

Deep infiltrating endometriosis: relation between severity of dysmenorrhoea and extent of disease

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BACKGROUND: Little is known about the precise nature of the relationship between dysmenorrhoea (DM) and endometriosis. Our aim was to evaluate the relationship between the severity of DM in women with posterior deep infiltrating endometriosis (DIE) and indicators of the extent of their disease. **METHODS:** Various indicators of the extent of DIE were recorded during surgery in 209 women. The severity of their DM was assessed with a pain scale. The scale was retrospective for 155 women and prospective for 54. Correlations were sought with an ordinal logistic regression model with cumulative odds. **RESULTS:** On univariate analysis the following variables were related to the severity of DM: number of previous surgical procedures for endometriosis; revised American Fertility society classification; extensiveness of adnexal adhesion; Douglas obliteration; size of the posterior DIE implant; extent of the sub-peritoneal infiltration by the posterior DIE (rectal, vaginal or both versus sub-peritoneal only). Current infertility was associated with less severe DM. After multiple regression analysis, presence of a rectal or vaginal infiltration by the posterior DIE and extensiveness of adnexal adhesion were the only factors that remained related to DM severity. **CONCLUSIONS:** The concept of ‘very deep infiltrating endometriosis’, defined as implants invading the wall of the pelvic organ, should be tested in future classification systems specifically addressed to the prediction of endometriosis-related pain.

Key words: classification system/deep infiltrating endometriosis/dysmenorrhoea

Introduction

The association of dysmenorrhoea (DM) with endometriosis is well recognized. Although DM is very common in the general population of women (Jamieson and Steege, 1996), it is especially frequent among those with endometriosis (Williams and Pratt, 1977; Mahmood *et al.*, 1991; Al-Badawi *et al.*, 1999). Furthermore, one case–control study reported a trend between the risk of endometriosis and the severity of DM (Cramer *et al.*, 1986), which suggests that the more extensive the disease is, the greater the severity of associated DM. Systems of endometriosis classification, such as the revised American Fertility Society classification (R-AFS) (The American Fertility Society, 1985), have been developed to help standardize evaluation of the extent of disease (Schenken, 1998). Several studies, however, have failed to correlate its extent, as measured by the AFS score, with the severity of dysmenorrhoea (Fedele *et al.*, 1990; Marana *et al.*, 1991; Vercellini *et al.*, 1996; Porpora *et al.*, 1999). Furthermore, little is known about the precise nature of the relationship between endometriosis and DM (Vercellini, 1997).

Deep infiltrating endometriosis (DIE) is a particular form of endometriosis that penetrates >5 mm under the peritoneal surface (Koninckx and Martin, 1994). These lesions are considered very active and are strongly associated with pelvic pain symptoms (Koninckx *et al.*, 1991). DIE implants are located in specific locations, primarily the posterior area (Cornillie *et al.*, 1990; Chapron *et al.*, 2003). Posterior DIE can involve uterosacral ligaments (Chapron and Dubuisson, 1996), torus uterinus (retrocervical area of the uterus where the uterosacral ligaments join together (Kamina, 1984), the posterior vaginal wall and the anterior rectal wall (Martin and Batt, 2001; Chapron *et al.*, 2003). DIE implants are rather poorly reflected in the R-AFS classification (Dubuisson and Chapron, 1994; Koninckx and Martin, 1992). This may explain why studies assessing disease extent with this classification have failed to observe correlations with DM severity.

Since 1992, we have conducted continuous assessment by collection of data concerning women operated on in our department for DIE. In a previous retrospective study based on the first 225 women, we made an attempt to correlate distinct painful symptoms to location and characteristics of DIE

