Association of cervical cryotherapy with inadequate follow-up colposcopy

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KEY POINTS FOR CLINICIANS

- Based on this study, cervical cryotherapy increases the risk that a follow-up colposcopic examination will be inadequate.
- Further studies are needed to determine the most effective treatment for mild cervical dysplasia and possible local effects of cryotherapy.

■ OBJECTIVE We studied the anatomic changes that occur in the ectocervix after cryotherapy and the role these changes play in the adequacy of follow-up colposcopic examination.

■ STUDY DESIGN We retrospectively reviewed patients' charts.

■ POPULATION Between January 1, 1991, and December 1, 1995, 268 women underwent 2 colposcopic examinations in 7 state-run public health clinics.

■ OUTCOMES MEASURED The likelihood that a follow-up colposcopic examination would be inadequate.

■ RESULTS Of the 268 women who underwent 2 colposcopic examinations during the study period, 83 had cryotherapy, 24 had loop excision of the ectocervical portion or cervical conization, and 96 had no procedure. Sixty-five were excluded because of missing data. Subjects were similar with respect to age, whether endocervical curettage was performed, presence of cervical dysplasia or human papilloma virus, and whether glandular involvement was noted. Patients who had cryotherapy had an increased likelihood of inadequate follow-up colposcopic examination compared with women who had no procedure (adjusted odds ratio = 18.7, 95% confidence interval = 7.0–49.8).

■ CONCLUSIONS Undergoing cryotherapy of the uterine cervix increases the risk that a follow-up colposcopic examination will be inadequate. Given the reported high rates of regression of mild and moderate cervical dysplasia and the risks posed by possibly unnecessary procedures performed after inadequate colposcopic examination, a trend toward less aggressive therapy and watchful waiting may be appropriate but should be investigated in a controlled clinical trial.

■ KEY WORDS Colposcopy; cervical dysplasia; cervical cryotherapy. (*J Fam Pract 2002; 51:526–529*)

Cryotherapy is an accepted procedure for treating low-grade cervical dysplasia.[1,2] Only minor modifications of the precise technique of cryotherapy application have occurred since its inception. Currently the double-freeze technique of cryotherapy is an accepted treatment for mild and focal moderate dysplasia of the uterine cervix.[3] Cervical cryotherapy is used widely not only because of its proven efficacy but also because of its ease of use in the outpatient setting and lack of known significant side effects. The procedure can be performed in the office setting without the use of local or general anesthesia, making it superior to the more invasive procedures performed before the availability of cryotherapy (eg, cervical conization and hysterectomy).

There has been limited investigation of the effects of cryotherapy on the anatomy of the uterine cervix. Whereas one study showed that cryotherapy has no effect on subsequent fertility or pregnancy outcome,[4] another in adolescents reported cervical stenosis and pelvic inflammatory disease as possible treatment side effects.[5] In addition, a study published in 1984 by Jobson and Homesley reported higher rates of retraction of the proximal squamocolumnar junction into the endocervical canal in patients undergoing cryotherapy compared with patients undergoing carbon dioxide laser ablation[6]; 47% of the follow-up colposcopic examinations were inadequate in that study population. Adequacy of colposcopic examination is defined as complete visualization of the

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transformation zone, visualization of the entire lesion, if present, and correlation between cytologic and histologic findings and the colposcopist's impression.[7] Failure to meet any one of these criteria leads to an inadequate colposcopic examination requiring further, more invasive evaluation. This study compared the rate of adequate and inadequate colposcopic examinations in women with and without a history of cryotherapy. Other factors found to influence the adequacy of follow-up colposcopy also are described.

METHODS

We performed a retrospective cohort study using data collected from 7 of 14 state-run public health clinics. These 7 sites included rural and urban clinics. All women undergoing at least 2 colposcopic examinations in these clinics between January 1, 1991, and December 1, 1995, were included. Women underwent initial colposcopic examination after an abnormality was noted on a screening Pap test. Only women who had both colposcopic examinations in the same clinic were included. Care provided in these clinics included Pap test screening, colposcopic examinations, and treatment of identified cervical dysplasia with cervical cryotherapy, conization, and loop excision of the ectocervical portion (LEEP). State-contracted physicians trained in obstetrics and gynecology followed women who attended these clinics.

