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Therapeutic Potential of Topical Combination of Ethinyl Estradiol (50 µg) and Levonorgestrel (250 µg) in the Management of Verruca Vulgaris in a Tertiary Care Hospital: A Prospective Study

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Abstract

Background: Verruca vulgaris is a common cutaneous infection caused by Human Papilloma Virus (HPV). Although several treatment modalities such as cryotherapy, salicylic acid, electrocautery, and immunotherapy are available, recurrence, pain, cost, and treatment resistance remain significant concerns. Recent studies suggest that estrogen and progesterone may exert antiproliferative effects on HPV-infected keratinocytes and modulate local immune responses, thereby facilitating viral clearance.

Aim and Objectives: To evaluate the efficacy of topical application of a combination of Ethinyl Estradiol (50 mcg) and Levonorgestrel (250 mcg) in the treatment of verruca vulgaris and to assess associated adverse effects.

Materials and Methods: A hospital-based prospective study was conducted in the Department of Dermatology, Venereology and Leprosy at Santhiram Medical College and General Hospital, Nandyal, from June 2025 to August 2025. Thirty clinically diagnosed patients with verruca vulgaris aged 5–50 years were included. After obtaining informed consent, paring of the wart was performed. A paste prepared by crushing a combination oral contraceptive pill containing Ethinyl Estradiol (50 mcg) and Levonorgestrel (250 mcg) was mixed with a petroleum jelly and applied topically over the lesion under occlusion for three consecutive days. Patients were assessed after one week and one month.

Results: Among 30 patients, 21 (70%) were males and 9 (30%) were females. Eighteen patients (60%) belonged to the 5–25 years age group. After one week, 15 patients (50%) showed approximately 50% reduction in wart size and verrucosity, 8 patients (26.7%) demonstrated partial resolution of about 20%, and 7 patients (23.3%) showed

no improvement. At one month, complete resolution was observed in 10 patients (33.3%), partial resolution of approximately 50% was noted in 15 patients (50%), while 5 patients (16.7%) showed no response. Adverse effects were minimal and included pruritus in 6 patients (20%) and erythema in 3 patients (10%).

Conclusion: Topical application of Ethinyl Estradiol and Levonorgestrel paste appears to be an effective, inexpensive, and well-tolerated therapeutic option for verruca vulgaris. The treatment demonstrated promising clinical outcomes with minimal adverse effects and may serve as a useful alternative to conventional therapies.

Keywords: Verruca vulgaris, Human Papilloma Virus, Ethinyl Estradiol, Levonorgestrel, Oral Contraceptive Pills, Topical Therapy, Warts.

Introduction

Verruca vulgaris is a benign epidermal proliferation resulting from infection by Human Papilloma Virus (HPV). It is one of the most common viral skin infections encountered in dermatological practice and affects individuals of all age groups, particularly children and young adults.

Human papillomaviruses are non-enveloped double-stranded DNA viruses belonging to the Papillomaviridae family. More than 200 HPV genotypes have been identified, among which HPV types 2, 4, 27, and 57 are commonly associated with common warts. The virus gains entry through minor abrasions in the skin and infects basal keratinocytes. Subsequent viral replication leads to epidermal hyperplasia, hyperkeratosis, papillomatosis, and the characteristic verrucous appearance.

Although spontaneous regression may occur through cell-mediated immunity, many lesions persist for prolonged periods and may spread through autoinoculation. Commonly employed treatment modalities include salicylic acid, cryotherapy, electrocautery, radiofrequency ablation, laser therapy, topical immunomodulators, and immunotherapy. However, recurrence, pain, pigmentary changes, scarring, cost, and the need for repeated treatment sessions remain major limitations.

Recent advances in HPV biology have highlighted the role of sex hormones in regulating HPV-infected epithelial cells. Estrogen receptor α has been shown to be overexpressed in HPV-positive keratinocytes. Experimental studies have demonstrated that estrogen suppresses viral oncogene transcription, inhibits cellular proliferation, reduces cell viability, and promotes apoptosis in HPV-infected epithelial cells.

Progesterone similarly augments apoptosis mediated by HPV proteins E2 and E7. Furthermore, estrogen and progesterone influence local immune responses by decreasing pro-inflammatory cytokines such as IFN-γ, IL-12, and TNF-α while increasing anti-inflammatory cytokines including IL-10 and TGF-β.