Table I. Characteristics of the 209 women in the study

| | No | Mean \pm 1 SD | % |
|---|-----|-----------------|------|
| Age (years) | | 30.9 \pm 5.3 | |
| BMI (kg/m ²) | | 21.0 \pm 2.8 | |
| Gravidity | | 0.6 \pm 1.0 | |
| Parity | | 0.3 \pm 0.7 | |
| No. with previous surgery for endometriosis | 100 | | 47.8 |
| Main operative indication ^a | | | |
| Chronic pelvic pain symptoms ^b | 186 | | 89.0 |
| Infertility ^c | 110 | | 52.6 |
| Ovarian cyst | 29 | | 13.9 |
| No. of distinct DIE implants per woman | | 1.3 \pm 0.6 | |
| AFS stage ^d | | | |
| I | 43 | | 20.6 |
| II | 69 | | 33.0 |
| III | 52 | | 24.9 |
| IV | 45 | | 21.5 |
| No. with endometrioma | 57 | | 27.3 |

^aNine women had three indications; 98 had two indications; 102 had one indication.

^bIncluding urinary tract symptoms and gastrointestinal symptoms.

^c1 year without conception.

^dAmerican Fertility Society stage based on The American Fertility Society, 1985.

DM = dysmenorrhoea; DIE = deeply infiltrating endometriosis; BMI = body mass index; No. = number.

(Fauconnier *et al.*, 2002). Surprisingly, we failed to correlate severe DM with any of the characteristics of the DIE implants. However, in this study DM was not evaluated in a standardized way in a questionnaire. The purpose of the present study is therefore to evaluate the relationship between indicators of disease extent and intensity of DM (using a standardized measurement) in a population of women with posterior DIE.

Materials and methods

Population study

This study includes all the women who underwent surgery for infertility, pelvic pain symptoms (including DM, deep dyspareunia and non-menstrual pain) or adnexal masses between June, 1992 and December, 2000 and were diagnosed with posterior DIE. This determination was made during the diagnostic phase of the surgery (The American Fertility Society, 1993) and was based on the macroscopic appearance of the lesion, using the following criteria: (i) palpable and visible nodule or induration in the posterior area (Koninckx *et al.*, 1996); (ii) dark blue nodule visible at the posterior vaginal wall at speculum examination (Vercellini *et al.*, 1996). DIE was considered histologically-confirmed when endometrial glands and stroma were present at microscopic examination. We excluded those women who had previously had a DIE nodule resected and those who were no longer menstruating.

Variables

All the women assessed the severity of their DM, but the method used depended on the study period. During the 'retrospective' period (from June, 1992 to December, 1999) DM intensity was assessed retrospectively with an 11-point numeric scale (Garry *et al.*, 2000). Two questionnaires were mailed to the women operated on—in 1997 for the women operated on between 1992 and 1996, and in 2001 for the women operated on between 1997 and 1999. During the 'prospective' period (from January, 2000 to December, 2000), DM intensity was assessed prospectively with a 10 cm visual analogue

scale (Peveler *et al.*, 1996) recorded during the month before surgery by means of a self-assessed questionnaire. Details of the questionnaire items used to assess DM for both of the study periods are given in Table V. In order to standardize the measurement of the intensity of DM, we recoded both scales into four quartiles, defined separately for each of the two study periods. Accordingly, DM severity was defined in four ordered categories, labelled mild, moderate, severe and extreme.

Disease extent indicators were coded onto a standardized data sheet according to the surgical report, the revised AFS scoring sheet, the anatomic drawing, the degree of the surgical procedure and the result of rectal endoscopic ultrasound (Chapron *et al.*, 1998).

Disease stage was scored according to the R-AFS classification (The American Fertility Society, 1985), and the individual items and all subscores for implants and adhesions were also recorded. The original staging was systematically verified by the author (A.F.). Other variables recorded included size of the biggest endometrioma as well as cumulative endometrioma size, number of distinct DIE implants, size of the posterior DIE implant (defined as the maximum diameter of the lesion assessed during the diagnostic phase of the surgery) and cumulative size of all DIE implants. The extent of the sub-peritoneal infiltration by the posterior DIE was classified as follows: (i) sub-peritoneal only when the DIE implant involved only the sub-peritoneal tissue (including uterosacral ligaments, torus uterinus, or retro-peritoneal tissue underlying the pouch of Douglas); (ii) rectal when the DIE implant involved the muscularis propria of the bowel either at histological examination or at rectal endoscopic ultrasound (Chapron *et al.*, 1998), when the women did not have complete resection and (iii) vaginal when a partial colectomy was required to remove the DIE (Donnez and Nisolle, 1995; Anaf *et al.*, 2001; Chapron *et al.*, 2001) or when a dark blue nodule was present in the posterior vaginal fornix at the speculum (Vercellini *et al.*, 1996).

