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# Difference Between Cryotherapy and Follow Up Low Grade Squamous Lesion of Cervix Uteri

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## ABSTRACT

**Introduction:** Cervical cancer can be successfully prevented by effective treatment. **Aim:** Analyse of success of cryotherapy in LSIL and ASCUS. **Materials et methods:** In retrospective study between January 2016 to March 2017, 3244 PAP test were analysed. 257 patients who had been diagnosed with LSIL and ASCUS from PAP smear were divided in two groups: women who had HPV positive, colposcopic positive and cytologic finding of LSIL or ASCUS treated with cryotherapy and women with LSIL, ASCUS and negative colposcopy.  $\chi^2$  test was used for statistical analysis of data. **Results:** Analysis of 3244 PAP smears showed negative for intraepithelial lesion or malignancy (NILM) in 90,10% (N-2923), and abnormal in 9,8% (N-321) of women. ASCUS was found in 4,8% (N-156) and ASC-H in 0,2% (N-6), LSIL in 3,1% (N-101), HSIL in 0,64% (N-21). The average age of patients with ASCUS lesion was  $41 \pm 12$  years. After cryotherapy, HSIL had progression in 1,5% (N-1), persistence in 6,3% (N-4) and regression in 91,7% (N-58). Progression occurred in 10,5% (N-4) of HSIL, persistence in 52,6% (N-20) and regression in 36,7% (N-14) in 38 women with LSIL lesion after repeated PAP test. Progression occurred in 8% (N-10) of LSIL and 4% HSIL (N-5), persistence in 58% (N-72) and regression in 29,8% (N-37) in 124 women with ASCUS lesion after treatment and repeated PAP test. Difference in progression lesions in HSIL between women with cryotherapy (1,5%) and follow-up (10,5%) after LSIL is not significant, but progression to CIN II occurred after cryotherapy. CIN III or cervical cancer was not found. **Conclusion:** Cryotherapy prevents progression of LSIL in HSIL and in cervical cancer. Because of that cryotherapy is successful method in prevention of cervical cancer.

**Keywords:** cryotherapy, HPV, ASCUS, LSIL.

## 1. INTRODUCTION

Cervical cancer can be successfully prevented if timely identification of precancerous lesions is followed by effective treatment (1). Women with low squamous grade (LSIL) have minimal potential for developing cervical malignancy, while those with high grade lesions are at high risk of progression to malignancy (2). In managing women with LSIL, the goal is to prevent possible progression to invasive cancer while avoiding over-treatment of lesions that are likely to regress. Management of LSIL is based upon correlation of the cervical cytology findings, colposcopic impression, cervical biopsy results, and individual patient characteristics, such as age, pregnancy, and the likelihood of compliance with treatment recommendations (3).

Untreated LSIL has a risk of 13% for diagnosis of High grade squamous lesion (HSIL) at two-year follow-up, which is the same as the risk for ASC HPV-positive or LSIL cytology

results following a negative colposcopy. However, most cases of LSIL will remit spontaneously over time (4). The decision for treatment or observation should be based on the preferences of the patient and the physician. For most women, especially younger women, observation provides the best balance between risk and benefit and should be encouraged. Follow-up of untreated LSIL should include two cytology screening tests six months apart, with colposcopy for an ASC or higher-grade result, or a single HPV test with colposcopy if the test result is positive (5).

Cryotherapy is a method for the treatment of cervical precancerous lesions (6) that is considered the most suitable option to use in low-resource settings with underserved populations because it is low cost, requires no anesthesia or electricity, and has low complications rate (7). If the final diagnosis in a woman is a LSIL, the clinical management may take one of

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the following courses; either to (a) immediately treat the lesion or (b) follow the woman cytologically or colposcopically and then treat if the lesion is persistent or progressive after 18 to 24 months, and if regression occurs (8, 9, 10). After cryotherapy, healing of the cervix is grossly apparent by two or four weeks, cytological and colposcopic appearances will continue to reflect healing or regenerative effects for approximately three months (11, 12). Local cervical immunity in women with LSIL after cryotherapy is increased, an increase of IgA may partly support the clearance rate of HPV infection (13). If the follow-up visit reveals no evidence of persistent disease, the woman is advised to participate in the screening programme. If persistent disease is found during the follow-up visit, appropriate investigations and appropriate treatment should be carried out.

