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Research Article

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Research Comparison of The Effectiveness of Wart Immunotherapy with Intralesional Interferon A2b Versus Cryotherapy: A Randomized, Blinded, Parallel-Group Clinical Trial

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Abstract

Objective: Determine the effectiveness of treatment with interferon α2b in patients with recalcitrant warts treated in the Dermatology Outpatient Clinic during the 2022-2023 administration.

Method and instrument: This are an analytical, longitudinal, cohort, experimental and prospective study.

Results: It is concluded that there are significant statistical differences between the number of warts and the treatment used. The side effects of intralesional application of IFN α2b were pain (64%) and necrosis (52%). The IFN α2b group required 5 sessions for complete healing in 50% of cases. The effectiveness of the treatment was 80% for IFN α2b vs 68% for cryotherapy, with no statistically significant differences.

Introduction

Warts are infections manifested as proliferations of the skin and/or mucous membranes caused by DNA viruses known as human papillomaviruses (HPV) [1]. Warts that persist for more than two years or have not responded to at least two different treatment modalities are termed recalcitrant warts [2].

There are approximately 80 HPV serotypes. High-risk oncogenic HPV types (16, 18, 31, 33, 35, 45, 51, 52, 58, 59) are most prevalent in Africa and Latin America, with HPV 16 being the most common worldwide [3,4]. The latency period after inoculation is approximately 2–9 months. The most frequent types of warts include common warts, flat warts, palmoplantar warts, periungual warts, filiform warts, and condyloma acuminatum [1].

Diagnosis is clinical and can be confirmed by polymerase chain reaction (PCR). Treatment options include topical applications of salicylic acid and retinoic acid, cryotherapy, intralesional bleomycin, imiquimod, electrocoagulation, electrosurgery, and retinoids [1].

Immunotherapy for recalcitrant warts includes topical imiquimod, bleomycin, intralesional application of vitamin D3, purified protein derivative (PPD), tuberculin, Candida albicans extract, interferon alpha-2b, and systemic supplements such as zinc, propolis, and echinacea. The cure rate for various immunotherapy treatments (intralesional, topical, and systemic) reaches up to 60%, noting that no treatment is 100% effective [5].

Interferon alpha-2b is a group of proteins that prevent viral replication or help virus-infected or tumor cells to die. Among its mechanisms of action, interferon alpha-2b has immunomodulatory, antiproliferative, anti-apoptotic, and regulatory effects. It is used for various conditions, including skin cancers (melanoma and non-melanoma), mycosis fungoides, Kaposi's sarcoma, granulomatous disease, and non-dermatological diseases such as hepatitis B and C [6,7,8].

It can be administered topically, systemically, subcutaneously, or intralesionally. Intralesional use is performed with prior topical anesthesia, using 300,000 IU at a frequency of once every 14 days for approximately seven applications. The injected wart shows signs of involution, such as loss of hyperkeratosis, perilesional edema and erythema, and loss of pain. When these changes occur, administration is discontinued [3].

Adverse reactions include pain at the injection site, pharyngitis, viral infection, nausea and vomiting, growth retardation, worsening of suicidal thoughts, necrosis at the injection site, melena, nasal bleeding, and psoriasis. It is contraindicated in patients with hypersensitivity, hepatic or renal insufficiency, children and adolescents with depression and suicidal ideation, transplant recipients, seizures, and epilepsy. Interactions have been observed with neurotoxic, cardiotoxic drugs, and theophylline [9].

Materials and Methods

This study is a randomized, non-inferiority controlled trial with two arms. It is analytical, longitudinal, cohort-based, experimental, and prospective in design. The trial was conducted at a medical center of the National Health Fund (Caja Nacional de Salud), specifically at the PAISE Polyclinic in La Paz, Bolivia.

Inclusion Criteria:

- Patients aged between 18 and 70 years.
- Presence of recalcitrant warts measuring between 5 and 10 mm in diameter.
- Preserved mental faculties.
- Immunocompetent status.

Exclusion Criteria:

- Patients with severe systemic diseases.
- Pregnant women.
- Individuals participating in other wart-related studies.

The total population considered for the study comprised 300 patients. A sample size of 25 patients per group (totaling 50 patients) was calculated. This calculation was based on an anticipated complete wart elimination rate of 80% with intralesional interferon alpha-2b (IFN α2b) and an assumed 60% elimination rate with cryotherapy, with a non-inferiority margin set at 15%. The sample size determination employed the non-inferiority formula as outlined in relevant literature.

The study was self-funded. The instrument utilized was IFN α2b at a concentration of 3,000,000 IU, adjusted to 300,000 IU per intralesional application. Each patient received between 3 to 5 intralesional applications. Prior to administration, patients provided written informed consent. A total of 5 to 10 injections were administered at two-week intervals.

