Prediction of Pain Before Biopsy: An Experimental Pain Assessment During Endometrial Sampling

Biyopsiden Önce Ağrının Öngörülmesi: Endometrial Örnekleme Sırasında Deneysel Ağrı Değerlendirmesi

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ABSTRACT Objective: Experimental human pain models have been used as a predictor of pain producing interventions. We prospectively evaluated whether the assessment of experimental pain perception using the modified tourniquet test before the procedure could predict the level of pain scores during endometrial sampling. **Material and Methods:** Sixty premenopausal women who underwent endometrial biopsy for abnormal uterine bleeding were prospectively enrolled in the present study. The day before biopsy, a modified submaximal effort tourniquet test was performed on all patients. During the test, pain scores were recorded at 30, 60, 90 and 120 seconds after inflation of the blood pressure cuff. Pain scores were also recorded during cannula introduction into the uterus and endometrial biopsy. Pain was assessed using a visual analogue scale (VAS). **Results:** There was a significant correlation between the VAS scores in the tourniquet test and the VAS scores during cannula introduction and the VAS scores during endometrial biopsy ($p<0.0001$). The most significant correlation was found between the VAS scores during endometrial biopsy and the VAS 90-second scores during the tourniquet test ($p<0.0001$, $r=0,836$). **Conclusion:** A simple and quick tourniquet test could be useful to identify patients who may experience severe pain during endometrial biopsy. In light of our data, personal adjustment of analgesic treatment would increase the patient acceptability and compliance with the procedure.

Key Words: Biopsy; pain measurement

ÖZET Amaç: Ağrı yaratan girişimlerde öngörüde bulunmak için deneysel insan modelleri kullanılmıştır. İşlemden once modifiye turnike testi kullanılarak deneysel ağrı algısının değerlendirilmesinin endometrial örnekleme sırasında ağrı skorlarının düzeyini öngörüp göremeyeceğini prospektif olarak değerlendirdik. **Gereç ve Yöntemler:** Bu çalışmada anormal uterin kanama için endometrial biyopsi yapılan altmış premenopozal kadın prospektif olarak kaydedildi. Biyopsiden önceki gün tüm hastalara modifiye submaksimal efor turnike testi uygulandı. Test sırasında, kan basıncı manşonu şişirildikten sonraki 30,60,90 ve 120. saniyelerde ağrı skorları kaydedildi. Ağrı skorları aynı zamanda kanül uterusa girdiği sırada ve endometrial biyopsi sırasında da kaydedildi. Ağrı vizüel analog skala (VAS) kullanılarak değerlendirildi. **Bulgular:** Turnike testi , kanülün girişi ve endometrial biyopsi sırasındaki VAS skorları arasında anlamlı ilişki vardı ($p<0.0001$). En anlamlı ilişki endometrial biyopsi sırasındaki VAS skoruyla turnike testi sırasındaki 90. saniye VAS skoru arasında bulundu ($p<0.0001$, $r=0,836$). **Sonuç:** Basit ve hızlı bir turnike testi endometrial biyopsi sırasında ciddi ağrı çekebilecek hastaları belirlemek için yararlı olabilir. Bizim verilerimiz ışığında, ağrı kesici tedavinin bireysel olarak ayarlanması hastanın işleme uyumunu artıracaktır.

Anahtar Kelimeler: Biyopsi; ağrı ölçümü

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Endometrial biopsy is a very common investigation performed for various indications, such as abnormal uterine bleeding, postmenopausal bleeding, abnormal cytology and infertility. Although it is usually performed as an outpatient procedure under either local or no anesthesia,

patient acceptability and compliance with the procedure might be difficult because of associated pain.[1-6]

Pain is a subjective experience, and the patient's perception of pain during endometrial biopsy changes from person to person. Some individuals seem to be highly sensitive to pain during this procedure, whereas others seem to be not. To date, several studies have been evaluated the role of different anesthetical methods including paracervical block, deep paracervical block, intrauterine lidocaine, topical spray lignocaine, and conscious sedation to relieve this pain.[7-9] On the other hand, analgesic requirement during the procedure is highly variable among women. In this respect, it is important to determine which patient would feel severe pain during endometrial biopsy.

Experimental human pain models have been used as a predictor of procedure- related pain. Pain induced by electric current, heat, pressure, ice-water and ischemic stimuli are the most commonly used methods of experimental human pain assessment.[10] Although several studies have examined the experimental pain response as a predictor of outcomes after pain producing interventions,[11] the relationship between the experimental pain assessment before endometrial biopsy and pain scores during the procedure has not been previously reported. Therefore, the aim of the present study was to evaluate whether the assessment of experimental pain perception using the modified tourniquet test before the biopsy procedure could predict the pain scores during endometrial biopsy.