Chart review was used to determine the adequacy of the initial examination, whether an intervening procedure was done, and the adequacy of follow-up colposcopic examination. Adequacy was documented by the physician performing the colposcopic examination with the use of a standard form consistent among clinics. The accepted criteria for adequacy were used, and each colposcopic examination was documented as adequate or inadequate based on the colposcopist's findings. Charts were reviewed and data were abstracted by 3 reviewers. Cervical biopsy results, presence of human papilloma virus (HPV) noted on routine cytology, endocervical curettage (ECC) results, and routine demographic data also were recorded. The management and therapeutic protocols were consistent across the 7 clinics.

Women were excluded from the analysis if (1) they had cryotherapy performed before their initial colposcopic examination (n = 1), (2) the date of the initial colposcopic examination was not available (n = 36), (3) information confirming the type of treatment used between colposcopic examinations was unknown (n = 32), (4) initial colposcopic examination was inadequate (n = 16), or (5) the adequacy of the follow-up colposcopic examination was not documented (n = 6). The total number of women excluded was 65 because some women met multiple exclusion criteria.

The management after initial colposcopic examination was done according to whether the women had cryotherapy, cone, LEEP, or no procedure between initial and follow-up colposcopic examinations. Univariate analysis of the association between the management group with clinic of treatment, performance of ECC, biopsy results, presence of HPV, and cytologic presence of glandular atypia was performed. Mean age and duration (interval between initial and follow-up colposcopic examinations or between the procedure and follow-up examination) were calculated for all groups.

The odds ratio of an inadequate follow-up colposcopic examination was estimated for type of treatment (cryotherapy, cone/LEEP) compared with no treatment, age, clinic where treatment was provided, performance of ECC, biopsy results, presence of HPV, and presence of glandular atypia. The 95% confidence intervals about the relative odds estimates were calculated. Mean age and duration between initial colposcopy and follow-up colposcopy were calculated for the groups with adequate and inadequate follow-up colposcopic examinations.

Multivariable logistic regression analysis was used to evaluate the association of adequacy of follow-up colposcopic examination with age (years), clinic where colposcopic examination was performed, duration (days), whether or not ECC was performed, biopsy results from the initial colposcopic examination, presence of HPV, and presence of glandular atypia noted on initial colposcopy. Biopsy results were categorized as normal or abnormal in the model that is reported. The stepwise backward elimination technique was used to evaluate the best model. The 95% confidence intervals about the adjusted odds ratio were calculated.

The Pearson chi-square test was used to test the significance of the association between binary variables. The significance of the difference between means was tested with the one-way analysis of variance. Data were analyzed with the personal computer version of the Statistical Package for the Social Sciences (SPSS/PC+ version 8.0).

RESULTS

Between January 1, 1991, and December 31, 1995, 3225 women underwent colposcopic evaluation or treatment at 7 county colposcopy clinics in Oklahoma. Two hundred sixty-eight of these women underwent 2 examinations during the study period. There were 203 of 268 subjects available for analysis after exclusions for missing data. Eighty-three patients (41.1%) had cryotherapy, 24 (11.9%) underwent a cone biopsy or a LEEP procedure, and

TABLE 1

Characteristics of patients with and without cryotherapy between initial and follow-up colposcopy

Characteristic	Cryotherapy (n = 82)	Cone or LEEP (n = 24)	No procedure (n = 96)	*P**
Mean age (y)	24.6	26.5	23.8	.229
Mean duration† (d)	565	319	339	.004
ECC (%)	80.2	75.0	67.1	.135
Cervical dysplasia (%)				< .001
Normal	21.7	19.0	39.5	
Mild dysplasia	58.0	23.8	45.3	
>Mild dysplasia	20.3	57.1	15.1	
HPV (%)	72.6	52.4	60.4	.130
Glandular atypia (%)	23.9	38.1	17.8	.125

*Pearson χ^2 for proportions and analysis of variance for means.
†Duration from treatment (cryotherapy) or examination to follow-up colposcopic examination.
ECC, endocervical curettage; HPV, human papilloma virus; LEEP, loop excision of the ectocervical portion.

