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CLINICAL STUDY

Endometriosis features and dienogest tolerability in women with depression: a case-control study

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ABSTRACT

Objective: Primary aim of this study was to investigate endometriosis characteristics of patients with psychiatric conditions or depression. The secondary aim was to study tolerability of dienogest in this context.

Methods: This observational case-control study included endometriosis data from patients visiting our clinic from 2015–2021. We collected information from patient charts and in phone interviews based on a structured survey. Patients with surgical confirmed endometriosis were included.

Results: 344 patients fulfilled the inclusion criteria: $n = 255$ no psychiatric disorder, $n = 119$ any psychiatric disorder and $n = 70$ depression. Patients with depression (EM-D, p=.018; p=.035) or psychiatric condition (EM-P, p=.020; p=.048) suffered more often from dyspareunia and dyschezia. EM-P patients had more often primary dysmenorrhoea with higher pain scores (p=.045). rASRM stage or localisation of lesions did not differ. EM-D and EM-P patients discontinued dienogest treatment more often related to worsening of mood (p= .001, p=.002).

Conclusion: EM-D or EM-P had a higher prevalence of pain symptoms. This could not be attributed to differences in rASRM stage or location of endometriosis lesions. Strong primary dysmenorrhoea might predispose to develop chronic pain-based psychological symptoms. Therefore, early diagnosis and treatment are relevant. Gynaecologist should be aware of the potential impact of dienogest on mood.

SHORT CONDENSATION

Women with endometriosis and psychiatric disorders especially have more dyschezia and dyspareunia, independent from rASRM stage, depth of infiltration and localisation of endometriosis lesions. Dienogest has an impact on mood especially in already prone patients.

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Introduction

Endometriosis (EM) is an inflammatory proliferative chronic disease affecting 5–10% of women of reproductive age [1,2]. A combination of immunological, environmental, anatomical, and emotional factors are discussed as pathomechanisms for the ectopic growth of endometrial tissue [1,2]. Patients can be without symptoms or suffer significantly from dysmenorrhoea, dyspareunia, dyschezia, dysuria, and chronic pelvic pain [3]. Infertility can be a long-term consequence. Comorbidities of EM include migraine, depression, and autoimmune diseases [3,4].

For research purposes, surgery, and confirmation of endometriosis lesions by biopsy is recommended.

The individual and social burden of endometriosis compromises patients' relationships, physical and mental well-being independent of the endometriosis stage and is estimated to be responsible for 40% of chronic pelvic pain complaints and 35% of female infertility cases [3,5].

Psychiatric disorders, mainly anxiety and depression, are common in women suffering from endometriosis [3,6,7]. It is yet unclear if anxiety and depression in EM patients are a consequence of EM-associated pain or a different condition. A meta-analysis of genome-wide association (GWAS) studies revealed a shared genetic aetiology for endometriosis and depression [4]. Such a genetic connection of both conditions might result in a special phenotype of EM.

The 19-nortestosterone derivative dienogest (DNG) is broadly used for endometriosis treatment [8,9]. It exerts a strong suppressive effect on endometrial growth and modifies the inflammatory microenvironment of endometriotic lesions [8]. Like other progestins, DNG may exert a negative impact on mood in a subset of women (5.1%) [10]. It is relevant to understand, if women with endometriosis and depression or other psychiatric conditions can without concern be treated with this progestin.

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The primary aim of the current study was to examine if women with endometriosis and psychiatric conditions on one hand and diagnosed depression on the other hand differ regarding endometriosis symptoms, rASRM stage and localisation from women with endometriosis alone. The second aim was to assess DNG tolerability by analysing the duration of use and reasons for discontinuation. Improved understanding of the comorbidity might contribute to earlier diagnosis, other therapeutic approaches, and reduction of the long-term negative impact on psychiatric well-being.

Methods

For this observational case-control study we identified endometriosis patients who visited our outpatient clinic of the Department of Gynaecology at University Hospital Zurich from 2015 to July 2021. Charts were included if endometriosis was confirmed by operation and biopsy and rASRM score was reported. The severity of endometriosis is classified by the American Society of Reproductive Medicine (rASRM) score and the #ENZIAN classification describing the location, amount, depth, and size of endometriotic lesions, involvement of pelvic structures, the extent of pelvic adhesions, and obstruction of the fallopian tubes [11]. We included premenopausal women aged 18–55 years who, after informed consent, agreed to participate in a telephone interview. The study was part of a larger study investigating the potential impact of comorbidities on endometriosis features.

