



Original Article

EVALUATION OF THE EFFICACY AND SAFETY OF INTRALESIONAL 5-FLUOROURACIL IN KELOID

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Abstract:

Background: Keloid is an area of overgrowth of fibrous tissue that usually develops after healing of skin injury and extends beyond the original defect. The existing treatment modalities include intralesional steroids, cryotherapy, silicone gel sheets, verapamil and 5- fluorouracil (5-FU).

Methods: An open label study on 48 keloids in 35 subjects attending the Department of Dermatology in Dhaka Medical College Hospital during June 2017 and November 2017. Patients with keloids of 10cm and less along the longest diameter in the age group 18-75 years, Keloids with signs of infection, History of hypersensitivity and/or intolerance to 5-FU were included in the study.

Results: Majority 21(60.0%) patients had single site keloid and 14(40.0%) had multiple site keloid. Majority 54.3% patients had keloids size 2-5 cm. All patients had pain and hyperpigmentation, 5(14.3%) had pustules, 3(8.6%) had necrosis and 1(2.9%) had ulceration. The median keloid area before the treatment was 4 with an inter quartile range of 1.5 to 7.8 and this is compared with post treatment area, median 1.5 and inter quartile range 0.6 to 4. Wilcoxon signed rank test was used to assess the reduction in the size of keloid before and after treatment which was significant. (P<0.001).

Conclusion: Majority patients had single site keloid. All patients had pain and hyperpigmentation. low dose intralesional 5-FU is safe and effective modality in the treatment of keloids.

Introduction

Keloid is an area of overgrowth of fibrous tissue that usually develops after healing of skin injury and extends beyond the original defect. The existing treatment modalities include intralesional steroids, cryotherapy, silicone gel sheets, verapamil and 5-fluorouracil (5-FU).¹ Intralesional injection of high dose of 5-FU for keloids acts by necrosis of fibroblasts and low dose has shown to reduce fibroblast proliferation and cause apoptosis. There are only a few clinical studies using low dose 5-FU for keloids.² The pathogenesis of keloids remains controversial. Although there is a lack of consensus about an ideal standard therapy, there is a significant need for an effective treatment protocol because keloids are common and tend to recur. The incidence of keloids is reported to be 4.5% to 16% in darker-skinned individuals.³ Although many treatment options have already been described in the literature, there is no universally accepted treatment resulting in permanent hypertrophic or keloid scar ablation. The lack of adequately long-term powered randomized controlled trials does not permit to establish definitive conclusions with implications for routine clinical practice.⁴

Materials methods:

This is an open label study on 49 keloids in 35 subjects attending the Department of Dermatology in Dhaka Medical College Hospital during June 2017 and November 2017. Patients with keloids of 10cm

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and less along the longest diameter in the age group 18-75 years, Keloids with signs of infection, History of hypersensitivity and/or intolerance to 5-FU were included in the study. A total dose of around 1ml of 5-FU (10mg/ml) injected into the lesion depending upon the size of keloid once in 2 weeks for a period of 3 months with a dose of around 0.1ml at each injection site after obtaining informed consent. Lignocaine is added in patients who experience pain during injection. The initial assessment was done by single investigator at baseline regarding site, size, extent and progression of keloids. Clinical assessment was done by the same investigator at each visit following the injection along with photographic documentation. The clinical responses were graded as grade 0, no improvement (No reduction in size from baseline); grade I, mild improvement (<25% reduction from baseline); grade II, moderate (25%-50% reduction from baseline); grade III, good improvement (50%-75% reduction).

Results:

Majority 12(34.3%) patients belonged to age 41-50 years. The mean age was found 39.7±12.3 years (Table I). Male was found 19(54.3%) and female was 16(45.7%). Male female ratio was 1.18:1 (Figure 1). Majority 14(40.0%) patients had keloid in duration of 1-5 years. The mean duration of keloid was 6.2±3.7 years (Table II). 23(65.7%) patients had spontaneous keloid and 12(34.3%) had trauma keloids (Figure 2). Majority 21(60.0%) patients had single site keloid and 14(40.0%) had multiple site keloid (Figure 3). Majority 54.3% patients had keloids size 2-5 cm (Figure 4). All patients had pain and hyperpigmentation, 5(14.3%) had pustules, 3(8.6%) had necrosis and 1(2.9%) had ulceration (Table III). The median keloid area before the treatment was 4 with an inter quartile range of 1.5 to 7.8 and this is compared with post treatment area, median 1.5 and inter quartile range 0.6 to 4. Wilcoxon signed rank test was used to assess the reduction in the size of keloid before and after treatment which was significant. (P<0.001) (Table IV). Majority 45.7% patients had good and fair response, 34.3% had excellent outcome and 20.0% had poor response (Table 5).

