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Original Research

Evaluation of Stress Hormone Levels, Preoperative Anxiety, and Information Needs before and after Hysteroscopy under Local Anesthesia in Relation to Transvaginal Procedures under General, Short-Term Anesthesia

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Abstract

Background: Hysteroscopy is currently the gold-standard procedure in the evaluation of the uterine cavity and treatment of intrauterine lesions as it is minimally invasive and has high diagnostic efficiency. According to previous observations, many patients are afraid of minimally invasive procedures performed under general anesthesia. They are also afraid of procedures that, according to them, may be associated with pain. To address this issue, in this study, the levels of stress and anxiety, and biochemical parameters indicating the hormonal response in terms of the stress response in hysteroscopic procedures under local anesthesia were compared with those of traditional surgical procedures and uterine cavity curettage procedures under general, short-term anesthesia. **Methods**: This study included 184 participants: 153 women undergoing diagnostic or operative mini-hysteroscopy procedures with the use of a hysteroscope of a reduced diameter under local, paracervical anesthesia without the participation of an anesthesiologist, and 31 women undergoing hysteroscopy or uterine cavity curettage under general, intravenous, short-term anesthesia with the participation of an anesthesiologist. To determine cortisol and prolactin levels using electrochemiluminescence, blood was collected from the patients on the day of admission to the hospital, i.e., the day of surgery, in the morning, while fasting. An original survey questionnaire, the Amsterdam Preoperative Anxiety and Information Scale (APAIS) and the Visual Analogue Scale (VAS) were used as research tools. The questionnaires were completed by the patients themselves 60 min before the surgery. **Results**: APAIS: no significant differences in anxiety and information demand scores were observed between the study groups. Anxiety before surgery was significantly higher than that before anesthesia in both groups. Similarly, information demand for surgery was significantly higher than that for anesthesia in both groups. VAS: no significant differences in anxiety and stress scores were observed between the groups. No significant differences in prolactin and cortisol levels were observed between the groups. **Conclusions**: It can be concluded that it is necessary to apply the interventions that reduce the anxiety of the patients and inform patients about the planned course of the procedure, since higher levels of anxiety before the procedure result in a significant increase in procedure duration, which in turn can increase the pain experienced by the patients.

Keywords: hysteroscopy; minimally invasive procedures; general anesthesia; local anesthesia; cortisol; prolactin; Amsterdam Preoperative Anxiety and Information Scale (APAIS); Visual Analogue Scale (VAS)

1. Introduction

Hysteroscopy is currently the gold-standard procedure in the evaluation of the uterine cavity and treatment of intrauterine lesions as it is minimally invasive and has high diagnostic efficiency [1–6]. Worth noting is the possibility of removing submucosal myomas by morcellation during hysteroscopy, using tubes of appropriate diameter, while in 2014 the Food and Drug Administration (FDA) issued a warning against performing this procedure during laparoscopic surgery (updates in 2020 and 2022 as a draft - recommended limiting the use of laparoscopic power morcellation to certain appropriately selected women and performing only with a tissue containment system) [6–8]. Since direct visualization and treatment of lesions can be performed using hysteroscopy, it has replaced uterine cavity curettage procedures [9–12]. Previously, endoscopes that are 10 mm or more in diameter, a speculum, bullet forceps, and Hegar's dilators were used in hysteroscopy, which allowed for the dilatation of the cervical canal, necessitating the use of general anesthesia due to the accompanying pain [11,13]. Nowadays, resectoscopes with a lower diameter are increasingly used to reduce the discomfort experienced by the patient, limit the costs, and shorten the duration of hospitalization [1,12–16], which can allow this procedure to be performed without requiring short-term intravenous anesthesia [13,17].

Anxiety and pain symptoms occur in patients before, during, and after surgery. Currently, preoperative ques-

tionnaires are used to assess fear, anxiety, and pain, such as the Amsterdam Preoperative Anxiety and Information Scale (APAIS) and the Visual Analogue Scale (VAS). Using these questionnaires, appropriate preoperative treatment and postoperative care can be established [18,19]. The primary advantage of the APAIS that distinguishes it from other scales is that it assesses, besides the level of anxiety, the level of need for information regarding anesthesia and the procedure, which is extremely important for medical personnel caring for surgical patients [19]. The VAS is a 100-mm-long segment, of which one end is marked with the number 0 and the other end with 10. It is used most often to assess pain; in addition, it is a well-established method in the evaluation of other somatic and psychological symptoms. The major advantages of VAS are its ease of use and patient-friendly characteristic, as well as its very short execution and interpretation time. Due to these features, the VAS can be successfully used to assess and monitor the severity of fear/anxiety/stress in elderly patients and patients with severe clinical conditions [19]. Although short-term stress can be adaptive, pain or nonpain-related stressors can induce maladaptive responses, which in turn can increase cortisol secretion and condition a sensitized physiological stress response [20]. Cortisol and prolactin are described as two potential biochemical markers of chronic stress in the literature [21]. Cortisol is a steroid hormone secreted in the striatal layer of the adrenal cortex [22]. Blood cortisol concentrations show a diurnal rhythm, with the highest concentration observed in the morning (the morning peak of cortisol upon awakening) and the lowest around midnight [23]. Studies on the relationship between severe condition/severe illness or extensive surgical intervention, and serum cortisol levels show an increase in cortisol levels in patients with serious illness or undergoing surgery [24]. However, evaluating the effect of procedures as minimally invasive or "minor" on the concentration of the hormone secreted under stress is difficult. Prolactin is a hormone secreted in the anterior lobe of the pituitary gland [25]. Physiologically, prolactin secretion is regulated by dopamine, and its concentrations show a diurnal rhythm. One of the stimuli to prolactin release is sleep, and other stimuli include physical exertion and emotional state. However, although it is well established that prolactin levels increase in response to stress, the findings of Studerus *et al*. [26] do not support the notion that increased prolactin levels among patients not previously treated with antipsychotics with a clinically high risk of psychosis or first-episode psychosis are attributable specifically to stress [26]. Severe stress [27] and irregular sleep times and durations may lead to impaired prolactin release. In addition, a "positive coupling" between prolactin levels and the adrenal response to stress stimuli has been reported: the higher the prolactin level, the higher the adrenocorticotropic hormone concentration [28].