MATERIAL AND METHODS

This prospective study included 75 premenopausal women with normal Pap tests, who underwent endometrial sampling for abnormal uterine bleeding, between January 2008 and June 2008. Fifteen patients were excluded from the study: seven of them refused to participate in the study, and eight did not meet the inclusion criteria (cervical stenosis in four, acute cervicitis in three, and epilepsy in one). Therefore, the study included 60 women who underwent endometrial sampling for abnormal uterine bleeding.

All patients were evaluated with a detailed history and physical examination. Any patient with a history of severe medical illness (e.g., heart failure, diabetes mellitus, neurologic disease), chronic pain conditions including fibromyalgia, arthritis, chronic pelvic pain that might lead to pain, cervical stenosis, pregnancy, suspected pelvic inflammatory disease, acute cervicitis or need for coincident endocervical curettage as well as any patient who was currently on analgesic treatment was excluded from the study.

Before attending for endometrial sampling, a written informed consent was obtained from all patients, and the study protocol was approved by the Medical Ethics Committee of the University of Mersin School of Medicine, and we conformed to the ethical guidelines of the 1975 Helsinki declaration. No participant was given sedation or local anesthesia. During endometrial sampling procedure, patients were placed in a lithotomy position, and a bimanual examination was performed to assess the size and the position of the uterus. The cervix was exposed with a bivalve speculum and cleaned with betadine (10% povidine-iodine solution). The 5 mm Karman Vacuum Aspirator Curette was then pushed into the uterine cavity for a minimum of 4 passes to ensure full sampling. Each suction sample was fixed in 10% formaldehyde and stained with haematoxylin-eosin stain. To maintain consistency and limit confounding variables, all procedures were performed by the same gynecologist (A.D.) who used the same technique to sample the endometrium on an outpatient basis.

The day before endometrial biopsy, a modified submaximal effort tourniquet test was used to evoke ischemic pain.[10] First, the nondominant arm was occluded with a standard blood pressure cuff inflated to 20 mmHg higher than the patient's own systolic blood pressure to abolish arterial blood supply and to render the arm hypoxic. Patients were then instructed to perform 20 hand grip exercises. Ischemic pain threshold was determined by recording the time (seconds) when subjects first reported hand or forearm discomfort. Ischemic pain tolerance was determined by recording the time (seconds) when subjects could no longer endure their ische-

mic arm pain. During the test, pain scores were recorded 30, 60, 90 and 120 seconds after inflation of the cuff. We also recorded pain scores during cannula introduction into the uterine cavity and endometrial biopsy. The pain scores were recorded using a visual analogue scale (VAS), and a trained nurse instructed the patients before the procedure how to score their pain.[12] According to the VAS, 0 corresponded to no pain and 10 to the greatest pain imaginable. The relationships between the VAS scores in the tourniquet test, those during cannula introduction and endometrial sampling were examined. The most commonly used methods of experimental human pain assessment include electrical, heat, pressure, ice water, and ischemic pain. We used a modified submaximal effort tourniquet test as an ischemic pain procedure.

Statistical data analysis was performed using "The Statistical Package for Social Sciences, version 11.5, for Windows (SPSS, Chicago, III)". Since VAS scores did not show normal distribution, the relationship between the VAS scores during the biopsy procedure and tourniquet test were evaluated using Spearman's rank correlation analysis. A P value less than 0.01 was considered statistically significant.

RESULTS

Mean age of the patients in the present study was 45.87 ± 9.08 years (as mean ± SD) (range 30 to 55). VAS scores in the tourniquet test and at various stages of the endometrial biopsy were shown in Figure 1. Median VAS scores in the tourniquet test at 30, 60, 90 and 120 seconds were 2 (range 1 to 6), 4 (range 2 to 8), 5 (range 3 to 9) and 7 (range 3 to 10), respectively.

Table 1 shows the Spearman's rho correlation coefficients among the VAS scores in the tourniquet test, during cannula introduction and endometrial biopsy, and P values belong to these correlation coefficients. A significant correlation was found between the VAS scores in the tourniquet test, cannula introduction and endometrial biopsy ($p< 0.01$). The most significant correlation was found between the VAS scores during endometrial biopsy and the VAS 90-second scores in the tourniquet test ($p< 0.01$, $r= 0.836$; Table 1 and Figure 1). Another significant correlation was found between the VAS scores during endometrial biopsy and the VAS 60-second scores in the tourniquet test ($p< 0.01$, $r= 0.607$; Table 1 and Figure 1). These relations can be interpreted as substantial correlations. No major complications occurred, and no patient required admission to hospital after the procedure. Only one patient experienced vasovagal syncope and recovered spontaneously.

TABLE 1: Spearman's rank correlation coefficient between visual analog scale scores in tourniquet test and endometrial biopsy.

