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Minimal clinically important difference for pain on the VAS scale and the relation to quality of life in women with endometriosis

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ABSTRACT

Objectives: The minimal important difference can be helpful in interpreting data from clinical trials. The objective of the study was to calculate the minimal important difference for improvement on the VAS scale for women with endometriosis.

Study design: A prospective study was conducted to evaluate the effect of pertubation with lignocaine on dysmenorrhea and quality of life in women with endometriosis. Data collected in the trial were used for additional analyses in the present descriptive study. Eligible women ($n = 37$) had endometriosis with pain > VAS 50 mm (visual analogue scale).

Main outcome measures: In a questionnaire, women evaluated their maximum pain on the VAS- scale during every menstrual period before and after treatment. They also estimated the changes in overall pain level by answering the response categories "much better", "somewhat better", "about the same", "somewhat worse" or "much worse". The women were grouped according to their own estimation of change in pain intensity after four months. The minimal important differences for change on the VAS scale correlate to the mean change for women who felt "somewhat better" ($n = 18$) excluding those who were pain free ($n = 2$).

Results: The minimal important difference for improvement on the VAS scale was found to be −39 mm and/or −49%.

Conclusion: If the patients have a pain level of at least 50 mm on VAS scale at inclusion, the cut off for success in clinical trials is suggested to be defined as an either >40 mm or a >50% decrease on VAS scale. Trial registry ClinicalTrials.gov Identifier: NCT01329796.

Introduction

Pain in the lower part of the abdomen is one of the main symptoms in endometriosis, a disease affecting 6–10% of all fertile women [1]. Dysmenorrhea is often the first symptom but other pain symptoms that may occur over time is non-menstrual pelvic pain, deep dyspareunia, dyschezia and chronic pelvic pain [2]. The pain can occur intermittently throughout the menstrual cycle or be continuous [3].

Women with chronic pelvic pain report worse health related quality of life (HRQL) compared to healthy women [4] and the impairment in quality of life is related to the degree of pain [5]. Women with endometriosis thus have impaired HRQL compared to women without endometriosis [4,5] and even worse than women with depression [6].

Numerous pain scales have been used in clinical trials for assessment of endometriosis associated pain [7]. For clinical trials in endometriosis, an 11-point NRS (Numerical/numeric Rating Scale) is recommended by ASRM (American Society for Reproductive Medicine) as primary outcome measure whereas the quality of life questionnaire Endometriosis Health Profile-30 (EHP-30) is proposed as secondary outcome measure [8]. The NRS is a segmented numerical version of the visual analogue scale (VAS) [7].

The VAS scale is measured in millimeters and range from 0 (no pain) to 100 (worst pain imagined). It is the most frequently used pain scale and is regarded as a valid instrument for evaluating chronic pain during endometriosis [7–9]. The VAS scale is more precise and potentially more sensitive to change than the NRS

Abbreviations: ASRM, American Society for Reproductive Medicine; EHP-30, Endometriosis Health Profile-30; HRQL, health related quality of life; IQR, interquartile range; Max, maximum; MCIC, minimal clinically important change; MCID, minimal clinically important difference; MID, minimal important difference; Min, minimum; MWU, Mann Whitney test; NRS, Numerical/numeric Rating Scale; PRO, patient reported outcomes; QOL, quality of life; RCT, randomized controlled trials; SD, standard deviation; VAS, visual analogue scale.

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and also allows simplified inclusion criteria [7,10]. An inclusion criteria of VAS >50 mm is often used in clinical studies [7,11,12].

The EHP-30 questionnaire is the only Quality of life (QOL) scale that has been validated for use in women with endometriosis and has proved to be reliable, valid and responsive to change [8,13–16]. It comprises two parts: a core questionnaire, which consists of five scales with a total of 30 items applicable to all women with endometriosis. The other part is the modular questionnaire, which does not necessarily apply to all women with endometriosis. It consists of six scales and contains a total of 23 items. Within the scales the items are summed to create a raw score and each scale is then translated into a score ranging from 0 (best health status) to 100 (worst health status). All scale scores should be presented separately [17].

QOL and most pain scales are patient reported outcomes (PRO) which are outcomes based on reports that comes directly from the patients. Patient ratings of pain are reliable [8] but it is difficult to interpret the results from clinical trials including PRO. Effects of an intervention on health status should ideally be analyzed in two ways; as mean differences between patient groups in the change in scores and as the difference in the proportion of patients in both groups exhibiting clinically significant change as defined by the minimal important difference (MID) [18,19].

