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Chronic postsurgical pain and neuropathic symptoms after abdominal hysterectomy

A silent epidemic

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Abstract

Chronic postsurgical pain (CPSP) is an important clinic problem. It is assessed that prevalence of chronic pain extends to 30% but it is contended that there are various risk factors. We aimed to evaluate the prevalence of chronic pain after hysterectomy, risk factors of chronicity, neuropathic features of pain, and sensorial alterations at surgery area.

Between years 2012 and 2015, 16 to 65 ages old patients that electively undergone total abdominal hysterectomy bilateral salpingo-oophorectomy and passed minimum 3 months after surgery were included to study. Visual analog scale (VAS) and Douleur Neuropathique 4-questionnaire (DN-4) surveys were used to evaluate pain symptoms, algometry device was used for evaluating abdominal pressure threshold and Von Frey Filament was used for sensorial alterations.

Ninety-three of 165 eligible patients were included to study. As the groups were compared by demographic data, no difference was obtained ($P > 0.05$). There was no difference between groups regarding patient and surgery attributes ($P > 0.05$). Most frequently performed incision type was Pfannenstiel. Neuropathic symptoms were observed in 90 patients (96.8%). Sensorial alterations as hypoesthesia and hyperesthesia were detected around abdominal scar in 18 patients (19.4%) with pinprick test.

Neuropathic symptoms should not be ignored in studies evaluating CPSP and a standard methodology should be designed for studies in this topic.

Abbreviations: CPSP = chronic postsurgical pain, DN-4 = Douleur Neuropathique 4-questionnaire, TAH-BSO = total abdominal hysterectomy with bilateral salpingo-oophorectomy, VAS = visual analog scale.

Keywords: chronic postsurgical pain, DN-4, hysterectomy, neuropathic pain, pain assessment, prevalence

1. Introduction

Chronic postsurgical pain (CPSP) is a phenomenon that has only recently been considered important.[1] Long-lasting pain has the potential to become chronic. CPSP is now considered possible after almost all types of surgery[2,3] and emerges not only after large surgeries, such as amputation and thoracotomy, but also smaller surgeries such as inguinal hernia, with a 6% to 7% risk of becoming chronic.[2–4] The mechanism underlying CPSP remains incompletely understood, but neuronal damage occurring during surgery and/or a continuous inflammatory response may alter the patient's sense of pain.[5] Several factors, including intensities of preoperative and postoperative pain, the approach and type of surgery, and genetic factors, contribute to the risk of pain chronicity.[6] Nevertheless, limited information is available about pain chronicity after gynecological operations.

Hysterectomy is a common gynecological operation, with annual rates of 1.8/1000 in Denmark, 4.1/1000 in Finland, and 5.4/1000 in the USA.[7–9] Hysterectomy can be performed by abdominal, vaginal, subtotal, or laparoscopic surgery and is an ideal model for postoperative pain studies.[10] Reported pain percentiles still vary from 5% to 32% independent of surgery type.[3,11] Such wide differences in the prevalence rates of pain are due to differences in criteria used to define pain. Many studies have pain as a primary outcome parameter, with detailed descriptions regarding location, density, frequency, and possible etiology. However, there have been no studies regarding the neuropathic characteristics of posthysterectomy pain. Therefore,

Editor: Kazuo Hanaoka.

The journal's comments regarding English were standard comments sent to all authors. They were not specific to your document, which was well edited and grammatically correct.

The authors have no conflicts of interest to disclose.

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Medicine (2016) 95:33(e4484)

Received: 6 June 2016 / Received in final form: 11 July 2016 / Accepted: 11 July 2016

http://dx.doi.org/10.1097/MD.0000000000004484

the present study was performed to assess the incidence of pain chronicity after abdominal hysterectomy, risk factors of chronicity, neuropathic features of pain, and sensorial alterations in the operated area.

