

Comparison of the Effectiveness of Topical Podophyllin, Cryotherapy, CO2 Laser and Cryotherapy + CO2 Laser in Condyloma Acuminata in Females.

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ABSTRACT

Background: Condyloma acuminata, the most common sexually transmitted viral disease of genitalia is caused by Human Papilloma Virus (HPV). **Methods:** The present work was designed as a randomized interventional study during the period from November 2016 to October 2017. **Results:** A total of 80 non pregnant sexually active female patients were included in the study. In this study the mean age of the patients was 23 years. Out of total 80 patients, 67 had affected partners. The mean duration of complete clearance was 3.6 weeks for podophyllin, 4.8 weeks for cryotherapy, 2 weeks for CO2 laser and 1.8 weeks for CO2 laser + cryotherapy. In CO2 + cryo group, complete clearance was seen in all 20 lesions, in CO2 alone group 17 lesions, cryo alone showed complete clearance in 13 patients and in podophyllin group the number was 15. **Conclusion:** This study shows that CO2 laser + cryotherapy is most effective treatment followed by CO2 laser alone and podophyllin.

Keywords: Condyloma acuminata, Human papilloma virus and Interventional.

INTRODUCTION

Condyloma acuminata, the most common sexually transmitted viral disease of genitalia is caused by Human Papilloma Virus (HPV).^[1] In recent times, CA has emerged as a disease of major public concern because of its high prevalence, sexual mode of transmission, its association with various neoplasia, HIV, difficulty in treatment and high rates of recurrence. The worldwide prevalence of infection with Human Papilloma Virus (HPV) in women without cervical abnormalities is 11-12%.^[2] Genital warts are sexually transmitted, with transmission rates of 60%, but materno-fetal transmission may also occur.^[3] The incubation period varies from 2 weeks to 8 months Human Papilloma Viruses comprise a large group of approximately 120 genotypes that infect epithelia of the skin or mucosa and most commonly cause benign papillomas.^[1] Condyloma acuminata are typically caused by HPV 6 or 11 which are considered low risk types. Persistent infection with high risk HPV types predominantly HPV 16 and 18,^[4,5] are the primary and major cause of cervical cancers and a subset of vaginal, vulvar, penile, anal,

oropharyngeal and rarely squamous cell carcinoma of the digits.^[6] Genital warts are associated with adverse psychological effects resulting in decreased quality of life and increasing medical care costs.^[7,8] At present there is no specific antiviral therapy available to cure HPV infection.^[9] Destructive or ablative therapies for genital warts include cryotherapy, Trichloroacetic acid (TCA) application, electrosurgery, curettage, scalpel or scissors excision, laser vaporisation and photodynamic therapy with topical aminolevulinic acid.^[10,11]

It has been estimated that genital HPV infection is present in 30-50% of sexually active adults and of them 1% have genital warts. They present as soft, pink, elongated and sometimes pedunculated lesion, usually multiple, especially on moist surfaces. Sites of involvement include

- Inside the vagina or anus
- Outside the vagina or anus
- Cervix

The treatment of EGW poses a therapeutic challenge. If not treated, they may resolve spontaneously, increase in size or number, or remain unchanged depending upon the patient's immunological status [12]. A wide range of therapeutic options are available for treatment of CA like cytotoxic agents (Trichloroacetic acid, Phenol, Podophyllin, 5-Fluorouracil, Retinoids and Bleomycin), physical ablation (Electrical destruction and Cryotherapy), immunomodulation (Imiquimod, Interferon, purified protein derivative and the HPV

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vaccine) and CO₂ laser. Although a large armamentarium of therapies are available, but no definitive therapy has emerged as the ideal standard of care in the treatment of CA. All methods are fraught with the uncertainty of achieving a complete cure and high possibility of recurrence of lesions. Aim of this present study was to evaluation of the efficacy of topical podophyllin, cryotherapy, CO₂ laser and cryo + CO₂ laser in the treatment of genital warts in females.

MATERIALS AND METHODS

Non pregnant sexually active female patients were included in the study. This clinical study was performed from November 2016 to October 2017 on 80 patients with genital wart in Rama Medical College, Hapur, Ghaziabad, U.P. and A. K. Jha Amar Skin And Laser Institute, Patna. Patients were randomly divided into 4 groups, each having 20 patients. Of the total 80 patients, 20 received podophyllin solution, 20 received cryotherapy, 20 received CO₂ laser and 20 were treated with cryotherapy + CO₂ laser. A solution of freshly prepared topical 25% podophyllin in compound

tincture of benzoin was applied accurately and in enough amount to cover the wart area, adjoining areas were protected by applying petroleum jelly. It was allowed to dry for 10 minutes and washed off after 4 hrs. In cryotherapy the wart and 2mm of the normal surrounding margin were frozen using liquid nitrogen at -196 celsius. In laser therapy group, after local anaesthesia the wart and a 2mm surrounding margin of normal skin were evaporated in focal distance of laser light using CO₂ laser at a fluency of 4.5 J/cm². In the last group the lesions were first subjected to cryotherapy and then to CO₂ laser. Patients whose lesions got cleared completely were observed for upto 8 weeks to evaluate the recurrence. Clinical photographs were taken at each visit.

