

## CRYOTHERAPY AS A MODALITY FOR TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA

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### Abstract

**Aim:** The study was done to determine the effectiveness of Cryotherapy in treatment of cervical intraepithelial neoplasia I,II and III.

**Background:** Cryotherapy is a time proven ablative method of treating lower grades of cervical dysplasia. It is done using compressed CO<sub>2</sub> or 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. It is performed using a double freeze or single freeze technique. Currently the double freeze technique of cryotherapy is an accepted treatment for mild and focal moderate dysplasia of the uterine cervix.

**Material and Methods:** A clinical observational study was undertaken at a tertiary care teaching hospital on 30 selected patients from the outpatient department of Obstetrics and Gynaecology over a period of 3 years.

**Results:** Overall clinical improvement following cryotherapy was seen in 67.43%. Cure rates in CIN I was 80.9%, in CIN II 71.4% and in CIN III 50.0%.

**Conclusion:** Cryosurgery is an effective treatment of cervical lesions with negligible side effects or minor complications. It is the most favoured ablative technique for treatment of lower grades of cervical intraepithelial neoplasia like CIN I and CIN II.

**Keywords:** Cervical intraepithelial neoplasia, Colposcopy, Cryotherapy.

### 1. Introduction

The word Cryo is derived from the Greek word "Kryos" which means icy cold. Cold has been used for medical purposes since as early as 2500 B.C. when Egyptians first used cold compressors for infected wounds and fractures.

Cryotherapy is done using compressed CO<sub>2</sub> or 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 the ice ball results in crystal formation within cervical tissue, leading to tissue destruction (cryonecrosis).

Cryotherapy is performed using a double freeze or single freeze technique. The double freeze technique involves applying coolant continuously for a 3-min freeze, followed immediately by a 5-min thaw, followed by another 3-min freeze. The single technique consists of continuously freezing for 5-min. Currently the double freeze technique of cryotherapy is an accepted treatment for mild and focal moderate dysplasia of the uterine cervix<sup>1</sup>.

The success of cryotherapy is determined by five factors : patient anatomy, pathology, equipment, technique and physician skill. The location of the lesion, vascular supply and the potential crypt involvement include anatomical variability. The lesion size and severity of disease determine pathologic factors. For cryotherapy to be

effective – entire squamocolumnar junction must be visualized; women with unsatisfactory colposcopy should not be treated with cryotherapy. Also for better results with cryotherapy entire lesion should be visualized and should not go into canal more than 5mm. A minimal lateral spread of freeze of 7mm as 2mm recovery zone and 5mm lethal zone is clinically necessary for satisfactory treatment of CIN<sup>2</sup>.

Cryotherapy is a favoured ablative technique for CIN. Small sized cervical intraepithelial neoplasias (<2.5 cm<sup>2</sup>) respond favourably to cryotherapy but larger lesions (>2.5 cm<sup>2</sup>) have a higher failure rate<sup>3</sup>.

### 1.2 Aims and Objectives

Present study was done to determine the effectiveness of cryotherapy in treatment of cervical intraepithelial neoplasia I,II and III.

### 2. Material and Methods

**Setting** -The prospective study was carried out in the Department of Obstetrics and Gynaecology of tertiary care medical institute of Northern India after approval from Ethical Committee.

**Study populaton:** Thirty selected women who had reported with complaints of contact bleeding per vaginum, excessive or persistent vaginal discharge, irregular vaginal bleeding or spotting and repeated genital infections during the study

period of 3 year, fulfilling the inclusion criteria were enrolled in the study after an informed consent.

Women who were pregnant, who had invasive cervical cancer or in whom the lesions extended into the endocervical canal were excluded.

An informed written consent was taken for each case. After thorough history and clinical examination, Pap smear was taken followed by colposcopy on day 10-12<sup>th</sup>. Colposcopically directed biopsy of abnormal areas was taken and the women were then categorized as having CIN I, CIN II and CIN III. All the women in three groups were treated with cryotherapy by double freeze technique and were followed at regular intervals at 3 months, 6 months for 2 years after cryotherapy to know the effect of cryotherapy on CIN.

### 3. Results

Of thirty women enrolled in the study, 21 had CIN I, 7 had CIN II and 2 had CIN III. On regular follow-up at 6 months after cryotherapy, 17 of 21 (80.9%) women with CIN I showed complete healing of lesions while in 4 (19%) women the lesion healed incompletely. Of 7 women with CIN II, 5 (71.4%) had complete healing while in 2 (28.5%) the lesions were incompletely healed. Similarly in 2 women with CIN III, only 1 (50%) had her lesions completely healed. Thus it shows that cryotherapy is an effective modality of treatment for lower grades of lesions like CIN I and CIN II where as it is less effective in treatment of higher grades of lesions like CIN III and those with larger lesions.