2. Materials and methods

2.1. Patients

The Sakarya University Faculty of Medicine Ethical Council provided approval for this prospective sectional study (approval number: 16214662.050.01.04/26, date: 24/02/2014). Patients aged 16 to 65 years at a minimum of 3 months after elective total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO) performed between 2012 and 2015 at Sakarya University Education Research Hospital were included in the study. The records of the patients were obtained from the hospital's electronic database. All patients provided informed consent for inclusion in the study.

Demographic data (age, weight, height, surgery indication, surgery type, previous pelvic operations, and previous vaginal or caesarean deliveries) were recorded for all patients included in the study. Characteristics related to surgery (surgery type, anesthesia technique, method and length of abdominal incision, and postoperative analgesia technique) were identified.

Patients with a history of uterine prolapse, endometriosis, malignant diseases, or psychiatric diseases, and patients undergoing laparoscopic hysterectomy, subtotal abdominal hysterectomy, vaginal hysterectomy, or emergent hysterectomy were excluded from the study.

2.2. Pain assessment

Pain severity was evaluated both at rest and in motion according to a visual analog scale (VAS) (0: no pain to 10: worst pain imaginable). The probability of developing chronic neuropathic pain was assessed during regular postoperative examination in the pain clinic using the Douleur Neuropathique 4-questionnaire (DN-4, Table 1).[12] All patients underwent physical examinations. Surgical incision types were identified and incisions were measured. The superior and inferior parts of horizontal incisions as well as the right and left parts of midline vertical incisions were divided into 6 areas (Fig. 1). These regions were evaluated in a noninvasive manner using a pressure algometer to assess sensitivity to pain and to confirm pressure perception (Fig. 2). The algometer, which is a device to measure mechanical stress, uses a coil with a rubber end that has a circular pressure surface 1 cm in diameter and provides the result in kg/cm^2 with a minimum of 25 g caliber and 2.5 kg/cm^2 quadrant. Before algometry, a pressure of 4 kg was applied with the pulpous region of the thumb to the mid-point of the incision, which is one of the main control points. A force was then applied to 6 separate predefined areas to allow the patient to differentiate between the pain sensation and the pressure sensation. This procedure was repeated several times. Measurements were performed with the algometer in 1-kg increments with a minimum interval of 15 to 20 seconds between measurements. Three measurements were carried out for each of the 6 areas, and every first measurement value was ignored. The average of the latter 2 values was recorded. Localization of pain was recorded (mid-pelvis, distal lower extremity, vagina, groin, abdominal scar, phantom). A number 5.88 von Frey filament (Touch Test Sensory Evaluator Kit; North Coast, Inc., Gilroy, CA, USA) was used to assess hypoesthesia and hyperesthesia along the abdominal scar. Patients were asked if and when the pinprick sensation became more and less painful.

Table 1

DN4 questionnaire, Turkish version[10].

Question 1: Dose the pain have one or more of the following characteristics?	
Burning	Yes (1)/No (0)
Painful cold	Yes (1)/No (0)
Electric shocks	Yes (1)/No (0)
Tingling	Yes (1)/No (0)
Question 2: Is the pain associated with one or more of the following symptoms in the same area?	
Pins and needles	Yes (1)/No (0)
Itching	Yes (1)/No (0)
Examination of patient	Yes (1)/No (0)
Question 3: Does the pain located in the area where the physical examination was done reveal one or more of the following characteristics?	
Hypoesthesia to touch	Yes (1)/No (0)
Hypoesthesia to pinprick	Yes (1)/No (0)
Question 4: In the painful area, can the pain be caused or increased by brushing?	Yes (1)/No (0)

Total score = 10. If the patient score is ≥4, neuropathic pain is diagnosed.
DN-4 = Douleur Neuropathique 4-questionnaire.

