Cervical cleaning improves Pap smear quality

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Abstract

Background: Cervical Papanicolaou (Pap) smear screening is an effective method of detecting cytological changes in the cervix before they lead to cervical cancer. However, the quality of a Pap smear can be compromised by inflammatory exudate, inadequate cellularity or failure to sample the transformation zone. We evaluated the effect of routine cervical cleaning on Pap smear quality.

Methods: In a primary care setting, we compared the quality of Pap smears obtained after cervical cleaning (with a dry, oversized cotton swab) with the quality of historical control slides obtained from the same women without prior cervical cleaning. The results for both groups were then compared with statistical averages for the province of British Columbia.

Results: Inflammatory exudate was reported in 1 (0.3%) of the 334 study smears and 72 (11.0%) of the 652 control smears ($p < 0.001$). Inadequate endocervical or metaplastic squamous cells were reported in 11 (3.3%) of the study smears and 90 (13.8%) of the control smears ($p < 0.001$). Inadequate cellularity was reported in 13 (3.9%) of the study smears and 9 (1.4%) of the control smears ($p = 0.01$). There were similar statistical differences between the study group and provincial averages. The results for the control group did not differ significantly from provincial averages (inflammatory exudate, 11.3%; inadequate endocervical cells, 14.7%; and poor cellularity, 2.7%).

Interpretation: Prior cervical cleaning with an oversized cotton swab was associated with a lower frequency of smears with inflammatory exudate or inadequate endocervical cells and, to a lesser degree, a higher frequency of smears with inadequate cellularity.

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Over the past 50 years, the incidence of and mortality from invasive cervical cancer in British Columbia have been reduced by approximately 80%, primarily because of that province's Cervical Cancer Screening Program.[1] The Papanicolaou (Pap) test used by the screening program has a reasonably high sensitivity and is inexpensive and simple to perform. Nonetheless, sampling methods are inconsistent, and cytological interpretation is subjective, allowing some cases of cervical cancer to be missed. In British Columbia the false-negative rate for Pap smears is estimated at between 3% and 7%.[2]

More than 600 000 cervical Pap smears are interpreted annually through the BC Cervical Cancer Screening Program.[2] Of these, 3% to 4% are unsatisfactory, and 25% are limited for interpretation because of poor quality due to the presence of inflammatory exudate, inadequate endocervical or metaplastic cells, or inadequate cellularity. In 1999, 52% of unsatisfactory smears were obscured by inflammatory exudate, and 46% had inadequate cellularity.[2] Thirty-four percent of limited-quality smears were obscured by inflammatory exudate, and 61% had inadequate endocervical or metaplastic cells, which indicates failure to sample the transformation zone.[2] A total of 190 000 smears were unsatisfactory or limited for interpretation; 70 000 of these had inflammatory exudate.[2]

Ideally, unsatisfactory and limited-quality smears should be repeated promptly. In reality, only one-third of unsatisfactory smears are repeated within 12 months and three-quarters within 36 months.[2] Lack of repeat testing in cases of inadequate smears means potentially missed cancers.

Enhancement of Pap smear quality by routine use of a cytobrush has been shown,[3–5] but cervical cleaning has received limited attention. Cleaning with acetic acid in colposcopy clinic settings has been evaluated, with mixed results. Two studies suggested a greater proportion of slides with inadequate cellularity.[6,7] Another suggested no difference in smear quality.[8] Some office manuals and guides recommend cleaning the cervix before obtaining a Pap smear[9,10] but do not give specific advice or provide evidence supporting this recommendation.

