Predictors of pain during oocyte retrieval

Yoon Frederiksen[1,*], Mimi Y. Mehlsen[1], Signe M.S. Matthiesen[1,2], Robert Zachariae[1,3], Hans Jakob Ingerslev[4,5]

[1]*Department of Psychology, Aarhus University, 8000 Aarhus, Denmark*

[2]*Aarhus Municipality. Family, children and youth, Department of projects and development, Interventions for children and families*

[3]*Department of Oncology, Aarhus University Hospital, 8000 Aarhus, Denmark*

[4] *Centre for Preimplantation Genetic Diagnosis/The Fertility Clinic, Aarhus University Hospital, Brendstrupgaardsvej 100. 8200 Aarhus N, Denmark*

5Faculty of Health, Aarhus University, Vennelyst Boulevard 9, 8000 Aarhus C

Corresponding author:

Yoon Frederiksen, PhD-fellow

Department of Psychology, University of Aarhus

Bartholins allé 9, 8000 Aarhus, Denmark

Email: yoonf@psy.au.dk

Abstract

Introduction: Pain during oocyte retrieval remains prevalent despite detailed and specific pain management protocols. Exploring the role of psychosocial risk factors of pain during the oocyte retrieval could identify possible targets for prevention. The present study assessed pain prevalence and possible risk factors for experiencing extreme pain levels in a large cohort of women receiving assisted reproductive technologies (ART) treatment.

Methods: Participants were 810 first attendees about to begin treatment with ART. The participants completed questionnaires at three time points: at their 21st day of the cycle, during the waiting time before the oocyte retrieval surgery, and after the oocyte retrieval.

Results: Fifty-one (6.9%) of the women reported the oocyte retrieval to be very or extremely painful. The results of a multiple logistic regression indicated that the significant predictors of high pain intensity, measured before the oocyte retrieval, were negative gynecological experiences and side effects of hormonal treatment. Variables measured after the oocyte retrieval associated with pain intensity were higher levels of anxiety during the oocyte retrieval, lower levels of perceived control, and longer duration of the procedure.

Discussion: The findings of the present study may help to identify those women who are at increased risk of experiencing unacceptable pain levels during oocyte retrieval procedures and the medical staff is advised to take psychological factors into account.

Introduction

Infertility treatment with *In Vitro Fertilisation* (IVF) or *Intracytoplasmic Sperm Injection* (ICSI) involves oocyte retrieval (OR), where oocytes are collected by transvaginal ultra-sound-guided follicle aspiration. This is a potentially painful procedure, primarily due to needle perforation of the vaginal wall and ovary.

Various protocols have been investigated in search for the best model, but a recent Cochrane review failed to identify one particular procedure as better than others [1].

It is widely accepted that the pain experience is related not only to biological factors, and several psychosocial factors have been found to influence pain intensity and pain tolerance [2] . Anxiety, for example, has been described to be associated with lower pain threshold [3], and the feeling of being in control associated with more efficient pain coping. Many women in fertility treatment are anxious, not only in relation to the OR procedure itself, but they also display various levels of anxiety related to the involuntary childlessness in general [5]. Being treated for infertility often induces feelings of not being in control over one's own body, and the lack of control could contribute to less efficient pain coping, thereby exacerbating the pain experience [7, 8]. In addition, a number of common physical symptoms e.g. nausea, fatigue, swelling of the womb experienced throughout treatment cycles could sensitize the body and contribute to the feelings of helplessness over longer periods of time [8],adding to the feeling of loss of control.

Although much research in general pain management and pain relief has been conducted with other clinical populations [12, 13, 14], our knowledge about the role of medical, procedural, and psychosocial factors in relation to acute OR-related pain remains limited. In spite of a seemingly safe and effective pain relief protocol, OR is considered to be one of the most stressful and painful parts of an IVF or ICSI treatment, and a minority (6%) has been found to consider OR to be unacceptable [15, 16]. Hence, better understanding of OR-related pain with the aim of reducing pain is still a major goal, only surpassed by the goal of improving the chances of achieving a pregnancy [4, 17, 18]. With the perspective of developing preventive strategies, the aim of the present study was to identify women at risk of

experiencing intolerable pain levels during oocyte retrieval by exploring possible medical, procedural, and psychological predictors of intolerable pain.

Methods

Patients

In the present study we approached 1578 eligible women undergoing their first IVF-treatment cycle at the Fertility Clinic, Aarhus University Hospital, between Oct. 2001 and Sept 2006. Other data from this sample has previously been published [4]. A total of 837 women (53%) from this sample agreed to participate. The inclusion criteria were: 1) first IVF-cycle, 2) no previous attempts with IVF-treatment, and 3) ability to read and understand Danish. Exclusion criteria were 1) Preimplantation Genetic Diagnosis, which involve atypical treatment with more intense hormone stimulation and prolonged egg-retrieval procedures and 2) acute change in treatment type, e.g., from insemination to IVF due to too many follicles.