Statistical analysis

Univariate associations between DM severity and the variables considered were sought with a separate ordinal logistic regression model with cumulative odds (Ananth and Kleinbaum, 1997; Manor *et al.*, 2000). Subsequently, variables associated with DM severity at a threshold of $P = 0.20$ were entered into a multiple ordinal logistic regression model. Backward stepwise selection was used to retain variables with a P -value = 0.05 in the final multiple regression model. All continuous variables were recoded into ordered categorical variables. The reference classes were those with the lowest values. The parameter values for the final model were estimated by the maximum likelihood method; the adjusted odds ratios and their 95% confidence intervals were calculated from the model's coefficients and their standard deviations. The odds ratio represents the likelihood of being in a category of more severe dysmenorrhoea. Similar analyses were conducted for women with histologically-confirmed DIE. Because the results could vary according to the way DM was recorded, we also performed subgroup analysis on both periods of the study.

All analyses were performed with Stata Statistical Software 6.0 (Stata Corporation).

Results

Of the 349 women eligible for the study, 140 were excluded for the following reasons: amenorrhoea, nine cases (2.6%); previous resection of DIE, 12 cases (3.4%); inadequate description of the posterior DIE, 13 cases (3.7%); and failure to respond to the questionnaire, 106 women (30.4%). The

Table II. Severity of DM according to r-AFS score items and other indicators of the extent of the disease

