GENERAL GYNECOLOGY

Cotton-tipped applicator test: validity and reliability in chronic pelvic pain

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OBJECTIVE: We sought to assess the concurrent validity and interrater reliability of the cotton-tipped applicator (CTA) test as a screening tool for diagnosis of cutaneous allodynia in patients with viscerally related chronic pelvic pain (CPP).

STUDY DESIGN: We performed a prospective cohort comparative observational study of referred patients to a gynecology clinic with CPP. A total of 22 females with CPP were compared to 23 pain-free controls and 12 cyclic pain patients. Participants were evaluated by 2 clinicians. The CTA test was performed to detect the appearance of pain in dermatomes of T10-L1.

RESULTS: Interrater reliability resulted in 98% agreement for the 3 study groups. CTA test showed 73% sensitivity and 100% specificity for differentiating patients with CPP from pain-free patients.

CONCLUSION: The CTA test had excellent interrater reliability and concurrent validity for diagnosis of cutaneous allodynia in CPP patients with visceral diseases versus controls.

Key words: chronic pelvic pain, cotton-tipped applicator test, cutaneous allodynia, visceral disease

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Chronic pelvic pain (CPP) causes disability and distress, significantly compromises quality of life, and affects health care costs.[1] The American Congress of Obstetricians and Gynecologists has estimated that 15-20% of women in the age group 18-50 years have experienced pain of >1 year's duration and 4% continue to have ongoing persistent pain.[2] The Society of Obstetricians and Gynecologists of Canada defines CPP as a pain lasting for ≥6 months, with incomplete relief despite treatment and significantly impaired function at home/work.[3] CPP is a multicausal disease. While a multidisciplinary approach to management of these patients often proves to be effective, it still does not explain why some women continue to experience daily pain that is irresponsive to large doses of pain medications.[4,5] The concept of the central sensitization may help to explain this medical problem.

Central sensitization seems to be a common feature of chronic pain conditions. The concept of neuroplasticity explains the changes in the function of the central nervous system, particularly at the dorsal root ganglion.[6] The stimuli for the changes are multifactorial. Severe or prolonged visceral pain from organs in the pelvis appears to be one of the significant contributing factors. Visceral pain is typically localized by the brain's sensory cortex by visceral afferents to the respective spinal cord level.[7] Visceral afferents follow a segmental distribution. Visceral afferent fibers are poorly myelinated and the action potentials may easily spread from them to impact adjacent somatic nerves. As a result, visceral pain may at times be referred to dermatomes that correspond to the impacted somatic nerve fibers.[8] In addition, both peripheral somatic and visceral nerves often synapse in the spinal cord at the same dorsal horn neurons. These neurons, in turn, relay sensory information to the brain. The cortex recognizes the signal as coming from the same dermatomes regardless of its visceral or somatic nerve origin. If noxious stimuli such as inflammatory process following endometriosis or pelvic inflammatory diseases continue for a prolonged period of time, neurons within spinal cord display increased excitability. This is termed "central sensitization." In the case of the pelvis, it is associated with increased efferent activity that results in aberrant activity in pelvic organs. This persistent central hyperexcitability might cause an increase in perception of pain in visceral organs. Referred pain tends to be localized in areas corresponding to the dermatome and myotome that are supplied by the affected viscus, or remote from the inciting stimulus in an area supplied by the same neural segment as the injured organ. Creation of pain from an innocuous stimulus in the related cutaneous areas is referred to as cutaneous allodynia.

Viscerosomatic pain referral has been evaluated by pain threshold measures and abdominal wall thermography tests. Pain threshold measure tests have been validated with the identification of chronic pain states.[9-11] Current methods for identifying patients with pain hypersensitivity are sufficiently complex to limit their widespread application in clinical settings.[12] The cotton-tipped applicator (CTA) test has been introduced to iden-

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tify this group of patients.[13] In an exploratory evaluation of the ability of 3 bedside tests in discriminating visceral disease from nonvisceral disease among women with CPP, the CTA test for cutaneous allodynia appeared to have the greatest likelihood of predicting preexisting or ongoing visceral disease.[14]

The aim of the present study was to assess the test reliability and validity as a screening method by testing the presence of cutaneous allodynia among women with or without CPP. We hypothesized that this test was reliable, feasible, and valid for assessing cutaneous allodynia.

