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Responsiveness of the Endometriosis Health Profile-30 questionnaire in a Swedish sample: an observational study

K. Wickström[1], J. Spira[2], G. Edelstam[3]

[1] Karolinska Institutet, SE-171 77 Stockholm, Sweden and Danderyd Hospital, Stockholm
[2] Karolinska Institutet, SE-171 77 Stockholm, Sweden and InSpira Medical AB, Tyresö
[3] Karolinska Institutet, SE-171 77 Stockholm, Uppsala University, SE-751 85 Uppsala and Danderyd Hospital, Stockholm (Sweden)

Summary

Objective: The objective was to evaluate the responsiveness of the Endometriosis Health Profile-30 (EHP-30) questionnaire in a Swedish sample. *Materials and Methods:* Forty-two patients with endometriosis were included in a prospective observational study. *Main outcome measures*: The changes on the EHP-30 questionnaire after pertubation treatment were compared with the patients' self-estimated change in pain intensity. The responsiveness to change was evaluated with effect sizes and significance of change (paired *t*-test). The changes in scores between those who improved / not improved were compared with independent *t*-test. *Results*: The changes in the scores were significant for all dimensions on the core questionnaire ($p = 0.04–0.0002$) for improved patients in contrast to the patients in the stable group where there were no significant changes in any dimension ($p = 0.16–0.63$). The effect sizes were large (> 0.8) on all core scales except for self-image (0.51) for the improved patients and small on all scales in the non-improved (stable) group (- 0.17−0.35). There were significant differences between the improved and the stable group considering change in most of the core EHP-30 scores. *Conclusions*: The EHP-30 is responsive to improvement on all core scales and is acceptable, understandable, and applicable in this Swedish sample.

Key words: Endometriosis; Pain; Quality of life; EHP-30; Responsiveness.

Introduction

Endometriosis is defined by the presence of viable endometrial tissue outside the uterine cavity. It affects 6-10% of all fertile women and up to 35-50% of females with dysmenorrhea and/or infertility, which are the main symptoms of endometriosis [1, 2].

Women with endometriosis have impaired health-related quality of life compared to women without endometriosis [3, 4], and even worse than women with depression [5]. It appears that women with chronic pelvic pain and conditions that are associated with chronic pain (such as endometriosis) report worse health-related quality of life compared to healthy women [6] and the decreased quality of life is related to the degree of pain [4, 7].

There are several questionnaires for evaluating health-related quality of life and the questionnaires could be generic or disease specific. For endometriosis, three disease specific questionnaires have been developed (Bodner 1997 [8], Colwell 1998 [9], and Jones 2001 [10,11]). In the Endometriosis Health Profile-30 (EHP-30) questionnaire, developed by Jones *et al*., the questions were patient-generated. The EHP-30 has proved to be reliable, valid and responsive to change [10, 12, 13]. When the responsiveness of the EHP-30 initially was evaluated, complete data were obtained for 40 patients, and the study showed that only one scale (social support) on the core questionnaire failed to demonstrate any responsiveness. The EHP-30 questionnaire has been shown to be more responsive to change compared to the generic tool Short Form-36 (SF-36) in patients with endometriosis [12, 14].

The EHP-30 questionnaire comprises two parts. The core questionnaire consists of five scales (pain, control and powerlessness, emotional well-being, social support, and self-image) and contains 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 (work life, relationship with children, sexual intercourse, infertility, medical profession, and treatment) and contains a total of 23 items [11]. Within the scales the items are summed to create a raw score. Each scale is then translated into a score ranging from 0 (best health status) to 100 (worst health status) and the scales are intended to be presented separately [15].

For clinical trials in endometriosis, the EHP-30 questionnaire is proposed by American Society for Reproductive Medicine (ASRM) as secondary outcome measure, whereas an 11-point Numerical/numeric Rating Scale (NRS), which measures pain, is recommended as primary outcome measure [16].