| Variable | DM severity | | | | P |
|---|------------------------------|----------------------------------|--------------------------------|---------------------------------|---------------------|
| | Mild No. (%) ^a | Moderate No. (%) ^a | Severe No. (%) ^a | Extreme No. (%) ^a | |
| Age (years) | | | | | |
| <29 | 19 (27.1) | 12 (17.1) | 14 (20.0) | 25 (35.7) | NS ^b |
| 29–33 | 12 (18.5) | 17 (26.2) | 16 (24.6) | 20 (30.8) | |
| >33 | 17 (23.0) | 16 (21.6) | 22 (29.7) | 19 (25.7) | |
| Parity | | | | | |
| 0 | 38 (23.3) | 33 (20.2) | 43 (26.4) | 49 (30.1) | NS ^b |
| 1 | 8 (24.2) | 8 (24.2) | 6 (18.2) | 11 (33.3) | |
| ≥2 | 2 (15.4) | 4 (30.8) | 3 (23.1) | 4 (30.8) | |
| Women with infertility | | | | | |
| No | 21 (19.3) | 23 (21.1) | 27 (24.8) | 38 (34.9) | NS ^b |
| Yes | 27 (27.0) | 22 (22.0) | 25 (25.0) | 26 (26.0) | |
| No. previous surgery for endometriosis ^c | | | | | |
| 0 | 34 (31.2) | 29 (26.6) | 22 (20.2) | 24 (22.0) | 0.0003 ^b |
| 1 | 10 (16.7) | 10 (16.7) | 17 (28.3) | 23 (38.3) | |
| ≥2 | 4 (10.0) | 6 (15.0) | 13 (32.5) | 17 (42.5) | |
| R-AFS Stage ^d | | | | | |
| I | 13 (30.2) | 9 (20.9) | 10 (23.3) | 11 (25.6) | 0.05 ^b |
| II | 16 (23.2) | 17 (24.6) | 15 (21.7) | 21 (30.4) | |
| III | 14 (26.9) | 13 (25.0) | 11 (21.1) | 14 (26.9) | |
| IV | 5 (11.1) | 6 (13.3) | 16 (35.6) | 18 (40.0) | |
| Cumulative size of DIE implants | | | | | |
| <1 cm | 3 (20.0) | 7 (46.7) | 3 (20.0) | 2 (13.3) | NS ^b |
| 1–3 cm | 30 (25.4) | 24 (20.3) | 25 (21.2) | 39 (33.1) | |
| >3 cm | 15 (19.7) | 14 (18.4) | 24 (31.6) | 23 (30.3) | |
| No. of distinct DIE implants | | | | | |
| 1 | 38 (23.5) | 36 (22.2) | 39 (24.1) | 49 (30.2) | NS ^b |
| 2 | 8 (21.6) | 7 (18.9) | 8 (21.6) | 14 (37.8) | |
| ≥3 | 2 (20.0) | 2 (20.0) | 5 (50.0) | 1 (10.0) | |
| Size of the posterior DIE implant | | | | | |
| <1.7 cm | 21 (29.2) | 20 (27.8) | 16 (22.2) | 15 (20.8) | 0.01 ^b |
| 1.7–2.2 cm | 17 (24.3) | 14 (20.0) | 15 (21.4) | 24 (34.3) | |
| >2.2 cm | 10 (14.9) | 11 (16.4) | 21 (31.3) | 25 (37.3) | |
| Extent of the sub-peritoneal infiltration | | | | | |
| Sub-peritoneal only | 43 (28.7) | 38 (25.3) | 34 (22.7) | 35 (23.3) | 0.0001 ^b |
| Rectal | 3 (13.6) | 2 (9.1) | 7 (31.8) | 10 (45.5) | |
| Vaginal | 1 (5.6) | 3 (16.7) | 5 (27.8) | 9 (50.0) | |
| Both | 1 (5.3) | 2 (10.5) | 6 (31.6) | 10 (52.6) | |
| Associated bladder DIE implant | | | | | |
| No | 45 (22.7) | 44 (22.2) | 49 (24.7) | 60 (30.3) | NS ^b |
| Yes | 3 (27.3) | 1 (9.1) | 3 (27.3) | 4 (36.4) | |
| Cumulative surface of superficial peritoneal implants | | | | | |
| 0 | 11 (16.2) | 14 (20.6) | 19 (27.9) | 24 (35.3) | NS ^b |
| ≤3cm | 18 (24.0) | 17 (22.7) | 19 (25.3) | 21 (28.0) | |
| >3 cm | 19 (28.9) | 14 (21.2) | 14 (21.2) | 19 (28.9) | |
| Endometrioma | | | | | |
| None | 35 (21.7) | 35 (21.7) | 39 (24.2) | 52 (32.3) | NS ^b |
| Unilateral | 11 (28.2) | 10 (25.6) | 9 (23.1) | 9 (23.1) | |
| Bilateral | 2 (22.2) | 0 (0.0) | 4 (44.4) | 3 (33.3) | |
| Cumulative size of endometriomas | | | | | |
| 0 | 35 (21.7) | 35 (21.7) | 39 (24.2) | 52 (32.3) | NS ^b |
| ≤3 cm | 5 (19.2) | 9 (34.6) | 6 (23.1) | 6 (23.1) | |
| >3 cm | 8 (36.4) | 1 (4.5) | 7 (31.8) | 6 (27.3) | |
| Size of the largest endometrioma | | | | | |
| 0 | 35 (21.7) | 35 (21.7) | 39 (24.2) | 52 (32.3) | NS ^b |
| ≤3 cm | 5 (17.9) | 9 (32.1) | 7 (25.0) | 7 (25.0) | |
| >3 cm | 8 (40.0) | 1 (5.0) | 6 (30.0) | 5 (25.0) | |
| Extent of adnexal adhesions ^e | | | | | |
| 0 | 29 (29.9) | 21 (21.6) | 21 (21.6) | 26 (26.8) | 0.03 ^b |
| <12 | 10 (16.9) | 18 (30.5) | 15 (25.4) | 16 (27.1) | |
| ≥12 | 9 (17.0) | 6 (11.3) | 16 (30.2) | 22 (41.5) | |
| Douglas obliteration ^e | | | | | |
| absent | 37 (29.4) | 29 (23.0) | 28 (22.2) | 32 (25.4) | 0.009 ^b |
| partial | 9 (16.4) | 11 (20.0) | 14 (25.5) | 21 (38.2) | |
| complete | 2 (7.1) | 5 (17.9) | 10 (35.7) | 11 (39.3) | |

^aRepresents the percentage of women with this degree of severity of DM.

