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Symptomatic endometriosis of the posterior cul-de-sac is associated with impaired sleep quality, excessive daytime sleepiness and insomnia: a case–control study

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ABSTRACT

Objective: To assess the impact of endometriosis of the posterior cul-de-sac on quality of sleep, average daytime sleepiness and insomnia.
Study design: This age-matched case–control study was conducted in a tertiary referral centre for the diagnosis and treatment of endometriosis between May 2012 and December 2013. It included 145 women with endometriosis of the posterior cul-de-sac (cases; group E) and 145 patients referred to our Institution because of routine gynaecologic consultations (controls; group C). This study investigated whether sleep is impaired in patients with endometriosis of the posterior cul-de-sac. Sleep quality, daytime sleepiness and insomnia were assessed using the following self-administered questionnaires: the Pittsburgh Sleep Quality Index, the Epworth sleepiness scale and the Insomnia Severity Index, respectively. The primary objective of the study was to evaluate sleep quality in the two study groups. Secondary outcomes of the study were to assess average daytime sleepiness and insomnia in the two study groups.
Results: The prevalence of poor sleep quality was significantly higher in group E (64.8%) than in group C (15.1%; $p < 0.001$). The prevalence of excessive daytime sleepiness was significantly higher in group E (23.4%) than in group C (12.9%; $p = 0.033$). Patients of group E experienced subthreshold insomnia (29.0%) and moderate clinical insomnia (16.6%) significantly more frequently than patients in group C (24.4% and 5.0%; $p = 0.002$).
Conclusion: A substantial proportion of women with endometriosis of the posterior cul-de-sac experiences poor sleep quality, excessive daytime sleepiness and insomnia.

Introduction

Deep infiltrating endometriosis is commonly associated with pain symptoms and infertility; it deteriorates quality of life, sexual function and represents a relevant social burden [1–4]. Several studies investigated the impact of endometriosis on the psychological status of patients, finding a correlation between this condition and mental disorders (such as anxiety and depression) [5–9]. Sleep is an important physiological process for humans. It is essential for proper cognitive function and for human survival [10]. Poor sleep quality is a symptom of many sleep and medical disorders [11] and it inevitably reduces quality of life. Sleep disturbance is a common complaint of women with chronic pelvic pain [12]. Recently, a relationship between pain and sleep disturbances has been described in patients with endometriosis [13]; however, only sleep quality was evaluated, while other typical aspects related to sleep impairment (such as daytime sleepiness and insomnia) were not assessed.

The current study investigated quality of sleep, average daytime sleepiness and insomnia in patients with endometriosis of the posterior cul-de-sac and in healthy controls (without history of endometriosis and/or infertility). The primary objective of the

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study was to evaluate sleep quality in the two study groups. The secondary objectives were to assess average daytime sleepiness and insomnia in the two study groups.

Methods

This age-matched case–control study was performed between May 2012 and December 2013 in a referral institution for the diagnosis and treatment of endometriosis. It included women of reproductive age. Cases (group E) had histological diagnosis of endometriosis of the posterior cul-de-sac. Controls (group C) were recruited among women who underwent routine gynaecologic consultations; criteria for exclusion from the control group were: suspicion of endometriosis based on evaluation of symptoms (absence of dysmenorrhea, dyspareunia, chronic pelvic pain and dyschezia), gynaecological examination and transvaginal ultrasonography; history of infertility; previous diagnosis of endometriosis; gynaecological, intestinal and urological diseases causing abdominal pain (e.g. pelvic congestion syndrome, bladder pain syndrome). Exclusion criteria for both study groups were: severe underlying comorbidities (cardiovascular, respiratory, renal, haematological, endocrine, hepatic, gastrointestinal, neurological, or psychiatric); pregnancy; suspicion or diagnosis of oncological pathology; use of gonadotropin releasing hormone analogues [14]; restless legs syndrome; night shift work; use of antiallergic drugs and narcotics; and inability to sign the informed consent form or to complete the study questionnaires. Cases underwent laparoscopic excision of endometriosis while controls did not undergo any type of surgery.

The intensity of pain symptoms (dysmenorrhea, non-menstrual pelvic pain, deep dyspareunia and dyschezia) was recorded by using a 100 mm visual analogue scale (VAS).

Sleep quality, excessive daytime sleepiness and insomnia were assessed using the Italian validated versions of the Pittsburgh Sleep Quality Index (PSQI) [15], the Epworth sleepiness scale (ESS) [16] and the Italian translation of the Insomnia Severity Index (ISI) [17], respectively. The PSQI is used to measure the quality and patterns of sleep; a total score ≤ 5 indicates good sleep quality while a total score > 5 was indicates poor sleep quality [11]. The ESS is developed to measure average daytime sleepiness. A total score ≥ 10 indicates excessive daytime sleepiness [18]. The ISI is developed to measure insomnia. A total score between 0 and 7 corresponds to not clinically significant insomnia, between 8 and 14 to subthreshold insomnia, between 15 and 21 to clinical insomnia (moderate), between 22 and 28 to clinical insomnia (severe) [17].