Ovarian stimulation, oocyte retrieval and fertilization

Ovarian stimulation was performed as previously described [18, 19]. In brief, two protocols were followed using either clomiphene citrate (Clomivid®) or a standard long down-regulation protocol using Suprefact® nasal spray followed by ovarian stimulation with FSH or HMG (Humegon®, Puregon® or Gonalf®). Monitoring of the follicular development was performed by vaginal ultrasound. HCG (Pregnyl®) was administered when three or more follicles had reached a follicular size of at least17 mm.

The oocyte retrieval was performed under ultrasound guidance with either an 18G single lumen-needle or 16G double lumen-needle. The women were under sedation with 0,125 mg Halcion® (Triazolam) and received 1 g paracetamol one hour prior to the oocyte pick-up followed by 10 ml Carbocain® as local anesthesia into each side of the upper vagina. During the procedure, the women received Triazolam 0.125 mg orally and Fentanyl intravenously at a standard dose of 100ug, supplemented as necessary to 125 or 150ug. After the procedure, the women were placed in a recovery room for observation for at least 2 hours.

Procedure

Patients, questionnaires and time-points have previously been described in detail [4]. In brief, the women received oral and written information about the study and an invitation to participate. Women agreeing to participate received a baseline questionnaire package at their first scheduled appointment around the 21th day of the cycle (t1). When attending the clinic for oocyte retrieval, both women and their partners were asked to complete a second short questionnaire while waiting for the procedure, asking about concerns about the oocyte retrieval procedure and hormonal treatment side effects (t2). After the oocyte retrieval and after the effects of the sedation had subsided (t3), the women filled in a third questionnaire concerning their pain during oocyte aspiration. The physician registered medical and technical details about the procedure and the patient, including reason for infertility and number of eggs retrieved during the oocyte retrieval procedure. At this point, the woman's partner, the physician, and the nurse also gave their estimate of the patient's level of pain.

The possible associations between psychosocial factors, medical factors, and perceived pain were evaluated at to two time points: *before* the procedure (t1 and t2) and *after* the procedure (t3).The study was approved by the local Regional Ethics Committee and was approved by the Danish Data Protection Agency.

Measurements

Socio-demographic data as well as reproductive characteristics were obtained with a brief self-report questionnaire. Medical information was obtained from medical records.

Independent variables

Before the oocyte aspiration

Depressive symptoms were measured with the Beck Depression Inventory-II (BDI) [17]. This scale has been validated with numerous clinical populations and had an internal consistency of 0.71 (Cronbach's Alpha) in the present sample. State anxiety was measured using the State-Trait Anxiety Inventory (STAI-Y2) [20]. The internal consistencies of the STAI range from 0.86 to 0.95 in various populations.

Gynecological experience was measures with four questions related to pain and discomfort experienced during gynecological examination: 1) *Have you previously experienced pain during a gynecological examination?* 2) *To which degree do you experience gynecological examinations to be uncomfortable*? 3) *How painful is a gynecological examination for you, in general?* and 4) *To which degree do you feel burdened by the pain experience?* The items were treated as a scale, and demonstrated an internal consistency of 0.89. Likewise, two questions concerning menstruation (pain and discomfort) were transformed into a single scale named *menstruation experience:* 1) *To which degree do you experience pain in relation to your menstruation period, in general?* and 2) *to which degree do you feel burdened by pain during menstruation?* Internal consistency was 0.94 in the present sample. Both scales used 7-point Likert scale response formats with scores ranging from "0" = no pain/no discomfort/not at all burdened to "6" = extremely uncomfortable/extremely painful/extremely burdened. Additional questions asked about "hormonal treatment side-effects"; e.g., subjective reporting of headaches and hot flushes, "expected discomfort during the procedure", "distress concerning the expected level of discomfort during the OR", "apprehension about OR discomfort" and "concern about the result of OR", all rated on 7-point Likert scales. Medical factors included female BMI, previous ectopic pregnancies, spontaneous abortions, and induced abortions.

After the oocyte aspiration procedure

Post-procedural subjective evaluations included questions about "feelings of nervousness", "perceived contact with the staff" and "the perceived importance of the contact", "how anxious were you" and "perceived control" during the OR procedure, all rated on a 7-point Likert scales. Medical variables recorded included needle type (single or double-lumen), number of oocytes harvested, clinician credential, and procedure duration.

Dependent variable

Pain during OR

After the procedure, the women rated their perceived pain intensity ("how intense was your pain during the oocyte retrieval") on a 7-point Likert scale with responses ranging from "no pain at all" ("0") to "extreme pain" ("6"). The woman's partner, the physician, and the nurse also rated their estimates of the woman's level of pain on 7-point Likert scales.