Materials and Methods

This research was carried out as a prospective cohort comparative observational trial. Subjects were recruited from referred patients to Calgary Chronic Pain Clinic and Foothills Medical Center from 2010 through 2011. The date of entry was the date of approval of the ethics application at the University of Calgary. Subjects were invited to participate in the study by a nurse practitioner or a researcher during a clinical consultation for the management of chronic pain. The presence of pelvic visceral disease (eg, endometriosis and adenomyosis) as a possible cause of CPP was determined based on a documented operative record from the health records of the Calgary Health Region of Alberta Health Services. Potential participants were given an explanation of the study and the opportunity to ask questions. Five women declined to participate due to time constraints, severity of their pain, or no specific reasons. After obtaining written informed consent, the participants' demographic information and medical history were reviewed. Subjects were then allocated into 3 groups based on their description of presence of pain:

- 22 women with chronic continuous pelvic pain of ≥6 months' duration, not controlled with standard treatment.
- 12 women with cyclic pelvic pain of ≥6 months' duration, not controlled with standard treatment (sample of convenience).
- 23 women who had no pelvic pain and were referred to Foothills Medical Center for other gynecological reasons.

The standard treatment for pelvic pain was defined as having at least 1 pelvic surgery including a diagnostic or operative laparoscopic surgery, abdominal or vaginal hysterectomies, hormone therapy such as continuous oral contraceptive pills, progesterone therapy and Mirena intrauterine device, mild analgesics and narcotics.

Exclusion criteria for participation in the study included pregnant/breast-feeding women; women with major medical illnesses such as lupus, diabetes mellitus, or neurologic diseases; and those who did not provide written consent.

CTA test

Two trained clinicians performed the CTA test to determine the presence or absence of CA. Using a table of random numbers, the order of testing was determined. Testing was done during the 5th-10th days of the participant menstrual cycle if menstruating to avoid possible variation in pain sensitivity across different stages of menstrual cycle.

Abdominal test

A CTA was gently passed down from the midclavicular line under ribs on each side of the abdomen to the supra pubic area. It was then directed across the abdomen in the region of the T10-L1 dermatomes. Subjects were instructed to report the appearance of pain by giving signals to clinician. If the sensation suddenly changed and produced a sharp painful sensation despite gentle pressure, the test was considered positive. The participants were asked to score the severity of pain based on visual analog scale. The entire area was marked with a washable marker and a photograph was taken. After the area was washed, the process was repeated by the second observer. The time frame for performing the evaluations by the 2 raters was between 5-15 minutes. For a video presentation of the abdominal test, refer to "Demonstration of Cutaneous Allodynia in Association with Chronic Pelvic Pain" by Jarrell."[13]

The primary outcome was measured based on a dichotomous "yes/no" response.

Test validity

Concurrent validity assessment was based on observing the rates of cutaneous allodynia among those with continuous pain due to pelvic visceral disease and those with no pain. For further assessment of validity the rates of cutaneous allodynia between pain subjects and those with cyclic pain was assessed.[15,16]

Test reliability

Interrater reliability was measured based on the raters' agreement on the presence or absence of cutaneous allodynia in each of the 3 groups.[15,16]

Based on preliminary data and clinical experience, it was expected that 80% of women with continuous pain would have a positive CTA test and that no one without pain would show a positive CTA test. Assuming a significance level of .05, a sample size of 20 patients in each group would give >95% power to detect such a difference. Descriptive statistics were used to summarize participant characteristics. The Mann-Whitney *U* test was used to compare duration of pain and pain intensity between the continuous and cyclic pain groups.