These observations provide a scientific basis for the topical use of oral contraceptive pills containing Ethinyl Estradiol and Levonorgestrel in the treatment of cutaneous warts. The present study was undertaken to evaluate the efficacy and safety of this novel therapeutic approach.

Aims and Objectives

- To evaluate the efficacy of topically applied Ethinyl Estradiol (50 mcg) and Levonorgestrel (250 mcg) combination in the treatment of Verruca vulgaris.
- To assess local adverse effects associated with topical application of the hormonal preparation.

Materials and Methods

A hospital-based prospective interventional study was conducted in the Department of Dermatology,

Venereology and Leprosy at Santhiram Medical College and General Hospital, Nandyal, Andhra Pradesh, from June 2025 to August 2025. The study included a total of 30 patients with clinically diagnosed Verruca vulgaris who attended the Dermatology Outpatient Department during the study period. Participants were selected by a convenience sampling technique based on their fulfillment of the eligibility criteria and willingness to participate in the study. Data were collected from patients after obtaining informed written consent. The study was undertaken to evaluate the therapeutic response to the selected intervention in Verruca vulgaris. Ethical clearance was obtained from the Institutional Ethics Committee prior to the commencement of the study, and all patient information was kept confidential in accordance with established ethical guidelines.

Inclusion Criteria

The inclusion criteria for the study comprised patients aged between 5 and 50 years of either sex who were clinically diagnosed with Verruca vulgaris. Only those patients who were willing to provide written informed consent and comply with the prescribed follow-up schedule were enrolled in the study. In the case of participants below 18 years of age, written informed consent was obtained from their parents or legal guardians prior to inclusion in the study.

Exclusion Criteria

The exclusion criteria included patients who were unwilling to participate in the study or comply with the follow-up schedule. Individuals younger than 5 years or older than 50 years were excluded. Pregnant and lactating women, patients with a known allergy to the components of the oral contraceptive pill (OCP), and those with ulcerated or infected verrucae were not considered for inclusion. Patients presenting with genital warts and immunocompromised individuals were also excluded from the study.

Procedure

After obtaining written informed consent from the participants, the wart surface was pared using a sterile surgical blade (Parker No. 15) to remove the overlying hyperkeratotic tissue. The topical paste was prepared by thoroughly crushing a combination tablet containing Ethinyl Estradiol (50 mcg) and Levonorgestrel (250 mcg) into a fine powder and uniformly mixing it with petroleum jelly to obtain a homogenous paste. The prepared paste was applied directly over the pared Verruca vulgaris lesion and covered with a protective adhesive bandage to ensure occlusion. The paste was applied once daily for three consecutive days. Baseline clinical photographs were taken prior to the initiation of treatment for documentation and assessment purposes. Patients were subsequently followed up at the end of one week and one month after treatment, during which clinical evaluation and photographic documentation were performed to assess therapeutic response and monitor for any adverse effects.

Figure 1: Crushing the OCPs and mixing with

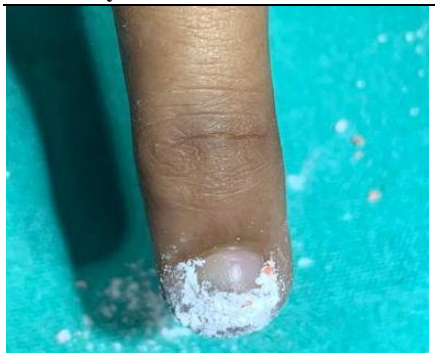


Figure 2: Paste applied over pared wart

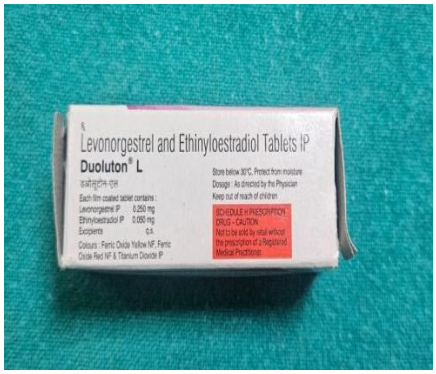


Figure 3: OCPs – Ethinyl Estradiol(50mcg) and Levonorgestrel(250mcg)

Statistical analysis

The collected data were tabulated and analyzed using descriptive statistics. Frequencies and percentages were used to summarize demographic details, treatment response and adverse effects.