**2. AIM**

Analyse of success of cryotherapy in women with LSIL and ASCUS.

**3. PATIENTS AND METHODS**

In retrospective study which was conducted between January 2016 to March 2017, 3244 PAP test were analysed. Total amount of 257 patients who had been diagnosed with LSIL and ASCUS from PAP smear were divided in two groups:

- a) Women who had HPV positive, colposcopic positive and cytologic finding of LSIL or ASCUS treated with cryotherapy and
- b) Women with LSIL, ASCUS and negative colposcopy.

Cryotherapy was done using compressed N<sub>2</sub>O refrigerant with the aim of creating an ice ball with a depth of freeze denoted by a peripheral margin of 4-5 mm of frost. The hypothermia produced by ice ball, results in ice crystal formation within cervical tissue leading to tissue destruction. To freeze the lesion, the cryoprobe is placed on the cervix, covering the entire lesion but not touching the vaginal wall. The coolant gas is allowed to flow through the channels in the metal tip of the cryoprobe.

Cryotherapy treatment is performed using cryosurgical unit (model MGC-200) and double-freeze technique. The double-freeze technique involves applying the coolant continuously for 3-min freeze, followed immediately by 5-min thaw, followed by another 3-min freeze. Results of study were gained comparing LSIL and ASCUS after cryotherapy and LSIL and ASCUS after observation (follow-up). X<sup>2</sup> test was used for statistical analysis of data.

**4. RESULTS**

Analysis of 3244 PAP smears showed negative for intraepithelial lesion or malignancy (NILM) in 90,10% (N-2923), and abnormal in 9,8% (N-321) of women. ASCUS was found in 4,8% (N-156) and ASC-H in 0,2% (N-6), LSIL in 3,1% (N-101), HSIL in 0,64% (N-21). The average age of patients with ASCUS lesion was 41 ± 12 years (Table 1).

Demographic Data	Results
Age	41±12
BW	68±10,2
Result of PAP smears (N,%)	3244 (100%)
NILM	2923 (90,10%)
Abnormal PAP smears	321 (9,8%)
Atypical	
ASC-US	156 (4,8%)
ASC-H	6 (0,18%)
Atypical glandular cells	37 (1,14)
LSIL	101 (3,11)
HSIL	21 (0,64)

**Table 1. Demographic data of our sample**

	Cryotherapy	Observation	Total
LSIL	63	38	101
ASC-US	32	124	156

**Table 2. Women follow-up 12 months after cryotherapy and observation**

Cryotherapy LSIL	NILM	ASCUS	CIN I	CIN II
63	55	3	4	1
100%	87,3%	4,7%	6,3%	1,5%
Results	87,3%	12,5%		

**Table 3. Follow-up results of women with LSIL 12 months after cryotherapy. NILM: negative for intraepithelial lesion or malignancy**

After cryotherapy, HSIL had progression in 1,5% (N-1), persistence in 6,3% (N-4) and regression in 91,7% (N-58) in this period of time (Table 3).

Observation LSIL	NILM	ASCUS	LSIL	HSIL
38	11	3	20	4
100%	28,9%	7,8%	52,6%	10,5%
Results	28,9%	7,8%	52,6%	10,5%

**Table 4. Follow-up results of women with LSIL 12 months after observation**

Progression of LSIL to HSIL occurred in 10,5% (N-4), persistence in 52,6% (N-20) and regression in 36,7% (N-14) in 38 women after repeated PAP test (Table 4).