2.3. Statistical analysis

The Chi-square test was used to compare categorical data, which are shown as counts (n) and percentages (%). The Kolmogorov–-Smirnov normality test was used to check the normality of continuous data. The Mann–Whitney *U* test was used to compare nonparametric numerical data between 2 groups. The Kruskal–-Wallis test was used to compare nonparametric numerical data between groups. The Friedman test was used to compare abdominal pain pressure thresholds among 6 areas (A1–A6).

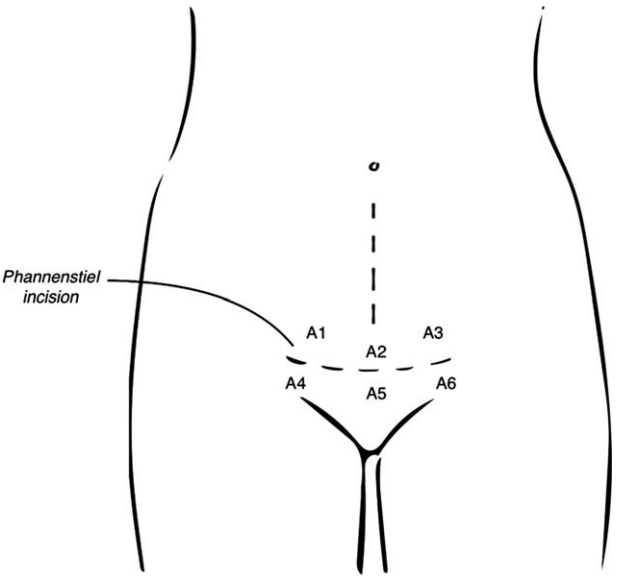

Figure 1. The pain assessment locations of the incision in the abdomen.

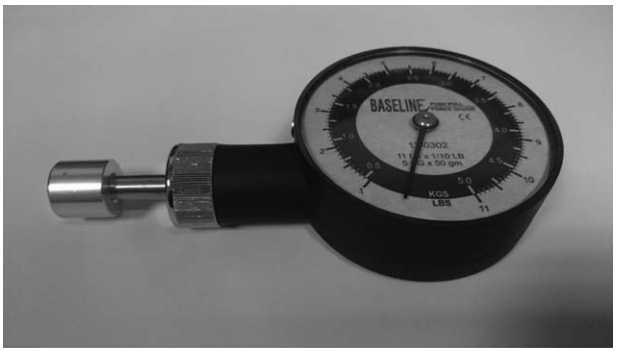

Figure 2. Algometer.

Wilcoxon rank sum test was used to compare abdominal pain pressure thresholds between 2 areas (upper and lower areas of the incision line). Numerical data are presented as means ± standard deviation. In all analyses, $P < 0.05$ was taken to indicate statistical significance. Analyses were performed using commercial software (IBM SPSS Statistics Version 22.0; IBM Corp., Armonk, NY).

3. Results

A total of 165 patients underwent hysterectomy from 2012 to 2015. Thirty-four patients could not be reached via the telephone numbers registered in the hospital system. The remaining 131 patients were called by telephone. Two patients had died and 3 patients had undergone another unrelated abdominal surgery. Eleven patients refused to participate in the study. Eighteen patients who had undergone vaginal hysterectomy and 6 patients who had undergone subtotal hysterectomy were excluded from the study. The remaining 93 patients who had undergone TAH-BSO were finally included in the study. Of these 93 patients, 65 (69.89%) with absence of pain (VAS score of 0) were classified as the Non-Pain group and 28 patients (30.1%) with abdominal pain (VAS score of 1–10) were classified as the Pain group.

3.1. Demographic characteristics

There were no differences in demographic data or patient and surgical characteristics between the groups (both $P > 0.05$) (Tables 2 and 3). The average time that had passed since the operation time was 14.85 ± 6.15 months (range, 5–26 months); there was no significant difference between the 2 groups ($P > 0.05$) (Table 2).

