

CLINICAL EFFICACY OF LOW DOSE INTRALESIONAL 5-FLUOROURACIL (5-FU) IN THE TREATMENT OF KELOIDS

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ABSTRACT

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).¹⁻⁶ But none have shown to be very effective.

OBJECTIVE

To evaluate the clinical efficacy of low dose intralesional 5-FU in the treatment of keloids.

RESULTS

A total of 30 keloids in 15 subjects were assessed for the efficacy of low dose intralesional 5-FU. Out of 30 keloids, 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% as assessed by photographic methods.

CONCLUSION

From this study it has been concluded that low dose intralesional 5-FU is safe and effective modality of in the treatment of keloids.

KEYWORDS

Keloids, Intralesional 5-FU, Low Dose.

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INTRODUCTION

Keloid is an area of overgrowth of fibrous tissue that usually develops after healing of skin injury and extends beyond the original defect. They are primarily of cosmetic concern, sometimes can be disfiguring. The existing treatment modalities include intralesional steroids, cryotherapy, silicone gel sheets, topical retinoic acid, tacrolimus, imiquimod, colchicine, verapamil and 5-fluorouracil (5-FU).¹⁻⁶ But none have shown to be very effective. 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.^{7,8}

Need for the Study

The existing treatment modalities including intralesional steroids, cryotherapy, silicone gel sheets, imiquimod, verapamil and high dose 5-FU have not shown to be very effective and there are only a few clinical studies using low dose 5-FU for keloids. Hence, the study is being undertaken.

OBJECTIVE

To evaluate the clinical efficacy of low dose intralesional 5-FU in the treatment of keloids.

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MATERIAL AND METHODS

Study Design

An open label study on 30 keloids in 15 subjects attending the Department of Dermatology in a Tertiary Care Hospital during June 2012 and November 2012.

Inclusion Criteria

Patients with keloids of 10cm and less along the longest diameter in the age group 18-75 years were included in the study.

Exclusion Criteria

Keloids with signs of infection.

History of hypersensitivity and/or intolerance to 5-FU.

Women in the age group 18 to 45 years who have not completed the family.

Dosage Schedule

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.

Parameters Studied

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

from baseline). Patients were followed up at end of 1, 2, 3 and 6 months after the last injection to look for further reduction in size and/or if any recurrence of keloids. Side effects of the drug were recorded at each visit. Results were tabulated and the clinical efficacy was assessed using appropriate statistical methods.

Statistical Analysis

The data were analyzed using SPSS V19 software. The descriptive statistics of reduction in size of keloids were analyzed and expressed in terms of median and Interquartile Range (IQR) since the data was skewed. Wilcoxon signed rank test was used to find the statistical significance in the reduction in size of keloids. P value of less than 0.05 was considered for statistical significance.

RESULTS

A total of 30 keloids in 15 subjects were assessed for the efficacy of low dose intralesional 5-FU. Out of 15 patients, 13 were males and 2 were females. The age range was 19-63yrs. The duration of keloids varied from 10 months to 16 years.

The onset was spontaneous in 10 and in 5 followed by trauma. In 13 patients the progression was gradual, but in 2 rapid. Nine patients had keloid at single site and in 6 at multiple sites. In 4 patients keloid size was less than 2cm, 8 had size between 2-5cm, and in 3 it was more than 5cms. Four patients had previous history of taking topical treatment for keloids and 11 patients had not sought treatment. Family history of keloid and diabetes was evident in 1 patient each. Lignocaine was added in 3 patients to reduce the pain. 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.

Out of 30 keloids in 15 patients, 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. 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).

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 - Interquartile Range

Out of 30 keloids among 15 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% as assessed by photographic methods.

DISCUSSION

Keloid is an area of overgrowth of fibrous tissue that usually develops after healing of skin injury and extends beyond the original defect. They are primarily of cosmetic concern, sometimes can be disfiguring. The existing treatment modalities include intralesional steroids, cryotherapy, silicone gel sheets, topical retinoic acid, tacrolimus, imiquimod, colchicine, verapamil and 5-fluorouracil (5-FU).¹⁻⁶ But none have shown to be very effective.

The present study has been aimed at finding the clinical efficacy of low dose 5-FU for keloids. The results were comparable to other studies involving higher dose of 5-FU and combination of % FU and triamcinolone.^{2,4,9}

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.^{7,8}

The side effects noted were few in the form of pain, pustulations and necrosis which did not warrant discontinuation of therapy.

CONCLUSION

From this study, it has been concluded that low dose intralesional 5-FU is safe and effective modality in the treatment of keloids.

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Fig. 1: Before Treatment



Fig. 2: After Treatment 2nd Visit



Fig. 3: After Treatment 3rd Visit