DISCUSSION

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The complex interplay of events following injury of the skin does not always eventuate in a normal, smooth skin surface. Rather, the skins often respond to injury with proliferation of fibrous tissue. When tissue response to injury is exaggerated, the result is hypertrophic scar or keloid. Hypertrophic scars and keloids have been known since very early times and were mentioned in the Smith Papyrus from between 3000 and 2500 BC. View idea about the current In this study we tried to give a clear idea on definition, incidence, aetiopathogenesis, clinical picture and recent advances in the management of keloidal scars.[158]

The present work comprised two interrelated parts, first clinical and second histological.

The main theme of the clinical part is to evaluate the effect of timed , local injections of 5 fluorouracil on the future scar following surgical excision of keloid, hypertrophic scar and wide scar.

The course of 5 fluorouracil consist of one injection in the site of half of the scar after healing then every month in the same half for ten months at concentration of 50 mg for a total of 10 treatments and compared with half of the scar that was not injected.

The current evaluation of treatment depended on 4 clinical signs and symptoms of scar, which include vascularity, pigmentation, thickness and pliability. The overall effect on improving these clinical findings was estimated and graded as good if 3 or 4 out of these 4 clinical signs and symptoms were improved, average if 2 were improved and poor if 1 or non of these finding was improved. These results were evaluated after a period of 10 months in both groups.

Overall good response was obtained in 75% (15 cases out of 20) of the halves injected with 5- fluorouracil whereas average response was the result in 10% (2 out of total of 20 patients), and poor results in 15% (3 out of total of 20 patients). This is in contradistinction to the results in the control (non injectable halves) group where good results where achieved in 35% (7 out of total of 20 patients) and average result was obtained in 25 % (5 out of 20 patients), and poor results in 40% (8 out of total of 20 patients).

As regard the results in extensive dermal scar : in the injectable halves the good result was obtained in 100% (3 out of total of 3 patients) and in the non injectable halves the good result was obtained in 66.7% (2 out of total of 3 patients), and average result in 33.3% (1 out of total of 3 cases). In hypertrophic scar group the good result in the injectable halves was obtained in 62.5% (5 out of total of 8 patients), average result in 12.5% (1 out of total of 8 cases), and poor result in 25% (2 out of 8 cases).While in the non injectable halves the good result was obtained in 12.5% (1 out of total of 8 cases), average result in 25% (2 out of total of 8 cases), and poor result in 62.5% (5 out of total of 8 cases). In keloid group the good result in the injectable halves was obtained in 77.8 (7 out of total of 9 cases), average result in 11.1 (1 out of total of 9 cases) and poor result in 11.1 (1 out of total of 9 cases).While in the non injectable halves the good result was obtained in 44.4% (4 out of 9 cases), average result in 22.2% (2 out of 9 cases),and poor result in 33.3% (3 out of total of 9 cases).

Dr. Haurani, et al presented a prospective study on the treatment of problematic scars with 5-FU. Keloids were treated with 5-FU following excision, and hypertrophic scars were treated without excision. Both patient groups were followed using questionnaires about scar symptomatology and by measuring the scar volume. The use of scar volume as a quantitative measure is a good objective approach to studying treatment efficacy. The authors report a recurrence rate of only 19% when keloids are resected and then treated with 5-FU, and a 50% median decrease in scar volume in the hypertrophic scars during the period of the study.(159)

Muhammad Aslam Khan compared the use of intralesional triamcinolone acetonide and its combination with 5 fluorouracil in the treatment of keloid and hypertrophic scars in terms of reduction in initial height of the scar. The randomized controlled trial was conducted at the Department of Plastic Surgery, King Edward Medical University, Lahore, from March 2011 to December 2012. It comprised patients of both genders having keloids or hypertrophic scars (1cm to 5cm in size) having no history of treatment for the scars in preceding 6 months. Those who were pregnant, planning pregnancy or lactating were excluded. The subjects were divided into two groups: Group A received intralesional triamcinolone acetonide alone; and Group B received triamcinolone acetonide + 5 fluorouracil. Eight injections were given at weekly interval. Scars were assessed 4 weeks after the completion of treatment on a five-point scale. The 150 subjects in the study were divided into two equal groups of 75(50%) each. Good to excellent results were seen in 51(68%) cases in Group A compared to 63(84%) in Group B. Frequency of complications was 18(24%) and 6(8%) in Group A and Group B respectively. (160)