3.2. Intraoperative features

All patients included in the study population had undergone TAH-BSO under general anesthesia with inhalation agents, and there were no cases of laparoscopic surgery. Postoperative analgesia was provided by intravenous patient-controlled analgesia in 52 cases (55.9%) and with epidural patient-controlled analgesia in 41 cases (44.1%) ($P > 0.05$). The most common incision type was Pfannenstiel, and neither incision type nor length contributed to chronic pain ($P > 0.05$) (Table 3). Pain and menorrhagia/metrorrhagia, which were the major hysterectomy indications, showed no significant association with the occurrence of chronic pain ($P > 0.05$).

3.3. Localization and characteristics of pain

Evaluation of pain localization indicated that more than 1 area was affected, with the abdominal scar being the most frequent area (14 patients, 50%) followed by groin pain (11 patients, 39.2%) ($P > 0.05$) (Table 4). The least frequent type was lower back pain, which was seen in only 1 patient (3.6%).

The DN-4 survey revealed neuropathic symptoms in 90 patients (96.8%). The number of patients with a DN-4 score of ≥4 points was significantly greater in the Pain group than in the Non-Pain group ($P < 0.05$) (Table 3). Neuropathic pain was assessed in 30 patients with a DN-4 survey score of ≥4 points, and 14 (46.7%) showed a correlation with the VAS score. Sixty patients had no neuropathic pain (DN-4 score of <4) according to the DN-4 survey but had symptoms of neuropathy; 13 (21.7%) showed a correlation with VAS evaluation, while the remaining 47 (78.3%) had a VAS score of 0.

Table 2

Demographic data of patients after TAH-BSO.

	Total (n = 93)	Non-Pain group (n = 65)	Pain group (n = 28)	*P*
Age	51.86 ± 7.3	52.46 ± 8.07	50.46 ± 4.92	0.404
Weight	77.63 ± 12.63	77.05 ± 12.54	79 ± 12.98	0.528
Height	160.75 ± 5.48	160.83 ± 6.09	160.57 ± 3.8	0.933
BMI	30.10 ± 5.10	29.86 ± 5.10	30.67 ± 5.17	0.516
Employment				
Employed	3 (3.2)	2 (3.1)	1 (3.6)	
Housewife	86 (92.5)	60 (92.3)	26 (92.9)	**0.049***
Retired	4 (4.3)	3 (4.6)	1 (3.6)	
Marital status				
Married	5 (5.4)	2 (3.1)	3 (10.7)	0.159
Single	88 (94.6)	63 (96.9)	25 (89.3)	
Children	2.3 ± 1.26	2.37 ± 1.28	2.14 ± 1.21	0.498
Operation time, mo	14.85 ± 6.15	14.4 ± 5.89	15.89 ± 6.73	0.206
Diabetes mellitus				
Yes	82 (88.2)	57 (87.7)	25 (89.3)	1.000
No	11 (11.8)	8 (12.3)	3 (10.7)	

Data are given by mean average ± standard deviation and percentiles.

* $P < 0.05$ statistically significant.

BMI = body mass index, TAH-BSO = total abdominal hysterectomy with bilateral salpingo-oophorectomy.

Table 3

Distributions and comparisons of the patient characteristics.

