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Original Article

Comparing the Efficacy of Intralesional Verapamil Hydrochloride vs Triamcinolone Acetonide in Treatment of Keloids/ Hypertrophic Scars

Rozeena Tumrani, Malik Muhammad Hanif, Tahir Hassan, Nazia Hanif
Department of Dermatology, Sheikh Zayed Medical College/ Hospital, Rahim Yar Khan.

Abstract

Objective: To compare the mean VSS score of intra lesional Verapamil Hydrochloride vs Triamcinolone Acetonide in treatment of keloids/ hypertrophic scars.
Study type, settings & duration: This non randomized controlled trial was conducted in Sheikh Zayed Hospital, Rahim Yar Khan from July 2019 to June 2020.
Methodology: In this study the cases of either gender and age more than 12 years were included irrespective of duration of keloid via non probability consecutive sampling. A total of 100 cases were included. The cases were divided into two equal groups by lottery method. The cases in group A were treated with intralesional Triamcinolone (40mg/ml) while group B was treated with intralesional Verapamil (2.5mg/ml).In both groups, session was repeated every 3 weeks for a maximum of 8 sessions or until complete flattening of the scar. Patients were accessed on the basis of Vancouver scar scale (VSS). VSS score was compared between both groups pre and post treatment.
Results: The mean age in group A and B was 22.16±9.01 vs. 22.68±8.93 years respectively (p =0.49). The mean duration of keloid or scar was 6.58±1.54 months in group A and 6.46±1.42 in group B with p =0.31.VSS score after treatment was 2.41±1.19 vs 1.65±0.93 with respect to change in Pliability score and it was 1.61±0.81 vs 1.25±0.72 in terms of height in Verapamil vs Triamcinolone group with p values of 0.05 and 0.04 respectively.
Conclusion: There is statistically significant difference in Triamcinolone group with respect to change in Pliability score and height as compared to Verapamil.
Key words: Keloid, triamcinolone, verapamil, VSS.

Introduction

Keloids are not uncommon and are often seen in the Dermatological out patients to seek medical care. They are usually firm and tender sort of nodules and are commonly seen in upper part of the body and face.[1]The most common site is ear and especially ear lobules. Blacks and Asian population has higher tendency for its development. They are non-malignant lesions and are seen as a sequel of trauma, surgery, burn or inflammatory changes that have characteristic growth that goes beyond the margins of early lesions.[2]

Pathophysiology for its development is complex. Keloids comprises of enhance inflammatory and fibrotic deposition and has HLA association. The incidence is higher in cases with wound healing by secondary intention especially when healing time is more than 3 weeks. Apart from mild tenderness, the major concern is cosmetic disfigurement and also the partial dysfunction of the affected area and hence impact the quality of life.[3-4] The diagnosis is usually clinical and does not require any invasive workup. They are categorized on the basis of different severity scales; out of which Vancouver scar scale (VSS) is the salient one. VSS is a well developed and most commonly used scoring system for keloid/ hypertrophic scar grading system which has 0 to 13 points and depends upon the assessment of various variables i.e. vascularity, scar height, thickness, pliability and degree of pigmentation each carrying their own numbers according to severity. Operator dependency is the only concern; yet it is most widely used globally.[5]

Corresponding Author:
Rozeena Tumrani
Department of Dermatology
Sheikh Zayed Medical College/ Hospital, Rahim Yar Khan.
Email: r.tumrani@gmail.com

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Authors Contribution

MMH conceptualized the project. NH did the data collection. TH performed the statistical analysis and literature search. Drafting, revision & writing of manuscript were done by RT.

There are wide variety of treatment modalities, each carrying their own benefits and side effect profiles. These include topical gels, lasers, radiotherapy, intra lesional injections of triamcinolone, verapamil, steroids, interferon,[5] fluorouracil, imiquimod, flurandrenolie etc, cryosurgery and surgical excision.[4] The limitation regarding their usage is cost of the treatment and side effect profile. Surgical intervention is invasive and radiotherapy carries the risk of carcinogenecity.[6]

Steroids are still practiced as an anti inflammatory agent in the treatment of keloids by inhibiting the propagation of various inflammatory markers like FGF, PDGF. Triamcinolone acetonide (TAC) is the most commonly used intralesional corticosteroid for keloid treatment and is cheap and easily available with comparable efficacy.[7-8]