A trial has been carried out to evaluate the effect of pertubation with lignocaine on dysmenorrhea and quality of

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Table 1. — *Inclusion and exclusion criteria.*

Inclusion criteria	Exclusion criteria
• age > 20 years	• continuous treatment with medication that may increase risk for infection
• endometriosis verified by laparoscopy	• clinical signs of pelvic inflammatory disease
• dysmenorrhea or pelvic pain defined as a pain score of >50 mm (VAS)	• hyper reactivity to local anaesthesia
• normal Fallopian tubes	• fibroids > 2 cm
• regular menstrual cycles 21-35 days	• ongoing treatment with GnRH agonist
• treatment with oral contraceptives (OC) ongoing >1 month and continued during the trial	• ongoing continuous treatment with high-dose gestagens
• previous hormonal treatment discontinued > 1 month (OC, gestagens) and > 6 months (GnRH agonist)	• pregnancy
• no wish for pregnancy during the study	• peritubal adhesions
• normal Pap smear	• occluded Fallopian tubes
• negative chlamydia test	• inability to understand information or comply with study procedures
• negative pregnancy test	• participation in a clinical study within one year before the present study
• informed consent given and signed	• any disease or laboratory finding considered of importance by the investigator for not including the patient

life in patients with endometriosis. The results concerning dysmenorrhea demonstrated a significant reduction of pain after three pertubations with lignocaine compared to placebo [17]. Quality of life was evaluated with the EHP-30 questionnaire and a significant effect was seen on the social support scale, whereas there were no differences on the other dimensions [18].

When analysing the results from the EHP-30 questionnaires, the question was raised whether the results from our Swedish material of 41 patients was reliable. The hypothesis was that the EHP-30 questionnaire was applicable and responsive for change for all measured dimensions in the present sample.

The primary objective of this study was thus to evaluate the responsiveness and the applicability of the EHP-30 questionnaire in a Swedish sample. A secondary objective was to calculate the minimal important differences for the EHP-30 in the study population.

Materials and Methods

Study design, participants and procedures

A prospective interventional, double-blind, and randomised study was conducted to evaluate the effect of pertubation with lignocaine on dysmenorrhea and quality of life in patients with endometriosis. The study included 42 patients of whom 24 were randomised to active treatment and 18 to placebo. The pertubation treatments were given during three sequential menstrual cycles and comprised passing study solutions 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 [17]. The treatments were given at three outpatient settings in Stockholm, Sweden. The subjects were recruited through advertisements and from the gynaecological outpatient unit at the three participating clinics. The main inclusion criteria were presence of peritoneal or ovarian endometriosis verified by laparoscopy and dysmenorrhea with a pain score of > 50 mm on the visual analogue scale (VAS) (Table 1). The exclusion criteria included reduced patency in the fallopian tubes and the intention to achieve pregnancy during the forthcoming year. Written informed consent was obtained before any study related procedures and the Consolidated Standards of Reporting Trials (CONSORT) guidelines were followed.

The study was approved by the Medical Products Agency in Sweden, as well as by the Regional Ethical Review Board in Stockholm.

The effect on quality of life was evaluated with a Swedish translation of the EHP-30 questionnaire (Pharmacia UpJohn, 2001) which were initially filled out before the first treatment i.e. baseline. The follow-up took place after the 7th and 13th menstrual period, i.e. six and 12 months after initial treatment. At the time of the study, the EHP-30 had not been validated in Swedish. It was however considered the best available option since it is the only quality of life scale that has been validated for use in women with endometriosis [16].

Data collected in the randomised study were used to evaluate the responsiveness of the EHP-30 questionnaire and the patients in the lignocaine and the placebo groups were analysed all together. All dimensions and items on the core questionnaire were collected (i.e. 30 items). Since the EHP-30 questionnaire is extensive and time-consuming for the patients to fill out, only the score concerning sexual intercourse (five items) on the modular questionnaire was included. The effect on pain was evaluated with a pain questionnaire and was initially filled out at the menstruation before the first treatment, i.e. baseline. Thereafter they were completed after every treatment and follow-up took place after the 7th and 13th menstrual period, i.e. six and 12 months after initial treatment. On the pain-questionnaires, the participating patients were asked to estimate any 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”. This corresponds to the global question on the general quality of life questionnaire SF-36 and can be used to examine the responsiveness of an instrument [14].