Statistics

The IBM Statistics Package for the Social Sciences (SPSS) version 19.0 was used for statistical analyses. For all psychometric scales, the proportion of missing values was computed. To retain statistical power and reduce the risk of Type-2 error, in cases with <50% missing items, the missing values of the scale in question were substituted with the mean values for the remaining scale items for that individual, but only if internal consistency of the scale was high, i.e., Cronbach's $\alpha > 0.70$. In cases with >50% of items in the scale unanswered, the scale total scores for these individuals were excluded from the analysis. This method does not replace data for non-responding individuals but only missing items, when there is a high likelihood that this will not affect scale total scores. This method is a commonly used, robust, and recommended method [19].

To assess the prevalence of excessive pain, the dependent variable (pain intensity) was dichotomized into high and low pain, with scores of 5-6 categorized as high pain and scores 0-4 as low pain. This was considered a conservative choice to make sure we did not include women reporting medium pain levels in the high pain group. T-tests were used to compare the two pain groups with respect to socio-demographic factors, previous history of gynecological and menstruation experience, and concerns about the procedure and fertility-related factors e.g. needle size and duration of surgical procedure. Chi^2-tests were used for assessing between-group differences in level of education, marital status, cause of infertility, treatment method, and the clinical pregnancy rate. Multiple logistic regression analyses were used to identify statistically significant predictors of high vs. low pain in a multivariate model, while adjusting for medical factors of possible relevance to pain experience, including previous births, previous spontaneous

abortions, previous provoked abortions, needle type (categorized as single or double-lumen), and duration of the procedure.

Results

Comparing responders and non-responders

The response rate was 53% (837/1578). An additional 28 women were excluded due to incomplete questionnaires, various medical factors (e.g. puncture of cysts, spontaneous pregnancy, ovulation prior to oocyte retrieval, treatment cancellation), or moving away. The study group only differed from non-responders with respect to cause of infertility, with the study group having a larger proportion of male infertility factor. Other characteristics such as socio-demographic factors and previous health status were not obtainable for non-responders.

Attrition

Sixty-six women (8%) dropped-out at follow-up (t3). The only difference found between drop-outs and completers were that women who did not complete the questionnaires at t3 were more likely to be smokers (66%) than those who had completed the questionnaires (29%) ($Chi^2(5)=17.87$; $p=0.003$). For psychometric scales, only 0.5% missing items were observed for both BDI and STAI. As >50 % of the items were completed, missing items were replaced with mean values for the remaining scale items for each respondent.

Perceived pain

The mean pain level was 1.95 (SD 1.43) for the total sample. Women who reported the oocyte retrieval to be very or extremely painful (score = 5-6) were defined as belonging to the *high pain group* (HPG), while the remaining women (score 0-4) were considered belonging to the *low pain group* (LPG). The high-level pain group consisted of 51 women (6.9%) and the low-level pain group of 692 women (93.1%)

Comparing women with high and low pain levels

Socio-demographic and reproductive characteristics:

In the unadjusted analyses, infertility duration was statistically significantly longer in the low pain group (Mean: 31.86 months, SD: 23.2) than in the high pain group (Mean: 25.22 months, SD: 13.4) ($t(622)=2.881$; $p=0.006$). No other between-group differences were found for socio-demographic factors, treatment-related factors, cause of infertility, or infertility history. The results are presented in table 1.

[Insert table 1 near here]

Variables assessed prior to oocyte retrieval:

When examining possible predictors of pain, the variables were grouped into individual characteristics, partner statements, and medical factors. In the unadjusted analyses, HPG women had statistically significant higher subjective ratings of previous negative gynecological examination experience, pain and discomfort during menstruation, trait anxiety, depressive symptoms, expected discomfort, distress concerning the expected levels of discomfort, apprehension about OR discomfort, hormonal treatment side effects, and concerns about the result. Partners of HPG women expected their partner to experience more discomfort during OR than partners of LPG women. There were no between-group differences in the partner's concern about the result (success of the oocyte retrieval e.g. no of oocytes). Likewise, no between-group differences were found for any of the medical factors assessed. The results are presented in Table 2a.

[Insert table 2 (a and b) near here]

Variables assessed after the oocyte retrieval procedure

Of the four medical factors assessed after the procedure, only duration of the aspiration was associated with high pain in the unadjusted analyses. No between-group differences were found for needle size, BMI, or number of oocytes harvested. Several between-group differences were found for post-OR subjective measurements. HPG women thus reported higher scores on anxiety, nervousness, and lack of control than LPG women. No between-group differences were found for contact with the staff, the rated importance of the contact, or the clinician involved in the oocyte procedure (data not shown).

Furthermore, no differences were found between the clinical pregnancy rates in the two groups: $Chi^2(1) = 0.721$, $p = 0.396$. The results are shown in Table 2b.

