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Evaluation of Intralesional Injection of 5-fluorouracil in Treatment of Vitiligo

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Authors' contributions

This work was carried out in collaboration among all authors. Author DMAA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors DAMA and RAEl-T managed the analyses of the study. Author LHE managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Vitiligo is a chronic cutaneous disease characterized by depigmented patches that leave psychological impact on the patients. New treatment modalities have been developed to improve the results vitiligo with less side effects.
Objective: To evaluate intralesional injection of 5-fluorouracil in treatment of vitiligo.
Patients and Methods: The study included 20 localized stable vitiligo patients. Each patient was treated with intralesional injection of 5-fluorouracil every 2 weeks for 3 sessions followed by narrow band sessions twice weekly for 3 months.
Results: There was statistically significant repigmentation after treatment with intralesional 5-FU (mean of 50.30 ± 34.60, P value =0.001 Wilcoxon signed ranks test between before and after). 55% of patients showed >50% repigmentation. after 3 months therapy. Side effects were minimal and transient.
Conclusion: Intralesional injection of 5-FU is safe and effective in the treatment of vitiligo.

Keywords: 5-fluorouracil; carbon dioxide laser; vitiligo.

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1. INTRODUCTION

Vitiligo is an acquired depigmentary disorder that affects skin as well as mucous membranes [1]. It is idiopathic and characterized by absence of melanocytes [2]. It results from integration of multiple factors; genetic and environmental factors that work together to destroy the melanocyte with loss of its function, that can be represented clinically as a de-pigmented macules or patches [3,4].Various therapeutic options are currently used in vitiligo treatment, although often without complete satisfactory therapeutic outcome [5].

Application of 5-Fluorouracil (5-FU) after mechanical dermabrasion, as a treatment for vitiligo, was introduced by Tsuji and Hamada in 1983 [6]. The experimental studies enriched us with valuable information regarding the biological effect of 5-FU on melanocytes. 5-FU in low concentrations could selectively destroy keratinocytes within three weeks, while melanocytes continued to grow, multiply and produce melanin [7].

In our study, we used intralesional injection of 5-fluorouracil as a treatment of vitiligo.

2. PATIENTS AND METHODS

Research ethical approval (code no. 32701/11/18) was obtained before beginning of the study. The present study is a prospective study. It was carried out on 20 vitiligo patients who were recruited from the Outpatient Clinic of Dermatology and Venereology Department, Tanta University. They were either newly diagnosed patients with stable vitiligo or patients who stopped treatment for at least three months prior to our study. Patients with systemic or other dermatological diseases, current pregnancy and lactation, bleeding and coagulation disorders, history of keloid and hypertrophic scars, active cutaneous bacterial or viral infection in the area to be treated were excluded from this study. After signing informed consents, all patients were subjected to full history taking, general and dermatological examination.

2.1 Steps of the Procedure

One or more patches were chosen for treatment. The vitiligo lesions were cleaned with 70% alcohol. Local anesthesia (Topical Pridocaine cream; a mixture of Lidocaine 25% and Prilocaine 25%) was applied 30 minutes before procedure.

The chosen patches were subjected to intralesional injection of 5-fluorouracil 5% solution (50 mg/mL). At each point, 0.05-0.1 ml was injected with 1 cm apart using insulin syringe [8]. The procedure was repeated every 2 weeks for each patient until improvement reached or for 3 months maximum.

2.2 Evaluation of the Treatment

It was performed by photographs which were taken at baseline and at the end of treatment using Canon camera 13 Mega Pixels. The repigmentation responses were assessed by 1) Three dermatologists committee and expressed qualitatively as follows:

- (0%) = No change.
- (1 –25%) = Poor improvement.
- (26–50%) = Moderate improvement.
- (51 –75%) = Good improvement.
- (76–100%) = Excellent improvement.

2) Visual analogue system score was used as follows:

- 0-25% — poor response (Grade I).
- 26-50% — fair response (Grade II).
- 51-75% — good response (Grade III).
- 76-100% — excellent response (Grade IV).

2.3 Statistical Analysis

The collected data were organized, tabulated and statistically analyzed using SPSS software version 20 (IBM, Armonk, NY, USA). For quantitative data, the mean and standard deviation were calculated. The difference between 2 means was statistically analyzed. P-Value ≤.05 was considered statistically significant.

3. RESULTS

This study comprised 20 patients with localized stable nonsegmental vitiligo, 11 males and 9 females. The patient's demographics were shown in (Table 1).