We excluded patient charts without histologically confirmed endometriosis, and those with adenomyosis or scar endometriosis only. Furthermore, we excluded patients not willing to participate and cases, who could not be interviewed due to insufficient language knowledge.

Patients interested in participating after being contacted and informed by phone received a sheet with detailed study information. After obtaining written or oral consent, we conducted telephone interviews based on a modification of the 'Women's Health Symptom Survey Questionnaire' of the World Endometriosis Research Foundation adapted to our study question [12]. The modification included questions about the general history, medical conditions, use of medications and specific questions about psychiatric symptoms and diagnosis. Furthermore, we collected information on the use of dienogest, its duration and reasons for discontinuation. Before the start of the interview, the survey was validated in 50 test interviews, interviews were conducted by medical staff educated in evaluation of medical history, gynaecological and psychiatric disorders and able to clarify questions during the interviews. Current and past medication was evaluated, excluding a possible co-effect of other drugs on reported symptoms.

For the analyses, participants were divided into three groups: Group 1 (EM-O): patients without a history of psychiatric disorder, group 2 (EM-P): patients with any psychiatric diagnosis in their history, group 3 (EM-D): patients with a history of depression. Patients with a psychiatric disorder were specifically asked for their psychiatric diagnosis and about medical treatment at present and in the past. Patients without psychiatric disorders served as controls.

Endometriosis was staged using the revised American Society of Reproductive Medicine (rASRM) Score in the patient chart [13]. From the surgical records endometriosis localisation, depth of infiltration, and affected compartments were noted. In the interview, we used a pain score from 1–3 to describe the pain intensity, with 1 describing light pain, 2 describing moderate pain, and 3 describing severe pain.

Statistical analysis

Data was analysed using SPSS® statistics (IBM®, Armonk, New York, United States).

Shares in percent were used for categorical variables and means including standard deviation (SD) were used for numeric variables. To compare categorical variables among groups, we used Chi-Square or Fisher's exact test (expected frequencies <5), depending on expected frequencies.

To compare numeric variables between two groups, we used the independent sample t-test for normally distributed variables and Wilcoxon-Mann-Whitney test for not normally distributed variables.

A two-tailed p-value ≤ 0.05 was considered statistically significant.

The study was approved by the cantonal ethics commission of Zurich (BASEC Nr. 2021-00285) and registered on clinical Trials.gov (NCT04816357).

Results

The screening procedure is described in Figure 1. 344 women fulfilled the inclusion criteria (Figure 1). 119 patients reported any type of psychiatric condition (group 2, EM-P), 70 women had a history of depression (group 3, EM-D),

Group 2 (any psychiatric disorder) consisted of $n = 70$ (58.8%) women with depression, $n = 21$ (17.6%) women with adaptive disorders, $n = 18$ (15.1%) women with anxiety, $n = 10$ (8.4%) women with post-traumatic stress disorder and others (9.2%, $n = 11$). Prescribed psychiatric medication reported were selective serotonin uptake inhibitors (33.6%, $n = 40$), tricyclic antidepressants (2.5%, $n = 3$), lorazepam (2.5%, $n = 3$), monoamine oxidase inhibitors (0.8%, $n = 1$), norepinephrine–dopamine reuptake inhibitors (0.8%, $n = 1$).

Altogether, 20.3% ($n = 70$) of all endometriosis patients suffered from depression. 22.8% ($n = 16$) were currently taking dienogest (vs 22.2% ($n = 50$) patients without psychiatric disorder). 55.7% ($n = 39$) of patients with depression reported a history of dienogest intake (vs 47.5% ($n = 107$) patients without psychiatric disorders).

Baseline criteria did not differ between groups, except that BMI was higher in group 2 (Table 1). The percentage of women with a history of dienogest use did not differ between groups (Table 1).