All participants underwent the study procedures after providing both written and verbal informed consent.

Results

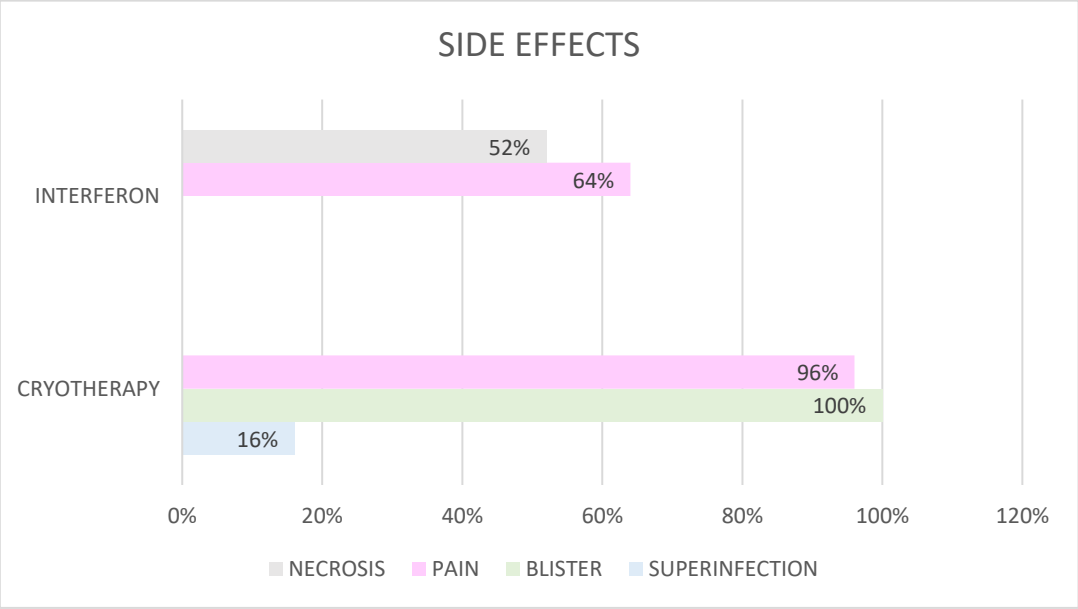
Table 1: Sociodemographic Characteristics of The Case Series.

GROUP	Variable	% (n)	p value
INTERFERON (25)			
	Female	40% (n=10)	0,57
	Male	60% (n=15)	
CRYOTHERPY (25)			
	Female	52% (n=13)	
	Male	48% (n=12)	
AGE	Group	media ± DE	p value
	Cryotherapy	35 ± 15,74	0,12*
	Interferon	42,6 ± 17,99	

Own elaboration.

Of the 50 patients studied, 25 were treated with IFN α2b and 25 with cryotherapy. The first group was predominantly female, with a mean age of 43 years, and the second group was predominantly male, with a mean age of 35 years (Table 1).

Chart 1: Bar chart, side effects of intralesional interferon alpha 2 beta treatment vs cryotherapy



Own elaboration.

All cases presented side effects (Chart 2), however, cryotherapy presented pain, superinfection, blisters, and erythema as side effects. In the intralesional IFN α2b group, we saw two predominant side effects: pain in 64% (n=16) and necrosis in 52 (n=13).

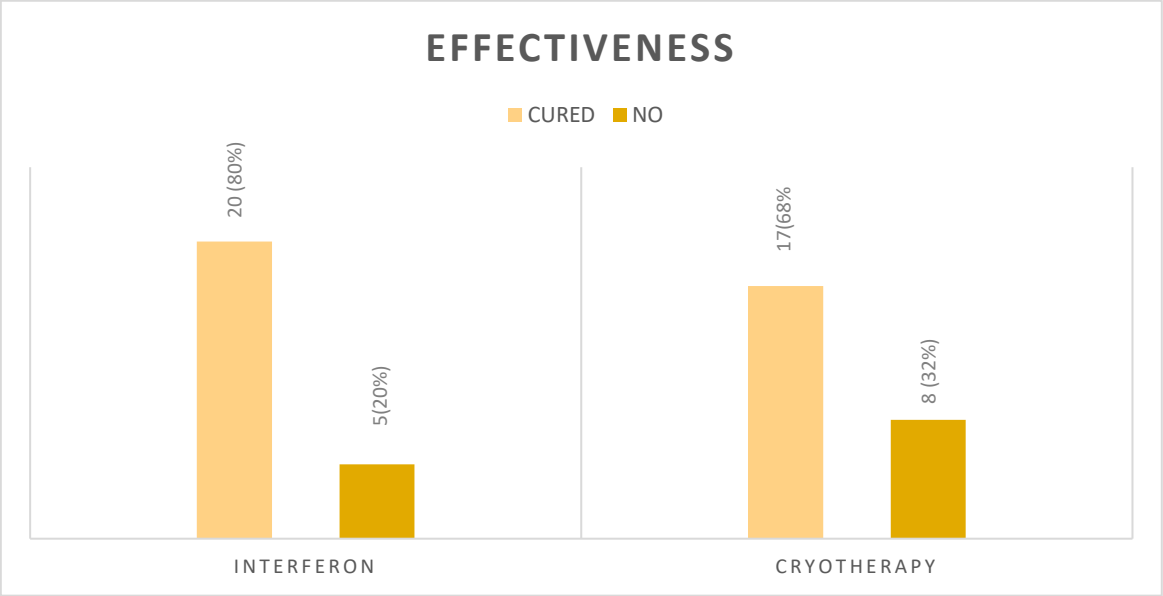
Table 2: Number of sessions required for the healing of recalcitrant warts in patients with intralesional interferon alpha 2 beta vs cryotherapy.