Factors associated with pain

In order to identify possible independent predictors of OR-related pain while adjusting for the influence of the remaining factors, a series of multiple logistic regression analyses were conducted with HPG vs LPG as the dependent variable. The predictors entered in the model were those found to differ significantly between the HPG and LPG in the unadjusted analyses.

For variables measured *before* the oocyte retrieval, negative gynecological experiences and hormonal treatment side effects were the only two variables remaining statistically significantly associated with high pain, when adjusting for the remaining variables. Higher ratings of previous negative gynecological experience or reporting hormonal treatment side effects increased the risk of being in the high pain group. Of the variables measured *after* OR, anxiety, perceived control, and duration of the procedure all remained statistically significant independent predictors of high pain, whereas nervousness ceased to be associated with intolerable pain. Higher pain intensity was associated with higher anxiety levels, lower degree of perceived control and longer duration of the procedure. In a final model, all statistically significant independent predictors were entered simultaneously. All variables remained significant predictors in the final model. The results are summarized in Table 3a and 3b.

[Insert table 3 (a and b) near here]

Discussion

In the present study, we examined the association of several medical, procedural, and psychosocial factors with pain during the OR procedure. The overall results suggest that factors such as hormonal treatment side effects, state anxiety, previous negative experiences with gynecological examinations, and perceived lack of control may be related to the pain experience. Furthermore, we found only one medical factor to

be associated with being in the high pain group (HGP), namely ‘duration of the procedure’. This appears to suggest that psychosocial factors are more important predictors of the OR-related pain experience than medical factors. Aspiration of oocytes is a crucial and anxiety-provoking part of IVF/ICSI fertility treatment [3, 23]. As a majority of the women may require repeated attempts in order to achieve a pregnancy, experiencing high levels of pain during the OR procedure may cause not only procedural problems such as prolongation, side effects, premature termination of the procedure, but also increased worry and distress.

Approximately 7% of the women in our sample found the oocyte retrieval procedure to be very or extremely painful; a result similar to an earlier finding by Højgaard et al. (2001) [13], who found that 6% reported unacceptable pain levels. Although 7% appears to be a relatively small number, other studies have shown that more than half of the women report moderate to high pain levels [3, 24], and our chosen cut-off (0-4 vs. 5-6) between high and low pain could be viewed as conservative. Nevertheless, even a small group of 7% with intolerable pain stresses the importance of identifying individual characteristics that may indicate need for special interventions to alleviate pain during the procedure.

The multidimensionality of the pain experience has been recognized for some time with the pain coping style of catastrophizing being among the core concepts [8, 25. 27]. Having thoughts about whether the OR procedure will be as painful or even more painful than former gynecological examinations, could result in magnification of the upcoming OR event, and the complex state of worry, anticipation and sadness associated with being involuntarily childless could for some of the women result in further worrying about the OR procedure. Furthermore, the fact that the OR procedure is a pivotal part of the whole fertility treatment may induce feelings of helplessness. The association between hormonal treatment side effects and belonging to the HPG could be explained by increased self-awareness of bodily symptoms as well as mood differences. The unpleasant changes may lead to negative cognitions about treatment as a whole, including the OR procedure, and result increased attention to pain [24].

Anxiety and lack of control during the OR procedure were two additional risk factors of experiencing high levels of pain. Pain and anxiety can be seen as reciprocal determinants. Pain can induce anxiety and anxiety, on the other hand, may exacerbate the pain experienced [25]. The association between anxiety and pain during oocyte retrieval has been reported by Cooper et al. (2000) too [12]. Furthermore, there is some evidence to suggest that women are more prone to anxiety as well as pain perception, which could explain why this relatively minor surgery is problematic, at least for a subgroup of women [29, 30].

Taken together, our findings indicate that within this large cohort of women treated for infertility, a number of psychosocial factors appear to be predictors of high levels of OR-related pain. The results are in line with the present knowledge of pain as a complex bio-psycho-social phenomenon and suggest that a broader understanding of the women's pain responses to the oocyte retrieval procedure is relevant when preparing and implementing pain management protocols in this population. Duration of the procedure was the only procedural factor that appeared to predict the HPG, and it might be expected that prolongation of an invasive and difficult procedure can be associated with elevated pain levels. Surprisingly, none of the other medical factors, e.g. needle size, previous abortions, female weight or the number of oocytes retrieved, were associated with pain. However, there may have been additional medical factors, e.g. diabetes and previous abdominal surgery, which were not taken into account, and which may have influenced pain levels as well. Interestingly, although previous gynecological experiences predicted being in the high pain group, the prevalence of endometriosis did not differ significantly between the two groups.

Clinical Implications

Emanating from the findings in the present study could be a structured infertility-specific interview with the aim of identifying women at risk of extreme pain. A next step could be in collaboration with the woman to decide on possible solutions if she is considered at risk of extreme pain. An important goal is to improve patient empowerment, rather than just altering dosage and pain relief medication. Shared

decision-making and exploring and addressing the patient's needs for alleviating pain and distress are core element of patient-centered care [28].