The patients were grouped according to their own estimation of change in pain intensity independent of treatment (lignocaine or placebo). The patients that estimated their pain to be “somewhat better” during and/or between periods were classified as better (n=17) and the patients that felt “somewhat worse” or “much worse” during and/or between periods were classified as worse (n=8). Patients that estimated their pain to be “about the same”

Table 2. — *Baseline data and data completeness.*

EHP-30	Baseline (n=41) Mean (SD) Min-max	Complete questionnaires Rate	%
Pain Question 1-11	51.3 (19.7) 13.6−95.5 n=40	100/103	97
Control and powerlessness Question 12-17	62.9 (21.3) 8.3−100 n=41	100/103	97
Emotional well-being Question 18-23	53.9 (16.7) 8.3−91.7 n=38	98/103	95
Social support Question 24-27	50.3 (21.6) 0−93.7 n=40	102/103	99
Self-image Question 28-30	30.2 (18.3) 0−58.3 n=40	102/103	99
Sexual intercourse Question C1-C5	41.5 (25.6) 0−100 n=38	92/103	89

Table 3. — *Change in EHP-30 in relation to change in pain intensity after six months.*

EHP-30	Worse n=8 Mean[a] (SD)	Same n=6 Mean[a] (SD)	Better = minimal important difference n=17 Mean[a] (SD)	Pain-free n=2 Mean[a] (SD)
Pain	3.7(10.4) n=8	-10.5 (10.4) n=5	-19.9 (18.8) n=17	-39.8 (37.0) n=2
Control and powerlessness	4.2(13.0) n=8	-10.4 (16.6) n=6	-25.7 (25.9) n=17	-50.0 (23.6) n=2
Emotional well-being	9.5(14.6) n=7	4.2 (20.7) n=6	-13.9 (21.4) n=15	-50.0 (17.7) n=2
Social support	0 (14.4) n=7	-8.3 (17.5) n=6	-12.9 (18.0) n=17	-50.0 (26.5) n=2
Self image	4.8 (15.1) n=7	-1.4 (12.3) n=6	-6.9 (15.6) n=17	-25 (23.6) n=2
Sexual intercourse	13.0 (16.0) n=5	-3.0 (15.6) n=5	-4.5 (27.8) n= 14	-27.5 (3.5) n=2

[a] Negative values indicate improved Quality of Life.

Table 4. — *Effect size and significance of change in relation to change in pain intensity after six months.*

EHP-30	Worse and same n=14		Better and pain-free n=19	
	Effect size[a]	*p*-value paired *t*-test	Effect size[a]	*p*-value paired *t*-test
Pain	-0.09	0.62	-1.22	<0.001
Control and powerlessness	-0.10	0.63	-1.24	<0.001
Emotional well-being	0.35	0.16	-1.04	0.006
Social support	-0.17	0.40	-0.84	0.003
Self image	0.11	0.62	-0.51	0.04
Sexual intercourse	0.15	0.38	-0.30	0.29

[a] Negative values on effect size indicate improved quality of life.

both during and between periods were classified as "same" (n=6) and the two patients that became "much better" both during and between periods were classified as pain free. One patient was removed from analysis since she could not be classified according to the above definition. She became pain free between periods whereas the pain during periods became worse.

The *improved group* consisted of the patients that were classified as better or pain free (n=19) and the *non-improved or stable group* of patients that were classified as same or worse (n=14).

In the EHP-30 questionnaire, if one or more items are missing from any dimension on the core and modular questionnaire, a scale score cannot be calculated for that individual [15]. Only the complete scores are presented for the different dimensions giving different number of patients in various dimensions. Furthermore, if any item was missing at any dimension at baseline, this specific score was withdrawn. The questionnaires collected after six months were used for the responsiveness analyses, whereas the data completeness analysis also includes the questionnaires collected after 12 months.

Statistical methods

For statistical analysis Excel 2007 was used. The responsiveness to change for the EHP-30 questionnaire was evaluated with effect sizes and significance of change in the improved and the stable groups. All the patients that were better or pain free (improved group) were compared with all the patients that felt the same or worse (stable group) independent of treatment group (lignocaine or placebo).

Effect size is one of the most commonly used methods for interpreting change in a score [19] and are an estimation of the magnitude of change in health status between two different times [20]. It is independent of sample size and can be calculated by dividing mean difference with pooled standard deviation (SD) [21]. An effect size of 0.2 indicates small change, 0.5 indicates a moderate change, and 0.8 a large change [21]. The signs of the effect sizes are influenced by the direction of the scoring of the scale. Negative effect sizes correlates to improved quality of life in the present material since a lower score indicate better quality of life.