Liquid-based cervical screening has recently been touted as a way of improving smear sensitivity, specificity and quality.[11–13] With this technology, samples are taken from the cervix and immediately rinsed in a fixative solution. The solution is then processed by a machine that automatically prepares a slide from the suspension of cells. However, in studies showing better screening results and specimen adequacy with this process, the sampling techniques used for conventional smears were not always optimal, and the role of cervical cleaning was overlooked.[11–13] A recent randomized controlled trial comparing liquid-based cervical screening technology with conventional Pap smear screening showed no difference in sensitivity or specificity and superior specimen quality with conventional smears.[14] The authors attributed their findings to careful cleaning of the cervix before the smears were obtained and suggested that the previously reported advantages of liquid-based technology are related solely to better sampling technique, including cervical cleaning.

We assessed the effect of routine cervical cleaning on Pap smear quality. A dry, oversized cotton swab was used for cleaning because of its minimal cost and simplicity of use.

Methods

The study, which was approved by the Clinical Research Ethics Board of the University of British Columbia, was performed in a 5-physician group practice in a rural town in northern British Columbia. The town has a catchment population of 18 000 and a balanced economic base of forestry, mining, farming and regional government services. Before the study, the Pap smear technique for all practitioners involved visualization of the cervix, no cervical cleaning or minimal cleaning with a small cotton swab, and a spatula scraping of the exocervix followed by cytobrush sampling of the endocervix, regardless of the site of the transformation zone. Each smear was prepared on a single slide and allowed to air dry. As part of a quality improvement initiative, practitioners began routinely cleaning the cervix with an oversized cotton swab (OB-GYN applicator, Solon Manufacturing, Solon, Me.) before obtaining smears. No training was provided other than instruction to clean the cervix with one or more large swabs until it was visibly free of exudate or mucus. The clinicians otherwise maintained their prior technique.

Consecutive cervical smears obtained after implementation of cervical cleaning formed the study sample. Smears from the vaginal vault were excluded. Clients were identified only by birth date and British Columbia Cancer Agency laboratory identification number. Data for the study smears were obtained from British Columbia Cancer Agency cytology reports.

The control smears consisted of the 2 most recent Pap tests performed before the study smear for each woman in the study group. Smears obtained before 1990 were excluded. Summaries of cytology history for each study subject were obtained from British Columbia Cancer Agency records and were used as the source of control data. When fewer than 2 historical smears were available for a given subject (i.e., women having their first or second Pap smear or those newly resident in British Columbia), an extra historical control smear was recorded (for a total of 3) from the next listed subject. Because some subjects had no historical smears and because no more than 3 smears were used for any subject, there were 16 fewer control smears than twice the number of study smears.

The British Columbia Cancer Agency has a centralized Cervical Screening Laboratory, which interprets all Pap smears obtained in the province. In the laboratory, the slides are rehydrated with glycerol according to the technique described by Koss.[15] Before 2000, Pap smears obtained in British Columbia were air-dried only. In 2000, guidelines recommending the use of fixative were introduced; however, our study took place before local implementation of these guidelines. Study and control slides were analyzed by the British Columbia Cancer Agency's Cervical Screening Laboratory; the interpreting cytotechnologists were unaware of any cleaning procedures.

The British Columbia Cancer Agency uses the following interpretive criteria for unsatisfactory smears: 75% or more of the slide obscured by blood or inflammatory exudate, less than 1000 cells present, excessively thick smear, poor cell preservation and lack of squamous cells (endocervical cells only). Slides deemed to be of limited quality for interpretation are those with adequate squamous cells but without endocervical or metaplastic cells (which indicates failure to sample the transformation zone) and smears with inflammatory exudate but that the cytotechnologist is still able to interpret. The baseline provincial proportion of smears with inflammatory exudate is 11.3%.[2] A 50% reduction in this rate was considered clinically significant. Sample size was calculated to detect a 50% reduction with 80% power at a p value of less than 0.05.