Strength and limitations

Although the general pain literature has confirmed pain as a multidimensional bio-psycho-social phenomenon [6], our study is one of the few so far that have explored the possible role of psychosocial factors for perceived pain in relation to the OR procedure while taking medical and treatment-related factors into account. Our study is, however, not without limitations. One possible confounder could be that if the women in the study appeared to be in need of more analgesics, this was administered, which may have influenced their pain ratings. Furthermore, the third questionnaire was completed in the recovery room, soon after the OR procedure, and some women could theoretically still have been sedated to some degree, which may have influenced their recall of the OR procedure. Moreover, the literature also suggests that cultural differences and beliefs influence pain responses; hence ethnicity and religion could perhaps be accountable for variations in pain intensity [35, 36, 37]. We did not ask specifically about ethnic and religious background, and despite Denmark being a highly secular and ethnic homogenous country, it cannot be ruled out that some of the participants in the present cohort may have cultural or religious backgrounds which may have influenced their pain experience. Although the present study was conducted between 2001 and 2006, women's experience of pain is still a pertinent problem, and the prevalence of high or intolerable pain in our study is similar to that found in similar studies [1]. Furthermore, the sedation, the analgesic procedure, and the clinical IVF protocols per se have not changed significantly. Furthermore, only approximate half of the originally eligible women were available for the final analyses. While this could have introduced selection bias, we found no statistically significant differences, neither between responders and non-responders, nor between participants and drop-outs with respect to medical characteristics, age, or smoking habits. Finally, we aimed to identify women at risk of extreme pain. By not analyzing a possible third group representing women with moderate pain, we may have missed a patient group that could also benefit from improved approaches to OR-related pain management.

Conclusion

The present study shows that although most women tolerate pain during OR well, a small subgroup was found to experience unacceptably high pain levels. With the perspective of developing possible preventive measures, the primary aim of the present study was to investigate whether it is possible to identify women who are at risk of experiencing intolerable pain levels during oocyte retrieval by pinpointing possible medical, procedural, and psychological predictors of intolerable pain. In a clinical perspective, the findings in the present study allow for improved understanding of the patient and an optimal and respectful response to the patients care and needs.

Authors' roles

R.Z., M.M. and H.J.I. participated in the concept and design of the study. Y.F., M.M. and S.M. were responsible for data collection and analysis. Y.F., M.M. and R.Z. drafted the manuscript. Y.F., M.M., S.M., R.Z. and H.J.I. interpreted data, revised drafts and approved of the manuscript.

Acknowledgements

The authors would like to thank the clinical staff at [collaborating clinics] for their cooperation and valuable feedback during the data collection. Moreover, we wish to express our gratitude to all the couples who took part in this study and spent time responding to the questionnaires.

Funding

The research was partly supported by an unrestricted grant from MSD and partly by a PhD scholarship from The Danish Agency for Science Technology and Innovation granted to Y.F. (AUID/144944/2009)

Conflict of interest

None to declare. No conflicts of interests are associated with this study or its publication

Current knowledge on the subject

Alleviating pain is still a relevant challenge, when undergoing the oocyte retrieval procedure.

Research in this area has mostly focused on improving pain protocols in relation to medical intervention and the exploration of psychosocial factors is sparse.

A subgroup of women seem to experience almost unbearable pain

- What this study adds

A subgroup of women is at risk of experiencing high pain levels and their gynecological history, experience of hormonal side-effects, anxiety levels during the oocyte retrieval procedure, as well as perceived lack of control are important predictive factors.

This knowledge, could aid, women at risk of an intolerable pain experience, to be identified with relatively little effort in clinical practice.

A patient centered approach could be beneficial in the planning and decision-making process in alleviating pain

References

[1] I. Kwan, S. Bhattacharya, F. Knox, and A. McNeil, “Pain relief for women undergoing oocyte retrieval for assisted reproduction,” Cochrane database Syst. Rev., vol. 1, p. CD004829, Jan. 2013.

[2] F. J. Keefe, M. Lumley, T. Anderson, T. Lynch, J. L. Studts, and K. L. Carson, “Pain and emotion: new research directions.,” J. Clin. Psychol., vol. 57, no. 4, pp. 587–607, Apr. 2001.

[3] A. L. Gejervall, E. Stener-Victorin, A. Cerne, K. Borg, and C. Bergh, “Pain aspects in oocyte aspiration for IVF,” Reprod. Biomed. Online, vol. 14, no. 2, pp. 184–190, Feb. 2007.

[4] S. M. Ebbesen, R. Zachariae, M. Y. Mehlsen, D. Thomsen, A. Hojgaard, L. Ottosen, T. Petersen, and H. J. Ingerslev, “Stressful life events are associated with a poor in-vitro fertilization (IVF) outcome: a prospective study,” Hum. Reprod., vol. 24, no. 9, pp. 2173–2182, Sep. 2009.