3.1 Repigmentation Response

Regarding the percentage of repigmentation, the excellent results were in 30% of the patients (Fig. 1). good in 25%, moderate in 15%, poor in 15%

and no improvement in 15% of the patients (Table 2). The percentage of improvement ranged from 0 –100% with a mean of 50.30 ± 34.60 and a median of 55.50 %. Regarding Visual Analogue System (VAS) score, the percentage of reduction ranged from 1-4 with mean 2.50 ± 1.24 and median 2.5.

There was a significant relation between the degree of improvement assessed by three dermatologists committee and the patient satisfaction (p=<0.001) and the visual analogue system (VAS) score (p=<0.001) (Table 2). There was statistically positive correlation between the percentage of improvement and the percentage of VAS score (r =0.952, p =<0.001) (Table 3).

3.2 Regarding Side Effects

All patients experienced tolerable pain during injection, only two patients complained of ulceration at site of injection which healed within one week after topical antibiotic.

4. DISCUSSION

Vitiligo, a common depigmenting skin disorder, its prevalence is 0.5–2% worldwide and about 1.2% in Egypt. It is characterized by absence of melanocytes that clinically causes non scaly, milky-white macules [9]. The available treatment methods have different indications and specific limitations. The treatment modalities can be classified into medical and surgical [10]. A lot of procedures were tried over years in terms of improving the clinical results with its impact on the quality of life of the patients and to decrease the possible side effects [11].

Fluorouracil (5-FU) has an antimitotic activity with selective cytotoxicity against rapidly proliferating keratinocytes which explains its efficacy in the treatment of non-melanoma skin cancers, actinic keratosis, nail psoriasis, and porokeratosis. 5-FU has been considered in vitiligo treatment after the observation of its induction of hyperpigmentation during treatment of psoriasis and skin tumors [12].

The current study included 20 patients with localized stable vitiligo, treated with intralesional 5 fluorouracil injection, every two weeks until improvement or maximum for 3 months.

One of the prominent findings in this study after 3 months of the treatment sessions was repigmentation which was excellent response in 30%, good in 25%, moderate in 15%, poor in 15% and no improvement in 15% patients.

Table 1. Clinical data of the studied cases (n = 20)

	n	%
Sex		
Male	11	55.0
Female	9	45.0
Age		
Min. – Max.	7.0 – 60.0	
Mean ± SD.	18.70 ± 13.60	
Median	(26.5 – 9.0)15.0	
Family history		
Negative	12	60.0
Positive	8	40.0
Skin type		
II	1	5.0
III	13	65.0
IV	6	30.0
Duration (years)		
Min. – Max.	1.0 –13.0	
Mean ± SD.	4.33 ± 3.58	
Median	3.0 (5.0 – 2.0)	
Site of vitiligo		
Extremities	10	50.0
Acral	7	35.0
Trunk	3	15.0

Table 2. Relation between degree of improvement assessed by three dermatologists committee with visual analogue system (VAS) score and patient satisfaction after intralesional 5-FUinjection

	Degree of improvement										Test of Sig.	p
	No (n=3)		Poor (n=3)		Moderate (n=3)		Good (n=5)		Excellent (n=6)			
	No.	%	No.	%	No.	%	No.	%	No.	%		
VAS score												
1	3	100.0	3	100.0	0	0.0	0	0.0	0	0.0	χ^2=	^{MC}p
2	0	0.0	0	0.0	3	100.0	1	20.0	0	0.0	25.416*	<0.001*
3	0	0.0	0	0.0	0	0.0	3	60.0	1	16.7		
4	0	0.0	0	0.0	0	0.0	1	20.0	5	83.3		
Min. – Max.	1.0 – 1.0		1.0 – 1.0		2.0 – 2.0		2.0 – 4.0		3.0 – 4.0		H=	0.002*
Mean ± SD.	1.0 ± 0.0		1.0 ± 0.0		2.0 ± 0.0		3.0 ± 0.71		3.83 ± 0.41		17.111*	
Median	1.0		1.0		2.0		3.0		4.0			
Patient satisfaction												
No	3	100.0	1	33.3	0	0.0	0	0.0	0	0.0	χ^2=	<0.001*
Slight	0	0.0	2	66.7	2	66.7	0	0.0	0	0.0	21.766*	
Satisfied	0	0.0	0	0.0	1	33.3	4	80.0	2	33.3		
Very satisfied	0	0.0	0	0.0	0	0.0	1	20.0	4	66.7		