Results

Table 1: Age Distribution

Age Group	Number of patients	Percentage
5 – 25 years	18	60%
26 – 50 years	12	40%

Graph 1: Age distribution

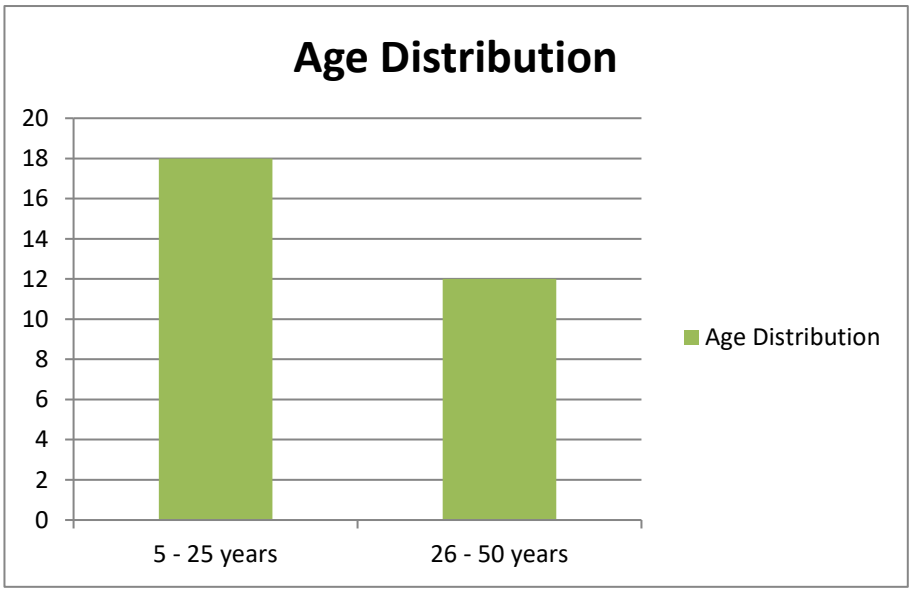


Table 2: Sex Distribution

Sex	Number Of Patients	Percentage
Male	21	70%
Female	9	30%

Graph 2: Sex Distribution

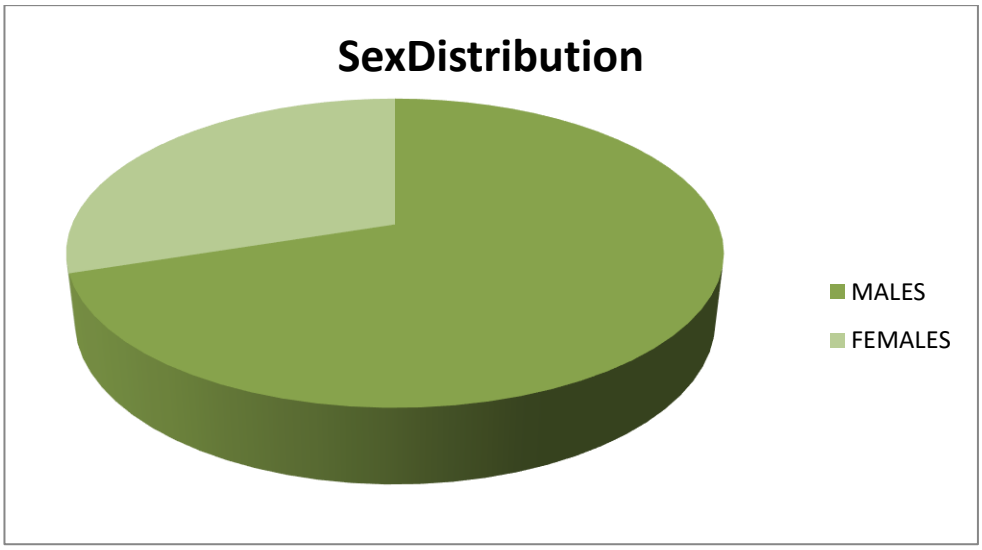


Table 3: Clinical Response After One Week

Response	Number of Patients	Percentage
50% reduction	15	50%
20% reduction	8	26.7%
No response	7	23.3%