[5] K. S. Bowers, “Pain, anxiety, and perceived control,” J. Consult. Clin. Psychol., vol. 32, no. 5, pp. 596–602, 1968.

[6] P. J. Quartana, C. M. Campbell, and R. R. Edwards, “Pain catastrophizing: a critical review,” Expert Rev. Neurother., vol. 9, no. 5, pp. 745–758, 2009.

[7] S. M. S. Matthiesen, Y. Frederiksen, H. J. Ingerslev, and R. Zachariae, “Stress, distress and outcome of assisted reproductive technology (ART): A meta-analysis,” Hum. Reprod., vol. 26, no. 10, pp. 2763–2776, 2011.

[8] D. Suthersan, S. Kennedy, and M. Chapman, “Physical symptoms throughout IVF cycles,” Hum. Fertil. (Camb)., vol. 14, no. 2, pp. 122–128, Jun. 2011.

[9] J. Bruce, A. J. Thornton, R. Powell, M. Johnston, M. Wells, S. D. Heys, A. M. Thompson, W. C. Smith, W. A. Chambers, N. W. Scott, and R. S. Group, “Psychological, surgical, and sociodemographic predictors of pain outcomes after breast cancer surgery: A population-based cohort study,” Pain, 2013.

[10] A. R. Gross, F. Kaplan, S. Huang, M. Khan, P. L. Santaguida, L. C. Carlesso, J. C. Macdermid, D. M. Walton, J. Kenardy, A. Soderlund, A. Verhagen, and J. Hartvigsen, “Psychological Care, Patient Education, Orthotics, Ergonomics and Prevention Strategies for Neck Pain: An Systematic Overview Update as Part of the ICON Project,” Open Orthop. J., vol. 7, pp. 530–561, Sep. 2013.

[11] S. Suhonen, M. Tikka, S. Kivinen, and T. Kauppila, “Pain during medical abortion: predicting factors from gynecologic history and medical staff evaluation of severity,” Contraception, vol. 83, no. 4, pp. 357–361, Apr. 2011.

[12] W. H. Cooper, S. M. Weaver, and D. M. Hay, “The psychological predictors of pain during IVF egg retrieval,” J. Reprod. Infant Psychol. Issue Reprod. pain, vol. 18, no. 2, pp. 97–104, 2000.

[13] H. J. Ingerslev, A. Hojgaard, J. Hindkjaer, and U. Kesmodel, “A randomized study comparing IVF in the unstimulated cycle with IVF following clomiphene citrate,” Hum. Reprod., vol. 16, no. 4, pp. 696–702, Apr. 2001.

[14] I. Kwan, S. Bhattacharya, F. Knox, and A. McNeil, “Conscious sedation and analgesia for oocyte retrieval during in vitro fertilisation procedures,” Cochrane database Syst. Rev., vol. (3), no. 3, p. CD004829, Jul. 2005.

[15] E. H. Ng, D. K. Chui, O. S. Tang, and P. C. Ho, “Paracervical block with and without conscious sedation: a comparison of the pain levels during egg collection and the postoperative side effects,” Fertil. Steril., vol. 75, no. 4, pp. 711–717, Apr. 2001.

[16] A. Hojgaard, H. J. Ingerslev, and J. Dinesen, “Friendly IVF: patient opinions,” Hum. Reprod., vol. 16, no. 7, pp. 1391–1396, Jul. 2001.

[17] A. T. Beck and R. A. & B. Steer G.K., Beck Depression Inventory Manual., vol. Second. San Antonio, Texas: The Psychological Corporation, Harcourt Brace & Company, 1996.

[18] C. D. Spielberger, R. L. & L. Gorsuch R., and P. R. & J. Vagg G.A., Manual for the STATE-TRAIT ANXIETY INVENTORY (FORM Y): Self-Evaluation Questionnaire. Palo Alto, California: Consulting Psychologist Press, Inc., 1983.

[19] J. L. Schafer and J. W. Graham, “Missing data: our view of the state of the art,” Psychol. Methods, vol. 7, no. 2, pp. 147–177, Jun. 2002.

[20] S. Lord and N. Robertson, “The role of patient appraisal and coping in predicting distress in IVF,” J. Reprod. Infant Psychol., vol. 23, no. 4, pp. 319–332, Nov. 2005.

[21] L. A. Shatford, S. E. Brown, A. A. Yuzpe, J. A. Nisker, and R. F. Casper, “Assessment of experienced pain associated with transvaginal ultrasonography-guided oocyte recovery in in vitro fertilization patients,” Am. J. Obstet. Gynecol., vol. 160, no. 4, pp. 1002–1006, Apr. 1989.

[22] E. Stener-Victorin, J. Kowalski, and T. Lundeberg, “A New Highly Reliable Instrument for the Assessment of Pre- and Postoperative Gynecological Pain,” Anesth. Analg., vol. 95, no. 1, 2002.