To assess concurrent validity, the χ^2 test was used to compare the CTA test's ability to distinguish between women with continuous pelvic pain vs those with no pelvic pain, and women with continuous pain vs cyclic pain. Sensitivity and specificity of the CTA test was reported with the corresponding exact 95% confidence intervals. Interrater reliability was measured using the proportion of agreement and McNemar test. Software (SAS 9.2; SAS Institute Inc, Cary, NC) was used for analysis.

Results

Of the 64 women enrolled in the study, 7 women were excluded from the continuous pain group due to causes other than visceral disease such as motor vehicle accident, trauma, or complications of their surgery. A total of 57 women were included in the analysis.

TABLE 1
Participant characteristics

Characteristic	Continuous pain (n = 22)	Cyclic pain (n = 12)	No pain (n = 23)
Mean age, y (SD)	35 (10)	37 (8)	39 (8)
G0, P0	11 (50%)	8 (67%)	8 (35%)
G>0, P0	1 (5%)	0 (0%)	4 (17%)
G>0, P>0	10 (45%)	4 (33%)	11 (48%)
Median duration of pain,[a] y	6 (IQR10)	5 (IQR 8)	N/A
	Range, 2–17	Range, 1–30	
Median pain intensity on VAS	6 (IQR 1)	5 (IQR 2)	N/A
	Range, 5–8	Range, 4–10	

G, gravidity; *IQR*, interquartile range; *N/A*, not applicable; *P*, parity; *VAS*, visual analog scale.

[a] Excludes n = 1 unknown in cyclic pain group.

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Population demographics are listed in Table 1. The mean age of participants, gravidity, and parity in the 3 study groups were similar. The median duration of pain was comparable in the continuous group and the cyclic pain group (6 vs 5 years). Patients in the continuous pain group had higher baseline pain intensity, all >5 on a visual analog scale of 0-10.

Assessment of validity

The CTA test reached excellent discrimination of continuous CPP cases from pain-free controls (*P* value < .001), with 73% sensitivity and 100% specificity (Tables 2 and 3). It also showed moderate discrimination of continuous CPP cases from cyclic pain controls (*P* value < .001), providing further evidence for concurrent validity.

Assessment of reliability

The CTA test showed 98% (95% confidence interval, 0.91–1.00) agreement between 2 raters with the McNemar test *P* value of .317 (Table 4). Only 1 participant in the continuous pain group tested positive by one clinician and negative by the second. The Figure depicts a few photographs of patients taken after each examiner performed the CTA test to highlight the degree of agreement between examiners.

Comment

Appropriate tests are invaluable to clinicians; they may be used to legitimize patients' concerns and reassure them about their prognosis. Unfortunately, many CPP patients interpret a physician's report of a normal test result as a statement that their anatomy is normal and their pain must be in their mind.[17] We used the CTA test as a screening method in patients with chronic pain to validate their concerns and to possibly avoid the expense and discomfort of repeating evaluations.

An evaluation of 3 bedside tests concluded that the CTA test appears to have a greater likelihood of identifying cutaneous allodynia in patients with a visceral source of pain compared to somatic sources of pain.[14] Consistent with the current study, it noted that patients with a history of preexisting or concurrent visceral disease showed a higher rate of cutaneous allodynia. The value of the test when positive would appear to indicate the presence of a current or previous visceral disease. When negative, it can provide some reassurance that presence of pain may not be due to central sensitization and the central sensitization has not yet developed in response to an internal visceral disease.

In addition, in the current study, 4 women with a hysterectomy and bilateral salpingo-oophorectomy for previous visceral disease had a negative test despite having a chronic pain state. Another woman in the continuous pain group had complete suppression of her menstruation for the last 3 years. This may indicate that the treatment of endometriosis with the induction of amenorrhea may be the first step in reversing the effects of neuroplasticity and helping these patients to combat the process of chronic pain state. This observation cannot be generalized due to limitations with the small number.