Graph 3: Response after 1 week

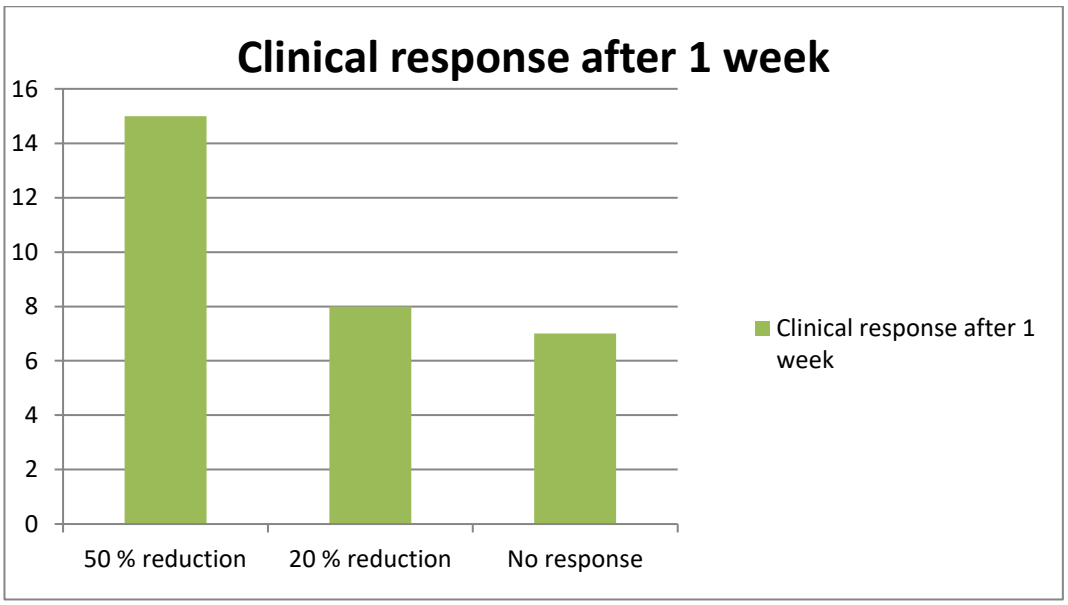


Table 4: Clinical Response After One Month

Response	Number Of Patients	Percentage
Complete resolution	10	33.3%
50% resolution	15	50%
No response	5	16.7%

Graph 4: Response After 1 Month

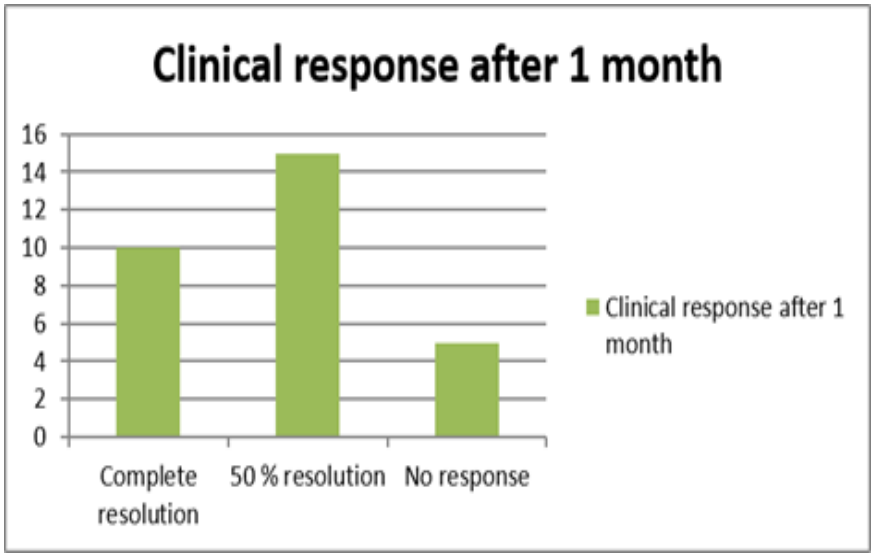
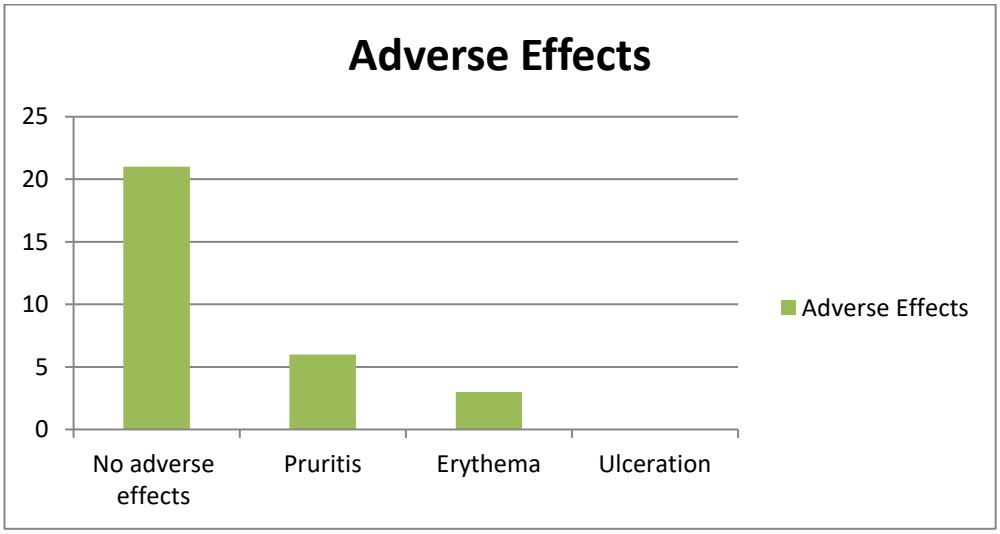


