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Efficacy Safety and Acceptibility of Intralesional Bleomycin in the Treatment of Ungual and Resistant Palmoplantar Warts

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Abstract: ***Aim and Objectives: This study was conducted to evaluate the role of intralesional (IL) bleomycin injection in resistant ungual and palmoplantar warts to know its efficacy and safety. Methodology: It was a Prospective observational study in which Seventeen Patients who met the inclusion and exclusion criteria were included comprising ten males and seven females. Injection Bleomycin was injected to the base of each wart until the lesion was blanched. The amount of injection was determined based on the size of the wart. Patients were checked on for eschar paring at two weeks and, if required, a second dose of bleomycin injection at four weeks. Results: Seventeen patients were enrolled in the study, comprising ten males and seven females, with age between 19 to 51 years. Wart clearance after four weeks of first dose were seen in seven patients, significant response in four, mild response in five patients and no response in one patient. After twelve weeks of treatments fourteen had complete clearance of warts, two had Significant clearance and one patient did not show any response. Most common side effect encountered was pain and burning sensation. Conclusion: Intralesional bleomycin appears an effective and safe treatment for resistant and difficult sites warts even at health institute with limited resources, as no specialized equipment is needed unlike cryotherapy or pulsed dye laser.***

Keywords: Bleomycin, human papilloma virus, intralesional, Palmoplantar, Ungual, electrodissection, cryosurgery

1. Introduction

Skin warts are benign growths induced by HPV infection in keratinocytes, resulting in apparent hyperkeratotic protrusions. All around the world, warts are prevalent and can appear at any age, however they are unusual in infants and the elderly. Over 100 HPV subtypes have been identified, each with a preference for a distinct location on the body.The clinical manifestation of warts varies according to the HPV type and infection site.Warts are often self-limiting and cure spontaneously over months or years, thus they can occasionally be left untreated.For pain, discomfort, functional impairment, aesthetic purposes, and the possibility of cancer, treatment is recommended. Different forms of treatment can be combined, but there is not a single treatment that works for every kind of wart. There is currently little proof that intralesional (IL) bleomycin can effectively treat resistant warts.[1-4] According to some reports, cure rates range from 14% to 99%, indicating positive outcomes.Therefore, we have carried out this study to evaluate the effectiveness, safety, and acceptability of IL bleomycin for treatment of resistant palmoplantar warts or periungual warts.

Aim and Objectives

This study was conducted to evaluate the role of intralesional (IL) bleomycin injection in resistant ungual or palmoplantar warts to understand its efficacy and safety

2. Methodology

It was a Prospective observational study which was done in the Department of dermatology in the tertiary care center of Eastern India from November 2022 to October 2023.The study included 17 patients, 10 of whom were male and 7 of whom were female, with age between 19 to 51 years. Written informed consent was obtained from each patient, and the ethical clearance was taken from ethical committee. Clinical and demographic profile including age, sex, and duration of warts and history of any previous treatment was noted. Throughout every visit, photographic records were maintained.Investigations including complete haemogram, liver and kidney function tests and serology for HIV were carried out at baseline and at the end of the study.

Inclusion Criteria:

1) Patient's age ≥18 years with resistant Palmoplantar or ungual warts who had never received injection bleomycin intralesionally in the past and any treatments in the last 3 months

Exclusion Criteria:

1) Pregnancy, hepatitis, or patients suffering from renal disease.
2) Patients suffering from vascular disorders or Raynaud's phenomenon
3) Patients who received treatment for verruca vulgaris within the previous three months
4) Patients with bleomycin hypersensitivity.
5) Patients who refused to give their consent for the study and did not come for follow up

Injection Technique: The injectable form of bleomycin was obtained in vials containing 15 mg [15 U] of powder. 5 ml of sterile water was required to reconstitute it.Isopropyl alcohol was used to wipe each wart and the surrounding skin prior to injection.To reach a final concentration of 1 U/ml, two parts 2% lignocaine and one part bleomycin preparation were mixed in a 26G insulin syringe.

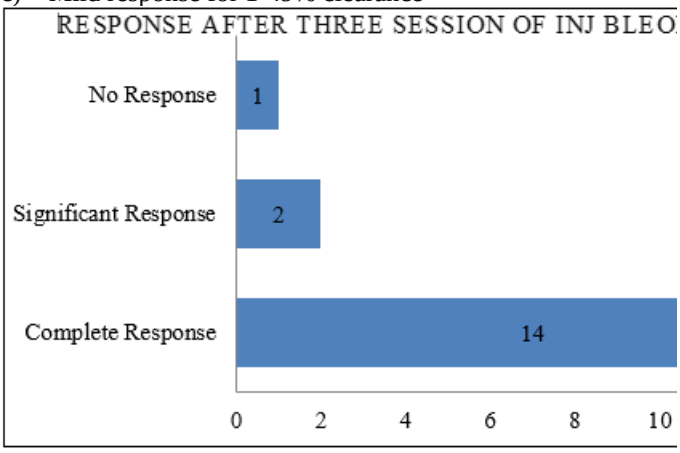
Injection bleomycin was administered at the base of each wart until the lesion was blanched. Depending on the size of the warts, the injection bleomycin dosage was determined. 0.2 ml was injected if the size of the wart was up to 5 mm, 0.5 ml if it was up to 10 mm, and 1.0 mL if it was more than 10 mm in size. The total volume administered during one therapy session was limited to only 2ml.