^bOrdered logistic regression

^cWomen with previous resected DIE were excluded.

^dIndividual item calculated according to the American Fertility Society Classification (The American Fertility Society, 1985).

DM = dysmenorrhoea; DIE = deeply infiltrating endometriosis; No. = number

Due to rounding the percentages may not all total 100.0%.

Table III. Determinants for severity of DM for all women and for women with histologically-confirmed DIE results from an ordinal multiple logistic regression analysis with cumulative odds

| Independent variable | Overall women <i>n</i> = 209 | | Women with histologically-confirmed DIE <i>n</i> = 142 | |
|---|---|----------|--|----------|
| | Adjusted OR for severity of DM ^a | 95% CI | Adjusted OR for severity of DM ^a | 95% CI |
| Extent of the sub-peritoneal infiltration | | | | |
| Sub-peritoneal only | 1 | Ref. | 1 | Ref. |
| Rectal | 2.5 | 1.1–5.9 | 2.8 | 1.0–8.2 |
| Vaginal | 4.1 | 1.6–10.2 | 4.1 | 1.6–10.7 |
| Both | 4.3 | 1.7–10.7 | 4.7 | 1.6–13.2 |
| Extent of adnexal adhesion ^b | | | | |
| 0 or <12 | 1 | Ref. | 1 | Ref. |
| ≥12 | 1.9 | 1.1–3.5 | 2.1 | 1.0–4.3 |

^aThe odds ratio represents the likelihood of being in a category of more severe dysmenorrhoea.

^bIndividual item calculated according to the American Fertility Society Classification (The American Fertility Society, 1985).

Adjusted OR = adjusted odds ratio; CI = confidence interval; Ref. = reference group; DM = dysmenorrhoea; DIE = deep infiltrating endometriosis.

proportion of non respondents did not differ by study period (31.3% for the retrospective period, versus 27.8% for the prospective period). Accordingly, the final study population included 209 women. Their characteristics are reported in Table I. Among the 209 women with surgical diagnosis of posterior DIE, 142 (67.9%) had implants confirmed histologically, whereas 47 (22.5%) had fibrotic implants and 20 (9.6%) did not have removal of their implants. Surgery for 155 women (74.2%) took place during the retrospective period, and for 54 (25.8%) during the prospective period. During the retrospective period the median time-lapse between surgery and the questionnaire was 2.2 years (range 0.2–4.7).

The mean value of the numeric DM scale was 6.9 ± 3.0 for the retrospective period and was divided into four quartiles: (i) <6, mean 2.3 ± 2.4 ; (ii) 6 and 7, mean 6.6 ± 0.5 ; (iii) 8, mean 8.0 ± 0.0 ; and (iv) 9 and 10, mean 9.5 ± 0.5 . For the prospective period, the mean value of the visual analogue DM scale was 5.8 ± 3.1 : (i) <3.6, mean 1.2 ± 1.0 ; (ii) from 3.6 to <6.8, mean 5.5 ± 1.0 ; (iii) from 6.8 to <8.1, mean 7.4 ± 0.3 ; and (iv) = 8.2, mean 9.1 ± 0.7 . Thus the final distribution of DM severity in the overall population was: (i) mild for 48 women (23.0%); (ii) moderate for 45 (21.5%); (iii) severe for 52 (24.9%); and (iv) extreme for 64 (30.6%).

On univariate analysis (Table II), the following variables were related to more severe DM: number of previous surgical procedures for endometriosis; R-AFS stage; extent of adnexal adhesion; Douglas obliteration; size of posterior DIE implant; extent of the sub-peritoneal infiltration (rectal, vaginal or both versus sub-peritoneal only). Current infertility was associated with less severe DM. After multiple regression analysis (Table III), extent of the sub-peritoneal infiltration and extensiveness of adnexal adhesion were the only factors that remained related to DM severity. The number of previous procedures for endometriosis was not included in the final model because it was strongly correlated with adnexal adhesion ($P = 0.007$). The final model did not change when we excluded the women without histologically-confirmed DIE (Table III). Stratified results according to the study periods are reported in Table IV. Although some associations becomes non-significant because of the lack of statistical power, the adjusted odds ratios were similar in both study periods.