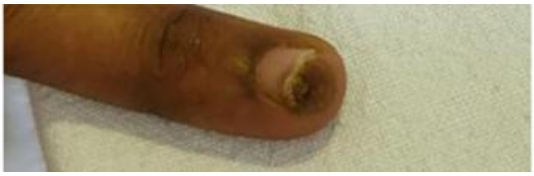
Table 5: Adverse Effects

Adverse Effects	Number of Patients	Percentage
No adverse effects	21	70%
Pruritis	6	20%
Erythema	3	10%
Ulceration	0	0%

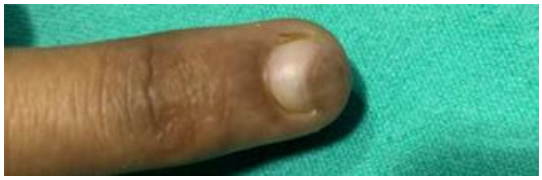
Graph 5: Adverse effects



Patient 1



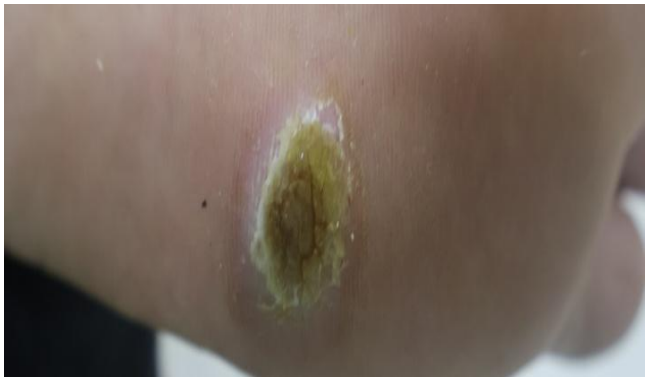
Before treatment



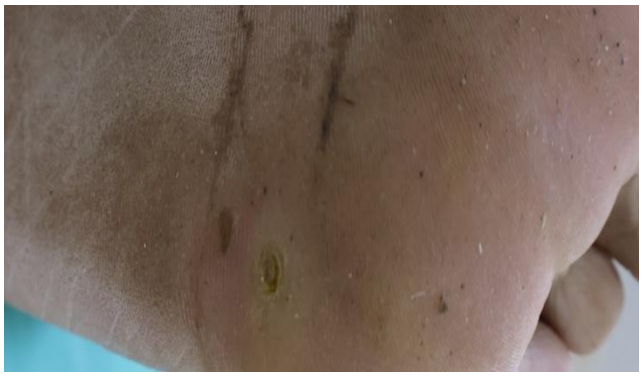
After 1 week

After 1 month complete resolution was seen

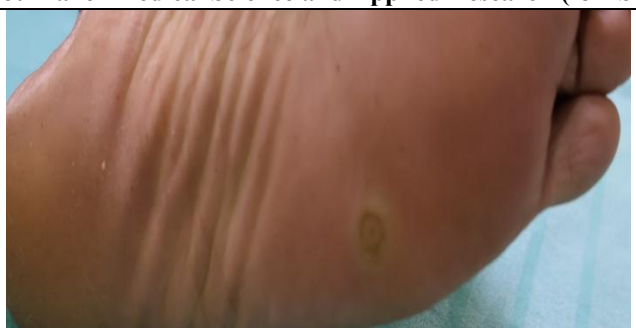
Patient 2



Before treatment

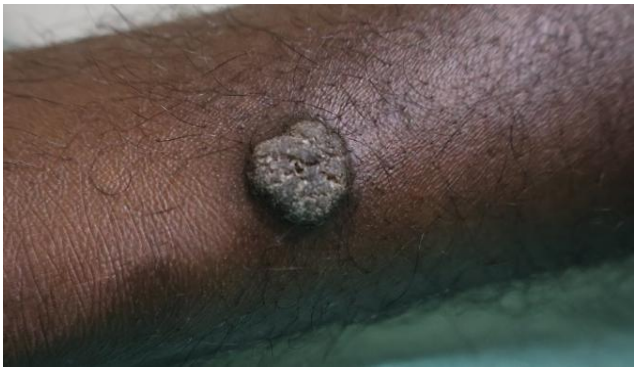


After 1 week

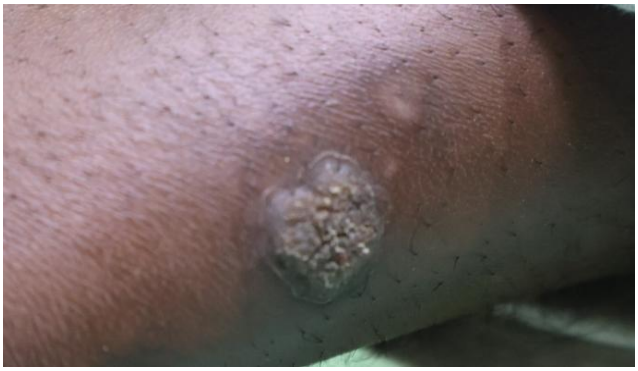


After 1month more than 50% resolution was seen

Patient 3



Before treatment



After 1 month no significant change was seen

Discussion

Management of verruca vulgaris continues to be challenging because of treatment resistance, recurrence, and patient discomfort associated with conventional therapies.

The present study evaluated a novel topical therapeutic approach using Ethinyl Estradiol and Levonorgestrel in the management of Verruca vulgaris.

The majority of patients belonged to the younger age group, reflecting the epidemiology of HPV infection. Male predominance was observed, accounting for 70% of participants.

Clinical improvement was evident in most patients. After one week, 76.7% of patients showed measurable regression of lesions. At one month, complete clearance occurred in 33.3% of patients and partial clearance in 50%.

The therapeutic effect may be attributed to multiple biological mechanisms.

Bristol et al. demonstrated that estrogen attenuates growth of HPV-positive epithelial cells by suppressing viral oncogene expression and reducing cellular proliferation.

Webster et al. demonstrated that estrogen and progesterone enhance apoptosis induced by HPV proteins E2 and E7.

