COMPARISON OF EFFICACY OF INTRALESIONAL TRIAMCINOLONE ACETONIDE VERSUS COMBINATION OF INTRALESIONAL TRIAMCINOLONE WITH 5-FLUOROURACIL IN TREATMENT OF KELOIDS: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Objective: To determine the efficacy of conventionally used Triamcinolone Acetonide (TCA) in the treatment of keloids versus its combination with 5 fluorouracil (FU).

Methodology: In this randomized control trial, 60 patients were included 30 in each group. A combination of triamcinolone and 5-FU was given to Group-A while Group B was administered intralesional triamcinolone in combination with 5 FU. The Efficacy was deemed as positive if post-treatment was a more than 70 % reduction in Patient and Observer Scar Assessment Scale (POSAS) from baseline.

Results: Mean age of the patients was 33.6±8.8 and 32.1±8.8 years in group-A and B, respectively. There were 12 males (40%) in group-A and 14 (46.7%) in group B. Females were 18 (60%) in group-A while 16 (53.3%) were in group B. Most of the patients were having Fitzpatrick skin type 4 in both groups. Efficacy was found to be 28 (93.3%) in group-A and 19 (63.3%) in group B (p=0.005). Stratification for age, gender, and Fitzpatrick skin type was also carried out.

Conclusion: This study concluded that the intralesional TCA was effective in 63.3% and a combination of intralesional 5-FU and TCA was effective in 93.3% of cases of keloids. This difference in efficacy is statistically significant (p=0.005).

Keywords: Fluorouracil; Hypertrophic Scars; Keloids; Triamcinolone Acetonide.

INTRODUCTION

The word "keloid" is derived from the Greek word `cheloid" meaning crab pincers.[1] Keloid and hypertrophic scars occur due to aberrant wound healing. It is a benign, fibroproliferative dermal tumor resulting from excessive deposition of scar tissue beyond the wound margins, invading the normal skin. It can occur spontaneously or after injuries to the skin such as piercing, scratching, acne, burns, and vaccination in genetically susceptible individuals.[2] These shiny, firm tumors with well-demarcated borders and irregular margins pose problems to both dermatologists and patients due to pain, pruritis, infection, cosmetic disfigurement, and recurrence associated with them. They occur equally in both genders, mostly between the ages of 10 to 30 years and the most common sites of involvement are mid chest, back, shoulders and earlobes.[3] Keloids are most commonly seen in African American, Asian and Hispanic populations, and an incidence of 6 to 16% has been reported in Africans.[3] Many treatment options are available for the reatment of keloids, the first line being intralesional triamcinolone injection, others include use of bleomycin, cryotherapy, pulsed dye laser, verapamil, silicone sheeting, tamoxifen and tacrolimus but none of treatment options has proved to definitely cure them and remain a challenge for dermatologists.[4] The excision of keloid leads to an even a bigger keloid and recurrence.[5-12] Triamcinolone acetonide which is a short acting steroid, has been used as gold standard until now but its efficacy is 71.23% and keloid recurs in 50% cases after 5 years of treatment. Triamcinolone acetonide (TCA) inhibits protein synthesis and fibroblast migration but causes atrophy of skin, pigmentation when used for a longer period.[6] 5-Fluorouracil is an antimetabolite which blocks synthesis of pyrimidine thymidine which is a nucleoside important for DNA synthesis and causes death of rapidly dividing

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cells.[7] A combination of 5 FU with triamcinolone showed the efficacy of 98% vs 62% of steroid alone.[8] 5 FU causes faster flattening of the scar as documented by several published studies but causes pain and skin ulceration when used solely. Khan et al found good to excellent results in 84% of patients receiving triamcinolone and a combination of 5 fluorouracil as compared to 68% in a group receiving triamcinolone alone.[9] In 96% of cases a combination of 5FU and TCA showed excellent results in contrast to TCA alone 72% of cases as reported by Sharma et al.[10] The rationale of the study is to achieve better results in the treatment of keloids in our local population as no such study has been conducted on our local population in the last 5 years. Patient and observer scar scale assessment is used in which both the dermatologist as well as patient will assess the keloid while other studies conducted have focused mainly on the appearance of a scar, we will also focus on the reduction of symptoms. Moreover, the results of the study will be shared with other health care professionals.

