

RESEARCH COMMUNICATION

Cervical Cytologic Abnormalities of Cervical Intraepithelial Neoplasia 1 Treated with Cryotherapy and Expectant Management during the First Year Follow-Up Period

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Abstract

Aim: To determine the frequency of cervical cytologic abnormalities in patients who were diagnosed as having CIN 1 and had undergone either cryotherapy or expectant management. **Methods:** A retrospective medical record review of 87 patients with colposcopic cervical biopsy-proven CIN 1, was undertaken including age, parity, menstruation status, cervical cytology reports, colposcopic findings, and cervical cytologic follow-up reports. There were 38 patients (43.7%) treated with cryotherapy and the remainder underwent expectant management. **Results:** Mean (SD) age of patients treated with cryotherapy was less than that of the patients who had expectant management (36.2 (9.4) vs 41.1 (9.4) years, respectively, $p=0.02$). There were no differences in the frequencies of cervical cytologic abnormalities between the groups at 6- and 12-month-follow-up visits (cryotherapy group vs expectant group: 18.4% vs 18.4% at 6-months and 19.2% vs 16.1% at 12-months). **Conclusion:** Cryotherapy and expectant management with cytologic surveillance had comparable frequencies of cytologic abnormalities during a 12-month follow-up period. Expectant management requires adherence to follow up and high quality cytology and colposcopy testing. Therefore, it should be reserved for these settings. Cryotherapy may be more reasonable in women who are likely to be lost to follow up and high quality cytology cannot be guaranteed.

Key Words: Cervical intraepithelial neoplasia - cryotherapy - expectant management - colposcopy

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Introduction

Cervical cancer is the most common leading cause of cancer death among Thai women (Deerasamee & Srivatanakul., 1999). It usually develops gradually and has a long preinvasive state. Regular Papanicolaou test (Pap smear) is the recommended modality in detecting preinvasive lesion of the cervix. "Atypia" is known as an early stage of abnormal Pap smear, of which the cells become slightly abnormal. After a while, atypia could turn into cancer. Colposcopy with directed biopsy provides a histological diagnosis following an abnormal Pap smear. Recommendation of treatment is then based on the histological diagnosis.

Cervical intraepithelial neoplasia (CIN) 1 is the most common form of CIN and up to 70% of CIN 1 spontaneously regresses (Schlecht et al., 2003; Hamm et al., 1998). The recommended management of women with a histological diagnosis of CIN 1 preceded by an atypical squamous cells of undetermined significance (ASC-US) or atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion (ASC-H) or low-grade squamous intraepithelial lesion (LSIL) is a follow-up with

either human papillomavirus (HPV) DNA testing every 12 months or cervical cytology assessment every 6-12 months, so-called expectant management (Wright et al., 2007). Another option for management of CIN 1 includes ablation method by using cryotherapy. However, both expectant management and cryotherapy require cytologic and/or colposcopic follow-up to detect progression, persistence, and recurrence of disease.

Both treatment modalities have been chosen by the preference of gynecologic oncologists. Although recent data indicate that expectant management of CIN 1 is safe, cost-effective and having high rate of spontaneous resolution of the disease (Richart & Wright., 1993; Hamm et al., 1998; Falls, 1999), many clinicians have routinely treated CIN 1 with cryotherapy (Creasman et al., 1981; Richart & Wright., 1993). Disadvantages of using cryotherapy such as cramping during and after the procedure, vaginal spotting and watery vaginal discharge have been reported (Jacob et al., 2005). On the other hand, patients treated with expectant management may experience the progression of CIN grading, resulting in a requirement for treatment with more invasive procedures (Richart & Barron., 1969; Richart & Wright., 1993). There

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have been no available data comparing the outcome of these 2 treatments in terms of cervical cytologic abnormalities. The purpose of this study was to determine the frequency of abnormal cytologic abnormalities during the 1-year-follow-up period in patients treated with cryotherapy and expectant management.

Materials and Methods

A retrospective study including 87 women with a histological diagnosis of CIN 1 preceded by ASC-US, ASC-H and LSIL cytology who attended the Gynecologic Oncology Clinic, Thammasat University Hospital between January 2004 to December 2008, was undertaken. The study was approved by the Ethics Committee of Faculty of Medicine, Thammasat University. Thirty-eight of them (43.7%) were treated with cryotherapy while 49 (56.3%) patients underwent expectant management. Medical records of those patients were reviewed for age, parity, menstruation status, cervical cytology report, colposcopic findings, cervical cytologic

Table 1. Clinical Characteristics of Enrolled Patients

Parameters		Expectant (n = 49)	Cryotherapy (n = 38)	P Value
Age group	20-39	21 (42.9)	28 (57.1)	0.084
	40-70	24 (63.2)	14 (36.8)	
Parity	Nulliparous	10 (20.4)	39 (79.6)	0.781
	Multiparous	6 (15.8)	32 (84.2)	
Menopause	No	39 (79.6)	10 (20.4)	0.135
	Yes	35 (92.1)	3 (7.9)	

Table 2. Colposcopic Findings before CIN 1 Diagnosis in all Patients

Treatment	Colposcopy*	
	Satisfactory	Unsatisfactory
Expectant	42 (85.7)	7 (14.3)
Cryotherapy	37 (97.4)	1 (2.6)