	Total (n = 93)	Non-Pain group (n = 65)	Pain group (n = 28)	*P*
Hysterectomy indication				
Pain	34 (37)	23 (35.9)	11 (39.3)	
Meno/metrorrhagia	52 (56.5)	38 (59.4)	14 (50)	0.485
Other	6 (6.5)	3 (4.7)	3 (10.7)	
Past abdominal surgery	0.67 ± 0.9	0.71 ± 0.95	0.57 ± 0.79	0.628
Vaginal delivery	2.11 ± 1.34	2.15 ± 1.37	2 ± 1.27	0.587
Abdominal incision				
Pfannenstiel	60 (64.5)	40 (61.5)	20 (71.4)	
Joel–Cohen	5 (5.4)	5 (7.7)	0 (0)	0.289
Vertical	28 (30.1)	20 (30.8)	8 (28.6)	
Incision length, cm	13.52 ± 2.51	13.71 ± 2.79	13.19 ± 1.98	0.899
Abdominal scar (pinprick)				
None	75 (80.6)	42 (73.7)	33 (91.6)	
Hypoesthesia	14 (15.6)	12 (21.1)	2 (5.6)	0.025
Hyperesthesia	4 (3.8)	3 (5.2)	1 (2.8)	
DN-4	2.43 ± 2.49	1.89 ± 2.14	3.7 ± 2.8	0.004
DN-4				
<4	60 (66.7)	47 (74.6)	13 (48.1)	0.028
≥4	30 (33.3)	16 (25.4)	14 (51.9)	

Data are given by mean average ± standard deviation and percentiles.

$P < 0.05$ statistically significant.

DN-4 = Douleur Neuropathique 4-questionnaire.

In this study, sensorial alterations such as hypoesthesia and hyperesthesia around the abdominal scar were identified in 18 patients (19.3%) with the pinprick test (Table 3). Hypoesthesia was the most common finding (14 patients, 15.6%). There were no differences among the 6 areas with regard to these sensorial alterations ($P > 0.05$) (Table 5). There were no differences between the 2 groups with regard to abdominal pressure or the pain detection threshold when the 6 areas were compared not only within themselves but also as the upper and lower parts of the incision scar ($P > 0.05$) (Table 5).

4. Discussion

This prospective cross-sectional study showed that pain became chronic in 30.1% of women following TAH-BSO, that preoperative pain status and menorrhagia/metrorrhagia were not risk factors for pain chronicity, and that the majority of patients included in this study developed neuropathic symptoms and sensorial alterations. Fourteen patients, corresponding to 15% of the study population, had positive findings according to both the DN-4 survey and VAS score. The VAS score is an indicator of the severity of pain, while the DN-4 survey reveals pain with a neuropathic character. Therefore, obtaining results using only a single evaluation criterion can be misleading. Beyaz et al[13] reported a postmastectomy pain incidence rate of 64.1% in women with breast cancer, while the ratio of women describing no pain but with neuropathic symptoms was 23.6%. Evaluation of these 2 conditions together indicated that 87.6% of patients had long-term effects after surgery. Similarly, 96.8% of patients in the present study experienced neuropathic symptoms over the long term.

The differences between studies in the prevalence and characteristics of CPSP are due to the absence of standard criteria and lack of precise evaluation methods.[14,15] Therefore, following Haroutiunian et al,[15] the present study of patients meeting all 4 criteria and at a minimum of 3 months after surgery was performed to evaluate not only the severity of pain but also its neuropathic characteristics. In the GENDOLCAT study, Montes et al[14] reported results similar to those of the present study regarding pain chronicity after abdominal hysterectomy (25.1% and 30.1%, respectively). In the GENDOLCAT study, the DN-4 survey was used and the rate of patients with neuropathic pain (DN-4 score of ≥4) after abdominal hysterectomy was 44.3% (55% after thoracotomy, 38.7% after hernia repair, 24.5% after vaginal hysterectomy). No information on patient counts with neuropathic symptoms (DN-4 score of <4) was provided in the same study.

Hypoesthesia is a finding of nerve damage, while hyperesthesia is an indicator of sensitization. Decreased neuronal function and

Table 4

Pain characteristics of VAS >0.

Pain after hysterectomy	Pain group, N (%)	*P*
Pain report—CPSP	28 (30.1%)	
Pain location (can report 1 or more)		
Groin	11 (39.2%)	
Abdominal scar	14 (50%)	
Vagina	2 (7.2%)	0.025
Lower back	1 (3.6%)	
Frequency		
Daily	7 (25%)	
Several times, wk	6 (21.4%)	
Several times, mo	15 (53.6%)	
Dyspareunia	0 (0%)	0.045
Analgesic consumption		
Paracetamol + NSAID	19 (67.9%)	
Opioids	1 (3.6%)	0.020
Not using	8 (28.6%)	

Data are given by percentiles.