**Table-I: Shows effect of Cryotherapy On Cervical Intraepithelial Neoplasia.**

Grade of CIN	Effect of cryotherapy on CIN after 6 months			Total
	Healed	Incompletely healed	Not healed	
<b>CIN I</b>	17 (80.9%)	04 ( 19%)	00 (0%)	21
<b>CIN II</b>	05 ( 71.4)	01 (14%)	01 (14%)	07
<b>CIN III</b>	01 (50%)	00 (0%)	01 (50%)	02
<b>Total</b>	23	05	02	30

**Table- II: Shows Comparison of Cure Rates of Cryotherapy in various Studies.**

Study	Follow-up months	Cure rates of Cryotherapy by CIN grade (%)			
		All	CINI	CIN II	CIN III
Townsend et al. (1979)	12+	93.0%	100.0%	94.6%	90.6%
Ferenczy (1985)	12	91.2%	97.0%	95.9%	71.0%
Kwikkel et al.( 1985)	18	86.0%	100.0%	75.0%	91.7%
Singh et al. (1988)	3-48	79.1%	86.7%	64.7%	80.0%
Yliskoski et al. (1989)	14-15	56.8%	53.6%	66.7%	-
Berget et al. (1991)	12-80	90.0%	90.0%	90.9%	86.4%
Present study	3-24	76.67%	80.9%	71.4%	50%

Cryotherapy cure rates by grade of CIN appeared relatively consistent across the seven randomized control trials, ranging between 86.0% and 94.6% for all grades, 90.9% to 100% for CIN I lesions, 75.0% to 95.9% for CIN II lesions and 71.0% to 91.7% for CIN III lesions.

### 4. Discussion

Cryotherapy is a time proven ablative method of treating lower grades of cervical dysplasia. In Gynaecology it is employed increasingly for the benign lesions of the lower genital tract. Cryotherapy is also used for the condylomatous lesions of vulva, vagina and also the endometrial hyperplasia, but the principle use of cryotherapy is to the cervix itself. As chronic erosions and ectropion are amongst the commonest gynecological lesions accounting for 80-90% of

patients attending Gynae O.P.D. Cryotherapy is relatively pain free and provides an ideal means of treating these common lesions in the conscious patient.

Cryotherapy is done using compressed CO<sub>2</sub> or N<sub>2</sub>O refrigerant. If an excellent contact between the cryoprobe tip and the ectocervix is achieved, N<sub>2</sub>O-based cryotherapy will achieve -89 degree C and CO<sub>2</sub> based system will achieve -68 degree C at the core of the ice ball and temperatures around -20 degree C at the edges. Cells reduced

to -20 degree C for one or more minutes will undergo cryonecrosis.

For cryotherapy to be effective – entire squamocolumnar junction must be visualized; women with unsatisfactory colposcopy should not be treated with cryotherapy. Also for better results with cryotherapy entire lesion should be visualized and should not go into canal more than 5 mm. A minimal lateral spread of freeze of 7mm as 2mm recovery zone and 5mm lethal zone is clinically necessary for satisfactory treatment of CIN<sup>2</sup>. Various studies have demonstrated that endocervical crypt (gland) involvement of cervical intraepithelial neoplasia (CIN) may penetrate up to 3.8 mm into the cervix. A freeze that causes cell death to 4mm should effectively eradicate 99.7% of lesions with gland involvement. Current recommendations are to produce an ice ball with a 5 mm lateral spread to accomplish this go<sup>4</sup>.

Small sized cervical intraepithelial neoplasias (<2.5 cm<sup>2</sup>) respond favourably to cryotherapy but larger lesions (>2.5 cm<sup>2</sup>) have a higher failure rate<sup>3</sup>.

The Alliance for Cervical Cancer Prevention (ACCP) conducted a systematic review of the literature on the use of cryotherapy as an out-patient treatment option for women with cervical intraepithelial neoplasia (CIN)—the precursor to cervical cancer and concluded that cryotherapy produced an overall cure rate of 89.5 percent. The data suggested that, overall, cryotherapy is as effective as other out-patient treatment methods. It resulted in higher cure rates for less severe lesions (CIN I and CIN II), more severe lesions (CIN III), especially larger lesions extending into the endocervical canal, have lower cure rates<sup>5</sup>.

A similar study was conducted to evaluate the effectiveness and safety of treatment of cervical precancerous lesions by nurses using cryotherapy and concluded that the cure rate for CIN I was 87.4% and for CIN I and CIN II 83.7% which was comparable with our study. They also concluded that cryotherapy is a safe, acceptable and effective treatment for ectocervical CIN lesions involving less than three fourths of the

cervix. It has no serious side effects and long term sequelae<sup>6</sup>.

2001 Consensus Guidelines, support the use of cryotherapy as an acceptable method of treatment of CINI and CIN II / CIN III provided that an appropriate follow-up is conducted.

### Conclusion

Cryotherapy is an effective treatment of cervical lesions with negligible side effects or minor complications. It is sophisticated, safe procedure with predictable uniform action. It has powerful hemostatic action and sealing effect on blood vessels. Healing is rapid and complete following cryotherapy as compared to other methods like electrocoagulation, diathermy cauterization etc.

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