With the increase in the availability of ultrasound (US) examinations, the detection of abnormalities within the uterine cavity is also increasing, along with the need to choose the appropriate treatment procedure. According to previous observations, many patients are afraid of minimally invasive procedures performed under general anesthesia. They are also afraid of procedures that, according to them, may be associated with pain. To address this issue, in this study, the levels of stress and anxiety, and biochemical parameters indicating the hormonal response in terms of the stress response in hysteroscopic procedures under local anesthesia were compared with those of traditional surgical procedures and uterine cavity curettage procedures under general, short-term anesthesia.

2. Materials and Methods

This study included 184 participants: 153 women undergoing minor gynecological procedures in the Reception Room Office (RRO), i.e., diagnostic or operative mini-hysteroscopy procedures with the use of a hysteroscope of a reduced diameter under local, paracervical anesthesia without the participation of an anesthesiologist, and 31 women undergoing hysteroscopy or uterine cavity curettage in the Central Surgical Office (CSO) under general, intravenous, short-term anesthesia with the participation of an anesthesiologist. All female patients were hospitalized, from February to August 2022, at the Gynecological-Obstetrical Clinical Hospital of the Poznan University of Medical Sciences.

2.1 Procedure of Qualifying Patients for Surgery

Patients who met the following criteria were selected for mini-hysteroscopy surgery under local anesthesia (using lignocaine): a history of abnormal uterine bleeding, changes in the uterine cavity such as endometrial polyps or small submucosal myomas, and hypertrophy of the endometrium. These patients reported good health without cardiovascular disease, had a negative history of sensitization to lignocaine and ketoprofen, were in phase I of their menstrual cycle or postmenopausal, and were selected for the procedure after a gynecological US examination. Patients who had heavy genital tract bleeding, inflammation of the vagina and/or cervix, and inability to avoid pregnancy during qualification for the procedure were excluded from the mini-hysteroscopy. During the aforementioned procedures, the patients were conscious and could observe the procedure in real time on a monitor.

Patients who met the following criteria were selected for hysteroscopy or uterine cavity curettage under general, intravenous, short-term anesthesia: changes in the uterine cavity such as endometrial polyps or submucosal myomas, and endometrial hypertrophy or patients who did not provide their consent to minimally invasive procedures. Additional criteria were neoplastic endometrial and cervical proliferations, abnormal uterine bleeding, and heavy bleeding. These patients were selected for the procedure after a gynecological US examination. Patients who had inflammation of the vagina and/or cervix during qualification for the pro-

cedure and inability to avoid pregnancy were excluded from the hysteroscopy or uterine cavity curettage.

2.2 Data Collecting

The medical history of the patients was collected during the selection for the procedure. The collected data included age, weight, height, past surgeries, allergies, the number and types of past births, the number of miscarriages, past cervical and endometrial procedures, and general health.

To determine cortisol and prolactin levels using electrochemiluminescence, blood was collected from the patients on the day of admission to the hospital, i.e., the day of surgery, in the morning, while fasting.

An original survey questionnaire, the APAIS, and the VAS were used as research tools. The questionnaires were completed by the patients themselves 60 min before the surgery.

2.3 The Questionnaires

An original survey questionnaire, the APAIS, and the VAS were used as research tools. The questionnaires were completed by the patients themselves 60 min before the surgery.

The APAIS contains six statements, of which four comprise an overall measure of preoperative anxiety (two on fear of anesthesia and two on fear of surgery) and the remaining two comprise a subscale assessing the need for information about anesthesia and surgery. The patients responded to each statement by selecting one of the responses rated on a 5-point scale in which 1 denoted "not at all" and 5 denoted "tremendously". The maximum score on the anxiety subscale and the subscale assessing the need for information was 20 and 10 points, respectively [16].

The VAS is a 100-mm-long section, of which one end is marked with the number 0 and the other end with 10. While assessing the level of anxiety/stress/pain, the patients chose by hand the point that most closely corresponded to their state, with 0 referring to "no anxiety/no stress/no pain" and 10 referring to the "highest imaginable anxiety/stress" or "anxiety/stress/pain most severe".