METHODOLOGY

This randomized controlled study took place at Lady Reading Hospital Peshawar's Department of Dermatology between April 2019 and October 2019. Patients coming to outpatient clinics between the ages of 18 and 50 who had one to three keloids ranging in size from 1 cm to 15 cm and who had Fitzpatrick skin types 2-5 were included in the research. The institution's research and ethics committee gave its blessing to the project, so it could go on. A block design was used to get written informed consent from all patients. Using the World Health Organization's (WHO) sample size calculation algorithm, data from 60 patients (30 in each group) was collected using a non-probability sampling technique. Patients with active infections (local or systemic) were eliminated because triamcinolone can suppress the immune response, and patients with known sensitivities to steroids or 5-FU were also removed because of the risk of hypersensitivity responses. Randomization was 1:1 for group A and group B, i.e., each upcoming patient was included in the next group; this randomization was supervised by another clinician. Group-A patients received a combination of triamcinolone and 5 fluorouracil at 4 weekly intervals and group-B received conventionally used triamcinolone. For a total of 24 weeks, group-A received intralesional 5-FU, 50mg/ml (0.9m1) + 0.1ml (0.1ml) of triamcinolone for each 1 cm region while group-B was administered with intralesional triamcinolone 40mg/ml. The patient and observer scar assessment scale was used at baseline and at end of treatment. The doctor and the patient filled out a proforma at the start of the treatment to assess the objective and subjective components of the scale and the efficacy of treatment determined at the end. Efficacy was deemed as positive if the post-treatment response was 70% or above the baseline. SPSS version 20 was used for the analysis of data. Categorical factors such as gender, effectiveness, and Fitzpatrick skin type were used to derive percentages. Means and standard deviations were computed for demographic variables such as age, duration, number of keloids, and POSAS score at presentation and at each follow-up visit for 24 weeks. Both groups' efficacy was stratified according to gender, age, duration of symptoms, Fitzpatrick skin type, and baseline POSAS score to look for evidence of effect modification. We performed a Chi-square post-stratification, with a p-value of 0.05 representing statistical significance.

RESULTS

A total of sixty participants participated in this trial (30 in each arm). Treatment in Group-A included both triamcinolone and 5-FU, whereas treatment in Group-B consisted of intralesional triamcinolone. Group-A patients were on average 33.68.8 years old, whereas group B patients were on average 32.18.8 years old (Table- 1 shows the Distribution of patients by age). In group A, there

Table 1: Distribution of patients by age

Age (Year)	Group-A (Triamcinolone and 5-FU)		Group-B (Triamcinolone)	
Ampicillin	No.	%	No.	%
18-30	10	33.3	14	46.7
31-50	20	66.7	16	53.3

Table 2: Distribution of patients by gender

Gender	Group-A (Triamcinolone and 5-FU)		Group-B (Triamcinolone)	
	No.	%	No.	%
Male	12	40.0	14	46.7
Female	18	60.0	16	53.3
Total	30	100.0	30	100.0

Table 3: Distribution of patients by Fitzpatrick skin type

Fitzpatrick skin type	Group-A (Triamcinolone and 5-FU)		Group-B (Triamcinolone)	
	No.	%	No.	%
1	1	3.3	4	13.3
2	10	33.3	9	30.0
4	16	53.4	14	46.7
5	3	10.0	3	10.0

Table 4: Distribution of patients by efficacy

Efficacy	Group-A (Triamcinolone and 5-FU)		Group-B (Triamcinolone)	
	No.	%	No.	%
Yes	28	93.3	19	63.3
No	02	06.7	11	36.7

