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Effect of flash lamp pulsed dye laser on discoid lupus erythematosus lesions

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Abstract:

The treatment of discoid lupus erythematosus with pulsed dye has been evaluated in recent years. The improvement of telangiectasia and erythema in cutaneous lesions was based on selective photothermolysis ablation of the dilated capillaries and venules. While the improvement in scar and atrophy was referred to the effect of pulsed dye laser on collagenase activity. We describe the results of discoid lupus erythematosus (DLE) lesions of 62 patients; they received treatment with FPD (585nm, 450µsec) with fluences ranged from 6.75 to 7.75J/cm². The overall clearance rate was 67.5%. Relapse had occurred in 7 patients. Few side effects were observed in the form of hyperpigmentation or hypopigmentation.

We confirm that pulsed dye laser is a good alternative treatment for discoid lupus erythematosus lesions.

Introduction

Classic discoid lupus erythematosus (DLE), the most common form of chronic cutaneous LE, begins as flat or slightly elevated, well demarcated

red-purple macules, or papules with scaly surface. Early DLE lesions most commonly evolve into larger coin-shaped (discoid) erythematous plaques covered by prominent adherent scales. The lesions slowly expand in association with active inflammation at the periphery, leaving scarring with atrophy and telangiectasias at the center. Chronic untreated cutaneous lupus erythematosus ends with marked scarring; with depressed and contracted lesions on the face, creating a wolf-like or lupus facieses [1]. DLE skin lesions are present in 15-30% of variously selected study populations of SLE [2], [3].

The demonstration of immunoglobulin and complement proteins in the dermal-epidermal junction of lesions from patients with DLE has led to renewed interest in immunologic abnormalities of these patients [4].

Standard medical therapy includes corticosteroids (topical or intralesional) and antimalarials. Other alternative therapies include auranofin, thalidomide, oral or topical retinoids, and immunosuppressive agents [5].

The flash lamp pulsed dye laser (585nm) was the first laser system specifically developed for the treatment of cutaneous vascular lesions such as port wine stains, telangiectasias and hemangiomas. It was based on selective photothermolysis, which aims to destroy the blood vessels of the cutaneous vascular lesions with minimal or no damage to the surrounding tissue [6].

Patients and methods:

This study was conducted on 62 DLE patients who presented to our dermatology laser outpatient clinic in the National Institute of Laser Enhanced Science (NILES), referred from Al- Haud Al-Marsoud dermatology hospital.

Patients of both sexes were included; 34 females, 28 males. Their age ranged between 12 and 63 years, all skin types were included with no prevalence to certain type. Follow up period was performed at 3, 6, 12 months after end of sessions.

Patients were diagnosed as classical type of DLE clinically, pathologically and verified serologically. Both localized and diffuse variants were included in the study.

Patients with signs and serological investigations suggestive of DLE activity, females during pregnancy or postpartum were excluded from the study.

Patients were divided into two groups according to distribution of the lesions; localized DLE (48 patients) and disseminated DLE (14 patients).

- Initial evaluation of patients to exclude the presence of SLE according to criteria stated by [7] was performed.
- Pre and post treatment biopsies were taken.
- Inter-rater reliability by two independent dermatologists at the beginning of the treatment and at the end of laser sessions to assess

the degree of improvement.

- Examination of the lesion to determine the following; site, size extent, distribution and the present clinical signs of the lesions.
- The signs of DLE were evaluated according to the severity as shown in table 1:

Table 1 .Evaluation of DLE signs

	None	Mild	Moderate	Severe
Erythema	-	+	++	+++
Telangiectasia	-	+	++	+++
Hyperkeratosis	-	+	++	+++
Atrophy	-	+	++	+++

- The degree of improvement was determined as the percent reduction in the clinical signs relative to normal surrounding skin in gradation of 10% to 100% rating.
- Patients were photographically documented with digital camera; Kodak DX 3700, 3.1 Mega pixels, 3 xs zoom before and after treatment. A written consent to be photographed was taken.
- Patients were evaluated every 2 sessions and at the end of treatment.

Laser procedure:

All the patients were treated by flash lamp pulsed dye laser; Candela SPTL-1 (Candela Corp., Wayland, Mass.) with wave length 585nm, pulse duration 450µsec and hand piece of spot size 5or 7mm. The energy density employed ranged from 6.5 J/cm² to 7.5 J/cm² (average 7 J/ cm²), depending on the test treatment performed 8 weeks previously.