Significance of change was calculated with paired Student's *t*-test. The different scores before and after treatments were compared. The changes in EHP-30 scores between the improved and the stable groups were compared with independent Student's *t*-test.

The minimal important differences **(**MID) for scores on EHP-30 correlate to the mean change for patients who felt "somewhat better" [22]. A negative value on the mean change means the EHP-30 score is lower at the follow up and thus that the patients are improved considering their quality of life.

Results

In total, 103 EHP-30 questionnaires were collected at different time-points, 41 at baseline, 36 after six months, and 26 after 12 months. The demographic of the study population was as follows: the mean age was 33.2 (± 5.1) years (min. 22 and max. 43 years) and the mean duration of endometriosis was 4.95 (± 4.2) years (min. 0 and max.16

Table 5. — *Change in EHP-30 for improved and not improved (stable) group after six months.*

EHP-30	Patients´ estimated change in pain intensity		
	Worse and same n=14 Mean (SD)	Better or pain-free n=19 Mean (SD)	*p*-value independent *t*-test
Pain	-1.7 (12.3) n=13	-22.0 (20.7) n=19	0.004
Control and powerlessness	-2.1 (15.9) n=14	-28.3 (26.2) n=19	0.002
Emotional well-being	7.1 (17.1) n=13	-18.1 (23.8) n=17	0.003
Social support	-3.8 (15.8) n=13	-16.8 (21.6) n=19	0.07
Self image	1.9 (13.7) n=13	-8.8 (16.8) n=19	0.07
Sexual intercourse	5 (17.2) n=10	-7.3 (27.0) n=16	0.21

years). Of the included patients, 65% were nulliparous, 19% had delivered once, and 14 % were multiparous with at least two children

Data completeness for the core scales was good. For the modular score sexual intercourse, data were complete in all 103 questionnaires, but 11/103 (11%) could not be analysed since patients reported they did not have sexual intercourse for other reasons (Table 2).

At the baseline, the analysed sample of 41 patients had the lowest score (i.e. best quality of life) on the dimension self-image and sexual intercourse and highest score (i.e. worst quality of life) on the dimensions control, powerlessness, and emotional well-being (Table 2).

On the pain-questionnaires, the participating patients were asked to estimate any changes in their overall pain level and after six months, 34 patients estimated their pain according to this question. One patient was excluded from analysis since she could not be classified as pain-free, better, same or worse.

The mean change on EHP-30 scores correlates with the patients' own estimation of change in pain intensity, indicating that the pain intensity is related to all dimensions of quality of life (Table 3). The improvement or deterioration in the quality of life was related to the improvement or deterioration in the pain intensity. The levels for MID corresponds to the mean change for patients evaluating their pain to be better (n=17) and excluding the two that were pain-free (Table 3).

For the patients in the improved group (better and pain free), the change in EHP-30 scores was significant for all dimensions except for sex. The effect sizes for changes were large for all dimensions except "self-image" (moderate change) and "sex" (small to moderate change, Table 4). Significance of changes and effect sizes were also calculated for patients in the stable group (same and worse). There were no significant changes in any dimension on the EHP-30 questionnaire in the stable group and the effect sizes were small, indicating that there was little change in health status (Table 4).

The change in the different EHP-30 scores between the improved (better and pain free) and the stable group (same or worse) after six months were compared with independent Student's *t*-test. There were significant differences for the change in EHP-30 scores for pain, control and powerlessness and emotional well being, whereas there was a tendency but no significant differences for social support and self-image (Table 5). The difference was not significant for the dimension of sexual intercourse.

The stable group was separated into two small subgroups and the effect sizes were calculated in the group that was "same" i.e. unchanged (n=6) and worse, (n=8) respectively.

There were no significant changes in any EHP-30 score in the same group ($p = 0.08-0.64$) or in the worse group ($p = 0.13-1$). The effect sizes were small in both subgroups except on two scales in the subgroup that felt the same, in which the effect size were moderate for pain (- 0.79) and for control and powerlessness (- 0.70). Thus, some of the scales displayed responsiveness in the small group that felt the same, but for the other dimensions, the effect sizes were small, indicating small changes in quality of life for patients reporting themselves to feel the same during periods.