	Tourniquet test (s)		Cannula introduction	
	Endometrial biopsy			
VAS 30	r=0.091	p>0.01	r=0.184	p>0.01
VAS 60	r=0.507	p<0.01	r=0.607	p<0.01
VAS 90	r=0.516	p<0.01	r=0.836	p<0.01
VAS 120	r=0.378	p<0.01	r=0.401	p<0.01

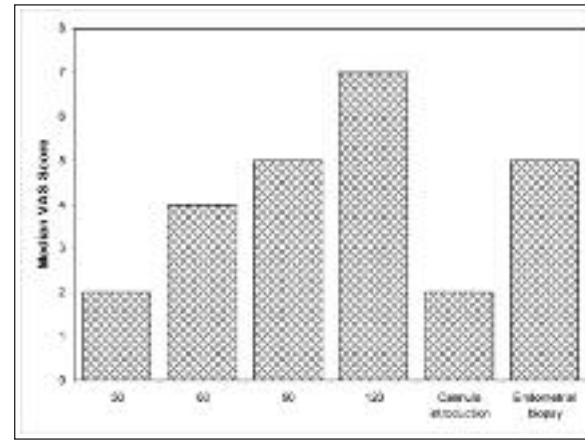

FIGURE 1: Median VAS scores in tourniquet test and biopsy procedure. VAS: Visual analog scale.

DISCUSSION

Endometrial biopsy is an established gynecologic office procedure to collect tissue for histologic evaluation of the endometrium.[1-6] It is associated with some discomfort and pain from the procedure itself which is one of the most common side effects. Although this procedure is considered safe and is commonly performed on an outpatient basis, the pain during endometrial biopsy is the most common reason for failure to complete the procedure.[13,14]

There have been several conflicting reports on various methods of pain relief during an endometrial biopsy, and the conflicting results can be explained as individual differences in pain sensitivity and variations in the pain assessment methods.[15-19] Because of the pain experienced during endometrial biopsy is highly variable among women, the level of pain intensity is critical.

Experimental human pain models have been widely used, and preoperative pain sensitivity has been found to predict for the severity of postoperative pain by several investigators.[11] However, no single best experimental pain test has been accepted in published reports. It has been reported that preoperative rating of an intense noxious thermal stimulus was strongly correlated with joint pain rating after anterior cruciate ligament repair.[20] Granot et al. demonstrated that preoperative experimental pain measurement was useful in identifying those patients who would experience severe pain after Cesarean section.[21] Similarly, Bisgaard et al. reported that preoperative experimental pain was significantly related to the intensity of postoperative pain in patients who underwent laparoscopic cholecystectomy.[22] Recently, Soyupek et al. found that there was a strong correlation between experimental pain assessment before biopsy and amount of pain experienced during the transrectal ultrasound guided prostate biopsy.[23]

The successful results of those previous studies led us to investigate an experimental human pain model for endometrial biopsy. We used a modified submaximal effort tourniquet test as an ischemic pain procedure, and the present study is the first one that shows the experimental pain assessment before the procedure can serve as a predictor of the pain experienced during endometrial biopsy.

In the present study, pain scores assessed by the modified tourniquet test before endometrial biopsy correlated significantly with the pain scores during the procedure. Moreover, the best correlation was found between the VAS scores during endometrial biopsy and the VAS 90-second scores in the tourniquet test. In this respect, the VAS 90-second scores in this experimental pain model may be useful in identifying those patients who will experience severe pain during endometrial biopsy.

It is important to identify and know which patients are more likely to have severe pain, since certain analgesics could be reserved for the patients who are at risk of pain intolerance. In addition, targeting this group before endometrial biopsy may eliminate the occurrence of intolerance due to pain and interruption of the procedure.

Experimental pain models are also used to investigate analgesic drug effects and are important tools to compare the analgesic potency of different drugs. To date, the analgesic potencies of pain relieving treatments during endometrial biopsy has not been investigated in experimental human pain models. As we did not perform any pain relieving methods in the present study, it was possible to evaluate the relationship between the experimental pain assessment before endometrial biopsy and pain scores during the biopsy procedure. In the light of these findings, additional prospective studies will be necessary to evaluate whether experimental pain assessment before the procedure could predict the analgesic potency of pain relieving treatments during endometrial biopsy. However, targeting the patients who will tolerate the procedure without anesthesia before endometrial biopsy could result in savings by avoiding unnecessary analgesic use.

CONCLUSION

The results of our study emphasized that there was a correlation between experimental pain assessment before biopsy and amount of pain experienced during the endometrial biopsy. We suggest that identifying those patients who might experience severe pain before endometrial biopsy may lead to changes in practice that would be cost effective and time efficient and patient satisfaction might be improved. Further studies will be needed to evaluate whether experimental pain assessment before the procedure could predict the analgesic potency of pain relieving treatments during endometrial biopsy.

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