The MID can be defined as the smallest difference in a score that the patients perceive as a change [18,20] and may vary by population and context [21,22]. The corresponding MCIC (minimal clinically important change) is sometimes used. The MID can be estimated using various methods and there is no consensus in the literature on what is the most appropriate technique [18]. The anchor-based methods examine the relation between scores on the target instrument and some independent measures i.e. anchors [18]. Within-patient global ratings of change i.e. transition questions can be used as an anchor to estimate the MID of an instrument [14,20–22]. A transition question requires the respondent to evaluate the change in their clinical status or their health status by answering the response categories much better, somewhat better, about the same, somewhat worse and much worse [14,21].

There are few studies defining the clinical relevant improvement on the VAS scale for patients with endometriosis. In a study from 2010, based on two randomized controlled trials (RCT), the minimal clinically important difference (MCID) for endometriosis-associated pelvic pain was determined to be 10 mm. The best separation between women rating themselves "minimally improved" and "improved" was found to be a decrease of 28 mm on the VAS scale [7,23]. The definition of responders in clinical trials in endometriosis has been suggested to be either a >30% or a >50% reduction in symptoms [8].

There is a need for more studies using anchor tools to determine the MID on the VAS scale for women with endometriosis. A trial has been carried out to evaluate the effect of pertubation with lignocaine on dysmenorrhea and quality of life in women with endometriosis [11,24]. Data collected in the trial were used for additional analyses in the present study.

The primary objective was to calculate the MID for change on the VAS scale for women with endometriosis, using the women's estimation of change in pain intensity as an anchor. A secondary objective was to examine whether this cut-off on the VAS scale also had significant effects on quality of life.

Methods

A prospective study was conducted to evaluate the effect of pertubation with lignocaine on dysmenorrhea and QOL in women with endometriosis. 42 women were included in the study. The pertubation treatments were given during three sequential menstrual cycles and comprised passing study solutions (lignocaine or placebo) through the uterine cavity and the Fallopian tubes via an intra-cervical placed balloon catheter. The detailed methodology of this trial has previously been described [11,24]. The main inclusion criteria were presence of peritoneal or ovarian endometriosis verified by laparoscopy and dysmenorrhea with a pain score >50 mm on the VAS scale. Written informed consent was obtained before any study related procedures. The study was approved by the Medical Products Agency in Sweden Nov. 8, 2006 (Dnr 151:2006/56028) and after amendment Dec. 12, 2007 (Dnr 151:2007/76934) as well as by the Regional Ethical Review Board in Stockholm Jan. 10, 2007 (Dnr 2006/1416-32) and after amendment Dec. 14, 2007 (Dnr 2007/1398-32).

The effect on pain was evaluated with a pain questionnaire including a VAS scale, initially filled out at the menstruation before the first treatment, i.e. baseline. They were thereafter completed during the 2nd, 3rd and 4th period, i.e. after every treatment and also during the 7th, 10th and 13th menstrual period, i.e. just over 6, 9 and 12 months after initial treatment. The maximum pain on the VAS scale during every menstrual period was recorded. In addition, the women were asked to estimate changes in their overall pain level during and between periods by answering the response categories "much better", "somewhat better", "about the same", "somewhat worse" or "much worse". The women's estimation of change in pain intensity was used as an anchor to evaluate the MID on the VAS scale [21].

The women were grouped according to their own estimation of change in pain intensity after four months independent of treatment. The women that estimated their pain to be "somewhat better" during and/or between periods were classified as better ($n = 18$) and the women that felt "somewhat worse" or "much worse" during and/or between periods were classified as worse ($n = 4$). Women that estimated their pain to be "about the same" both during and between periods were classified as same ($n = 11$) and the two women that became "much better" both during and between periods were classified as pain free. The MID for change on the VAS scale correlate to the mean change for women who felt "somewhat better" [20] excluding the two that were pain free.

The effect on QOL was evaluated with a Swedish translation of the EHP-30 questionnaire (Pharmacia UpJohn, 2001). It was filled out before the first treatment and during the 7th and 13th menstrual period. The women received the treatments before the 4th period and no treatments were given the subsequent two periods preceding the collection of the EHP-30 questionnaire after six months. All scales and items on the core questionnaire and also the sexual intercourse scale (five items) were collected. If one or more items were missing from any dimension, a scale score could not be calculated for that individual [17]. Only the complete scores are presented giving different number of women in various dimensions. Further if any item was missing at baseline, this specific score was withdrawn from further analysis concerning this specific dimension. A decrease on a score scale (i.e. negative change) at follow up implies that the patient has improved.

The change in QOL was compared between the group of women that improved more than the calculated MID on the VAS scale after four and/or six months and those who did not improve.

For statistical analysis Statsoft Statistica 10 and Microsoft Excel 2007 were used. The mean change in pain intensity on the VAS scale was calculated in the above groups. A negative value on the mean change means that the women were improved considering pain.

The changes on the different EHP-30 scores from baseline to follow-up after six months were compared between women who improved/not improved more than our calculated MID. The changes on different EHP-30 dimensions were compared between groups with Mann Whitney U test (MWU).