The data regarding the calcium channel blockers i.e. verapamil is also promising and works on the principle that they reduced the extracellular matrix production.[9-10] According to a study done by Saki et al, there was significant decrease in mean height of keloid/ scar which was 4.04±1.92 in verapamil group vs 2.97±2.07 in triamcinolone group at 6 weeks.[10]

Steroids are most commonly practiced and cheaper but have a side effect profile. In contrast to this, verapamil is relatively safer and has also shown reassuring results. There were very few studies where they were compared directly for outcome, rather these drugs were compared with other agents used for this disease. This study was therefore planned to compare these two to find the better one to decrease morbidity in such cases.

Methodology

This was a non randomized controlled trial, that was carried out during July 2019 to June 2020 at Sheikh Zayed Hospital, Rahim Yar Khan. In this study the cases of either gender and age more than 12 years were included irrespective of duration of keloid via non probability consecutive sampling. Majority of the cases that were excluded were either taking active treatment for Keloids with any of the other drug or were residing in far flung area and therefore follow up was not possible. The sample size of 110 (55 in each group) was calculated by keeping the confidence interval as 95%, power equal to 80% and 1:1 ration of both groups and mean height of keloid/ scar as 4.04±1.92 in verapamil group vs 2.97±2.07 in triamcinolone group at 6 weeks. There were 5 cases lost on follow up in each group and hence final data was collected as 50 in each group.

The cases were divided into two equal groups by lottery method. The cases in group A were managed with Triamcinolone and those in B with verapamil.

Before the therapy injection lignocaine was used as local anesthetic agent and then intra lesional injection i.e. Verapamil (2.5mg /ml) in group B and triamcinolone (40mg/ml) in group A every 3rd week and total eight injections were injected three weeks apart; or complete recovery was seen in the form of flattening of the lesions; whichever comes the first by using insulin syringes under full aseptic measures. Scar evaluation at each stage was done by same researcher on the basis of Vancouver scar scale (VSS).The mentioned scale scores the scars on 4 parameters: height, vascularity, pliability, and pigmentation. Scar height was accurately measured with a ruler in millimetres. Scar vascularity and pigmentation were assessed by visual inspection. Scar pliability was subjectively assessed by palpation. Out of total score 13, the cases were scored and cases with at least score of more than 5 were included. Final Vancouver scare scale (VSS) was assessed at 24 weeks of treatment and compared for both groups. Both the researcher and the data analyser were blinded in terms of the type of drug in each group.

The data was assessed by using SPSS version 24. Frequency and percentages were calculated for categorical data and mean and standard deviation for numerical data as it was normally distributed. Independent sample t test was used for numerical data like age, weight and duration of keloid/scar. Pre and post treatment VSS score was compared by using independent sample t test and p value of equal or less than 0.05 was taken as significant.

The Ethical approval was obtained from Ethical Review Committee of Sheikh Zayed Hospital, Rahim Yar Khan.

Results

In this study, a total of 100 cases were enrolled, 50 cases in each group. The mean age in group A and B was 22.16±9.01 vs 22.68±8.93 years respectively (p =0.49). The mean duration of keloid or scar was 6.58±1.54 months in group A and 6.46±1.42 in group B with p =0.31 as in Table-1. VSS score before treatment with respect to individual variables is shown in Table-2. VSS score after treatment with respect to individual variables is shown in Table-3. This difference was statistically significant in Triamcinolone group with respect to change in Pliability score and height with p values of 0.05 and 0.04 respectively.

Table 1: Study Variables. (n= 50 each)

Study Variables	*Group A*	*Group B*	*p value*
Age (years)	22.16±9.01 (range 10-40)	22.68±8.93 (range 12-36)	0.49
BMI (kg/m^2)	24.94±3.90 (range 20-31)	25.04±3.06 (range 20-32)	0.23
Duration of keloid/scar (months)	6.58±1.54 (range 4-9)	6.46±1.42 (range 4-9)	0.31

Table 2: Pre treatment VSS Score in both groups. (n= 50 each)