We found significant differences in endometriosis symptoms between women without and those with psychiatric conditions or depression (Table 2). Primary dysmenorrhoea tended to be more frequent in EM-P patient (p=.121) and associated with a significantly higher pain score (p=.045). More women with EM-P and EM-D suffered from dyspareunia (EM-P: OR 1.84 (95% CI 1.15 – 2.96); EM-D: OR 2.00

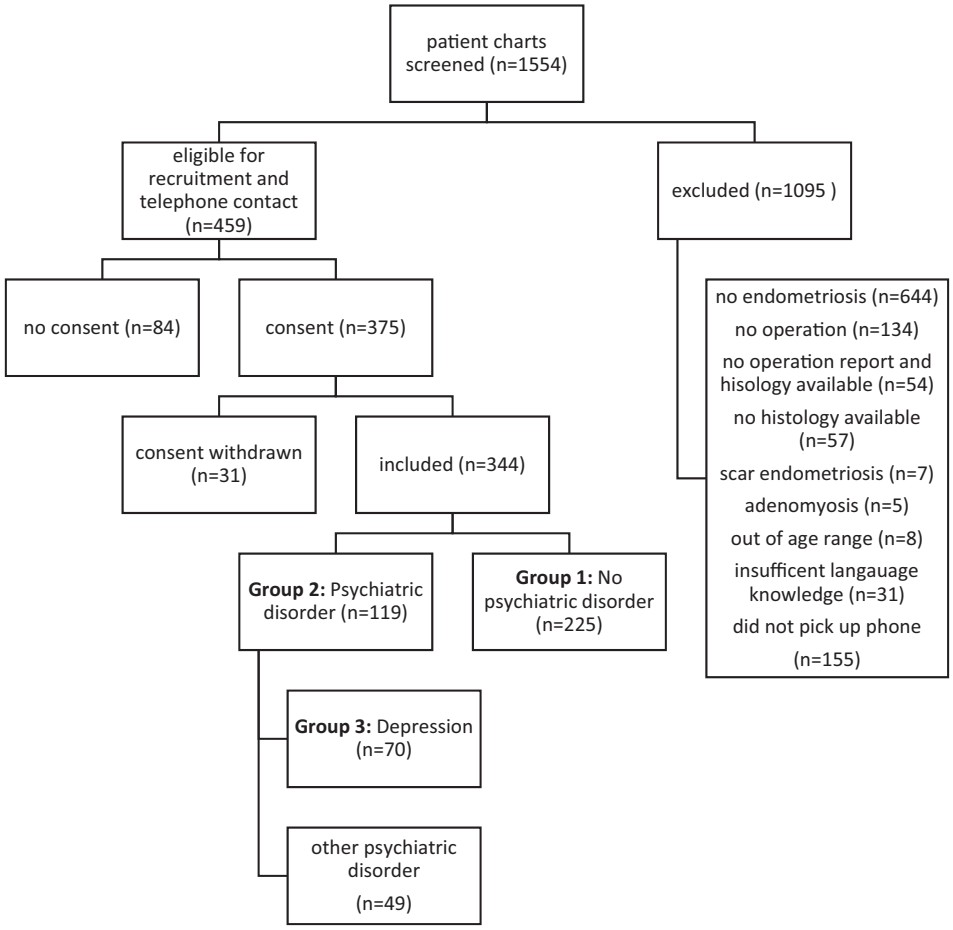

Figure 1. Inclusion and exclusion of patients.

Table 1. Baseline characteristics.

Characteristic	All ($n = 344$)	Group 1: No psychiatric disorder ($n = 225$)	Group 2: Psychiatric disorder ($n = 119$)	*p Value	Group 3: Depression ($n = 70$)	*p Value
Age years mean (SD)	36.0 (7.3)	35.9 (7.2)	36.7 (7.5)	.324	36.5 (8.0)	.558
BMI kg/m^2 mean (SD)	23.1 (4.0)	22.8 (3.7)	23.7 (4.4)	.043	23.8 (4.6)	.074
Age menarche years mean (SD)	12.8 (1.6)	12.7 (1.5)	12.9 (1.6)	.446	12.9 (1.8)	.354
Ever pregnant % (n)	40.4 (139)	39.1 (88)	42.0 (50)	.658	37.1 (26)	.768
Number of pregnancies mean (SD)	0.7 (1.1)	0.6 (1.0)	0.8 (1.1)	.258	0.7 (1.2)	.682
Age at first delivery years mean (SD)	29.8 (5.4)	29.5 (4.9)	30.2 (6.3)	.602	31.2 (6.1)	.241
Sport >1h/week % (n)	64.8 (223)	67.6 (152)	59.7 (71)	.145	58.6 (41)	.147
Ethnicity Caucasian % (n)	83.1 (286)	81.3 (183)	86.6 (103)	.219	81.4 (57)	.986
Ever use of Dienogest % (n)	72.1 (248)	71.1 (160)	73.9 (88)	.577	78.6 (55)	.220

n: number; BMI: Body mass index. *Compared to patients without psychiatric disorder.