RESULTS

This study shows that CO₂ laser + cryotherapy is most effective followed by CO₂ laser alone and podophyllin. Mean duration of treatment was also less and recurrence was also less frequent in patients treated with CO₂ laser + cryotherapy [Table 1].

Table 1: Shows the demographic of the patients.

Characteristics	Podophyllin	Cryotherapy	CO ₂ laser	CO ₂ + Cryo
Mean age of the patients	24 ± 1.3yrs	23 ± 0.95yrs	25 ± 0.9yrs	25 ± 1.5yrs
Duration				
< 4 months	06	08	05	08
> 4 months	14	12	15	12

Table 2: Shows the clinical characteristics of the patients.

Location of lesions				
Mons pubis	03	05	01	02
Labia majora	05	02	04	03
Perineum, Perianal	04	03	02	03
Vaginal orifice	08	10	13	12
Complete clearance	15 lesions	13 lesions	17 lesions	20 lesions
Mean duration of complete clearance	4.8 weeks	3.6 weeks	2 weeks	1.8 weeks

There was no significant difference between the four groups with regards to the age. Most genital HPV

infections occur during the first few years after the onset of sexual activity. In this study the mean age of the patients was 23 years. Out of total 80 patients, 67 had affected partner. The primary goal of the treatment is to reduce symptoms and remove symptomatic warts.

The mean duration of complete clearance was 3.6 weeks for podophyllin, 4.8 weeks for cryotherapy, 2 weeks for CO₂ laser and 1.8 weeks for CO₂ laser + cryotherapy. In CO₂ + cryo group complete clearance was seen in all 20 patients, in CO₂ alone group 17 patients, cryo alone showed complete clearance in 13 patients and in podophyllin group the number was 15 [Table 2 & 3].

Table 3: showing clearance of lesions and relapse at 8 weeks

	Podophyllin	Cryotherapy	CO ₂ laser	CO ₂ + cryotherapy
Complete clearance	15	13	17	20
Mean duration of complete clearance	4.8 weeks	3.2 weeks	2 weeks	1.8 weeks
Relapse	08	00	00	00

Table 4: showing side effects

Side effects	Podophyllin	Cryotherapy	CO ₂ laser	CO ₂ + cryotherapy
Erythema	04	06	03	07
Burning/itching	06	07	06	05
Ulceration	02	12	02	02
Secondary infection	00	02	00	00

At the end of treatment, overall side effects were more frequent in cryotherapy group [Table 4].

DISCUSSION

Different treatment modalities have been described for genital warts in females. All of them are associated with advantages and disadvantages. The appropriate treatment modality depends on the number, size and location of the lesions in addition to patient's immunological status. The ideal treatment is one that could clear the lesions completely with a minimal amount of pain, hypo or hyperpigmentation, scars, local and systemic adverse effects in addition to lower recurrence rates that are mostly achieved by physical ablative methods. CO₂ laser and cryotherapy are of those physical ablative treatment methods with less adverse effects and high clearance rates.^[13] Cryotherapy is one of the most effective treatments available for genital warts with clearance rates of about 79-88%.^[14] It is an inexpensive, easy applicable method with rapid destructive effect and no serious systemic side effects that make it a safe therapy in pregnancy. Although, it has some limitations such as risk of vaginal perforation in case of using liquid nitrogen, recurrence in lesions larger than the cryo probe and some local side effects including blistering and local necrosis.^[15] However, hypopigmentation and scar formation are reported rarely.^[15] Healing usually occurs in 1-2 weeks time after cryotherapy, although sometimes complete healing may take more than 2 weeks. Lasers are more complex and costly in comparison to other treatment options for genital warts, however mostly used in refractory external genital lesions.^[15]

Laser therapy needs local anaesthesia in most of the cases however it can be used in extensive and thick lesions effectively as it is able to penetrate the lesions deeper than generally occurs with cryotherapy.^[16] Due to the aforementioned reasons in addition to its painless act, rapid healing, limited rate of complication, infection and recurrence rates, and minimal risk of scarring, it could be considered as a safe and effective therapeutic method for genital warts even in childhood and pregnancy.^[17] Its adverse effects include pruritis, hypopigmentation and scar formation. Disadvantage of the CO₂ laser in comparison with cryotherapy is greater risk of scarring. CO₂ laser + cryotherapy is one of the most effective treatments available with clearance rates of about 80-92%. It has rapid destructive effect with no serious systemic side effects. The recurrence rate was also least (0.05%) with this modality. So it is most appropriate modality for genital warts in females. In a study done by Azizjalali et al,^[18] CO₂ laser was found to be more effective than cryotherapy and it is associated with lesser recurrence rate than cryotherapy (0.05% against 18%) which is comparable with our study (recurrence rate 0.08% against 0.2%).

In a study Bashi et al^[19] found cryotherapy required shorter period for clearance compared to podophyllin (2.3 weeks v/s 4.7 weeks), which is consistent with our study as well (3.6 weeks v/s 4.8 weeks). In a study by Nath et al,^[20] mean time for clearance of lesions with podophyllin was 3 weeks with recurrence rate of 30% in non pregnant females, which is comparable with our study where we had mean duration of clearance of 3.6 weeks with a recurrence of 40%.

CONCLUSION

We concluded from our study that out of the four modalities CO₂ + cryotherapy is the most effective modality with rapid clearance, least side effects and least recurrence rates.

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