Chi square = 7.954, P value = 0.005

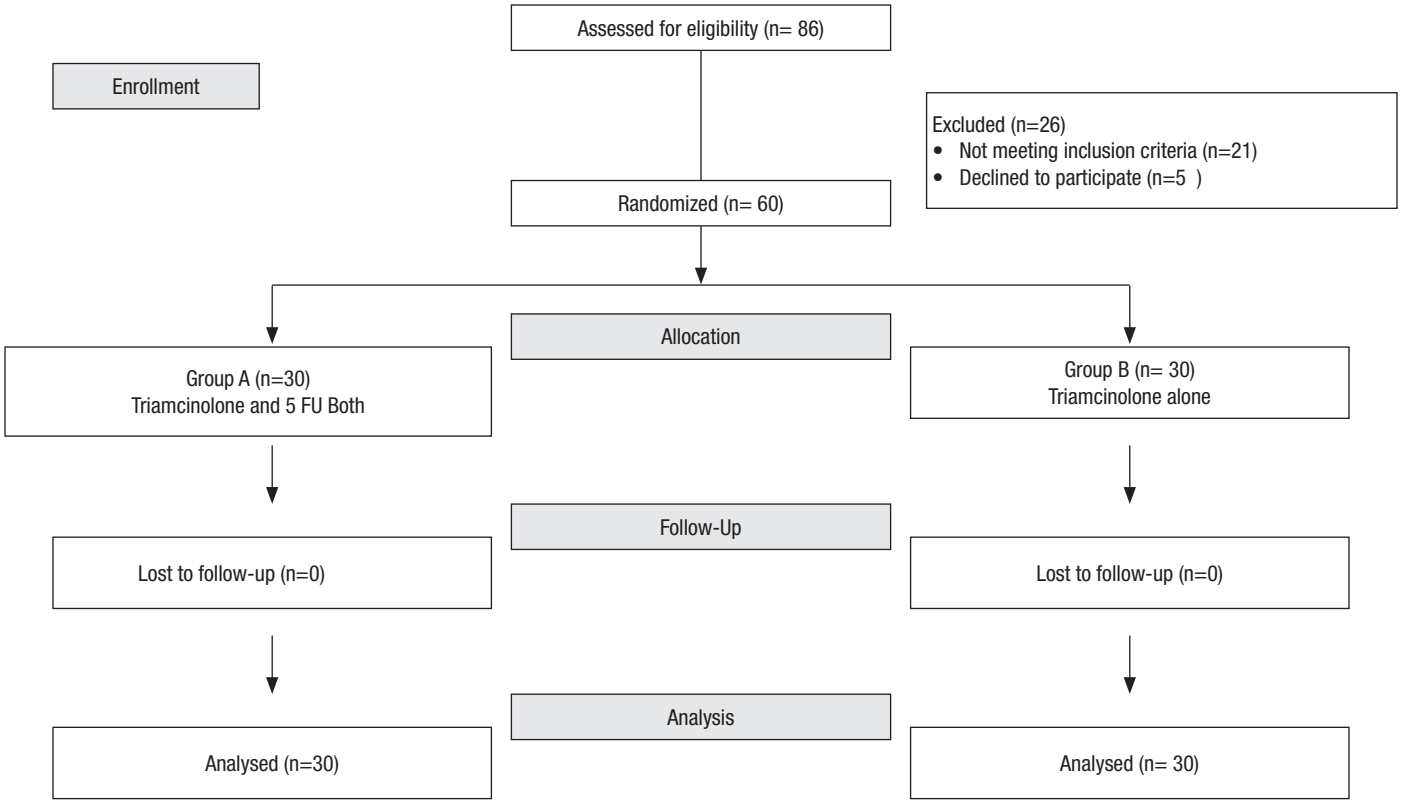

Figure 1: Consort diagram

were 12 men (40%) while in group B, there were 14 (46.7%). There were 18 women in group-A (60%) and 16 in group-B (53.3%). Table 2 shows the Distribution of patients by gender. In both groups, Fitzpatrick skin type 4 was the most common Table 3 shows the Distribution of patients by Fitzpatrick skin type. A total of 28 out of 30 participants in Group-A were effective, but only 19 out of 30 in Group-B were (p=0.005). Patients' Distributions Based on Efficacy are Shown in Table 4.

DISCUSSION

While there are a variety of treatments for keloids, none of them have been shown to result in a permanent cure.[11] Intralesional therapy, cryotherapy, radiation, pressure therapy, surgical excision, and various combinations thereof have all been mentioned as possible treatments. The benefits and drawbacks of triamcinolone acetonide, the most widely used first-line corticosteroid, are well established.[12-17]

Intralesional use of triamcinolone acts

by decreasing fibroblast proliferation, increasing collagen breakdown, inhibiting of inflammation, and decreasing endothelial proliferation.[18-20] Triamcinolone also cause reduces the levels of alpha-1-antitrypsin and alpha-2-macroglobulin levels, which are greater in keloidal tissue and cause inhibition of collagenase in human skin.[21,22] Dose varying from 10–40 mg/mL has been described in literature, to be effective. Dose of 40 mg/mL was chosen for our study. The most frequent adverse effects of triamcinolone are telangiectasia, skin atrophy, and dyspigmentation.[23]

The average ages of the participants in our research were 33.68±8 and 32.18±8 for groups A and B, respectively. This is consistent with data from studies conducted in other parts of the world, where the majority of patients were in their 30s and 40s.[24,25]

5FU in a dose of 50mg/ml when administered intralesionally has shown favorable results. Systemic complications of 5-FU, such as anemia, thrombocytopenia, and leucopenia are not reported, but local adverse effects include pain at injection site, burning, ulceration, and hyperpigmentation.[26] Triamcinolone when added to 5 FU in a ratio of 1:9 leading to absolute triamcinolone concentration of 4mg/ ml.[27-29]

For every two females in Group A, there were nearly two men in Group B, for a total of 60% of each. 60 percent of those in group-A were women, but only 53.3 percent of those in group-B were women. Similarly, to research by Afshan et al., there was a modest rise in the percentage of women represented.[2] Women's preoccupation with their appearance may possibly explain their increased participation. The current study indicated that when Triamcinolone was combined with 5-FU, it was more effective than when each component was used separately (p=0.005). Our results are consistent with those of the following trials, which found that a regimen including both 5FU and TAC was more effective than TAC alone. A recent meta-analysis by Ren et al. indicated that TAC with 5FU is superior to TAC alone in terms of efficacy and safety.[30-33]

Our analysis found that Fitzpatrick skin type 4 was the most common among the individuals we saw. Sreekar H et al. found similar results, reporting that people of color were at increased risk for developing keloids.[34]

CONCLUSION

The findings of this study showed that intralesional TCA for the treatment of keloids was successful in 63.3% of instances, whereas intralesional 5-FU plus TCA provided statistically significant outcomes in 93.3% of cases (p=0.005). The combination of 5 FU with TAC is preferred over TAC alone for the treatment of keloids because it results in a more favorable patient experience and better objective metrics.

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Author's Contribution

SN, AQ, and MMP helped in the collection of data and write-up for the manuscript. FS helped in the analysis and interpretation of data. SMN conceived the idea, designed the study, and write-up of the manuscript. Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.