Discussion

For women with posterior DIE, severity of DM was related to disease extent by two independent indicators: presence of a rectal or vaginal infiltration by the posterior DIE and the extensiveness of adnexal adhesion.

This study has two limitations. First, most of the women completed the pain questionnaire retrospectively. Because some of them received their questionnaire up to four years after operation, one may question what was really measured. Nevertheless, in studies comparing prospective and retrospective methods of pain measurement a fairly good correlation was found (Redelmeier and Kahneman, 1996), even after several years (Dawson *et al.*, 2002). Besides, when we analysed both periods separately, the results were similar in the prospective and retrospective parts of the study.

The second limitation is that inclusion of the women was based on the surgical diagnosis of posterior DIE, regardless of histological results. At our institution, indeed, diagnosis and treatment of DIE is based on the macroscopic aspect of the lesion, a method that has been shown to be effective (Cornillie *et al.*, 1990; Koninckx *et al.*, 1996). However for several women histology differed from the macroscopic aspect because some forms of DIE implants may have dense fibrotic tissue instead of gland and stroma (Coronado *et al.*, 1990; Brosens, 1994). Also, in certain cases histology was not available because women did not want extensive surgery, in particular when the posterior DIE was embedded in the rectal wall. For these women the diagnosis of rectal involvement was based on rectal endoscopic ultrasound, a method shown to have very good correlation with histological results (Chapron *et al.*, 1998; Fedele *et al.*, 1998). Nonetheless, two-thirds of the women in our study did have histologically-confirmed DIE, and the results did not change when we excluded the women without histological proof.

To the best of our knowledge, our study is the first to report a correlation between vaginal or rectal infiltration by DIE and DM severity. One previous study (Vercellini *et al.*, 1996), on the other hand, did not find any difference in DM severity when comparing women with or without vaginal wall infiltration. One explanation is that it studied all subtypes of endometriosis, unlike ours, which considered only patients with DIE.

Table IV. Determinants for severity of DM according to the study period

| Independent variable | Cases | Retrospective period <i>n</i> = 155 | | Prospective period <i>n</i> = 54 | |
|---|-------|--|-------|--|-------|
| | | Adjusted OR for severity of DM ^a (95% CI) | Cases | Adjusted OR for severity of DM ^a (95% CI) | Cases |
| Extent of the sub-peritoneal infiltration | | | | | |
| Sub-peritoneal only | 116 | 1 (Ref.) | 34 | 1 (Ref.) | |
| Rectal | 11 | 3.0 (1.0–9.2) | 11 | 2.4 (0.6–9.5) | |
| Vaginal | 15 | 3.9 (1.4–10.9) | 3 | 4.5 (0.6–36.1) | |
| Both | 13 | 3.9 (1.3–11.7) | 6 | 6.6 (1.2–35.3) | |
| Extent of adnexal adhesion ^b | | | | | |
| 0 or <12 | 120 | 1 (Ref.) | 38 | 1 (Ref.) | |
| ≥12 | 35 | 2.1 (0.8–3.4) | 18 | 3.0 (0.9–10.0) | |

^aThe odds ratio represents the likelihood of being in a category of more severe dysmenorrhoea.

^bIndividual item calculated according to the American Fertility Society Classification (The American Fertility Society, 1985).

Adjusted OR = adjusted odds ratio; CI = confidence interval; Ref. = reference group; DM = dysmenorrhoea; DIE = deep infiltrating endometriosis.