χ^2: Chi square test, MC: Monte Carlo, H: Kruskal Wallis test
*p: p value for association between different categories *: Statistically significant at p ≤ 0.05*

Table 3. Correlation between percentage of improvement assessed by the three-dermatologists committee and visual analogue system (VAS) score

	Percentage of improvement intralesionalv5-FU	
	r_s	P
VAS score	0.952*	<0.001*

rs: Spearman coefficient
**: Statistically significant at p ≤ 0.05*

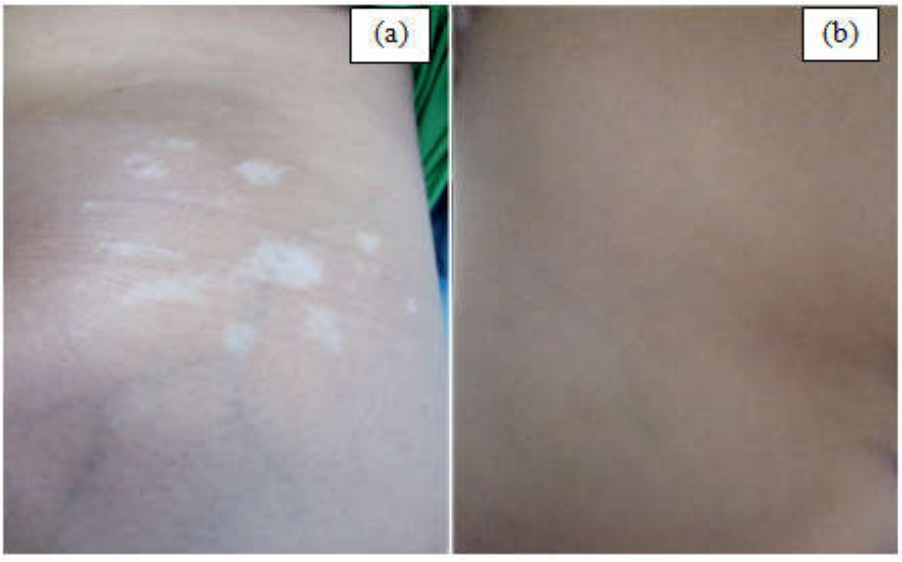

Fig. 1. Right side of back of trunk of female patient (a) before treatment (b) complete repigmentation after treatment with intralesional 5-FU

The mean percentage of improvement was (50.30 ± 34.60 SD) and a median of 55.5 in the treated lesions. These results agreed with Zohdy and Hussein [8] study showed the best overall

improvement with median 52.27, for patients with stable vitiligo treated with intralesional injection of 5-FU. On the other hand, the present study showed superior results than that of intradermal 5-FU injection combined with narrow-band ultraviolet in the study of Abd El-Samad & Shaaban, [13] as repigmentation >50% reported in 48.3% of the patients in the 5-FU side after 4 months while in the present study was 55% in 3 months.

Other studies treated stable vitiligo patients with needling followed by topical 5% 5-FU showed comparable results. The study of Shashikiran et al. [14] noted more than 75% repigmentation (excellent response) in 49% of the patches. Very good response with 50–75% repigmentation in 26% of the patches, 25–50% repigmentation in 11% of the patches, whereas 14% of the patches responded poorly with less than 25% repigmentation. Abd El-Samad [15] et al. demonstrated that excellent improvement occurred in 48% of 5- FU treated patches after microneedling and 40% of acral patches achieved excellent improvement (repigmentation >75%), while the study of Zahra et al. showed [16] excellent improvement (>75% repigmentation) in 47%.

As regarding Evaluation of the safety and tolerability of the therapeutic procedure Regarding the side effects. All patients experienced tolerable pain during injection, only two patients complained of ulceration at site of injection which healed within one week after topical antibiotic [17,18]

5. CONCLUSION

Intralesional injection of 5-FU showed excellent clinical results. The percentage and the degree of repigmentation achieved by the intralesional injection of 5-FU was significant compared to pretreatment evaluation.

CONSENT

After signing informed consents, all patients were subjected to full history taking, general and dermatological examination.

ETHICAL APPROVAL

Research ethical approval (code no. 32701/11/18) was obtained before beginning of the study. The present study is a prospective study. It was carried out on 20 vitiligo patients who were recruited from the Outpatient Clinic of Dermatology and Venereology Department, Tanta University

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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