2.4 Surgery Procedures

After a gynecological US transvaginal examination, the patients provided their consent to undergo the procedure by signing in an appropriate consent.

The following steps were involved in the process of preparing the patients for and carrying out the procedure at the RRO: 30 min before the start of the mini-hysteroscopy procedure, each of the selected patients was intravenously administered 100 mg of ketoprofen. Vital functions of the patients, i.e., heart rate, blood pressure, O_2 saturation, and respiratory rate, were monitored during the procedure. Ten minutes before the insertion of the mini-hysteroscope into the cervical canal, 10 mL each of 0.1% lignocaine solution was administered in two punctures, paracervically (the first 10 mL paracervically at 4 o'clock and the second 10 mL paracervically at 8 o'clock) using a needle (insertion depth of about 2 mm). The hysteroscopy procedure was performed without inserting bullet forceps and a speculum using a vaginoscope. The surgeons had varying levels of experience in performing hysteroscopy. The patients were placed on a "treatment table" in a position similar to that of a gynecological examination. As the dilating agent for the uterine cavity, a 0.9% NaCl solution with a continuous flow and pressure of 110 mm Hg was used, and the procedure was carried out using the "mini hystero-resectoscope" system. The patients who underwent this procedure were asked to assess the level of pain that occurred during the procedure using the VAS, with 0 referring to "no pain" and 10 referring to "the highest imaginable/most intense pain".

The following steps were involved in the process of preparing the patients for and carrying out the procedure at the CSO: procedures under intravenous anesthesia were carried out after the anesthesiologist administered anesthesia. Vital functions of the patients, i.e., heart rate, blood pressure, O_2 saturation, and respiratory rate, were monitored during the procedures. The procedures were performed using bullet forceps and a speculum. The surgeons who performed the procedures had varying levels of experience. The patients were placed on a "treatment table" in a position similar to that of a gynecological examination.

2.5 Statistical Analysis

For the analysis of data, TIBCO Software Inc (Palo Alto, CA, USA) version 13 (2017), Statistica (data analysis software system, version 13 (2017), Armonk, NY, USA), and Microsoft Excel (version 2019, Microsoft Office, Redmond, WA, USA) were used. Mann–Whitney U test was used for comparisons between the groups. Wilcoxon paired rank-order test was used for comparisons between anxiety scores before and after anesthesia and information demand scores. Using Kendall's tau test and the chi-square NW (highest reliability) test, the relationship between variables was examined. $p < 0.05$ was considered significant in all calculations ($*p < 0.05$; $**p < 0.01$; $***p < 0.001$).

3. Results

3.1 Characteristics of the Study Group

The age of the patients ranged from 18 to 82 years, and the average age was similar in both groups, 44 years in the CSO (46.29 $\pm$ 13.33) and 46 years in the RRO (47.49 $\pm$ 12.3). The body mass index (BMI) of the patients ranged from 14.95 to 60.84 kg/m^2, and the average BMI of the patients was also similar in both groups, 23.56 kg/m^2 in the CSO (25.94 $\pm$ 6.18) and 25.21 kg/m^2 in the RRO (25.78 $\pm$ 5.85). Procedure time ranged from 2 to 45 min and the average time was significantly longer (U = 689.5; $p < 0.001$) in the RRO group at 15 min (18.52 $\pm$ 7.58), whereas in the CSO group, it was 8 min (9.68 $\pm$ 6.94). The characteristics

of the study groups are shown in Table 1. The diagnosis of cervical dysplasia and endometrial hyperplasia was significantly more common in the CSO group, whereas myomas were more common in the RRO group. No other significant differences were observed between the groups.

3.2 APAIS

The results of the APAIS assessment are shown in Table 2. No significant differences in anxiety and information demand scores were observed between the study groups. Anxiety before surgery was significantly higher than that before anesthesia in both CSO (T = 0; $p = 0.01$) and RRO (T = 456.5; $p < 0.001$) groups. Similarly, information demand for surgery was significantly higher than that for anesthesia in both CSO (T = 0; $p = 0.01$) and RRO (T = 185; $p < 0.001$) groups. In addition, higher levels of anxiety before anesthesia were associated with higher levels of anxiety before surgery in both CSO ($\tau = 0.42$; $p = 0.036$) and RRO ($\tau = 0.56$; $p < 0.001$) groups. In the CSO group, a higher number of past births was associated with lower levels of preprocedure anxiety ($\tau = –0.48$; $p = 0.017$) and overall anxiety scores ($\tau = –0.46$; $p = 0.02$). In the RRO group, a positive correlation was observed between procedure time and pretreatment anxiety ($\tau = 0.15$; $p = 0.02$) and the need for information about the procedure ($\tau = 0.16$; $p = 0.016$). In addition, higher levels of anxiety were associated with a higher information demand (Table 3). Patients with higher education presented significantly higher anxiety scores and higher information needs (Table 4). Professionally active patients presented significantly higher anesthesia anxiety scores (Table 5).