(95% CI 1.12 – 3.58)) and dyschezia (EM-P OR 1.65 (95% CI 1.06 – 2.58); EM-D: OR 1.79 (1.04 – 3.07)).

At present the number of women using a pain killer more than 3 days/month was significantly higher in the EM-D group. Both, EM-P and EM-D patients reported more often to not respond to pain medications (p=.011; p=.015).

EM-D patients tended to have experienced more endometriosis surgeries (Table 2). Subanalyses revealed that the number of operations was not higher in patients with no response to analgesics. Women stating no response to analgesics ($n = 68$) did neither experience more surgeries, nor more often more than one surgery (Number of surgeries: EM-O 1.5 (SD 1.1); EM-D 1.9 (SD 1.6), $p = 0.288$; >1 surgery % (n): EM-$O = 26.5$ (9); EM-D 40.9 (9), $p = 0.259$).

Compared to group 1, localisation of the endometriosis lesions was less frequent in the ovaries, and there was a trend to more lesions in the rectovaginal septum in EM-D patients (Table 3). No differences were found regarding depth of infiltration, rASRM stage or number of affected compartments (Table 3). Although not significant, it might be of relevance that the percentage of women with infiltration >3cm was lower in women with depression (12.9% vs. 20.0%, p=.177), despite more pain.

Reasons to discontinue treatment with dienogest are presented in Table 4. Both, participants with any psychiatric condition and those with depression reported more frequently to have discontinued dienogest treatment because of worsening of mood (p=.002; p= .001) (Table 4).

Discussion

Findings and interpretation

In accordance with existing evidence, that women with endometriosis are prone to psychiatric diseases, the prevalence of depression in our trial was higher (20.3%) than in

Table 2. Endometriosis related clinical parameters.

Characteristic	All ($n = 344$)	Group 1: No psychiatric disorder ($n = 225$)	Group 2: Psychiatric disorder ($n = 119$)	*p Value	Group 3: Depression ($n = 70$)	*p Value
Endometriosis symptoms						
Dysmenorrhoea % (n)	74.5 (225) $N = 302$	73.6 (145) $N = 197$	76.2 (80) $N = 105$	.623	82.5 (52) $N = 63$	.130
Dysmenorrhoea start menarche % (n)	39.9 (130) $N = 326$	36.8 (78) $N = 212$	45.6 (52) $N = 114$	.121	40.9 (27) $N = 66$	.547
Score (0–3) mean (SD)	1.0 (1.3) $N = 323$	0.9 (1.2) $N = 210$	1.2 (1.4) $N = 113$	.045	1.1 (1.4) $N = 65$	.306
Dyspareunia % (n)	60.5 (208)	56.0 (126)	68.9 (82)	.020	71.4 (50)	.018
Dyschezia % (n)	45.6 (157)	41.8 (94)	52.9 (63)	.048	55.7 (39)	.035
Dysuria % (n)	17.4 (60)	16.4 (37)	19.3 (23)	.503	22.9 (16)	.222
Use of analgesics per menstrual bleeding						
Days mean (SD)	2.7 (2.6)	2.5 (2.4)	3.0 (2.8)	.123	3.1 (3.1)	.168
More than 3 days % (n)	21.5 (74)	18.7 (42)	26.9 (32)	.077	30.0 (21)	.043
Response to analgesics % (n)	70.1 (241)	72.4 (163)	65.5 (78)	.011	62.9 (44)	.015
Heavy menstrual bleeding % (n)	57.8 (199)	56.4 (127)	60.5 (72)	.468	62.9 (44)	.342
Endometriosis operations (EM-OP)						
Age at first OP years mean (SD)	31.7 (6.7)	31.6 (6.3)	31.8 (7.3)	.772	30.7 (6.9)	.330
≤20 years % (n)	4.9 (17)	3.6 (8)	7.6 (9)	.103	7.1 (5)	.198
≤29 years % (n)	37.5 (129)	36.9 (83)	38.7 (46)	.748	44.3 (31)	.267
Number of EM-OP mean (SD)	1.6 (1.0)	1.5 (0.9)	1.6 (1.0)	.239	1.7 (1.2)	.097
> 1 EM OP % (n)	35.5 (122)	32.4 (73)	41.2 (49)	.107	44.3 (31)	.060