$P < 0.05$ is accepted statistically significant.

CPSP = chronic postsurgical pain, NSAID = nonsteroidal antiinflammatory drugs, VAS = visual analog scale.

Table 5

Abdominal pain pressure thresholds of patients.

	Total (n = 93)	Non-Pain group (n = 65)	Pain group (n = 28)	*P*
A1	3.38 ± 2.76	3.22 ± 2.85	3.65 ± 2.64	0.502
A2	3.24 ± 2.71	2.87 ± 2.82	3.85 ± 2.43	0.104
A3	3.38 ± 2.83	2.98 ± 2.85	4.02 ± 2.73	0.146
A4	3.72 ± 2.84	3.65 ± 2.93	3.84 ± 2.72	0.904
A5	3.51 ± 2.89	3.09 ± 2.89	4.21 ± 2.81	0.164
A6	3.15 ± 2.82	3.19 ± 2.85	3.08 ± 2.83	0.685
P	0.314	0.132	0.155	
Top (A1 + A2 + A3)	3.33 ± 2.56	3.02 ± 2.68	3.84 ± 2.32	0.165
Bottom (A4 + A5 + A6)	3.47 ± 2.54	3.32 ± 2.67	3.72 ± 2.32	0.574
	0.608	0.314	0.658	

Data are given by mean average ± standard deviation.
$P < 0.05$ is accepted statistically significant.

increased sensitivity to a stimulus are often the most evident characteristics of neuropathic pain.[11] One of the most surprising findings of this study was that although hypoesthesia occurred in 14 patients (15.6%) and hyperesthesia occurred in 4 patients, only 3 were correlated with the VAS score. In fact, hypoesthesia or hyperesthesia alone is not sufficient to reflect complete sensorial alterations. Hypoesthesia and hyperesthesia are just 2 of the well-known symptoms or findings of neuropathy. It should be taken into consideration that the DN-4 questionnaire evaluates multiple neuropathic symptoms. While the patient count with pain alone was 28 (30.1%), that with neuropathic symptoms was 90 (96.8%) (DN-4 score of <4 + DN-4 score of ≥4), and these patients were evaluated 14.85 ± 6.15 months (range, 5–26 months) after their surgeries. Pinto et al[6] evaluated 93 patients with the DN-4 survey 4 months after hysterectomy and reported that 59 (63.4%) had a DN-4 score of <3 and 34 (36.6%) had a DN-4 score of ≥3. The most obvious result of this study was that all of the patients evaluated 4 months after hysterectomy had neuropathic symptoms.[6] A recent study indicated that CPSP ratios at 4, 12, and 24 months after abdominal surgery decline (25.1%, 9.9%, and 6.7%, respectively).[14] The nervous system begins sensitization with the first noxious stimulus, but usually becomes normal with recovery. Sensitization continues in some cases and contributes to the development of chronic pain.[2,10] Johansen et al[11] reported a positive correlation between pain severity and sensorial alterations in 51% of patients. Although the majority of patients with CPSP do not show symptoms of neuronal injury, the findings of Johansen et al[11] indicated that potential neuronal injury is an important factor for CPSP. Visser[16] referred to this phenomenon in 2006 as a silent epidemic.