Cryotherapy ASCUS	NILM	ASCUS
32	30	2
100%	93,7%	6,2%
Results	93,7%	6,2%

**Table 5. Follow-up results of women with ASCUS 12 months after cryotherapy**

After cryotherapy there was no progression into LSIL and HSIL, persistence occurred in 6,2% (N-2) and regression in 93,7% (N-30) in this period of time (Table 5).

Progression occurred in 8% (N-10) LSIL and 4% HSIL (N-5), persistence in 58% (N-72) and regression in 29,8% (N-37) in 124 women with ASCUS lesion after treatment and repeated PAP test (Table 6).

Observation ASCUS	NIML	ASCUS	LSIL	HSIL
124	37	72	10	5
100%	29,8%	58,0%	8,0%	4,0%
Results	29,8%	58,0%	8,0%	4,0%

Table 6. Follow-up results of women with ASCUS 12 months after observation

Cause	ASCUS (N-156)	LSIL (N-101)
HPV		
High risk	80 (51%)	72 (71%)
Absent	76 (48%)	28 (27%)

Table 7. Distribution of patients in relation to HPV infection

Patients with ASC-H lesion 0,2% (N-6) were transferred to biopsy of cervix where PH results showed 33% (N-2) Carcinoma in situ (CIS), 33% (N-2) HSIL and 33% (N-2) LSIL. High risk of HPV was found by 51% (N-80) women with ASCUS and 71% (N-72) women with LSIL.

## 5. DISCUSSION

A systematic review of cryotherapy performed in 2004 showed that cryotherapy is approximately 90% effective for all grades of CIN when assessed 1 year after cryotherapy, based mainly on studies from developed countries (14). Our results present cure rates of 89,3% (N-55) by women who underwent cryotherapy. Authors from Kenya cited cure rates of 81,4%, cure rates of 88% was achieved by nurses in Southern India and 97% overall by physician in Peruvia and Ghanaian (15, 16). After cryotherapy, progression of LSIL lesions in HSIL occurred in 1,5% (N-1), persistence of lesion in 6,3% (N-4). Sasieni found progression rates of CIN in 1,5% of women treated for CIN II or CIN III at age 20-24 who would have developed cervical cancer (17). Some authors wrote that majority of LSIL lesions regress without medical intervention (18). Consequently, over-treatment at early stages should be avoided, especially in young women, and follow-up periods should be encouraged to make HPV clearance and histologic regression successful (19). Our study shows regression of LSIL lesions in 28,9% (N-11) and ASCUS in 29,8% (N-37), but persistence in 52,6% (N-20) with LSIL and 58% (N-72) with ASCUS. Progression lesions in HSIL were found in 10% (N-4) after LSIL and 4% (N-5) after ASCUS of women who were observed. Barken cited that 13% to 16% of untreated LSIL in Denmark would have progressed to cancer (20). In his study Cortes found spontaneous regression of LSIL in 50% and progression in HSIL in 6% in the 2-year follow-up. Other authors found regression of LSIL in 57%, persistence in 32% and progression in HSIL in 11% (21, 22, 23,). Our analysis showed that the regression frequency was significantly lower ( $p < 0,05$ ) in women who had follow-up (28,9%), comparing with the group of women with cryotherapy (87,3%). Cryotherapy prevented progression of LSIL in HSIL and cervical cancer. Difference in progression lesions in HSIL between women with cryotherapy (1,5%) and follow-up (10,5%) after LSIL is not significant ( $p > 0,05$ ), but progression to CIN II occurred after cryotherapy. CIN III or cervical cancer was not found.

## 6. CONCLUSION

Cryotherapy prevents progression of LSIL in HSIL and in cervical cancer because in our study we found that there is a significantly less chance of LSIL progression after cryotherapy. In conclusion cryotherapy is a successful method in prevention of cervical cancer.

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- Authors' contribution: M.J., E.J, M.M, and A.H. were all directly involved in all aspects of research, from study design to reporting. All authors approved the final manuscript.

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