n: number; EM: endometriosis; OP: operation, for variables with differing n_{total} due to missing values, n_{total} is specified, *compared to patients without psychiatric disorder.

Table 3. Endometriosis localisation and stage.

Characteristic	All (n = 344)	Group 1: No psychiatric disorder (n = 225)	Group 2: Psychiatric disorder (n = 119)	*p Value	Group 3: Depression (n = 70)	*p Value
rASRM Grade mean (SD)	2.6 (1.1)	2.7 (1.1)	2.6 (1.1)	.540	2.4 (1.2)	.256
rASRM >1 % (n)	75.6 (260)	76.0 (171)	74.8 (89)	.804	71.4 (50)	.489
rASRM >2 % (n)	61.0 (210)	63.1 (142)	57.1 (68)	.280	52.9 (37)	.125
rASRM >3 % (n)	27.3 (94)	27.6 (62)	26.9 (32)	.895	24.3 (17)	.590
EM Infiltration				.518		.240
<1cm	59.9 (206)	57.8 (130)	63.9 (76)		68.6 (48)	
1–3cm	21.5 (74)	22.2 (50)	20.2 (24)		18.6 (13)	
>3cm	18.6 (64)	20.0 (45)	16.0 (19)		12.9 (9)	
EM Compartments mean (SD)	2.4 (1.2)	2.4 (1.2)	2.3 (1.2)	.406	2.3 (1.1)	.542
>1 % (n)	72.7 (250)	73.8 (166)	70.6 (84)	.528	75.7 (53)	.692
>2 % (n)	40.4 (139)	42.7 (96)	36.1 (43)	.240	37.1 (26)	.451
Localisation						
Rectovaginal septum % (n)	46.5 (160)	44.9 (101)	49.6 (59)	.407	57.1 (40)	.063
Rectum % (n)	11.6 (40)	12.0 (27)	10.9 (13)	.767	8.6 (6)	.427
Intestine % (n)	7.8 (27)	7.6 (17)	8.4 (10)	.781	11.4 (8)	.310
Ligaments/pelvic wall % (n)	70.9 (244)	70.2 (158)	72.3 (86)	.691	71.4 (50)	.792
Bladder % (n)	28.2 (97)	30.2 (68)	24.4 (29)	.251	21.4 (15)	.153
Extragenital locations % (n)	5.2 (18)	5.3 (12)	5.0 (6)	.908	4.3 (3)	1.000
Ovaries % (n)	53.8 (185)	57.8 (130)	46.2 (55)	.041	44.3 (31)	.056
Peritoneum % (n)	11.0 (38)	11.1 (25)	10.9 (13)	.958	10.0 (7)	.794

rASRM: revised American Society of Reproductive Medicine; EM: endometriosis; n: number. *compared to patients without psychiatric disorder.

the general population (5–10%) [6,14]. The percentage of women with onset of more severe dysmenorrhoea at menarche was higher in the EM-P group. Both, women with any psychiatric disorder (EM-P) and those with depression (EM-D) reported significantly more often dyspareunia and dyschezia and responded less to analgesics (Table 2). Despite more pain symptoms in both groups, there were no differences in rASRM stages or depth of infiltration, which is the parameter believed to be more associated with endometriosis pain (Table 3) [15]. In contrast, fewer patients with depression were diagnosed with more than 3 cm depth of infiltration (12.9% vs. 20.0% p=.240). Localisation of endometriosis lesions tended to differ between groups, with more lesions in the rectovaginal septum in EM-D patients (p=.063) and a trend to less lesions at the ovaries (Table 3). Within patients with dienogest treatment, those with depression or psychiatric problems mentioned significantly more often depression as reason for discontinuation (Table 4).