3.3 VAS

No significant differences in anxiety and stress scores were observed between the groups (Table 6). In the RRO group, a longer procedure time was associated with higher pain scores ($\tau = 0.14$; $p = 0.01$), and a higher number of past births was associated with lower pain scores ($\tau = –0.24$; $p < 0.001$). In addition, patients with higher education presented significantly higher anxiety scores (Table 7). No significant differences were observed in stress and pain ratings. Higher stress scores were associated with higher anxiety scores (Table 8), and higher pain scores were associated with higher anxiety scores (Table 9).

Pain was assessed only in patients after procedures under local anesthesia (the level of pain refers to the assessment of pain experienced during minimally invasive procedures under paracervical, vaginal anesthesia).

3.4 Prolactin and Cortisol

No significant differences in prolactin and cortisol levels were observed between the groups (Table 10). Patients with higher education showed significantly higher cortisol levels (Table 11). In addition, a higher age of the patients was associated with lower prolactin levels in both the CSO group ($\tau = –0.25$; $p = 0.049$) and the RRO group ($\tau = –0.13$; $p = 0.02$). Furthermore, in the RRO group, a higher number of past births was associated with lower prolactin levels ($\tau = –0.16$; $p = 0.004$), and a higher BMI ($\tau = –0.12$; $p = 0.02$) and a longer treatment time ($\tau = –0.14$; $p = 0.01$) were associated with lower cortisol levels. In the RRO group, higher prolactin levels were associated with higher cortisol levels ($\tau = 0.18$; $p = 0.001$). No correlation was observed between prolactin and cortisol levels, anxiety and information demand scores, or VAS scores for anxiety, stress, and pain.

4. Discussion

Thanks to the development of minimally invasive techniques, which allow examining individual body cavities, the cervical canal and the uterine cavity can be viewed using small instruments. The use of mini-hysteroscopy, both in reproductive and in peri- and postmenopausal patients, is currently the "gold standard" due to the short hospital stay, short recovery time, integration of clinical practice with the "see and treat" mode, and reduction in the need for additional interventions, such as the need for general anesthesia and performing the procedure in the operating room [1–5,29,30]. Despite the tremendous advances made in mini-hysteroscopy over the past 20 years, many women still experience discomfort and pain in various stages of this procedure, which is the most common factor for treatment discontinuation [31,32]. Thus, pharmacological and non-pharmacological methods of pain relief are widely used—both during the procedure [2,32,33] and in the following hours after the procedure. These pain relief methods are reported to be effective, less effective or non-effective by different groups of women [2,33–37].

Different stages of mini-hysteroscopy can result in different unpleasant sensations [38–40] and different intensities of pain; for example, women who had previously given birth by natural means usually perceive the passage of the hysteroscope through the cervical canal as less painful and the time of the procedure as shorter [29,41,42] or the pain level reported by them 60 minutes after procedure is lower [43]. Among the pain relief methods worth citing are the results of a randomized clinical trial conducted in 2021 by Gulucu *et al*. [44] in which they compared the severity of pain in two groups of women, depending on the temperature of the distension fluid used in the office hysteroscopy (37 °C *vs* 25 °C). They observed a statistically significant reduction in pain, assessed at specific moments of the procedure using the VAS scale during: the hysteroscope cervical ostium transition, and placement it in the uterine cavity and end of procedure in the group of women in whom the fluid used to dilate the uterine cavity had been pre-heated to 37 °C [44].

It is worth mentioning that the degree of pain experienced by the patient is determined by many factors, such as technical aspects, experience of the operator, ab-

Table 1. Characteristics of the group.

