriosis.

2. The *extent of negative impact* of chronic pelvic pain in endometriosis patients might *correlate with the energy requirement of physical activity* for which the negative impact is noted. Higher the energy effort requirement of a certain physical activity, deeper the negative impact of chronic pelvic pain.

3. *Smoking* might have a *destructive effect on self image* in patients treated for chronic pelvic pain due to endometriosis. Counseling to the patient should cover this issue before launching therapy for chronic pelvic pain.

4. Regular exercise and sport *might lower the effectiveness of painkillers* in endometriosis patients suffering from chronic pelvic pain.

5. Recommendations for daily clinical work based on the results:

a. In clinical centers dealing with endometriosis patients, a *consized questionnaire focusing on lifestyle variables* of patients should be included in the explorative phase of the disease. Thus, potential pitfalls in the therapy like heavy smoking lifestyle characteristic of the patient could be detected and addressed.

b. *Patient-tailored treatment strategies* should be provided to each individual endometriosis patient based on all medical and non-medical cofounders detected with regard of pain and endometriosis. Thus, disappointment resulted from unsuccessful therapy for both patient and medical care taker could be avoided.

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