The strict patient inclusion policy in the present study represents the most important difference from previous studies. Only patients who underwent TAH-BSO were included in this study. Abdominal hysterectomies have been associated with much more severe acute postoperative pain than vaginal or laparoscopic hysterectomies.[6] There is a tendency to perform vaginal hysterectomy because it rarely results in chronic pain compared with abdominal hysterectomy.[5,14] Other studies performed to evaluate CPSP after hysterectomy included patients who had undergone laparoscopic, subtotal, and vaginal hysterectomies, which would have affected the results.[17,18]

Presurgical pain is not an absolute indication for surgery. Current CPSP symptoms in 40% of women were assessed independent of surgery, and symptoms occurring before and after surgery were expressed as distinct from each other.[6] These results were consistent with other studies, and it has been hypothesized that a prolonged pain stimulus exacerbates the nociceptive system via sensitization of nociceptors and neurons belonging to the central and/or peripheral nervous system.[19] This will likely contribute to determination of the relationship between CPSP and nonsurgery-related pain.[6] Despite the marked differences in techniques used in abdominal and vaginal approaches, it has been reported that the surgical procedure type does not affect the occurrence of chronic pain.[17] Various types of tissue damage and inflammatory responses will inevitably occur after different surgical approaches. It is possible to compare noxious inputs to the central nervous system among different types of surgery. Although our study population underwent only a single surgery type, Brandsborg et al[10] evaluated 11 scientific studies, all of which had patient groups treated with different methodologies and multiple surgery types. In addition, there is no relationship between the abdominal hysterectomy incision type and pain chronicity. The Pfannenstiel incision causes chronic pain less frequently than does the Joel–Cohen incision, and although the Joel–Cohen incision is less traumatic, it is performed by pulling and severing rather than dissecting, thus causing central sensitization by damaging sensorial neurons.[5] The results of our study indicate that use of the Pfannenstiel incision, Joel–Cohen incision, or vertical incision does not contribute to the occurrence of chronic pain ($P = 0.025$).

The development of chronic pain due to marked nerve damage plays an important role in the occurrence of CPSP.[13,20] Although the Pfannenstiel incision during abdominal hysterectomy would be predicted to cause damage to the ilioinguinal and iliohypogastric nerves, it is unlikely to contribute to the occurrence of chronic pain.[21,22] Pain chronicity after abdominal hysterectomy is more closely related to preoperative factors and findings than intraoperative damage.

Although it has been reported that cutaneous sensorial alterations, preoperative pain, and hypersensitivity are correlated with early postoperative pain, there are only weak correlations between preoperative pain and hypersensitivity with chronic pain, and only minor roles are seen in long-term pain after hysterectomy.[23,24] In this study, cutaneous sensorial alterations were detected in 18 patients. Cutaneous hypersensitivity was localized at dermatomes of the uterus and surrounding pelvic organs.

Pelvic base pain sensitivity was measured with algometry in 19 healthy women, and this method was demonstrated to be reliable and applicable for measuring vaginal mechanosensitivity.[25] Another study indicated that lower preoperative pressure threshold

values before hysterectomy in patients with preoperative pain were correlated only with postoperative acute pain, not with chronic pain.[26] In this prospective cross-sectional study, a realistic evaluation could not be performed because of the absence of preoperative pressure threshold values. However, as we evaluated the incision areas, we showed that preoperative abdominal pressure threshold values do not contribute to pain chronicity because there was no significant difference between the patient groups.

There were 2 important limitations of this study. First, the sample size was too small to cover all risk factors. Second, the effects on the quality of life of patients diagnosed with neuropathic pain according to the DN-4, with pain according to VAS scoring, and with neuropathic symptoms could not be evaluated. However, this study was prospectively designed and the patient group was homogenous.

In conclusion, this is the first study to evaluate the prevalence of CPSP after hysterectomy in Turkey. The prevalence rate in our country is 30.1%. With addition of neuropathic symptoms after TAH-BSO, the prevalence rate is 96.8%, representing a silent epidemic. Use of the most suitable survey form is required to identify the neuropathic symptoms along with pain severity. Development of a suitable standardized methodology is required to identify specific target risk factors for future studies, and prospective randomized controlled studies regarding preventive approaches for posthysterectomy pain and neuropathic symptoms are needed.

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