Assessment and Follow-Up: Patients were checked on for eschar paring and a second bleomycin injection dosage at two and four weeks. The treatment was repeated using the same concentration and technique if the warts persisted or recurred after four weeks from the initial injection.

However, it was not repeated beyond three follow-up sessions. Pain, edema, oozing, crusting, and Raynaud's phenomenon were all reported as side effects of the injection at each subsequent visit. After their last intervention, patients were monitored for three months.

Response was categorized as

a) Complete response for 100% clearance
b) Significant response for 50-99% clearance
c) Mild response for 1-49% clearance
d) No response for 0% clearance



3. Result

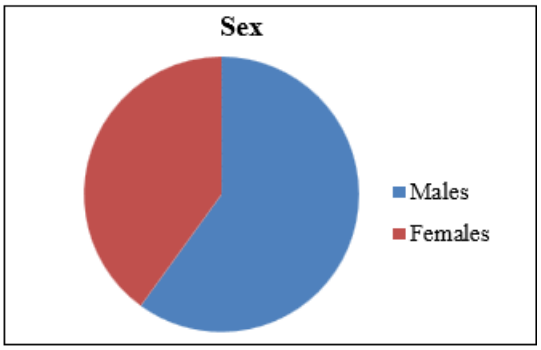
Seventeen patients were enrolled in the study, comprising ten males and seven females, with age between 19 to 51 years. The number of warts lesion varied from 1 to 8, localized over plantar surface in 4 patients, palmar surface in 7 patients,both palmar and plantar surface in 2 patients and ungual in 4 patients. Complete clearance of wart after four weeks of first intervention was seen in seven patients, significant response in four, mild response in five patients and no response in one patient. After 12 weeks of treatments 14 had complete clearance of warts, 2 had Significant clearance and 1 patient did not show any response. Pain and burning sensations were the most common side effects reported by all patients during injection. Seven patients developed hyperpigmentation at the injection site, which faded fully over time. None of our patients had any hematological or biochemical problems at the end of the study, and all the cured patients were quite delighted with the final result. (Likert scale-5)

Response after One Session of Inj Bleomycin Therapy

Response to treatment	No. of patients	Total warts cleared
Complete clearance	7	13
Significant clearance	4	16
Mild clearance	5	14
No response	1	1

Response after three session of inj Bleomycin Therapy

Response to treatment	No. of patients	Total warts cleared
Complete clearance	14	38
Significant clearance	2	5
No response	1	1



Ungual Wart

Blanching after inj bleomycin

Clearance of Lesion after 2 Dose of Inj Bleomycin

4. Discussion

Cutaneous warts are very common conditions seen in dermatology OPD. Although many lesions can be cleared on their own, many people choose to have them treated. It has long been a source of frustration for both patients and clinicians. These warts can greatly impair a patient's quality of life, causing feelings of embarrassment, fear of judgment from others, and irritation due to their persistence and tendency to reoccur.[5]Pain, functional impairment, cosmetic disfigurement, and cancer risk are the most common reasons for therapy.

A large number of treatment options are available for warts including electrodissection[6] cryosurgery[7], and different types of lasers[8-9], However none has proven to be 100% effective. Although bleomycin is yet not approved by USFDA for treatment of warts, it has shown excellent results in the treatment of warts in some studies[10-11]. For the treatment of challenging site-resistant warts, IL bleomycin (1 U/ml) had complete clearance rates of 41.17% and 82.35% following the first and third interventions respectively, in our trial. However, one patient did not show any response.

5. Conclusion

Intralesional bleomycin appears to be a successful and safe treatment for resistant and difficult-to-treat warts, even in health institutes with low resources, because no specific equipment is required, as opposed to cryotherapy or pulsed dye laser. Bleomycin can be simply administered via insulin needle without the use of specialized needles such as bifurcate or monojet needles. Furthermore, no systemic side effects, hematological or biochemical abnormalities were reported following the injections.

6. Limitations of the Study

Small study sample, absence of control group, short term follow-ups and use of only one bleomycin concentration are the main limitations of study

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Declaration of Interest: "The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper."

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