Table I

Distribution of the study patients by age (n=35)

Age (years)	Frequency	Percentage
11-20	1	2.9
21-30	3	8.6
31-40	7	20.0
41-50	12	34.3
51-60	9	25.7
>60	3	8.6
Mean±SD	39.7±12.3	

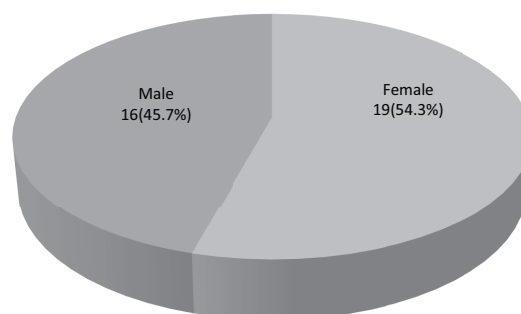


Fig.-1: Pie chart showing sex distribution of the patients (n=35)

Table II

Distribution of the study patients by duration of keloid (n=35)

Duration of keloid (years)	Frequency	Percentage
<1 year	3	8.6
1-5 year	14	40.0
6-10 year	11	31.4
> 10 year	7	20.0
Mean±SD	6.2±3.7	

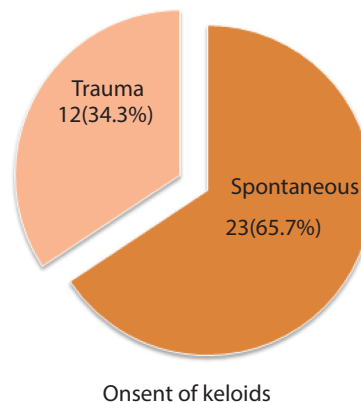


Fig.-2: Pie chart showing onset of keloids of the patients (n=35)

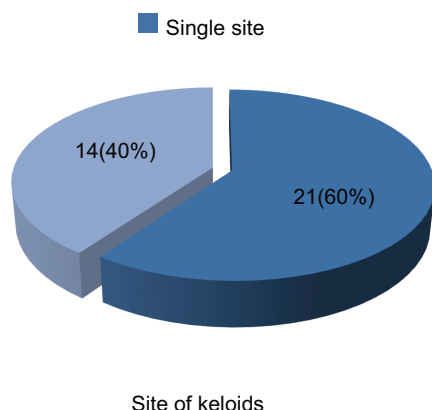


Fig.-3: Pie chart showing site of keloids of the patients (n=35)

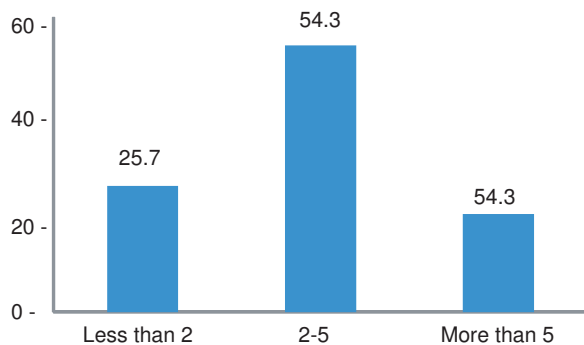


Fig.-4: Bar diagram showing keloids size of the patients (n=35)

Table III

Distribution of the study patients by side effects (n=35)

Side effects	Frequency	Percentage
Pain	35	100.0
Pustules	5	14.3
Necrosis	3	8.6
Hyperpigmentation	35	100.0
Ulceration	1	2.9

Table IV

Comparison of area of keloid- pre and post values

Keloid area	Pre treatment Median (IQR)	Post treatment Median (IQR)	p - value
Score	4.0(1.5 – 7.8)	1.5(0.6 – 4.0)	< 0.001

IQR – inter quartile range

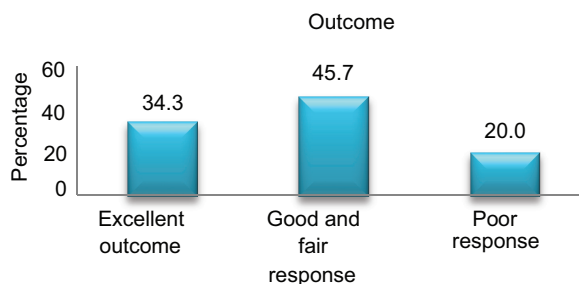


Fig.-5: Bar diagram showing outcome of the patients (n=35)

Discussion

In present study observed that the majority 12(34.3%) patients belonged to age 41-50 years. The mean age was found 39.7 ± 12.3 years. Similar observation was found Shivaswamy et al.¹ the age range was 19-63 yrs. Kontochristopoulos et al.⁵ study reported twenty patients aged 12 to 65 years were recruited to evaluate the efficacy of intralesional 5-fluorouracil (5-FU) in the treatment of keloids.