A collective breakdown of the sex data obtained from the 2 groups in the present work shows a female predominance over males (12 females and 8 males) in a ratio of 1.5:1. This female predominance goes in accordance with the theory that relates the effect of increased estrogen concentration to keloid formation. This may also be explained by the fact that females are more concerned about their appearance and hence seek medical advice more than males.

As regards age incidence in the groups (20 patients), most of them were between 20 and 3o years (60%). This was also the case in other studies. The reason for this is assumed to be that younger individuals are more frequently subjected to trauma, their skin has greater tension, the rate of collagen synthesis in young subjects is greater than older individuals and the effect of estrogen concentration on keloid formation. That is why many adult females with earlobe keloids date the formation of the scar to a recent injury although they had their lobes pierced in infancy.

Different etiological factors contributed to scar formation in the present study. Most of them .occurred after cut wound (70%), whether traumatic (50%) or after surgically-planned incisions (20%), others followed burn wounds (20%) ear piercing (10%). These are the well known precipitating causes of scar formation.

As regards the site of the lesions, 50 % of the patients suffered from scars in the face (10%) in the earlobes. other facial sites included auricles (15%), cheeks, mandibular area and forehead (25%). Arm lesions were 40% of the scars while the back of the shoulder 5 % and the foot 5%. This finding is in accordance with the theory of regional susceptibility to keloid and scar formation. Most of the above sites are keloid prone area.

Our results so far can favorably compare with those of other studies in the literature using other regimens. A recent study by Aradi et al studied 21 earlobe keloids that were treated using keloidectomy with core fillet flap and given intraoperative intralesional

steroid injections. This study showed an efficacy of 87.6%. Immediate recurrence was 9.5%, with an average of 29.9 months of follow up and with few complications encountered. Subjectively, 82.3% of patients were satisfied.[126]

Tredget et al showed a significant increase in the rate of scar improvement compared with the control period of time ($P = .004$) after injecting 9 patients with hypertrophic scars with 1 X 10^6 units of human recombinant IFN alfa-2b subcutaneously, daily for 7 days, and then 2 X 10^6 units administered 3 times per week for 24 weeks in total.[1] Scar assessment ($P < .05$) and scar volume ($P < .05$) also improved after 3 months of treatment. No recurrences were reported after stopping IFN therapy.[117]

Conejo-Mir et al reported that 66% of keloids (n = 20) did not recur after 3 years of follow-up after treating 30 keloids with ultrapulse carbon dioxide laser ablation followed by sublesional and perilesional injections of 3 million IU of IFN alfa-2b 3 times per week.[129]

In a 2008 prospective study, Lee et al reported decreases in depth (81.6%, $P = .005$) and volume (86.6%, $P = .002$) treating 20 keloids with a combination of intralesional TAC and IFN alfa-2b compared with only a non significant improvement ($P = .281$ and $P = .245$, respectively) obtained in 20 keloids treated with TAC alone.[130]

Intralesional injection was well tolerated by our patients, some complained of mild pain during injection. No significant complication occured.

In an attempt to verify the local effects of 5-fluorouracil on tissue and cells a histopathological study has been carried out.

Histopathological examination of the excised scar confirmed the clinical diagnosis. The keloid scar exhibited collagen fibers, which are abnormally large, dense, broad, glassy eosinophilic focally fragmented and arranged haphazardly. Few fibroblasts and numerous newly formed small blood vessels were found. In contrast hypertrophic scar exhibit collagen, which is discretely nodular, fibrillar, with fairly regular thickness of fibers with its long axis parallel to the epidermis. Fibroblasts are more seen in hypertrophic scar than in keloid.