Pathology procedure:

The histological sections were stained by hematoxylin & eosin, and by a trichrome stain; then subjected to evaluation by an ordinary light microscope. Epidermal thickness and blood vessels diameters were measured with micrometry.

Results

The overall obtained clearance rate was 67.54% assessed by both subjective and objective means.

Itching is recorded by all patients to increase during the first week after the laser session then gradually improved with subsidence of the lesion at the end of treatment.

Regarding the signs; it was found that erythema improved first with

complete clearance of 74% followed by telangiectasia which scored total clearance of 57.1% at the end of sessions. The highest incidence of complete clearance obtained was 85% which observed with hyperkeratosis; however atrophy and scarring were the last signs to show improvement with the least percentage of total clearance among clinical signs which were 5.8% for atrophy and 5% for scar.

Tables from (1-5) show the distribution of patients according to severity of each clinical sign and the number of patients that cleared completely at the end of treatment.

It should be taken into consideration that not all the patients presented the 5 clinical signs as the present clinical signs depend on the stage of the disease i.e. old lesions presented with telangiectasia atrophy and depigmented scar while new lesions presented with erythema ,telangiectasia, and hyperkeratosis only with no scar or atrophy.

Erythema:

At the beginning of treatment the total number of patients that had erythema was 50 patients distributed according to severity as follows; seven patients had mild erythema, while 30 patients were categorized as moderate and 13 patients were of severe erythema. At the end of laser sessions 34 patients were completely cured.

Although complete cure were not obtained in the other patients, variable degree of improvement could be observed as shown in [table 1](#).

[Table 2](#) Distribution of patients according to the severity of erythema before treatment after treatment

Before treatment									After treatment
+++		++		+		-ve			
%	No.	%	No.	%	No.	%	No.		
6	7	70	21	85.7	6	0	0	-ve	
1	5	23.3	7	14.3	1	0	0	+	
0	1	6.7	2	0	0	0	0	++	
100	13	100	30	100	7	0	0	total	

* The colored column shows the degree of improvement of severe erythema after treatment

Telangiectasia:

Thirty-five patients had telangiectasia with different degree of severity while 15 patients were negative (telangiectasia was not among the presented clinical signs) before treatment

Table 3. The distribution of patients according to severity of telangiectasia before and after treatment.

Before treatment									After treatment
+++		++		+		-ve			
%	No.	%	No.	%	No.	%	No.		
60	6	45.5	5	64.3	9	100	15	-ve	
30	3	36.4	4	35.7	5	0	0	+	
10	1	18.2	2	0	0	0	0	++	
100	10	100	11	100	14	100	15	total	

* The colored column shows the variable degree of improvement of the moderate degree of telangiectasia



Figure (1) patient represents erythema and telangiectasia before laser



Figure (2) after laser

Hyperkeratosis:

Hyperkeratosis was presented as a clinical sign in 40 patients and its improvement after treatment shows the highest clearance rate. The distribution of the severity of hyperkeratosis was as shown in table 9

Table 4. The distribution of patients according to the severity of hyperkeratosis before and after treatment.

Before treatment									After treatment
+++		++		+		-ve			
%	No.	%	No.	%	No.	%	No.		
66.7	2	76.5	13	95	19	100	10	-ve	
33.3	1	17.6	3	5	1	0	0	+	
0	0	5.9	1	0	0	0	0	++	
100	3	100	17	100	20	100	10	total	

**Figure (3)** follicular hyperkeratosis before laser**Figure (4)** after laser**Atrophy:**

Atrophy was presented in 26 patients, while 24 patients had no atrophy before treatment

Table 5. The distribution of patients before and after laser treatment according to severity of atrophy.

Before treatment									After treatment
+++		++		+		-ve			
%	No.	%	No.	%	No.	%	No.		
0	0	0	0	12.5	2	95.7	23	-ve	
0	0	75	6	87.5	14	4.3	1	+	
50	1	25	2	0	0	0	0	++	
50	1	0	0	0	0	0	0	+++	
100	2	100	8	100	16	100	24	total	

* The colored column shows that the two cured patients were of mild degree of atrophy

Scar:

Twenty-two patients had scar as one the presenting signs and 18 patients were scar free before treatment. Only one patient with mild scar showed complete clearance. On the other hand the rest of patients showed variable degree of improvement



Figure (5) atrophy and scar before laser



Figure (6) after laser

Table 6 . The distribution of scar patients according to the severity before and after treatment.