Results in the context of what is known

Prevalence of depression in our endometriosis patients is slightly higher than reported in previous studies, possibly related to differences in data collection and not histologically verified endometriosis diagnosis in other trials (14–15%) [16,17]. The finding, that rASRM stage is not associated with pain symptoms is in line with current literature [3,16,18]. Pain intensity seems to be more related to the localisation of deep infiltrating endometriosis [15,19].

The dysmenorrhoea rate of approximately 75% in our study is in line with findings in a recent cohort study including 1560 women [18]. We further found a prevalence of primary dysmenorrhoea in the range of the highly varying percentages reported in studies with adolescents ranging from 20–90% [20–22]. The earlier start of dysmenorrhoea in EM-D patients did not affect the mean age of first surgery (30.7 years EM-D vs. 31.6 years EM-O, p=.330). Considering the well-known consequences of

Table 4. Reasons for discontinuation of dienogest.

Adverse event leading to discontinuation % (n)	All (n = 177)	Group 1: No psychiatric disorder (n = 109)	Group 2: Psychiatric disorder (n = 68)	*p Value	Group 3: Depression (n = 41)	*p Value
Worsening of mood	14.7 (26)	8.3 (9)	25.0 (17)	.002	29.3 (12)	.001
Other psychiatric problems	22.0 (39)	20.2 (22)	25.0 (17)	.452	19.5 (8)	.927
Bleeding disorders	8.5 (15)	6.4 (7)	11.8 (8)	.241	12.2 (5)	.311
Headache, migraine	6.8 (12)	6.4 (7)	7.4 (5)	1.000	5.9 (2)	1.000
Gastrointestinal problems	6.2 (11)	5.5 (6)	7.4 (5)	.751	0 (0)	.189
Continuation of lower abdomen pain	11.3 (20)	14.7 (16)	5.9 (4)	.072	4.9 (2)	.157
Others	27.7 (49)	29.4 (32)	25.0 (17)	.897	19.5 (8)	.360

For variables with differing n_{total} due to missing values, n_{total} is specified, *compared to patients without psychiatric disorder.

long-term pelvic pain, delay of diagnosis could substantially contribute to psychiatric symptoms [16,23–25].

Deep dyspareunia is associated with deep infiltrating endometriosis [15,23,24]. The dyspareunia rate in our trial was higher (60.5%) than reported in survey-based studies (45%) and even higher in women with EM-D (71.4%) and EM-P (68.9%) [16,23,24]. In EM-D patients, this could potentially be attributed to the higher frequency of EM-lesions in the rectovaginal septum (p=.063). Our study does not allow final conclusions, but it might be worth to study deeper in future, if deep dyspareunia might be a special attribute of EM-D patients, as EM-P patients did not differ from EM-O patients regarding localisation. We found no differences in depth of infiltration between groups. Neither did we observe a higher prevalence of EM lesions at the ligaments/pelvic wall, what also has been reported to be associated with dyspareunia [15,23]. Some authors indicate, that dyspareunia is associated with a higher rate of depression, independent of the diagnosis of endometriosis [26–28]. Warzecha et al. found a significant positive correlation between the beginning of dyspareunia and depression in women with endometriosis, collecting data on symptoms with a written survey (n = 246 respondents) [16]. Also painful defaecation was associated with an increased risk of depression (OR = 7.7, 95% CI 1.4–42.3, p=.01) [16]. The prevalence for dyschezia in our trial (46%) is in line with other studies presenting data of patients with histologically confirmed endometriosis (45% to 52%) [16,18]. The OR in our study for dyschezia and depression was 1.65 (1.06 – 2.58). Prevalence of dyschezia was lower (25%) in a small cohort study with 96 patients without histological confirmation of the disease [24].

Endometriosis and depression share specific genetic polymorphisms. Women with the comorbidity might present with another phenotype of EM and more severe pain or respond less to treatment [29,30].

Insofar, pelvic pain might not be the only reason for the development of psychiatric conditions in EM patients, but predisposition might play a role as well [16,31].