Table 3. Size of Lesions from Pre-CIN 1 Diagnosis Colposcopic Findings

Treatment	1 quadrant	2 quadrants
Expectant	45 (91.8)	4 (8.2)
Cryotherapy	30 (78.9)	8 (21.1)

Table 4. Pap smear Results During Follow-up

Treatment	6 months		12 months	
	normal	abnormal	normal	abnormal
Expectant	40 (81.6)	9 (18.4)	26 (83.9)	5 (16.1)
Cryotherapy	31 (81.6)	7 (18.4)	21 (80.8)	5 (19.2)

Table 5. Pathology Reports after Colposcopic Biopsy

Colposcopic pathology		Expectant	Cryotherapy
At 6-months	No CIN	4 (44.4)	3 (42.9)
	CIN 1	4 (44.4)	4 (57.1)
	CIN 2-3	1 (11.2)	0 (0.0)
At 12-months	No CIN	3 (60.0)	5 (100)
	CIN 1	1 (20.0)	0 (0.0)
	CIN 2-3	1 (20.0)	0 (0.0)

No statistical difference between expectant and cryotherapy in any parameter

follow-up, and pathology.

Cytologic surveillance during the follow-up period in both groups consisted of repeated Pap smear testings every 6 months for at least one test. Patients who had abnormal Pap smear result underwent adjunctive colposcopic examination. Quality control of cytology is assured according to the routine quality control of the hospital. Outcome measure was the cytologic and colposcopic results at 12-month-follow-up visit.

Descriptive statistics were used to describe the patients' characteristics. Data are expressed in mean and standard deviation (SD). Correlation between cytologic and pathologic results were analyzed by using Chi-square test. A p-value of less than 0.05 was considered statistically significant.

Results

Of 87 patients included in the study, mean (SD) ages of the patients in expectant management group and cryotherapy group were significantly different [41.1 (9.4) and 36.2 (9.4) years, respectively]. Clinical characteristics of patients in both treatment groups are shown in Table 1. Colposcopic findings before CIN 1 diagnosis in majority of patients in both groups showed satisfactory colposcopy and one quadrant involvement lesion (Tables 2, 3).

During the follow-up periods, there were no differences in the frequencies of cervical cytologic abnormalities at 6 and 12 months after CIN 1 diagnosis between two treatment groups (Table 4).

Colposcopic directed cervical biopsy performed in the patients who had abnormal cytologic Pap smear results demonstrated both CIN-free and low grade (CIN 1) lesions in 15 of 16 patients (93.7%) and 9 of 10 patients (90%) at 6 and 12 months, respectively. At 6- and 12-month-follow-up visits, there was one patient in expectant management group for each visit had histological diagnosis of high grade lesion. Colposcopic pathology in each treatment group is shown in Table 5.

Fifty-seven of 87 patients (65.6%) had completed a 12-month-follow-up. Of these patients, 55 (96.4%) had a spontaneous regression of the disease, 1 patient had persistent disease and 1 patient had a progressive disease.

Discussion

Although several studies have shown a high rate of spontaneous regression of CIN 1 (Richart & Wright, 1993; Hamm et al., 1998; Falls, 1999; Schlecht et al., 2003). However, cytologic surveillance after CIN 1 diagnosis is necessary to detect progression, persistence or recurrence of the disease. Untreated CIN 1 entails a risk of persistence of 22-32% and a risk of progression of 13-17% (Nasiell et al., 1986; Ostor, 1993).

Our study showed a relatively low frequency of cervical cytologic abnormalities in both groups (16.1-19.2%) during the periods of 6- and 12-month-follow-ups. It might be explained by high rate of spontaneous resolution of the disease and the low accuracy of the Pap smear test in detecting cytologic abnormalities, i.e. 51% in a previous meta-analysis (McCrary et al., 1999).

Additionally, no difference in the frequency of cervical cytologic abnormalities during the follow-up period between 2 treatment groups. Several reasons might explain this result. Firstly, expectant management is as effective as cryotherapy treatment for patients with CIN 1. Secondly, number of patients who had large lesion (involved 2 quadrants) from colposcopic findings in expectant management group was less than that of the cryotherapy group (8.2 and 21.1%, respectively). Large lesion may have lower rate of spontaneous regression of the disease and higher rate of cervical cytologic abnormalities. Thirdly, mean age of the patients in cryotherapy group was less than that of the expectant management group. The difference in patients' age may affect this result. At 12-month-follow-up, most patients in both groups who had abnormal cervical cytology had pathologic results of CIN-free. This result confirmed that CIN 1 can spontaneously remit in a majority of cases without definite treatment.

The high rate of loss to follow-up at 12 months of 34.4% was observed in this study. The length of time between colposcopic diagnosis and recommended follow-up period may have an impact on compliance of the patients.

The expectant management requires adherence to follow up which can be problematic in most settings and particularly in low resource settings. Moreover, it requires high quality cytology and colposcopy testings which can be challenging in low resource settings. Cryotherapy may be more reasonable in women who are likely to be lost to follow up and/or if high quality of cytology cannot be guaranteed and in the setting where there is limited access to colposcopy.

In conclusion, cytology surveillance without cryotherapy appears reasonable in treating CIN 1 because of the high rate of spontaneous regression of CIN 1, but adherence to the follow-up should be emphasized to the patients during the follow-up visits.

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