96 (47.5%) underwent no procedure between initial and follow-up colposcopic examinations.

Table 1 shows characteristics of women who had cryotherapy, cone/LEEP, and no procedure. The groups were similar with respect to age, whether ECC was performed, presence of HPV, and whether glandular involvement was noted. There was an association between the degree of cervical dysplasia and the three treatment groups, which was expected because degree of dysplasia determines treatment modality. Women who had cryotherapy had follow-up colposcopy (mean = 565 days) later than women who had cone or LEEP (mean = 319 days) or no procedure (mean = 339 days; $P < .0001$).

Thirty-three percent (n = 67) had inadequate follow-up colposcopic examinations. These included a large proportion of women, 61.4%, who had cryotherapy (51/83) compared with 20.8% (5/24) of women who had cone or LEEP and 11.5% (11/96) of women who had no procedure.

Table 2 shows the relationship between inadequate second colposcopy and previous cryotherapy, cone/LEEP, abnormal cervical biopsy, ECC, presence of HPV, and presence of glandular atypia. Patients who had cryotherapy had an increased likelihood of inadequate follow-up compared with patients who had no procedure (adjusted odds ratio =18.67, 95% confidence interval = 6.99–49.81). Cone/LEEP increased the likelihood of inadequate follow-up but was not statistically significant. Age, duration, ECC, presence of HPV, or presence of glandular atypia did not increase the likelihood of subsequent inadequate colposcopic examination. Odds ratio estimates for different clinics are not reported but were imprecise due to small numbers.

TABLE 2

Likelihood of inadequate follow-up colposcopic examination*

Characteristics	Adjusted OR	95% CI
Cryotherapy	18.66	6.99–49.81
Cone or LEEP	3.01	0.78–11.58
Cervical dysplasia		
Mild	NA	
>Mild	NA	
ECC	NA	
HPV	NA	
Glandular atypia	NA	

*Logistic regression model included the clinic of colposcopy (not shown). Age (years) and duration (days; from treatment or first colposcopy to second colposcopy) were removed from the model by backward elimination.
CI, confidence interval; ECC, endocervical curettage ; HPV, human papilloma virus; LEEP, loop excision of the ectocervical portion; NA, not applicable; OR, odds ratio.

DISCUSSION

Undergoing cryotherapy of the uterine cervix increases the risk that a follow-up colposcopic examination will be inadequate. This agrees with the findings of Jobson and Homesley's 1984 study,[6] which looked at the efficacy of cryotherapy vs carbon dioxide laser ablation in the treatment of cervical dysplasia. Although it was not the focus of their study, a high rate of inadequacy was noted on follow-up colposcopic examinations after cryotherapy.

Because of the retrospective design of this study, we could not randomly assign women to a treatment group. However, the study groups were similar with respect to other variables potentially associated with the outcome measure. In addition, we attempted to control confounding variables by using multivariable analysis. By including the clinic where the examination was performed, we attempted to limit the effect of the subjective assignment of adequacy by the physician. This is a limitation of this study.

We found an association between the clinics where the follow-up colposcopist's examinations were performed and whether a follow-up examination was adequate or inadequate. The determination of adequacy depends on the physician's observations during the colposcopic examination. We were unable to measure the intra- or interobservation variation between the examinations. However, we attempted to control for this effect by including the clinic site in the multivariable analysis.

The current standard of care for inadequate colposcopic examination recommends more invasive evaluation with a procedure such as cervical conization or LEEP. This allows clarification of discordance between cytology, histology, and the colposcopist's impression; sampling of any lesion that may extend past the view of standard colposcopy; and histologic evaluation of the entire transformation zone. Given the reported high rates of spontaneous regression of mild and moderate cervical dysplasias with a watchful waiting approach,[8–12] we wonder whether we are performing unnecessary procedures (LEEP and conization) after cryotherapy as a result of inadequate follow-up colposcopic examinations. A study evaluating the pathologic findings of cone or LEEP specimens from inadequate colposcopic examinations after cryotherapy would help answer these questions. If there is no persistence or progression of dysplasia, then this would support the hypothesis that cryotherapy leads to unnecessary, invasive procedures. Further controlled trials are required to answer these questions.

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