Pap smear suitability for interpretation, presence of inflammatory exudate, adequacy of cellularity, and presence of endocervical or metaplastic squamous cells were recorded. The proportions of limited-quality and unsatisfactory smears in the study group due to inflammatory exudate, inadequate endocervical or metaplastic squamous cells, and inadequate cellularity were compared with the control group and with provincial averages using a χ^2 analysis. A Mantel–Haenszel procedure was performed to look for variation between individual practitioners. Provincial rates for each category were obtained from the British Columbia Cancer Agency Cervical Screening Program's 1999 and 2000 annual reports.[1,2]

Results

A total of 334 consecutive smears obtained in late 2000 and early 2001 formed the study group; these were compared with 652 historical controls, obtained between 1990 and 2000. The use of historical controls avoided possible bias arising from variations in ethnicity, comorbidity or socioeconomic status, but resulted in an older average age in the study group than in the control group (36.2 v. 33.8 years) (Table 1).

For 2 of the 3 measures of quality, the study smears had better quality than the control smears: inflammatory exudate was reported for 1 study smear (0.3%) and 72 controls (11.0%) ($p < 0.001$), and inadequacy of endocervical or metaplastic cells was reported for 11 study smears (3.3%) and 90 controls (13.8%) ($p < 0.001$). However, the pattern was reversed for inadequate cellularity: 13 study smears (3.9%) and 9 controls (1.4%) ($p = 0.01$) had this feature. Combined provincial averages for the years 1998 and 1999 were not statistically different from control results: 11.3% with inflammatory exudate, 14.7% with inadequate endocervical cells and 2.7% with poor cellularity (Table 2). The differences between the study group and provincial averages were similar to those between study and control slides (Table 2), with the exception of slides with inadequate cellularity, for which the overall proportion of study smears (3.9%) was not different from the provincial average (2.7%)

Table 1: Characteristics of women in study of quality of Papanicolaou (Pap) smears

	Group; no. (and %) of slides	
Characteristic	Study group *n = 334*	Control group *n = 652*
Marital status		
Single	61 (18.3)	Not available
Married or common-law	273 (81.7)	Not available
Age, yr		
< 20	15 (4.5)	46 (7.1)
20–29	93 (27.8)	222 (34.0)
30–39	103 (30.8)	206 (31.6)
40–49	75 (22.5)	117 (17.9)
50–59	40 (12.0)	58 (8.9)
≥ 60	8 (2.4)	3 (0.5)

(p = 0.09). Some control slides had combinations of inadequate endocervical or metaplastic cells with inadequate cellularity (2 slides) or with inflammatory exudate (4 slides).

About half (333 or 51%) of the control smears had been obtained by the 5 practitioners involved in the study. The proportion of limited-quality control smears obtained by study physicians was not significantly different from the proportion of those obtained by nonstudy practitioners, which suggests that there was no bias due to differences in baseline sampling techniques. The similarity between control smears and overall provincial results supports this finding.

As women age, the proportion of slides with inflammatory exudate and inadequate endocervical cells remains constant until age 50, at which point it begins to decrease.[15] Forty-eight (14.4%) of the study smears and 62 (9.5%) of the control smears were from women 50 years of age and older, but only 9 poor-quality smears were found in this age group: 3 in the study group and 6 in the control group. Exclusion of these smears did not alter the results.

More smears in the control group than in the study group showed benign squamous changes (4.7% v. 2.1%; p = 0.044) and squamous intraepithelial lesions (8.4% v. 4.2%; p = 0.013). The latter result would be expected, given that the incidence of squamous intraepithelial lesions decreases with advancing age. Also, for some abnormal controls, the subjects would have reverted to normal or received treatment by the time the study smears were obtained. The 2 groups did not differ significantly in the incidence of benign glandular changes (2.3% v. 1.8%; p = 0.27). The British Columbia Cancer Agency does not report the Bethesda categories of ASCUS or AGUS (atypical squamous or glandular cells of undetermined significance).

Mantel–Haenszel analysis of individual practice results showed that the increase in the proportion of smears with inadequate cellularity was limited to one practice. In this practice 9.0% of study smears and only 0.8% of control smears showed poor cellularity (p = 0.003). When data from this practice were excluded, 2.0% of study smears and 1.4% of controls had inadequate cellularity (p = 0.6); these values were similar to the provincial average of 2.7% (p = 0.54).