Extensive scar showed broad scar tissue made of collagen fibers parallel to the epidermis. Neither keloid collagen nor nodular collagen was noted.

Light microscope and ultra structural study of 5-floururacil injected keloid and hypertrophic scar after excision showed histological evidence of complete regression. Examination by H&E stain showed decreased thickness of the scar, decreased size of collagen bundles, fragmentation and fraying of the collagen fibers. Vascularity was remarkably diminished after treatment.

Histopathological examination of extensive scar showed no remarkable difference non injectable and injectable halves.

Examination by immunohistochemical stain for ki67 (a proliferating marker) showed mild positivity in the fibroblasts of keloid and hypertrophic scar before injection of 5-floururacil and absent after injection.

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SUMMARY

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Problematic scars occur as the result of an exaggerated wound healing of the skin following various types of injury. In addition to presenting a cosmetic concern, scars may be pruritic and restrict the range of motion. Certain patients and certain wounds are at higher risk for problematic scar formation. The cause of problemati scarc is unknown. Several theories have been proposed, though none has been proven.

Scars are extremely difficult to treat. Multiple treatments have been advocated in the past with varying degrees of success. Scars have been shown to respond to pressure therapy, intralesional steroids, systemic, chemotherapy, radiation, topical silicon, retonic acid and laser treatment. But until now there is no universally accepted treatment modality resulting in permanent scar ablation.

The aim of this work was to assess the efficacy of local injection of 5-fluorouracil. A chemotherapeutic drug, on recurrence of surgically excised problematic scars.

This study included 20 patients divided into three groups:

Group 1: Include (9) patients whose Keloids were surgically excised and thereafter treated by intrascar injections of 5flourouracil at special intervals according to a proposed protocol.

Group 2: Include (8) patients whose Hypertrophic scars were surgically excised and thereafter treated by intrascar injections of 5flourouracil at special intervals according to a proposed protocol except one patient the scar injected without surgical excision.

Group 3: Include (3) patients whose extensive dermal scars were surgically excised and thereafter treated by intrascar injections of 5flourouracil at special intervals according to a proposed protocol.

The final clinical analysis was based on comparisons between halves injected with 5 fluorouracil and halves not injected in the same patients. The response to treatment was evaluated after 10 months follow up period clinically and histopathologically.

The current evaluation of treatment depended on 4 clinical signs and symptoms of scars which included thickness, pliability, vascularity and pigmentation of the resulting scar. the overall effect on improving these clinical findings was estimated and graded as (good) (3 or 4 out of these 4 clinical signs and symptoms were improved) (average) (if 2 were improved) and poor (if 1 or non of these findings was improved. The result were tabulated and were statistically analyzed.

The result of the present work compare favorably with those of similar studies. evaluation of the overall results of I patients in the present work showed good response in 75 % of the patients average response in 10 % and poor response in the remaining 15%in injectable halves. In non injectable halves. The control 40 % of the patients showed poor response 25% showed average response, while 35% of patients showed good response.

Histopathological examination of specimens obtained from injectable and non injectable halves before and after treatment showed the keloid scar exhibited collagen fibers, which are abnormally large, dense, broad, glassy eosinophilic focally fragmented and arranged haphazardly. Few fibroblasts and numerous newly formed small blood vessels were found. In contrast hypertrophic scar exhibit collagen, which is discretely

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Light microscope and ultra structural study of 5-floururacil injected keloid and hypertrophic scar after excision showed histological evidence of complete regression. Examination by H&E stain showed decreased thickness of the scar, decreased size of collagen bundles, fragmentation and fraying of the collagen fibers. Vascularity was remarkably diminished after treatment.

Histopathological examination of extensive scar showed no remarkable difference non injectable and injectable halves.

These histopathological findings matched well with the clinical findings in this study.

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CONCLUSIONS

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Intralesional injection of 5fluorouracil is a safe and effective measure in treating keloid and hypertrophic scars but has no role in widened scars. Benefits were maintained for at least 10 months after completion of therapy. Intralesional 5 fluorouracil should be considered an option for patients suffering from keloid and hypertrophic scars.

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