Discussion

The present baseline data on the EHP-30 is consistent with studies from U.K. and Australia [12, 13, 23]. Data completeness for the core scales were high for all dimensions (89-99%) and only a few questions remained unanswered. The relatively low dropout rate was probably partly due to a limited number of modular items. The sample in this clinical trial seems to have normal distributions on all the different scores with few patients at extreme values. The EHP-30 questionnaire has been shown to have low ceiling and floor effects [13].

The social scale on the EHP-30 questionnaire failed to demonstrate responsiveness in the original English version, [12] but in the present material, the EHP-30 questionnaire seems to be highly responsive to change in health status for *all* scales on the core questionnaire. This is in concordance with a Dutch study from 2013 in which responsiveness was demonstrated for all scales on the EHP-30 core questionnaire [24]. The sample size in the present study was small but similar to the sample size used by Jones *et al.* [12].

The health-related quality of life was linked to pain intensity in the present study. A correlation between the mean change on the EHP-30 scores and the patients' own estimation of change in pain intensity was found. The fact that pain intensity is related to quality of life is in concordance with earlier studies [4, 7]. The present authors used the patients' estimation of change in pain intensity as an anchor to evalu-

ate responsiveness since pain is in relation with quality of life [25]. However, the long recall period of pain may constitute a bias.

In the improved group there were significant changes on all core scales on the EHP-30 questionnaire and the effect sizes were moderate to large, indicating that the EHP-30 is highly responsive to change. Also, there were no significant changes in any dimension on the EHP-30 questionnaire in the stable group and the effect sizes were small indicating that there was little change in health status.

There were significant differences between the improved and the stable groups for the change in EHP-30 scores for pain, control, powerlessness, and emotional well-being whereas there was a tendency but not significant differences for social support and self-image. It is important that there is a significant difference between those groups when evaluating the effect in a clinical study.

In the small group of patients that evaluated their pain to be the same (n=6), the present authors found moderate effect sizes for pain and control and powerlessness but there were no significant changes (paired *t*-test) in the change in the different EHP-30 scores. Thus, some of the scales displayed responsiveness in the small group that felt the same, but for the other dimensions, the effect sizes were small, indicating small changes in quality of life for patients reporting themselves to feel the same during periods. Similar results have been obtained when another quality of life questionnaire was evaluated, displaying responsiveness on some of the scales in the stable group (Colwell e*t al.* [9]). The reason for the improved quality of life, even if the pain intensity is the same, might be an effect of placebo and of Tender, Love, and Care when participating in a clinical study [26-28]. It can also be due to recall bias and the fact that other aspects than pain have an influence on quality of life.

For patients that felt worse with pain intensity (n=8), the effect sizes were much smaller than in the improved group, and the changes on the different EHP-30 scores were not significant, indicating that the EHP-30 questionnaire is not as responsive in the deteriorate direction. Again, this is in accordance with the responsiveness of Colwell's Quality of Life questionnaire, where it was found to be moderate to high for the patients who improved, but low to moderate in the impaired group [9]. Also in the Dutch study, the mean changes for those who deteriorated were smaller than for those who improved on all core scales [24]. There is evidence for asymmetry in worsening and improvement in patient reported outcomes [25].

The levels for MID in the present study population were higher for emotional well-being and social support but lower for control and powerlessness, pain, and self-confidence, compared to Jones' study. In comparison with the study by van de Burgt *et al*., the levels for MID were larger for all dimensions [24]. The MID for social support was -13 compared to -10 in the Dutch study and +1.7 in the British study, supporting the thesis that the EHP-30 questionnaire is sensitive to change even for the dimension social support.

The data from this limited observational study show that the EHP-30 is sensitive to change on all dimensions on the core questionnaire and can detect differences in health-related quality of life at a level that is important and detectable for the patients.

Conclusions

The EHP-30 questionnaire translated in Swedish seems to be acceptable, understandable, and applicable in the present Swedish sample. The EHP-30 is responsive to improvement on all dimensions on the core questionnaire.

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Corresponding Author:
G. EDELSTAM, M.D., Ph.D.
Uppsala University, SE-751 85 Uppsala
and Danderyd Hospital AB, SE-182 88
Stockholm (Sweden)
e-mail: Greta.Edelstam@ds.se