Findings like a significant correlation between prevalence of depression and mean age of dysmenorrhoea onset however support the idea that chronic pain generates the development of psychiatric disorders [16]. A meta-analysis by Gambadauro et al. found, that pain is the main factor determining the prevalence of depression in women with chronic pelvic pain with or without confirmed endometriosis [7].

Our findings support the theory proposed by Laganà of a vicious cycle of psychological diseases amplifying endometriosis-related pain, resulting in worsening of psychopathological symptoms [3].

That women in the EM-D group responded less to analgesics could be related to the well-known increased pain perception in patients with depression [32]. EM-D patients also tended to experience more operations (32.4 vs. 44.3% p=.060). Chronic pain results in increased pain sensitivity potentially due to associated alteration in brain structure and function [33]. Central and peripheral hypersensitivity in endometriosis patients is suggested [33].

Clinical Implications

For patients with strong primary dysmenorrhoea, optimised pain management and further evaluation of the course of pain might prevent chronification, neuroplastic changes in pain memory and development of psychiatric comorbidities. Our data suggest, that especially in adolescents without response to medical treatments diagnosis of endometriosis by laparoscopy and specific treatment might contribute to prevent chronification of pain symptoms. Today ultrasound and MRI have improved but limited sensitivity, especially in the case of discrete endometriosis lesions.

Awareness for the potential comorbidity depression in women with EM is relevant, as hormonal treatment, especially progestin-only treatment, is known to negatively affect mood in a subset of women [10]. It is unknown, how women with pre-existing psychiatric conditions tolerate the continuous use of the progestin dienogest. In the VIPOS trial, a higher risk for new depression or worsening of depression could not be excluded [34]. In our trial, six months discontinuation rates with dienogest did not differ between groups. However, EM-P and EM-D women reported significantly more often worsening of mood as a reason for discontinuation (Table 4). Consequently, we would recommend close monitoring of patients with pre-existing psychiatric problems.

Research Implications

Patients suffering from endometriosis and depression share increased pain perception. It is suspected, that one of the reasons are shared gene polymorphisms, but further research is needed to confirm this supposition [29,30]. The detected trend of more rectovaginal endometriosis in women with depression needs to be confirmed in larger studies, as well as the trend to more endometriosis surgeries for women with primary dysmenorrhoea. Further studies are also needed to evaluate the correlation of onset of psychiatric diseases and dysmenorrhoea onset at menarche.

Strengths and limitations

Strengths of our study include the histologically confirmed diagnosis and the detailed collection of information related to endometriosis and psychiatric symptoms in a personal interview and not in a survey only. Phone interviews conducted by medical experts allowed clarifications whenever needed. We can however not exclude some recall bias related to questions addressing symptoms in the past. A limitation might be, that we had no access to reports from psychiatrists. However, clarification and distinction of depression from other psychiatric disorders was achieved during the phone interview. Data for the group with all psychiatric disorders probably are influenced by results of the huge group of women with depressions. This was considered when interpreting the results.

Conclusion

Women with endometriosis and depression or other psychiatric conditions have a higher prevalence of dyschezia, and dyspareunia, independent from rASRM stage, depth of infiltration and localisation of endometriosis lesions. They also respond less to analgesics. The onset of stronger pain already at menarche, together with the high delay to first operation, might boost the development of alterations in brain structure and function which results in increased pain sensitivity. It is feasible that some of the psychological conditions observed in our study have evolved from chronic pain. Early diagnosis and treatment of endometriosis, especially strong primary dysmenorrhoea is therefore highly important.

Only women with depression tended to have more often rectovaginal lesions. Further studies are needed to evaluate if this could be an indicator for a shared hereditary trait. Gynaecologists should be aware of the impact of dienogest on mood in women with psychiatric conditions.

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Ethical approval

The study was approved by the cantonal ethics commission of Zurich (BASEC Nr. 2021-00285) on 16.03.2021 and registered on clinical Trials.gov (NCT04816357).

Author contributions

HD analysed and interpreted raw data, wrote the article, supervised data collection, performed sample checks for correct coding of data, performed interview training with students and served as a contact person for students. GM conceptualised the study, led the study, co-analysed, and interpreted the data and revised the manuscript. PI provided the patient charts and revised the manuscript. JM, AM, AN and MN added expertise and revised the manuscript. CK and LP collected the data, performed the interviews, and revised the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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