		Group		χ^2	p
		CSO	RRO		
Education	Primary	1 (7.14%)	1 (0.95%)	5.45	0.24
	Occupational	0 (0%)	13 (12.38%)		
	Secondary	4 (28.57%)	35 (33.33%)		
	Bachelor's	2 (14.29%)	10 (9.52%)		
	Master's	7 (50%)	46 (43.81%)		
Place of residence	Rural	5 (35.71%)	39 (37.14%)	3.93	0.42
	City <50 thousands	1 (7.14%)	28 (26.67%)		
	City 50–200 thousands	2 (14.29%)	11 (10.48%)		
	City 200–500 thousands	2 (14.29%)	8 (7.62%)		
	City >500 thousands	4 (28.57%)	19 (18.1%)		
Marital status	Spinster	2 (14.29%)	13 (12.38%)	0.06	1.00
	Married	10 (71.43%)	78 (74.29%)		
	Widowed	1 (7.14%)	7 (6.67%)		
	Free status	1 (7.14%)	7 (6.67%)		
Employment status	Employed	0 (0%)	3 (2.86%)	10.71	0.10
	Physical work	3 (21.43%)	21 (20%)		
	Mental work	8 (57.14%)	53 (50.48%)		
	Not working professionally	2 (14.29%)	8 (7.62%)		
	Learning/studying	1 (7.14%)	0 (0%)		
	Retirement	0 (0%)	17 (16.19%)		
	Pension	0 (0%)	3 (2.86%)		
Number of births	0	8 (25.81%)	37 (24.18%)	4.17	0.38
	1	9 (29.03%)	33 (21.57%)		
	2	9 (29.03%)	66 (43.14%)		
	3	5 (16.13%)	14 (9.15%)		
	4	0 (0%)	3 (1.96%)		
Miscarriages/premature births	Yes	6 (19.35%)	26 (16.99%)	0.10	0.75
	No	25 (80.65%)	127 (83.01%)		
Previous treatments	Yes	18 (58.06%)	74 (48.37%)	0.97	0.32
	No	13 (41.94%)	79 (51.63%)		
Gynecological surgeries	Yes	4 (12.9%)	36 (23.53%)	1.89	0.17
	No	27 (87.1%)	117 (76.47%)		
Infertility	Yes	2 (6.45%)	2 (1.31%)	2.78	0.25
	No	25 (80.65%)	123 (80.39%)		
	No data	4 (12.9%)	28 (18.3%)		
Diagnosis	Cervical dysplasia and/or cervical polyp	3 (9.68%)	8 (5,23%)	16.82	0.01**
	Uterine myomas	0 (0%)	22 (14.38%)		
	Endometrial hyperplasia and/or abnormal uterine bleeding	16 (51,62%)	63 (41,18%)		
	Endometrial polyp and/or infertility	12 (38.71%)	60 (39.21%)		
Pain during intercourse	Yes	5 (35.71%)	22 (20.95%)	1.40	0.24
	No	9 (64.29%)	83 (79.05%)		
Pain during defecation	Yes	0 (0%)	2 (1.9%)	0.51	0.48
	No	14 (100%)	103 (98.1%)		
Pain during urination	Yes	0 (0%)	1 (0.95%)	0.25	0.62
	No	14 (100%)	104 (99.05%)		
Pain during daily activities	Yes	2 (14.29%)	5 (4.76%)	1.56	0.21
	No	12 (85.71%)	100 (95.24%)		

CSO, Central Surgical Office; RRO, Reception Room Office.

**$p < 0.01$.

Table 2. Type of surgery *vs* APAIS.

	Group						U	*p*
	CSO			RRO				
	M ± SD	Min–Max	Me [Q1–Q3]	M ± SD	Min–Max	Me [Q1–Q3]		
I[a]	2.43 ± 1.09	1–5	2 [2–3]	2.58 ± 1.19	0–5	2 [2–3]	678	0.59
II[b]	1.71 ± 0.83	1–3	1.5 [1–2]	1.97 ± 1.02	1–5	2 [1–2]	651.5	0.43
III[c]	4.14 ± 1.75	2–8	4 [3–4]	4.56 ± 2.06	2–10	4 [3–6]	656	0.48
IV[d]	2.79 ± 1.05	2–5	2 [2–4]	2.92 ± 1.14	1–5	3 [2–4]	666.5	0.53
V[e]	2.64 ± 0.84	2–5	2.5 [2–3]	2.55 ± 1.14	1–5	2 [2–3]	687	0.68
VI[f]	5.43 ± 1.83	4–10	4.5 [4–7]	5.45 ± 2.14	1–10	5 [4–7]	710.5	0.80
VII[g]	9.57 ± 3.3	6–18	8 [8–11]	10.01 ± 3.84	3–20	9 [8–13]	663	0.52
VIII[h]	2.5 ± 1.09	1–5	2 [2–3]	2.66 ± 1.12	1–5	3 [2–4]	673	0.56
IX[i]	3.29 ± 1.2	2–5	4 [2–4]	3.13 ± 1.17	1–5	3 [2–4]	687	0.64
X[j]	5.79 ± 2.15	3–10	6 [4–7]	5.79 ± 2.09	2–10	6 [4–8]	718	0.85

APAIS, Anxiety and Information Scale; CSO, Central Surgical Office; RRO, Reception Room Office; M, mean; SD, standard deviation; Min, minimum; Max, maximum; Me, median; [a] Fear of anesthesia 1; [b] Fear of anesthesia 2; [c] Fear of anesthesia ([a] Fear of anesthesia 1 + [b] Fear of anesthesia 2); [d] Fear of surgery 1; [e] Fear of surgery 2; [f] Fear of surgery ([d] Fear of surgery 1 + [e] Fear of surgery 2); [g] Fear ([c] Fear of anesthesia + [f] Fear of surgery); [h] Information demand—anesthesia; [i] Information demand—surgery; [j] Information demand ([h] Information demand—anesthesia + [i] Information demand—surgery).

Table 3. Kendall's tau correlation coefficient for assessing the relationship between information demand and anxiety levels.