TABLE 2
Cotton-tipped applicator test outcomes

Primary outcome	Continuous pain (n = 22)	No pain (n = 23)	χ^2 test *P* value
Positive CTA test	16 (73%)	0 (0%)	< .001
Negative CTA test	6 (27%)	23 (100%)	
Secondary outcomes	**Continuous pain (n = 22)**	**Cyclic pain (n = 12)**	
Positive CTA test	16 (73%)	1 (8%)	< .001
Negative CTA test	6 (27%)	11 (92%)	

CTA, cotton-tipped applicator.

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TABLE 3
Sensitivity and specificity of cotton-tipped applicator test in detecting continuous pain vs no pain (n = 45)

Variable	Percent	95% confidence interval
Sensitivity	73	50–89%
Specificity	100	85–100%

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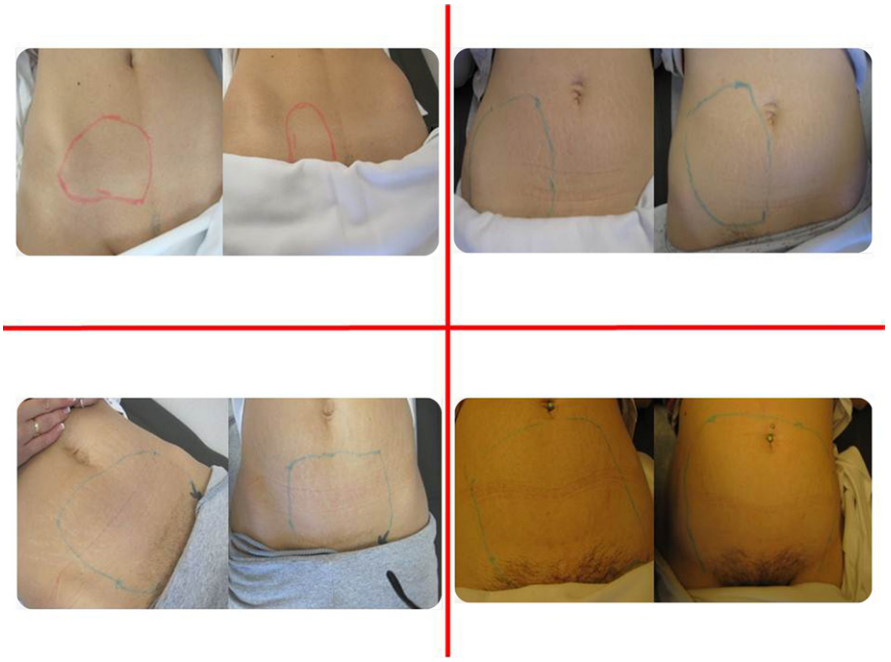
FIGURE
A sample of the CTA test photographs



Two photographs set side by side depict the same patient.

CTA, cotton-tipped applicator.

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Only 1 patient in the cyclic pain group showed a positive CTA test. She had documented endometriosis on her operative report and 10 years of severe dysmenorrhea. Her young age may predict that she may end up having chronic pain state if not treated aggressively to reverse the effects of endometriosis.

This project evaluated an effective office procedure, a noninvasive method that requires no sedation and can be repeated as desired in follow-up evaluations. It can be easily undertaken at the bedside. It is not time-consuming and is well tolerated by patients. The device is inexpensive, small, and easy to use. The CTA test can provide clinicians with a useful practical approach and may have significant implications in the recognition of central sensitization.

The strengths of the study are the consistency with our understanding of central sensitization[18] and previous studies of cutaneous allodynia[14] as well as the significant findings related to validity and reliability. However, it should be noted that a high percent agreement does not always indicate that the raters are correct. In our study, since the sensitivity and specificity are high, it can be extrapolated that a high percent agreement infers that both raters are correct.

The limitations of the study include the small number of cases. The clinicians were not blinded to the pain condition of patients, which could affect the results of the CTA test especially in the pain-free controls.

Further studies of this simple test in the clinical environment appear warranted.