Before treatment								After treatment
+++ severe		++ Moderate		+ Mild		-ve		
%	No.	%	No.	%	No.	%	No.	
0	0	0	0	9.1	1	94.7	17	
33.3	1	75	6	90.9	10	5.3	1	
33.3	1	25	2	0	0	0	0	
33.3	1	0	0	0	0	0	0	
100	3	100	8	100	11	100	18	total

Effects of clinical variants on clearance of DLE lesions

Effect of size of the lesion, duration of illness, site of the lesion, type of DLE and age were studied in relation to clearance rate.

Evaluation of the clearance rate at the end of laser sessions revealed that specific sites responded favorably than other sites.

Upon this observation the sites were divided according to its response to treatment into responsive sites and less responsive sites

The less responsive sites were found on the scalp, lips and eye brow while the responsive sites include the rest of the body.

The clearance rate found to be higher in responsive sites than the less responsive sites and this relation proved to be of highly statistical significance $p=0.004$.

New lesions were found to respond better than old lesions and the former recorded higher clearance rate.

Regarding type of DLE; the mean of clearance rate of localized DLE group was higher than that of disseminated DLE which proved to be of high statistical significance $p=0.010$

Age of the patients was found to have a significant effect on the clearance of the lesions. Patients younger than 35 years respond better to treatment by laser and scored higher rate of clearance than those who were older than 35 years which means that clearance rate decreased with advance in age.

Among the previously outlined factors and their relations to the clearance rate; it was found that age and duration of illness were the only significant independent variables that affect the clearance rate while the size of lesions was considered to be a dependent variable as shown table 15

Table 6.Effect of multivariate on clearance rate

Before treatment								After treatment
+++ severe		++ Moderate		+ Mild		-ve		
%	No.	%	No.	%	No.	%	No.	
0	0	0	0	9.1	1	94.7	17	
33.3	1	75	6	90.9	10	5.3	1	
33.3	1	25	2	0	0	0	0	
33.3	1	0	0	0	0	0	0	
100	3	100	8	100	11	100	18	

*The complete cure occurred in one patient of mild degree of scar as shown in the colored column

Patients were subjected for follow up period starting one month after the end of laser sessions then at 3, 6 and 12 months.

The data of follow up revealed that 42 patients committed the follow up period on regular basis as they were instructed. Relapse occurred in 7 patients; one male and six females. Their ages ranged between 17-42 years. Four patients were of skin type III while the other three were of skin type IV, V, and VI.

It is worthy to mention that 4 relapsed patients were on concomitant systemic treatment; chloroquine during laser treatment and follow up period. Results of effects of both clinical factors of the patients and the characteristics of DLE lesions on occurrence of relapse could be figured out as follows:

1. Both skin type and type of DLE have relation with relapse and this relations found to be of high statistical significance
2. Age, sex and site of lesions have minimal effects on relapse that of no statistical significance.
3. Concomitant treatment has no effect on relapse and this was proved statistically.

In this study 20 patients developed side effects; 17(85%) patients had transient hyperpigmentation which fade after 3-6 months and 3 (15%) patients had hypopigmentation.

Effect of pulsed dye laser on pathological characteristics of DLE:

Improvement of the pathological findings of DLE was confirmed by recording the following changes in post laser biopsies which include; decrease of hyperkeratosis and follicular horny plugging, marked decrease of perivascular and periadenxal mononuclear inflammatory infiltrates. Decrease of the dermal edema, blood vessels diameter and epidermal thickness were recognized and confirmed by measuring before and after laser treatment. Improvement of the basal layer changes as loss of normal organization and vacuolation were much improved after laser treatment. Figure (7) show the pathologic characteristics of DLE and Figure (8) show signs of improvement previously mentioned.