Information demand	Group					
	CSO			RRO		
	Anesthesia	Surgery	In total	Anesthesia	Surgery	In total
I[a]	0.49*	0.46*	0.47*	0.33***	0.26***	0.32***
II[b]	0.2	0.02	0.16	0.23***	0.11	0.19**
III[c]	0.4*	0.27	0.36	0.29***	0.2**	0.26***
IV[d]	0.41*	0.71***	0.54**	0.28***	0.25***	0.29***
V[e]	0.47*	0.73***	0.58**	0.21**	0.25***	0.25***
VI[f]	0.47*	0.76***	0.6**	0.26***	0.26***	0.29***
VII[g]	0.57**	0.59**	0.6**	0.31***	0.25***	0.31***

CSO, Central Surgical Office; RRO, Reception Room Office; [a] Fear of anesthesia 1; [b] Fear of anesthesia 2; [c] Fear of anesthesia ([a] Fear of anesthesia 1 + [b] Fear of anesthesia 2); [d] Fear of surgery 1; [e] Fear of surgery 2; [f] Fear of surgery ([d] Fear of surgery 1 + [e] Fear of surgery 2); [g] Fear ([c] Fear of anesthesia + [f] Fear of surgery).
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

normalities of the reproductive organs, the total duration of the procedure, and the psychological profile of the patient [10,34,45,46]. A similar relationship was observed in the present study: patients in the RRO group reported more severe pain with the increase in the duration of the procedure. In fact, pain sensations may be compounded by the high level of anxiety felt by women prior to the procedure; anxiety may be a factor that hinders and prolongs the procedure, and it is reflected in the negative experience of the procedure, despite its proper course and smooth execution [2,6,42,43,47].

To address the complexity of the problem of pain and anxiety in patients undergoing mini-hysteroscopy procedures, the present study attempted to assess the severity of anxiety and stress and pain levels depending on the anesthesia used and simultaneously measure cortisol and prolactin levels before the procedure. Serum prolactin levels are subject to diurnal fluctuations (with the peak secretion around 3 AM), decrease with age, and increase with BMI, and its increase may be related to the stress experienced [48–52]. In the present study, a decrease in prolactin levels was observed in older patients, which is consistent with the findings of Roelfsema *et al.* [48] but no relationship between prolactin levels and BMI was observed, and the level of anxiety experienced by the patients before the procedure did not correlate with their serum prolactin levels. A decrease in prolactin levels in relation to the number of deliveries was observed, which is consistent with the study conducted by McCoshen *et al.* [53].

Table 4. Education *vs* APAIS.

	Education						U	*p*
	Higher			Other				
	M ± SD	Min–Max	Me [Q1–Q3]	M ± SD	Min–Max	Me [Q1–Q3]		
I[a]	2.75 ± 1.26	0–5	3 [2–4]	2.33 ± 1.03	1–5	2 [2–3]	1388	0.04*
II[b]	2.03 ± 1.02	1–5	2 [1–3]	1.81 ± 0.97	1–5	2 [1–2]	1527.5	0.20
III[c]	4.78 ± 2.1	2–10	4 [3–6]	4.15 ± 1.9	2–10	4 [3–5]	1411	0.06
IV[d]	3.08 ± 1.12	1–5	3 [2–4]	2.7 ± 1.11	1–5	3 [2–3]	1409	0.06
V[e]	2.78 ± 1.13	1–5	3 [2–4]	2.3 ± 1.04	1–5	2 [2–3]	1304	0.02*
VI[f]	5.82 ± 2.17	1–10	6 [4–7]	5 ± 1.96	2–10	5 [4–6]	1338	0.02*
VII[g]	10.6 ± 3.84	3–18	10 [8–13]	9.15 ± 3.59	4–20	8 [7–11]	1352	0.03*
VIII[h]	2.88 ± 1.1	1–5	3 [2–4]	2.37 ± 1.09	1–5	2 [1–3]	1318.5	0.02*
IX[i]	3.38 ± 1.13	1–5	4 [3–4]	2.87 ± 1.18	1–5	3 [2–4]	1329	0.02*
X[j]	6.26 ± 2.01	2–10	6 [5–8]	5.24 ± 2.08	2–10	5 [4–7]	1257	0.01**

APAIS, Anxiety and Information Scale; M, mean; SD, standard deviation; Min, minimum; Max, maximum; Me, median; [a] Fear of anesthesia 1; [b] Fear of anesthesia 2; [c] Fear of anesthesia ([a] Fear of anesthesia 1 + [b] Fear of anesthesia 2); [d] Fear of surgery 1; [e] Fear of surgery 2; [f] Fear of surgery ([d] Fear of surgery 1 + [e] Fear of surgery 2); [g] Fear ([c] Fear of anesthesia + [f] Fear of surgery); [h] Information demand—anesthesia; [i] Information demand—surgery; [j] Information demand ([h] Information demand—anesthesia + [i] Information demand—surgery).
*$p < 0.05$; **$p < 0.01$.

Table 5. Professional activity *vs* APAIS.