Grupo		**media ± DE**	**p valor**
Number of sessions required			
Cryotheraphy		2,8 ± 2,02	<0,001*
Interferon		5,8 ± 2,61	

Own elaboration.

In the cryotherapy group the number of sessions required was 2.8 and in the intralesional IFN α2b group it was 5.8 sessions.

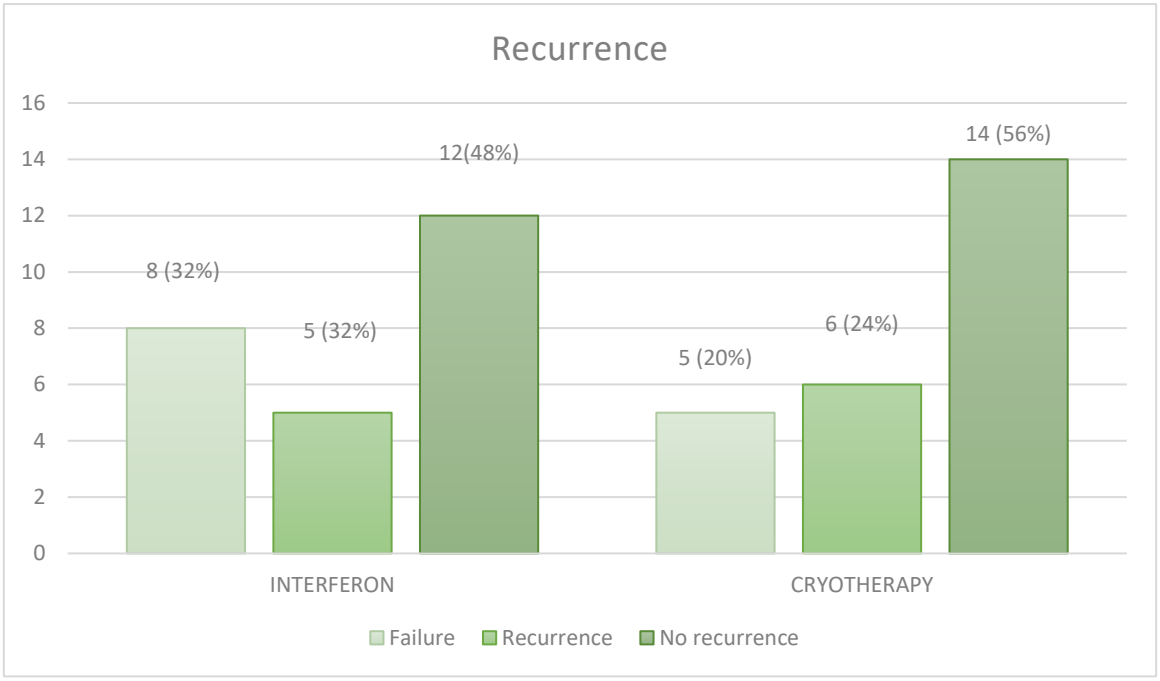
Chart 2: Effectiveness of the outcome of treatment with intralesional interferon α2b, in the case series.



Own elaboration.

Regarding the results of treatment with intralesional IFN α2b: 80% (n=20) were cured, with a 20% (n=5) failure rate. In the interferon cryotherapy group, the cure rate was 68% (n=17). No statistically significant differences were observed.

Chart 3: Bar chart showing recurrence at 6 months after treatment in both groups (cryotherapy vs. intralesional interferon alpha 2 beta).



Own elaboration.