Figure (7) DLE histopathological changes before laser

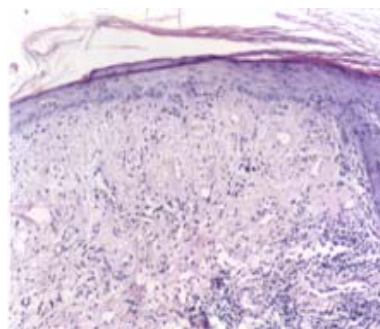


Figure (8) after laser

Discussion

Chronic discoid lupus erythematosus (CDLE) is a skin disease characterized by the presence of well-defined, raised erythematous lesions that spread slowly with an irregular outline while the centers of the lesions heal with scaling, atrophy, and scarring. Eventually, the three events: erythema, hyperkeratosis, and atrophy follow each other. Active areas often show telangiectasia [8].

The flash lamp pulsed dye laser (FPDL) 585 nm with pulse duration 450 μ s was the first medical laser to develop specifically for the treatment of vascular cutaneous disorders. It proved to be efficacious and successfully used for the treatment of port wine stains, hemangiomas and telangiectasias based on the principle of selective photothermolysis, which aims to destroy the blood vessels of the vascular lesions [9] because of its highly selective targeting of the oxyhemoglobin molecule, thermal energy is released in this very specific target within the vessel-the red blood cell. The short pulse duration of this energy (450 μ s) spared the tissue around from thermal damage [10], [11].

In 1986, Henderson and Odom [12] treated characteristic plaques of DLE patient with carbon dioxide laser and observed a dramatic clinical and cosmetic improvement of the cutaneous lesion. Hypopigmentation in the tested areas and reactivation of DLE in the periphery were described as side effect [12].

[13], [14] used argon laser in treatment of DLE, they documented successful trial. [15] presented a case of lupus erythematosus telangiectoides in which the main feature is telangiectasia, cutaneous atrophy was also present. They used FPDL (585nm) at fluence of 7.25 -8.75 J/cm² in five treatment sessions with 5mm spot size and a pulse duration 450 μ s (SPTL-1, Candela). One year later [16] reported on 4 patients with telangiectatic chronic erythema of cutaneous lesions in patients with systemic lupus erythematosus treated with

the same laser specifications and parameters; but the fluence used ranged from 6.75-7.75J/cm² in this study.

[17] Published on a group of 12 patients with different forms of lupus erythematosus. In 10 patients, the lesions LE was limited to the skin while two patients had systemic LE (SLE). They were treated with the pulsed dye laser 585nm and an impulse duration of 0.3-0.45 ms (photo Genica V, Cynosure Inc,) they used handpiece with an impulse diameter of 5mm, 7mm, and 10 mm. Depending on the spot size used, the applied fluences were 3.4-3.5 J/cm² for 10mm handpiece, 3-7J/cm² for 7 mm handpiece, and 6-7 J/cm² for 5mm handpiece ,no anesthesia was used with their patients and they continue the sessions until no further improvement was achieved the number of laser sessions range from 1-10 in their study. In the most recent Egyptian study done by [18], 4 patients of DLE were treated by using PDL at either a wavelength of 585nm and short pulse duration and fluence of 6-8.4 J/cm² for treating erythema mainly, and a wavelength of 600 nm and long pulse duration and fluence of 3.8-7 J/cm² for treating telangiectasia at an interval of 4 weeks between sessions.

All the available published studies focused on the effect of pulsed dye laser as a tool for treatment of vascular lesions hence the improvement of erythema and telangiectasia as they represent the vascular component of DLE lesions neglecting its effects in treatment of other clinical signs that contribute DLE lesions as hyperkeratosis, atrophy and scarring

In this study 62 patients that were selectively chosen to be of classical type of DLE without systemic involvement and this was verified by serological investigation .Flashlamp pulsed dye laser 585nm with pulse duration 450μs was used (SPTL-1, Candela). 5mm and 7mm spot size were used for small and large size lesions respectively. The energy density employed ranged from 6.5to 7.5 J/cm² (average 7 J/ cm²).

The present study included, all skin types except skin type I as it is rare in Egyptians. Observations have raveled that patients with dark skin type as IV-VI needed more laser sessions and this could be explained by the proposal of [19] concerning melanin absorption of visible light and its competition with oxyhemoglobin so in patients with darker skin types more of the laser energy will be absorbed within the pigmented epidermis ;this can result in insufficient energy reaching blood vessels and increased incidence of unwanted post inflammatory hyperpigmentation hence the need of more sessions .