The official Italian version Endometriosis Health Profile (EHP-30) was used to measure quality of life [19–21].

Patients completed the questionnaires in a silent room in privacy and then put the completed questionnaires in opaque sealed envelopes with a reference number to identify the case. Patients in group E fulfilled the questionnaires at the time of being scheduled for surgery (3–4 months before the operation). Patients in group C fulfilled the questionnaires after the gynaecologic consultation. The study conformed to the Declaration of Helsinki and women were informed on the study design and on the aims of this research; those who were enrolled in the study signed an informed written consent before participation. Ethic committee approval was obtained (393REG2015) and the study was registered on clinicaltrial.gov (NCT02027142).

Statistical analysis

The sample size was defined in an arbitrary way on the basis of the novelty of the study and the lack of available literature on the impact of endometriosis on sleep features at the time of the study design. The normal distribution of continuous variable data was evaluated with the Kolmogorov–Smirnov test. Categorical variables were analysed using the chi-squared test. The comparisons of continuous variables were performed by using the *t*-test or Mann–Whitney Rank Sum test accordingly to data distribution, between two groups of patients. Among more than two subgroups of patients, the comparisons of continuous variables were performed by using one way analysis of variance and analysis of variance on ranks accordingly to data distribution. The correlations between the PSQI score and the EHP-30 domain scores and between the PSQI score and the intensity of dysmenorrhea were performed using the Spearman Rank Order Correlation test.

Univariate and multivariate analysis were used to identify independent factors potentially affecting the sleep quality. Factors presenting significant correlation ($p < 0.05$) or a tendency towards association ($p < 0.10$) with the outcome of interest were entered into a multinomial regression model.

Data were analysed using the SPSS software version 20.0 (SPSS Science, Chicago, IL, USA).

Results

Out of 351 consecutive women approached for the study, 294 accepted to participate (149 cases and 145 controls), yielding a response rate of 83.8%. In group E, at surgery, four patients with suspected endometriosis had no histological confirmation and were excluded from the study. Therefore, 145 patients were included in group E and 145 in group C. Table 1 describes the characteristics of the study population.

The prevalence of poor sleep quality was higher in group E (94/145 patients; 64.8%, 95% C.I., 56.5–72.6%) than in group C (27/145 patients; 18.6%, 95% C.I., 12.3–24.9%; $p < 0.001$). The scores of the PSQI are detailed in Table 2.

In group E, no significant association was observed between sleep quality and use of hormonal treatments ($p = 0.536$), type of hormonal treatment ($p = 0.270$) and history of infertility ($p = 0.876$). No significant difference was reported in the prevalence of pain symptoms between patients with good and poor sleep quality, while patients with poor sleep quality experienced a higher intensity of dysmenorrhea and chronic pelvic pain (Table 3). A positive correlation was found between the PSQI scores and the intensity of chronic pelvic pain (Spearman correlation coefficient = 0.459, $p < 0.001$) while a strong positive correlation was observed between the PSQI scores and the intensity of dysmenorrhea (Spearman correlation coefficient = 0.764, $p < 0.001$). All EHP-30 domain scores were better in patients who experienced good sleep quality (Table 3). No significant correlation was reported between the PSQI score and all EHP-30 domains scores ($p > 0.05$ for all comparisons).

The mean (±SD) ESS score was worse in group E (6.2 ± 3.9) than in group C (4.5 ± 3.2; $p = 0.017$). The prevalence of excessive daytime sleepiness was significantly higher in group E (34/145 patients; 23.4%, 95% C.I., 16.5–30.3%) than in group C (17/145 patients; 11.7%, 95% C.I., 6.5–16.9%; $p = 0.014$).

In group E, excessive daytime sleepiness was not associated with the presence of dysmenorrhea ($p = 0.754$), chronic pelvic pain ($p = 0.948$), dyschezia ($p = 0.957$) and dyspareunia ($p = 0.968$). Furthermore, no association was found also with the intensity of dysmenorrhea ($p = 0.860$), chronic pelvic pain ($p = 0.698$), dyschezia ($p = 0.137$) and dyspareunia ($p = 0.547$). No association was reported between patients with and without excessive daytime sleepiness and the use of hormonal treatments ($p = 0.851$) and between excessive daytime sleepiness and the type of hormonal treatment ($p = 0.443$). No significant difference was reported in all EHP-30 domain scores between patients with and without

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