Table V. Evaluation of DM during the two study periods

| Study period | Questionnaire items |
|---|--|
| Retrospective period June 1992–December 1999 | Questionnaire mailed postoperatively (1997 and 2001) <i>Before your operation did you experience pain during menstruation (Yes/No) If yes, could you rank the intensity of the pain on a scale between 0 and 10</i> |
| Prospective period January–December 2000 | Preoperative self-assessed questionnaire <i>Based on your last three menstrual cycles please indicate the average intensity of your menstrual pain by placing a cross on the following scale (minimum = no pain; maximum = most unbearable pain that you could imagine)</i> |

Neural invasion by DIE has been shown to correlate with the severity of DM (Anaf *et al.*, 2001). Thus, one possible explanation of the correlation between DM and vaginal or rectal infiltration is that implants that penetrate the wall of adjacent organs will have a closer relation with nerve fibres than those which do not. A second explanation is that associated inflammatory changes in the adjacent organs, due to penetration of DIE, may also explain this association. Contrary to superficial endometriosis, DIE is usually associated with inflammatory cells (Cornillie *et al.*, 1990). A third explanation is that the ratio between glandular structures and fibrosis, and also the patterns of cyclical differentiation, may differ when the DIE penetrates the wall of the adjacent organs. Indeed histological components vary according to the location of the endometriosis (Cornillie *et al.*, 1990; Brosens, 1994; Bonte *et al.*, 2002). One may hypothesize that as the depth of infiltration increases, the glandular components will become more numerous and active.

Our study, like others (Muzii *et al.*, 1997; Porpora *et al.*, 1999), emphasises the role of adnexal adhesion in endometriosis-related DM. Pelvic adhesions have been found to be associated with severe DM in a population of subfertile women regardless of the presence of associated endometriosis (Forman *et al.*, 1993). Moreover, the treatment of severe adnexal adhesions (whatever the aetiology) has been shown to be

effective in alleviating pain (Duffy and diZerega, 1996). The mechanism by which adnexal adhesions cause DM has not yet been explained.

Surprisingly, neither the presence nor the characteristics of endometriomas were found to correlate with the severity of DM. Our findings, similar to those from other studies, (Vercellini *et al.*, 1996; Porpora *et al.*, 1999;) suggest that the noteworthy association between pain and endometrioma may be explained by adnexal adhesion. In our opinion however, adhesion may not be the sole factor contributing to the relationship between DM and endometrioma. Indeed, one previous study on women with endometriomas has found that increased vascularization and high CA 125 level may be determinants for pain (Alcazar, 2001). Future prospective research on endometriomas is needed to clarify how they produce pain.

A classification system that correlates positively with disease prognosis is important in developing and assessing treatment. The relationship between the R-AFS stage and DM is rather inconsistent. Some studies have found such a correlation (Buttram, 1979; Fedele *et al.*, 1992; Muzii *et al.*, 1997), while many others have not (Fedele *et al.*, 1990; Vercellini *et al.*, 1996; Stovall *et al.*, 1997; Porpora *et al.*, 1999; Gruppo Italiano per lo Studio dell'Endometriosi, 2001). In the present study, the linear trend between R-AFS stage and DM

severity was explained in part by the severity of adnexal adhesion and by obliteration of the pouch of Douglas (itself strongly related to the degree of adjacent visceral infiltration by the DIE implant). The quantification of DIE implants in the R-AFS system did not, on the other hand, appear to explain DM severity at all. This finding points out the need to improve the classification system when dealing with pain. Indeed, although DIE implants are differentiated from superficial implants, no quantification of depth is considered in the R-AFS classification (Hoeger and Guzick, 1999). Because depth of infiltration correlates with pain (Koninckx *et al.*, 1991), proper quantification of depth is extremely important. One interesting classification includes three types of posterior DIE and is based on physiopathological mechanisms (Koninckx and Martin, 1992). The correlation between this classification and the severity of pain symptoms was unfortunately not studied. In the present study we aimed to quantify indirectly the depth of posterior DIE according to the presence or non-presence of the infiltration of the wall of an adjacent organ. This classification was found to correlate with the severity of DM. If our results are confirmed by others, the concept of very deep infiltrating endometriosis, defined as implants invading the wall of the pelvic organ, should be tested in future classification systems specifically addressed to the prediction of endometriosis-related pain.

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