Based on the principle of selective photothermolysis proposed by [20] and the vascular selectivity of the flashlamp pulsed dye laser (585nm) cutaneous vascular lesions were treated successfully where the target oxyhemoglobin in cutaneous blood vessels is selectively thermally damaged that resulted in coagulative necrosis of red cells and subsequent reduction in the number and size of cutaneous blood vessels. FPDL proved its efficacy in treatment of port wine stains and hemangiomas in children [21] and that explained the effectiveness of FPDL in treatment of DLE as erythema and telangiectasia are

of the main clinical signs.

The microvascular damage may affect collagen or collagenase activity within the scar. Thermal damage to abnormal collagen may allow remodeling and reduction in endothelial cell volume that can affect type V collagen. Mast cell alteration after laser irradiation may be of importance. [22], [23].

On basis of the explanation proposed by previous authors, the improvement of scars and atrophy of patients in this study could be explained. [25], [26], [27].

[24] Treated 48 patients using fluences ranged from 6.5-7.5J/cm² and they have an 88% average improvement, with total resolution in 20% after 4.4 treatment sessions. They found also that facial scars less than one year old achieved better results than non facial scars older than one year.

Comparing the results of complete clearance of scar in this study(5%) to what has been obtained by [24] could be referred to the chronicity of the scars (more than one year) as scarred tissue led to limited depth of penetration of the laser and reduced number of blood vessels.

Explanation of improvement of hyperkeratosis and the pathological changes of DLE is concerned with the role of dye laser in the modulation of the inflammatory response of CLE. It has been observed that the endothelial cell activation plays an important role in the pathogenesis of lupus. This role could be due to the fact that higher levels of adhesions molecules on the surface of the endothelial cells, such as soluble E-selectin are correlated with active disease in LE patients [28].

[29] Suggested that the selective destruction or coagulation of the vessels leads to a modulation of the inflammatory network and a regression of local lesions of DLE.

The activation of photosensitizing substance in the serum and lymphocytes of LE patients could be demonstrated by irradiation at a wavelength of 360-400nm [30], [31] while the action spectrum of LE does not include yellow light (585nm) dye laser [16]. It is well established that light energy in the ultraviolet (UV) spectrum may precipitate or aggravate the disease in lupus erythematosus [32].

[17] proposed that with laser therapy, the applied light is monochromatic and there is strong evidence that the induced pathogenic mechanism are different from those caused by irradiation over a UV spectrum.

In the study done by [33], they stated that no induction of new lesions during treatment with FPD. L.

Both age of patients and duration of illness have significant inverse relationship with the clearance rate which mean that with younger patients and short duration of illness the response to laser treatment is much better

than those of older age or with long duration of illness that was expressed in the obtained higher clearance rate of the former group.

Regarding the pathological process of DLE the three events; erythema, hyperkeratosis and atrophy follow each other. Active areas often show telangiectasia then healing occurred with scarring [34].

When atrophy and scarring occurred, the number of cutaneous blood vessels is significantly reduced in the scarred tissue which is targeted by this laser [17].

On basis of what had been mentioned, explanation of higher clearance rate in new lesions that related to the short duration of illness before the process of scarring had taken place.

An important observation has been found in this study on evaluation of the clearance rate at the end of treatment in relation to the sites of the DLE lesions. Specific sites responded favorably than others and according to this observation the sites were divided into less responsive sites, namely scalp, eyebrow and lips and responsive sites in the rest of the body. Lower clearance rate was obtained with the less responsive sites

Both scalp and eyebrow undergo irreversible scarring alopecia [1] and as previously discussed the effect of scarring on the cutaneous blood vessels therefore decreasing the response of the lesion to the FPD. L.

On the other hand the poor response of the lips could be referred to the evaluation of response of port wine stain by dermatomal distribution proposed by [35], [36]. It revealed that the upper cutaneous lip is V2 dermatome that responds less favorably than V1 and V3 dermatome and they explained the difference in response as V2 skin could be slightly thicker with more adnexal structures and thus more vasculature and nerve endings. V2 dermatome includes the centrafacial part of the face (medial aspects of cheeks, nose, and upper cutaneous lip).

However in this study complete clearance of DLE lesions in the cheeks and nose was obtained so this postulation could not explain our result clearly.