In the intralesional interferon alpha-2b (IFN α2b) group, 20% of cases (n=5) experienced treatment failure. Conversely, the cryotherapy group exhibited a higher failure rate, with 32% of cases (n=8) not responding to treatment. Regarding recurrences among successfully treated patients, the IFN α2b group reported 6 cases, representing 24% (n=6) of the successful treatments. In the cryotherapy group, there were 5 recurrences, accounting for 20% (n=5) of the successful cases.

In terms of sustained treatment success without recurrence, the IFN α2b group achieved this in 14 cases, constituting 56% (n=14) of the total. The cryotherapy group had 12 such cases, representing 48% (n=12) of the total. These findings suggest that while both treatments have comparable rates of sustained success.

Discussion

In the intralesional interferon alpha-2b (IFN α2b) group, treatment failure occurred in 20% of cases (n=5). Conversely, the cryotherapy group exhibited a higher failure rate, with 32% of cases (n=8) not responding to treatment [3].

Regarding recurrences among successfully treated patients, the IFN α2b group reported 6 cases, representing 24% (n=6) of the successful treatments. In the cryotherapy group, there were 5

recurrences, accounting for 20% (n=5) of the successful cases [11].

In terms of sustained treatment success without recurrence, the IFN α2b group achieved this in 14 cases, constituting 56% (n=14) of the total. The cryotherapy group had 12 such cases, representing 48% (n=12) of the total [6].

These findings suggest that while both treatments have comparable rates of sustained success, the IFN α2b group demonstrated a lower overall failure rate compared to the cryotherapy group.

Conclusions

- The effectiveness of intralesional interferon alpha-2b (IFN α2b) treatment was 80%, compared to 68% for cryotherapy, with no statistically significant differences. Males were more frequently represented in the IFN α2b group (60%).
- Treatment of recalcitrant warts with intralesional IFN α2b resulted in a 24% recurrence rate, while cryotherapy had a 20% recurrence rate post-treatment.
- The most common side effects associated with intralesional IFN α2b were pain and necrosis.
- The number of sessions required for complete lesion clearance with intralesional IFN α2b varied; 50% of patients needed five or more sessions.
- To date, there is no treatment that guarantees 100% efficacy in curing common or recalcitrant warts. Therefore, the use of combination therapies may improve cure rates and reduce recurrence.

Conflict of Interest

The drug was obtained from the Argentine company Biosidus.

Bibliography

1. Arranz F. Las verrugas. Medicina Integral, 2001. 37 (9).
2. López-López D, Agrasar-Cruz C, Bautista-Casasnovas A, et al. Aplicación de cantaridina-podofilotoxina-ácido salicílico en las verrugas plantares recalcitrantes. Un estudio preliminar. Gac Med Mex. 2015;151 (1):14-19.
3. Recovered on 13 de abril de 2024, de http://chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://docs.bvsalud.org/biblioref/2022/02/195495/dermatol-pediatr-latinoam-2013-v11-n1 -p37-41.pdf
4. Rivera Z. René, Aguilera T. Jorge, Larraín H Angélica. EPIDEMIOLOGIA DEL VIRUS PAPILOMA HUMANO (HPV). Rev. chil. obstet. ginecol. [Internet]. 2002 [citado 2022 Nov 09]; 67(6): 501-506. Disponible en: http://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0717-75262002000600013&lng=es. http://dx.doi.org/10.4067/S0717-75262002000600013.
5. Thappa DM, Chiramel MJ. Evolving role of immunotherapy in the treatment of refractory warts. Indian Dermatol Online J. 2016 Sep-Oct;7(5):364-370. doi: 10.4103/2229-5178.190487. PMID: 27730031; PMCID: PMC5038096.
6. Hyun Jeong Ju, Hye Ree Park 1, Ji YOon Kim, Gyong Moon Kim, Jung Min Bae, Ji Hae Lee. Inmunoterapia intralesional para pacientes no genitalesletras: Una revisión sistemática y un metanálisis. 2022. Rev Ind Dermatologia: 88 (6):1-7.
7. Chandler, D.; Bewley, A. Productos biológicos en dermatología. *Productos farmacéuticos* **2013**, *6*, 557-578. https://doi.org/10.3390/ph6040557
8. Bolognia J. Dermatologia. 4ta edición. España. ElSelvier; 2018.
9. Bioferon. Interferon alfa 2 beta humano recombinante. Biosidus. Septiembre 2021.
10. Zhong B. How to Calculate Sample Size in Randomized Controlled Trial? J Thorac Dis [Internet]. 2009 [cited 2022 Dec 1];1(1):51. Available from: /pmc/articles/PMC3256489.
11. Potin M, Dahbar M, Chinchilla D, Alberto M, et al. Tratamiento de verrugas múltiples con interferón alfa 2b subcutáneo. Estudio prospectivo en 23 pacientes.2016. Dermatología Argentina. 22 (1).