Our findings are comparable with the randomized placebo-controlled trial by Zandi et al., who reported partial resolution in 93.3% and complete clearance in 73.3% of patients receiving topical OCP therapy.

The treatment was well tolerated. Adverse effects were mild and self-limiting. No ulceration, scarring, or secondary infection occurred.

The low cost, easy availability, painless administration, and favorable safety profile make this treatment particularly attractive in resource-limited settings.

Conclusion

The present study demonstrates that topical application of a combination of Ethinyl Estradiol (50 mcg) and Levonorgestrel (250 mcg) is an effective, economical, and safe treatment option for Verruca vulgaris. Significant clinical improvement was observed in the majority of patients, with complete resolution achieved in one-third of cases within one month. The treatment was associated with only mild and self-limiting adverse effects.

Given its affordability, ease of administration, and favorable safety profile, topical hormonal therapy may serve as a valuable alternative to conventional destructive methods, especially in resource-limited settings. Larger randomized controlled trials with longer follow-up periods are warranted to establish long-term efficacy and recurrence rates.

Limitations

- Small sample size (n=30).
- Lack of control group.
- Short follow-up duration.
- HPV typing was not performed.
- Histopathological confirmation was not done.
- Long-term recurrence could not be assessed.

List of abbreviations

HPV – Human Papilloma Virus

OCP – Oral Contraceptive Pill

EE – Ethinyl Estradiol

LNG – Levonorgestrel

IFN – Interferon

TNF – Tumor Necrosis Factor

TGF – Transforming Growth Factor

SPSS – Statistical Package for Social Sciences

DVL – Dermatology, Venereology and Leprosy

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