	Professional activity						U	*p*
	Yes			No				
	M ± SD	Min–Max	Me [Q1–Q3]	M ± SD	Min–Max	Me [Q1–Q3]		
I[a]	2.69 ± 1.22	0–5	3 [2–4]	2.19 ± 0.98	1–5	2 [1–3]	1044.5	0.046*
II[b]	2.02 ± 1.05	1–5	2 [1–3]	1.68 ± 0.79	1–4	2 [1–2]	1132	0.14
III[c]	4.72 ± 2.11	2–10	4 [3–6]	3.87 ± 1.65	2–9	4 [3–5]	1056.5	0.06
IV[d]	2.95 ± 1.13	1–5	3 [2–4]	2.77 ± 1.12	1–5	3 [2–4]	1242.5	0.45
V[e]	2.66 ± 1.16	1–5	2 [2–4]	2.29 ± 0.94	1–4	2 [2–3]	1121.5	0.15
VI[f]	5.58 ± 2.19	1–10	6 [4–7]	5.06 ± 1.86	2–8	5 [4–7]	1197.5	0.31
VII[g]	10.3 ± 3.94	3–20	9 [8–13.5]	8.94 ± 3.15	4–17	8 [7–11]	1122.5	0.14
VIII[h]	2.69 ± 1.12	1–5	3 [2–4]	2.52 ± 1.12	1–5	3 [2–3]	1248.5	0.47
IX[i]	3.24 ± 1.18	1–5	4 [2–4]	2.9 ± 1.14	1–5	3 [2–4]	1130	0.14
X[j]	5.93 ± 2.1	2–10	6 [4–8]	5.42 ± 2.08	2–10	5 [4–7]	1159.5	0.21

APAIS, Anxiety and Information Scale; M, mean; SD, standard deviation; Min, minimum; Max, maximum; Me, median; [a] Fear of anesthesia 1; [b] Fear of anesthesia 2; [c] Fear of anesthesia ([a] Fear of anesthesia 1 + [b] Fear of anesthesia 2); [d] Fear of surgery 1; [e] Fear of surgery 2; [f] Fear of surgery ([d] Fear of surgery 1 + [e] Fear of surgery 2); [g] Fear ([c] Fear of anesthesia + [f] Fear of surgery); [h] Information demand—anesthesia; [i] Information demand—surgery; [j] Information demand ([h] Information demand—anesthesia + [i] Information demand—surgery).
*$p < 0.05$.

Table 6. Group *vs* VAS.

	Group						U	*p*
	CSO			RRO				
	M ± SD	Min–Max	Me [Q1–Q3]	M ± SD	Min–Max	Me [Q1–Q3]		
Fear	3.71 ± 2.33	1–9	3.5 [2–5]	4.41 ± 2.66	0–10	4 [2–7]	630	0.36
Stress	4.29 ± 2.55	1–8	3.5 [2–7]	4.58 ± 2.65	0–10	4 [2–7]	700.5	0.73
Pain	–	–	–	3.36 ± 2.44	0–10	3 [1–5]	–	–

VAS, Visual Analogue Scale; CSO, Central Surgical Office; RRO, Reception Room Office; M, mean; SD, standard deviation; Min, minimum; Max, maximum; Me, median.

Table 7. Education *vs* VAS.

	Education						U	*p*
	Higher			Other				
	M ± SD	Min–Max	Me [Q1–Q3]	M ± SD	Min–Max	Me [Q1–Q3]		
Fear	4.82 ± 2.73	0–10	5 [2–7]	3.74 ± 2.41	0–10	3 [2–5]	1377.5	0.04*
Stress	4.88 ± 2.66	0–10	5 [2–7]	4.15 ± 2.59	0–10	3 [2–5]	1496	0.16
Pain	3.67 ± 2.65	0–10	4 [1–5]	3.27 ± 2.28	0–9	3 [1–5]	1221.5	0.51

VAS, Visual Analogue Scale; M, mean; SD, standard deviation; Min, minimum; Max, maximum; Me, median.
*$p < 0.05$.

Table 8. Kendall's tau correlation coefficient for assessing the relationship between APAIS and VAS stress.

VAS stress x	Group	
	CSO	RRO
I[a]	0.52**	0.59***
II[b]	0.07	0.43***
III[c]	0.33	0.54***
IV[d]	0.79***	0.65***
V[e]	0.71***	0.55***
VI[f]	0.8***	0.63***
VII[g]	0.57**	0.64***
VIII[h]	0.38	0.29***
IX[i]	0.74***	0.29***
X[j]	0.5*	0.31***

APAIS, Anxiety and Information Scale; VAS, Visual Analogue Scale; CSO, Central Surgical Office; RRO, Reception Room Office; [a] Fear of anesthesia 1; [b] Fear of anesthesia 2; [c] Fear of anesthesia ([a] Fear of anesthesia 1 + [b] Fear of anesthesia 2); [d] Fear of surgery 1; [e] Fear of surgery 2; [f] Fear of surgery ([d] Fear of surgery 1 + [e] Fear of surgery 2); [g] Fear ([c] Fear of anesthesia + [f] Fear of surgery); [h] Information demand—anesthesia; [i] Information demand—surgery; [j] Information demand ([h] Information demand—anesthesia + [i] Information demand—surgery).
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

Table 9. Kendall's tau correlation coefficient for assessing the relationship between APAIS and VAS pain.