[23] M. J. Sullivan, B. Thorn, J. A. Haythornthwaite, F. Keefe, M. Martin, L. A. Bradley, and J. C. Lefebvre, “Theoretical perspectives on the relation between catastrophizing and pain,” Clin. J. Pain, vol. 17, no. 1, pp. 52–64, Mar. 2001.

[24] C. Eccleston and G. Crombez, “Pain demands attention: a cognitive-affective model of the interruptive function of pain,” Psychol. Bull., vol. 125, no. 3, pp. 356–366, 1999.

[25] A. Jones and R. Zachariae, “Gender, anxiety, and experimental pain sensitivity: an overview,” J Am Med Womens Assoc, vol. 57, no. 2, pp. 91–94, 2002.

[26] R. B. Fillingim, C. D. King, M. C. Ribeiro-Dasilva, B. Rahim-Williams, and J. L. Riley, “Sex, gender, and pain: a review of recent clinical and experimental findings,” J Pain, vol. 10, no. 5, pp. 447–485, 2009.

[27] M. E. Robinson, E. A. Wise, C. Gagnon, R. B. Fillingim, and D. D. Price, “Influences of gender role and anxiety on sex differences in temporal summation of pain,” J Pain, vol. 5, no. 2, pp. 77–82, 2004.

[28] M. Stewart, J. B. Brown, A. Donner, I. R. McWhinney, J. Oates, W. W. Weston, and J. Jordan, “The impact of patient-centered care on outcomes.,” J. Fam. Pract., vol. 49, no. 9, pp. 796–804, Sep. 2000.

[29] K. H. Todd, “Pain Assessment and Ethnicity☆☆☆★,” Ann. Emerg. Med., vol. 27, no. 4, pp. 421–423, Apr. 1996.

[30] A. Cintron and R. S. Morrison, “Pain and ethnicity in the United States: A systematic review.,” J. Palliat. Med., vol. 9, no. 6, pp. 1454–73, Dec. 2006.

[31] A. M. Martinelli, “Pain and Ethnicity,” AORN J., vol. 46, no. 2, pp. 273–281, Aug. 1987.

Figure 1 Collapsed items into scales defining gynecological and menstruation experiences

Gynecological experience	**Menstruation experience**
1. Have you previously experienced pain during a gynecological examination?	1. To which degree do you experience pain in relation to your menstruation period, in general?
2. To which degree do you experience gynecological examinations to be uncomfortable?	2. to which degree do you feel affected by pain during menstruation
3. How painful is a gynecological examination for you, in general?	
4. To which degree do you feel affected by the pain experience?	

Table 1

Socio-demographic and medical characteristics

	Low pain		**High pain**		
	n	Mean (SD) or %	n	Mean (SD) or %	Range
Age	681	31.27 (3.9)	50	30.82 (3.5)	[21-40]
Marriage	690	6.4 (2.4)	50	6.4 (2.8)	[2-8]
Education					
Lower secondary high (7 years)	4	6.0%	3	0.0%	
Lower secondary general (8-10 years)	38	5.7%	3	4.0%	
Upper secondary high (11-13 years)	208	30.2%	15	34%	
Tertiery < master degree (14-17 years)	312	45.9%	23	44%	
Tertiery master degree (18 years)	120	17.6%	9	18%	
Type of procedure					
ICSI	258	39.4%	17	37.0%	
IVF long down regulation	351	53.6%	25	54.3%	
IVF mild hormone stimulation	46	7.0%	4	8.7%	
Cause of infertility and duration					
Ovulation factor	24	3.5%	2	4%	
Tubal	119	17.2%	11	22%	
Endometriosis	75	10.9%	3	6%	
Male	320	46.4%	20	40%	
Idiopathic	130	18.8%	12	24%	
Missing	22	3.2%	2	4%	
Duration of infertility (in months)	581	31.86 (23.20)	41	25.22 (13.40)	[0-228]