On discussing the effect of type of DLE on the clearance rate it is worthy to mention that the clearance rate of localized DLE lesions was much higher than that of disseminated DLE.

This may be explained by what [37] had found in their study. On measuring the activity of the disease in both localized and disseminated DLE; the former showed less activity hence the better response to laser treatment.

Both studies that have done by [15], [16] found that no clinical deterioration seen at 16 weeks follow up of the reported case.

In the study done by [17] relapse was seen after 6 months after complete

remission of the lesions in one case out of eight patients that were subjected to follow up for 7 months .

Regarding the sex, results in this study matched with that of both [17], [33] where an observation has been made that all their relapsed cases were females.

This may explained by the effect of hormonal changes on the cutaneous disease in lupus erythematosus that studied by [38]. They observed premenstrual and perimenopause flare of the lesions and improvement occurred after menopause. They also stated that the replacement therapy has no effect on exacerbation of the disease. In the present study two DDLE relapsed female patients developed SLE and verified by serological investigations. The relapse in the rest of female patients' could be referred to the effect of hormones exacerbation of the disease and appearance of new lesions. The relapsed male patient had been investigated serologically with no evidence of disease activity but this patient was heavy smoker and smoking is considered as one of the exacerbating factor as revealed by [39].

In the present study relapse has been found to occur more with disseminated DLE patients.

It could be suggested that the relapse is related to the activity of the disease which leads to appearance of new lesions and according to the study done by [37] to measure the activity of the disease in patients with cutaneous lupus erythematosus by applying the (SLAM); the Systemic Lupus Activity Measure proposed by rheumatologist they found that L-DLE patients had less active disease than D-DLE.

Comparing the results of relapse in patients who continue on concomitant treatment(systemic antimalarial) to those received no medications during laser treatment, it was surprising to found that relapse occurred more in those receiving systemic antimalarial. However it is worthy to mention that with development of very active disease, the antimalarials can not prevent such evolution [37].

The evidence of improvement of hyperkeratosis, horny plugs, edema and marked decrease in the inflammatory cellular infiltrates was shown in the post treatment biopsies compared to pre treatment one .The organization of the basal cell layer and absence of the liquefactive degeneration were another histological proof of clearance of DLE and this was matched with [33].

Measuring the blood vessels diameter before and after treatment has revealed that marked reduction in both numbers and diameters of blood vessels. These results were matched with what have been found by [16].

In this study measuring the epidermal thickness revealed that its decrease by two folds in comparison to pretreatment measurement

Previous Histological investigations of FPDLE tissue effects with hematoxylin

and eosin staining treatment in PWS patients have shown no [40] or minimal damage to the epidermis [41] at the light microscope level

By using the nitroblue-tetrazoliumchloride (NBTC) stain, that is a histochemical stain NBTC stain demonstrate the epidermal damage after FPD treatment in most of their studied cases

To our knowledge this study will be the first in literature that proved the occurrence of epidermal damage by measuring the epidermal thickness at the light microscope level and coincide with what [42] reported on using NBTC stain. The presence of epidermal damage explains the clinical frequency of crust formation [11] and the frequency of hyper -and hypopigmentation as the pigmented basal cell layer is a primary target for the thermal damage. Hence, avoidance of sun exposure seems essential before and during FPD therapy [42].

By the aid of this valuable histopathological study done by the previous authors many of the clinical findings in this study could be explained as the hyperpigmentation, hypopigmentation presented with dark skin type patients and their needs to more number of sessions to achieve clinical improvement .This concur with the results of [43] as they stated that the absorption of laser light in melanin leads to thermal damage of the epidermis and subsequently , to lower dermal energy fluences and less efficacy in vessel coagulation [44].In this study the development of side effects were found to be presented with the dark skin type and this concurs with that of [45],[43]; epidermal damage proved to be directly dependent on the intensity of epidermal pigmentation

Conclusions

Flash lamp pulsed dye laser were found to be an effective tool in treatment of DLE lesions. Best results were obtained if used in treatment of those fulfilling the following criteria; localized DLE lesions that are confined to the responsive sites as was found in this study that included the whole body except scalp, lips and eye brow. The clearance rate obtained with young age patients less than 35 years and short duration of illness was found to be associated with the best results.

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