VAS pain x	RRO
I[a]	0.13*
II[b]	0.1
III[c]	0.14*
IV[d]	0.18**
V[e]	0.24***
VI[f]	0.21**
VII[g]	0.18**
VIII[h]	0.13*
IX[i]	0.19**
X[j]	0.16*
XI[k]	0.19**
XII[l]	0.2**

APAIS, Anxiety and Information Scale; VAS, Visual Analogue Scale; RRO, Reception Room Office; [a] Fear of anesthesia 1; [b] Fear of anesthesia 2; [c] Fear of anesthesia ([a] Fear of anesthesia 1 + [b] Fear of anesthesia 2); [d] Fear of surgery 1; [e] Fear of surgery 2; [f] Fear of surgery ([d] Fear of surgery 1 + [e] Fear of surgery 2); [g] Fear ([c] Fear of anesthesia + [f] Fear of surgery); [h] Information demand—anesthesia; [i] Information demand—surgery; [j] Information demand ([h] Information demand—anesthesia + [i] Information demand—surgery); [k] VAS fear; [l] VAS stress.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

No significant differences in anxiety intensity and information demand, assessed using the APAIS, were observed between the groups: anxiety about the procedure itself was significantly higher than anxiety about anesthesia among patients in both CSO and RRO groups. Similarly, in both groups, the information demand related to the procedure itself was significantly higher than the information demand related to anesthesia. In both groups, higher levels of anxiety before anesthesia correlated positively with higher levels of anxiety before the procedure. No significant differences in the severity of anxiety and stress measured using the VAS were observed between the study groups.

Serum cortisol levels depends primarily on the circadian rhythm of secretion and the body's exposure to additional stressors—both, acute and prolonged stress [54–56]. Direct analysis of cortisol levels in relation to perioperative stress experienced is difficult, as the individual's personal ability to cope with stressful situations and the psychological and emotional appraisal play an important role in the hormonal response to the stressor [54–56]. Additionally, the genomic and non-genomic mechanisms of glucocorticoid action in the stress-response were described by Manou-Stathopoulou *et al*. [56]. Interesting study was conducted by Timmers *et al*. [57], they showed that an acute stress induction, combining physical and psychological stressors—increased heat pain thresholds, but not tolerance in healthy participants and the magnitude of this stress-induced hypoalgesic effect was predicted by cortisol reactivity and fear of pain. This is encouraging more attention to be paid to placing importance on stress reduction among patients undergoing medical procedures.

In the present study, no significant differences in prolactin and cortisol levels were observed between the study groups. In addition, no correlations between prolactin and

Table 10. Group *vs* prolactin and cortisol levels.

	Group						U	*p*
	CSO			RRO				
	M ± SD	Min–Max	Me [Q1–Q3]	M ± SD	Min–Max	Me [Q1–Q3]		
I[a]	12.47 ± 5.4	4.91–25.21	11.08 [8.2–16.21]	13.71 ± 7.47	3.01–46.89	11.93 [8.42–16.32]	2229	0.60
II[b]	372.45 ± 140.7	200.7–965.3	351.9 [282.4–420.02]	363.93 ± 147.42	109.4–983.7	340.9 [266–436.6]	2243	0.64

CSO, Central Surgical Office; RRO, Reception Room Office; M, mean; SD, standard deviation; Min, minimum; Max, maximum; Me, median; [a] Prolactin; [b] Cortisol.

Table 11. Education *vs* prolactin and cortisol levels.

	Education						U	*p*
	Higher			Other				
	M ± SD	Min–Max	Me [Q1–Q3]	M ± SD	Min–Max	Me [Q1–Q3]		
I[a]	12.92 ± 5.12	6.36–28.28	11.31 [8.96–16.23]	14.06 ± 6.77	4.91–37.06	12.96 [8.16–17.06]	1628	0.50
II[b]	371.3 ± 121.19	139.5–736.6	360.4 [288.7–425.4]	327.58 ± 110.54	109.4–631.9	334.6 [241.3–380.4]	1381	0.046

M, mean; SD, standard deviation; Min, minimum; Max, maximum; Me, median; [a] Prolactin; [b] Cortisol.

cortisol levels before procedure, anxiety and information demand scores, as well as VAS scores for anxiety, stress, and pain were observed. Thus, it can be concluded that the primary factors associated with changes in serum prolactin and cortisol levels are biological and that patients' feelings of stress and anxiety are mainly related to the procedure itself, rather than the type of anesthesia. Therefore, since performing the procedure under local anesthesia is safer, this solution can be implemented. A systematic review by Gambadauro *et al*. [42] on patients' anxiety related to hysteroscopy showed that the increase in the level of anxiety experienced by patients before this minimally invasive procedure was similar to that of patients undergoing major surgery under general anesthesia [42].

5. Conclusions

Therefore, it can be concluded that it is necessary to apply the interventions that reduce the anxiety of the patients and inform patients about the planned course of the procedure, since higher levels of anxiety before the procedure result in a significant increase in procedure duration, which in turn can increase the pain experienced by the patients.

Author Contributions

These should be presented as follows: KCW, KW designed the research study. AN, NIK, MM performed the research. MW provided help and advice on. KCW, KW analyzed the data. KCW, KW wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Patient enrollment methods, ways of obtaining the research material, and its storage were approved by the Bioethics Committee at the Poznan University of Medical Sciences (No 114/22).

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Conflict of Interest

The authors declare no conflict of interest. Karolina Chmaj-Wierzchowska, Katarzyna Wszołek and Maciej Wilczak are serrving as one of the Guest editors of this journal. We declare that Karolina Chmaj-Wierzchowska, Katarzyna Wszołek and Maciej Wilczak had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Gloria Calagna.

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