Variables	*Group A*	*Group B*	*p Value*
Vascularity	2.16±0.62 (range 0-3)	2.16±0.76 (range 0-3)	0.36
Pigmentation	1.39±0.61 (range 0-2)	1.53±0.58 (range 0-2)	0.75
Pliability	2.76±1.18 (range 0-5)	2.71±1.32 (range 0-5)	0.60
Height	2.18±0.73 (range 0-3)	1.92±0.85 (range 0-3)	0.54

Table 3: Post treatment VSS Score in both groups. (n= 50 each)

Variables	*Group A*	*Group B*	*p Value*
Vascularity	1.80±0.74 (range 0-3)	1.69±0.79 (range 0-3)	0.50
Pigmentation	1.16±0.59 (range 0-2)	1.22±0.61 (range 0-2)	0.52
Pliability	2.41±1.19 (range 0-5)	1.65±0.93 (range 0-5)	0.05
Height	1.61±0.81 (range 0-3)	1.25±0.72 (range 0-3)	0.04

Discussion

Hypertrophic scars and keloids are great cause of cosmetic disfigurement and mild functional dysfunction of the area involved and are result of enhanced inflammatory response due to unknown cause. They need early and prompt treatment to decrease further physical and psychological morbidity. There is always a need for better, safer and cheaper agent with minimal side effect profiles. Verapamil and triamcinolone are showing promising results for keloid treatment.[11-12]

In the present study, the efficacy was better in the Triamcinolone group with respect to change in Pliability score and height with *p* values of 0.05 and 0.04 respectively. The data regarding one to one comparison was lacking in previous studies. According to a recent randomized controlled trial to compare these two agents in terms of all the four variables of VSS it was seen that triamcinolone was better than verapamil in terms of height and pliability with *p* values of < 0.001 each but no statistically significant difference was noted in terms of vascularity and pigmentation.[10] Similarly, according to another study done by Shanthi et al, revealed reduction in size and vascularity of the keloids and scars with both of these agents and in one to one group. They also found triamcinolone as better agent than verapamil, however they didn't show good efficacy in terms of pigmentation.[5]

There was lack to data in terms of efficacy as overall tool to show efficacy; rather one to one variables were compared for assessment of VSS. However, individually and in comparison with other drugs, both of these agents have shown efficacy in good number of cases with minimal side effect profiles.[13-15] They further described that overall speed of reduction of the lesion was also better with Triamcinolone as compared to intralesional verapamil; though this difference was not statistically significant.

The study done by Ahuja et al also described that triamcinolone proved to be a better and faster agent to heal the keloids, but they lacked a statistically significant difference in both of these agents.[6]

According to a meta analysis done by Leventhal D et al to analyse the efficacy of different modalities tried for keloids and scar it was seen that data has supported Triamcinolone as drug with highest efficacy moreover, mean time taken to cure keloids and scars was also high; with no major side effect profiles.[16]

However, Ogawa found the surgical resection as the best treatment for keloids.[11]

In another study to label the efficacy in keloids and hypertrophic scars a randomized controlled trial was carried out by Abedini R et al where they compared similarly intralesional verapamil and triamcinolone and it was observed that 100% efficacy assessed on the basis of Vancouver scar scale (which was used in present study) was achieved by only Triamcinolone group as compared to verapamil.[17] This difference in efficacy of 100% in their study and 68% in present study can be due to difference in the operational definitions regarding efficacy.

Similar comparison was done by the study of Zamanian A et al where they found that intra group both of these agents led to significant reduction in size of lesions and other improvement parameters like erythema and pigmentation and triamcinolone was overall better drug but no significant difference was seen in both the groups. Similarly in the present study photographic evidence revealed clear improvement in both groups; yet triamcinolone was better in terms of VSS assessment. Furthermore, on confabulation of data regarding the confounders i.e. age and sex in their

study, they didn't found any significant association with any of these in both groups.[18]

In a study done by Saleem F et al where they compared a combination of [5] Fluoruracil along with triamcinolone versus triamcinolone only they found that the combination therapy led to efficacy in 98% of the cases as compared to TCA alone in 62% with p =0.001.[19] The data for comparison regarding variables like BMI and duration for its impact on outcome was not found.

There statistically significant difference in Triamcinolone group with respect to change in Pliability score and height as compared to Verapamil.

Conflict of interest: None declared.

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