In current study revealed that male was found 19(54.3%) and female was 16(45.7%). Male female ratio was 1.18:1. Kontochristopoulos et al.⁵ study observed that male was found 11(55.0%) and female was 9(45.0%). Gupta and Kalra⁶ study showed Out of 24 patients, 12 were males and 12 were females.

In current study majority 14(40.0%) patients had keloid in duration of 1-5 years. The mean duration of keloid was 6.2 ± 3.7 years. Shivaswamy et al.¹ the duration of keloids varied from 10 months to 16 years. Gupta and Kalra⁶ study showed six (54.5%) out of 11 patients with keloids of >5 years duration, in contrast to only 2 (15.4%) out of 13 patients with keloids of 15 years duration showed more than 75% flattening ($p < 0.05$). The duration of keloids ranged from 1 to 25 (mean 8.33) years. Kontochristopoulos et al.⁵ study showed it was shown that 82% of the patients having a disease duration of less than two years.

In current study observed that 23(65.7%) patients had spontaneous keloid and 12(34.3%) had trauma keloids. Shivaswamy et al.¹ study showed that the onset was spontaneous in 10 and in 5 followed by trauma.

In this study majority 21(60.0%) patients had single site keloid and 14(40.0%) had multiple site keloid. Shivaswamy et al.¹ nine patients had keloid at single site and in 6 at multiple sites.

In present study observed that the majority 54.3% patients had keloids size 2-5 cm. Shivaswamy et al.¹ showed in 4 patients keloid size was less than 2cm, 8 had size between 2-5cm, and in 3 it was more than 5cms Kontochristopoulos et al.⁵ the sizes of the lesions varied from 1 to >5 cm

In current study showed all patients had pain and hyperpigmentation, 5(14.3%) had pustules, 3(8.6%) had necrosis and 1(2.9%) had ulceration. Shivaswamy et al.¹ showed side effects were noted in the form of pain in 3, pustules in 2 and necrosis in 1 patient, which were self-limiting and not warrant drug withdrawal. Davison et al.³ of the 76 keloids treated with 5-FU (either with or without excision), 26 were painful (34%) and 27 presented with pruritus (36%). Pain resolved in 92% of these cases, with 2 patients reporting mildly increased pain after treatment. Gupta and Kalra⁶ the side effects observed in the earlier study were purpura at the injection site (30–40%), pain (100%) and localized superficial tissue sloughing (in 3–4 patients).

The median keloid area before the treatment was 4 with an inter quartile range of 1.5 to 7.8 and this is compared with post treatment area, median 1.5 and inter quartile range 0.6 to 4. Wilcoxon signed rank test was used to assess the reduction in the size of keloid before and after treatment which was significant. ($P < 0.001$). similar observation was found Shivaswamy et al.¹ study, they showed the median keloid area before the treatment was 4 with an interquartile range of 1.5 to 7.8 and this is compared with post treatment area, median 1.5 and interquartile range 0.6 to 4. To assess the reduction in the size of keloid before and after treatment which was significant. ($P < 0.001$).

In current study showed that the majority 45.7% patients had good and fair response, 34.3% had excellent outcome and 20.0% had poor response. Shivaswamy et al.¹ study observed that out of 35 patients, 4 showed <25% of clinical improvement from baseline, 8 had improvement between 26%-50%, 16 had improvement between 51%-75% and 2 had improvement of >75%. Gupta and Kalra⁶ overall, one third (8/24, 33.3%) of the patients showed an excellent outcome. Among the remaining two thirds, 6 (25%) patients each showed good and fair responses and 4 (16.6%) patients showed a poor response. Subjects receiving 5-FU revealed 70% with fair improvement and 30% with good improvement

on self-assessments at 32 weeks.⁷ Kontochristopoulos et al.⁵ reduction in keloid volume was noted in 95% of the cases with two patients improved by 25%, eight patients by 50%, eight patients by 75% and one showed complete resolution.

Conclusion

Majority patients had single site keloid. All patients had pain and hyperpigmentation. low dose intralesional 5-FU is safe and effective modality in the treatment of keloids.

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