Interpretation

Cervical cleaning was associated with a markedly smaller proportion of Pap smears obscured by inflammatory exudate. The proportion of study smears with inadequate cellularity was greater than that of the control group but was not different from provincial averages. The increase in smears with inadequate cellularity was limited to one practice, which suggests that smear quality is operator-dependent as well as technique-dependent. Explanations might include inadequate spatula pressure during sampling or overzealous cleaning beforehand.

Unexpectedly, cervical cleaning also resulted in significantly fewer smears with inadequate endocervical or metaplastic squamous cells. Control rates were consistent between study practitioners and other control practitioners, and the reduction occurred in all practices. Study physicians did not change their use of a cytobrush during the study. Perhaps cleaning the cervix reduces the amount of mucus picked up by the cytobrush and allows cells gathered from the endocervical canal to be more effectively deposited on the Pap smear slide. Obwegeser and Brack[14] reported a similarly low proportion of smears with no endocervical cells (3.6%) in a large series in which most smears were obtained after cervical cleaning.

The study design had limitations. Historical slides from subject women were chosen as controls to ensure comparability of the study and control populations. However, awareness of the study setting could have led to better sampling technique by study practitioners relative to their historical technique. A randomized study design would have

Table 2: Comparison of quality of Pap smears for study group with quality of Pap smears for control group and with provincial averages

Feature of Pap smear quality	Suitability for interpretation	Study group, no. (and %) of slides *n = 334*	Control group *n = 652**		Provincial average for 1998 and 1999 *n = 1 261 213*	
			No. (and %) of slides	*p*	% of slides	*p*
Normal	Satisfactory	309 (92.5)	487 (74.7)	< 0.001	71.4	< 0.001
Inflammatory exudate present	Unsatisfactory	0	14 (2.1)	0.0036	2.1	0.007
	Limited	1 (0.3)	58 (8.9)	< 0.001	9.2	< 0.001
Inadequate endocervical or metaplastic cells	Limited†	11 (3.3)	90 (13.8)	< 0.001	14.7	< 0.001
Poor cellularity	Unsatisfactory	8 (2.4)	9 (1.4)	0.25	1.7	0.33
	Limited	5 (1.5)	0	0.004	1.0‡	0.36

*Data sum to 658 because 6 slides had more than one poor-quality factor.
†The British Columbia Cancer Agency reports all smears with inadequate endocervical or metaplastic cells as "limited" for interpretation.
‡Data for 1998 only available from British Columbia Cancer Agency.

removed this potential bias. Nonetheless, if attention to cleaning the cervix resulted in better overall sampling technique and smear quality in our setting, then it is reasonable to expect improvement in other clinical settings.

The lower incidence of squamous intraepithelial lesions in study smears than in controls merits comment. With advancing age, the incidence of squamous intraepithelial lesions decreases. Ongoing surveillance and treatment of women with abnormal results during the interval between the control and study smears should explain the decrease seen in this study. There remains a concern that cervical cleaning could decrease the sensitivity or specificity of the Pap smear; however, the randomized trial by Obwegeser and Brack[14] provided reassurance that this is not the case. Randomization in our study would have removed bias caused by treatment or natural reversion of abnormal smears and would have provided additional reassurance that the difference was not due to an effect of cleaning on sensitivity.

Routine cervical cleaning with an oversized cotton swab before obtaining Pap smears should be considered as a method of improving Pap smear quality and enhancing the efficiency and effectiveness of cervical cancer screening programs. If, as suggested by Obwegeser and Brack,[14] this simple intervention improves smear quality to the same degree as liquid-based technology while preserving sensitivity and specificity, the high cost of liquid-based technology could be avoided.[11] Further study with randomized controls would help to confirm these results and refine ways to minimize the proportion of smears with poor cellularity.

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