TABLE 4
Interrater reliability of cotton-tipped applicator test (includes all 57 cases)

Variable	Rater 2 positive CTA	Rater 2 negative CTA
Rater 1 positive CTA	16 (28%)	1 (2%)
Rater 1 negative CTA	0 (0%)	40 (70%)
	Statistical result	**95% confidence interval**
McNemar test *P* value	0.317	N/A
Interrater reliability	98%	91–100%

CTA, cotton-tipped applicator; *N/A*, not applicable.

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Conclusion

In summary, this study showed that the CTA test has excellent concurrent validity with significant specificity and sensitivity, and excellent interrater reliability in the detection of central sensitization and cutaneous allodynia in patients with continuous pain due to visceral disease.

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REFERENCES

1. Dalpiaz O, Kerschbaumer A, Mitterberger M, Pinggera G, Bartsch G, Strasser H. Chronic pelvic pain in women: still a challenge. BJU Int 2008;102:1061-5.

2. American College of Obstetricians and Gynecologists. ACOG Committee on Practice Bulletins–Gynecology. ACOG practice bulletin no. 51: chronic pelvic pain. Obstet Gynecol 2004; 103:589-605.

3. Jarrell JF, Vilos GA, Allaire C, et al. Consensus guidelines for the management of chronic pelvic pain. J Obstet Gynaecol Can 2005; 27:781-826.

4. Baranowski AP. Chronic pelvic pain. Best Pract Res Clin Gastroenterol 2009;23:593-610.

5. Butrick CW. Chronic pelvic pain: how many surgeries are enough? [Erratum appears in Clin Obstet Gynecol 2007;50:xii.] Clin Obstet Gynecol 2007;50:412-24.

6. Vecchiet L, Vecchiet J, Giamberardino MA. Referred muscle pain: clinical and pathophysiologic aspects. Curr Rev Pain 1999;3:489-98.

7. Schorge JO, Williams JW. Williams gynecology. New York: McGraw-Hill Medical;2008.

8. Giamberardino MA. Referred muscle pain/hyperalgesia and central sensitization. J Rehabil Med 2003;(41 Suppl):85-8.
9. KuKanich B, Lascelles BD, Papich MG. Use of a von Frey device for evaluation of pharmacokinetics and pharmacodynamics of morphine after intravenous administration as an infusion or multiple doses in dogs. Am J Vet Res 2005; 66:1968-74.
10. Dong H, Sun H, Magal E, et al. Inflammatory pain in the rabbit: a new, efficient method for measuring mechanical hyperalgesia in the hind paw. J Neurosci Methods 2008;168:76-87.
11. Giamberardino MA. Women and visceral pain: are the reproductive organs the main protagonists? Mini-review at the occasion of the "European week against pain in women 2007." Eur J Pain 2008;12:257-60.
12. Nixdorf DR, Hemmaty A, Look JO, Schiffman EL, John MT. Electric toothbrush application is a reliable and valid test for differentiating temporomandibular disorders pain patients from controls. BMC Musculoskelet Disord 2009;10:94.
13. Jarrell J. Demonstration of cutaneous allodynia in association with chronic pelvic pain. J Vis Exp 2009;(28)pii.
14. Jarrell J, Giamberardino MA, Robert M, Nasr-Esfahani M. Bedside testing for chronic pelvic pain: discriminating visceral from somatic pain. Pain Res Treat 2011;2011: 692102.
15. Fletcher RH, Fletcher SW. Clinical epidemiology: the essentials, 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005.
16. Miller LA, McIntire SA, Lovler RL. Foundations of psychological testing: a practical approach, 3rd ed. Thousand Oaks, CA: SAGE Publications; 2011.
17. Levy BS. Diagnostic studies. In: Steege JF, Metzger DA, Levy BS, eds. Chronic pelvic pain: an integrated approach. Philadelphia: Saunders; 1998:101.
18. Giamberardino MA, Affaitati G, Lerza R, Lapenna D, Costantini R, Vecchiet L. Relationship between pain symptoms and referred sensory and trophic changes in patients with gallbladder pathology. Pain 2005;114:239-49.