Table 2

Perceived differences between the high pain and low level pain group

	Low pain			High pain				
	n	Mean	(SD)	n	Mean	(SD)	*t*	*P*
Variables measured before the oocyte retrieval								
Subjective rating								
Gynaecological experiences	677	6.31	(4.53)	49	10.27	(6.04)	4.49	0.000
Menstruation experience	684	6.30	(3.66)	50	8.40	(3.71)	3.95	0.000
Trait anxiety	681	34.05	(8.70)	50	38.60	(10.61)	2.98	0.004
Depression	684	7.05	(6.38)	50	9.32	(7.59)	2.08	0.042
Hormonal side-effects	614	1.80	(1.27)	45	2.64	(1.28)	4.31	0.000
Expected discomfort (during OR)	612	2.84	(1.33)	45	3.87	(1.38)	-4.99	0.000
Expected stress regarding the level of discomfort (during OR)	613	2.61	(1.30)	44	3.43	(1.35)	-4.04	0.000
Nervousness of the OR being uncomfortable	612	2.69	(1.60)	45	3.87	(1.50)	-4.78	0.000
Concern about the result	614	3.64	(1.58)	45	4.40	(1.51)	3.14	0.000
Partner rating								
Expected discomfort	618	3.04	(1.29)	45	3.64	(1.17)	3.06	0.002
Concern about the result	615	3.09	(1.59)	45	3.13	(1.69)	.17	NS
Medical factors								
Previous ectopic pregnancies	305	.09	(.37)	17	-	-	4.13	-
Previous spontaneus abortions	305	.15	(.47)	17	-	-	5.52	-
Previous births	305	.15	(.50)	17	.06	(.01)	.73	NS
Previous provoked abortions	305	.14	(.41)	17	.06	(.01)	.79	NS
Variables measured after the oocyte retrieval								
Subjective rating								
Anxiety during the procedure	690	1.03	(1.36)	50	2.56	(1.80)	5.81	0.000

Perceived control	686	3.87	(1.70)	50	2.10	(1.61)	7.12	0.000
Nervousness during the procedure	688	1.95	(1.57)	50	3.22	(1.87)	4.70	0.000
Contact with staff	687	47.85	(4.11)	50	46.86	(3.63)	1.67	NS
Importance of contact with staff	688	36.70	(2.92)	50	37.09	(2.89)	.907	NS
Medical factors								
Duration of the procedure	673	9.84	(5.75)	47	11.66	(6.54)	2.07	0.038
Needle size	675	1.32	(.47)	48	1.29	(.46)	.41	NS
Female BMI	554	23.40	(3.57)	39	24.43	(3.25)	1.74	NS
No. of oocytes retrieved	605	6.84	(4.33)	45	7.47	(4.15)	-.94	NS
Reproductive factors X^2	n	*%*		n	*%*			*P*
Clinical pregnancy	175	25.4		10	20			0.396
Missing data	239	34.6		18	36			

Table 3

Predictors of high pain intensity during oocyte retrieval

	Coefficient (B)	S.E	Wald	d.f.	Odds Ratio	95% CI	*P*
Variables measured before the oocyte retrival*							
Subjective rating							
Gynaecological experiences	0.085	0.036	5.534	1	1.084	[1.014, 1.168]	0.019
Menstruation pain and discomfort	0.053	0.049	1.184	1	1.054	[0.959, 1.159]	0.276
Trait anxiety (STAI-Y)	0.043	0.025	2.940	1	1.044	[0.994, 1.097]	0.086
Depression levels (BDI)	0.035	0.035	1.027	1	0.966	[0.902, 1.033]	0.268
Expected discomfort (during OR)	0.160	0.197	0.655	1	1.173	[0.797, 1.727]	0.418
Expected stress regarding the level of discomfort (during OR)	-0.219	0.192	1.297	1	0.803	[0.551, 1.171]	0.255
Nervousness of the OR being uncomfortable	0.119	0.170	0.493	1	1.126	[0.808, 1.570]	0.483
Hormonal side-effects	0.380	0.134	8.068	1	1.463	[1.125, 1.901]	0.004
Concern about the result	0.161	0.130	1.531	1	1.175	[0.910, 1.516]	0.216
Partner statement							
Expected discomfort	0.184	0.144	1.624	1	1.202	[0.906, 1.594]	0.203
Variables measured after the oocyte retrieval*							
Subjective rating							
Anxiety during the procedure	0.431	0.162	7.107	1	1.539	[1.121, 2.113]	0.008
Perceived control	0.461	0.103	20.164	1	0.631	[0.516, 0.771]	0.000
Nervousness during the procedure	0.042	0.162	0.069	1	1.043	[0.760]	0.793
Medical factors							
Duration of the procedure	0.070	0.022	10.326	1	1.073	[1.028, 1.120]	0.001
All the significant variables in one model*							
Gynaecological experiences	0.094	0.033	7.902	1	1.099	[1.029, 1.173]	0.005

Hormonal side-effects	0.0482	0.140	11.931	1	1.619	[1.232, 2.128]	0.001
Anxiety during the procedure	0.259	0.112	5.343	1	1.296	[1.040, 1.615]	0.021
Perceived control	0.476	0.119	16.088	1	0.621	[0.492, 0.784]	0.000
Duration of the procedure	0.081	0.024	11.478	1	1.084	[1.035, 1.136]	0.001

All variables used in the analysis are shown.

* N= 613 (Missing cases:196). Pseudo R^2-statistics: Cox and Snell, R^2 = 0.078, Nagelkerke R^2 = 0.195

** N= 616 (Missing cases:193). Pseudo R^2-statistics: Cox and Snell, R^2 = 0.105, Nagelkerke R^2 = 0.287