INTERNATIONAL JOURNAL OF ADVANCED BIOLOGICAL RESEARCH

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INTRA LESIONAL TRIAMCINOLONE ACETONIDE INJECTION IN THE TREATMENT OF CHRONIC RECALCITRANT PLAQUE PSORIASIS

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ABSTRACT
Psoriasis is a common, chronic, distressing skin disease of unknown etiology that affects 2-3% of the population. Until now, unfortunately, there is no unique curative systemic or topical treatment. Intra lesional injection of triamcinolone acetonide (3-10 mg/ml) is one of the known treatment option recommended for small resistant lesions for many years. The aim of this study was to induce atrophy by increasing the concentration of triamcinolone acetonide(15-20 mg/ml) for chronic recalcitrant hypertrophic plaque psoriasis. Forty patients with 167 lesions enrolled in this study, 84 lesions used as a control side and 83 lesions as a treatment side. Follow up was performed monthly for 6 months. The results of the injections were statistically significant except for trunkal lesions. Atrophy occurred in only 25% of the patients and in most of the cases were temporary resolving in few months.

KEY WORDS: psoriasis, intralesional, triamcinolone acetonide.

INTRODUCTION

Psoriasis is a common chronic, relapsing and disfiguring, inflammatory and proliferative disorder of the skin, in which both genetic and environmental influences have a critical role.[1] It affects about 2% of the U.S. population, [2] and in Iraq the incidence of psoriasis was 1.5%.[3] Psoriasis is considered to be a disorder of keratinocyte proliferation in the epidermis secondary to activated lymphocytes in the dermis; however the precise mechanism and sequence of interaction between keratinocytes and immune cells is not yet fully understood.[1]
The main pathogenic changes in psoriasis are:[1]

1-Epidermal hyper proliferation with loss of differentiation.
2-Dilatation & proliferation of dermal blood vessels.
3-Accumulation of inflammatory cells, particularly neutrophils & T-lymphocytes.

Chronic stable plaque type psoriasis (psoriasis vulgaris) occurs in the majority of patients as indolent lesions present for months or years and changing only slowly. Clinically the classical lesion of psoriasis presents as a sharply marginated erythematous papule, rich red in color with silvery –white scales. Scales are lamellar, loose and easily removed by scratching. Papules coalesce to form plaques with polycyclic and serpiginious patterns distributed mainly over the extensor surfaces of knees, elbows, lumbosacral areas, umbilicus and retro auricular areas .[4] Most stable plaque psoriasis should first be approached with topical therapy, which disrupts the patient's routine as little as possible. Tar preparations, vitamin D 3 analogues (calcipotriene), topical corticosteroids, anthralin and tazarotene are the mainstays of topical treatments. [2] Recalcitrant plaques of psoriasis have been treated by lasers (CO2 laser resurfacing, pulsed dye laser, and Excimer laser –generated 308-nm UVB radiation).[5] Intralesional triamcinolone acetonide 10mg/ml and triamcinolone hexacetonide (5mg/ml) can be infiltrated intradermally into localized psoriatic lesion by needle injection. This is a valuable technique in troublesome, small, resistant lesions on the back of the hands, especially the knuckles, intensely pruritic small plaques or lichenoid lesions. The effect is long-lasting & repetition of the injection may be unnecessary for several months.[1]

PATIENTS & METHODS

Study design

An open labeled clinical trial was performed on patients diagnosed clinically as having chronic recalcitrant plaque psoriasis attending the out-patient department of Dermatology and Venereology at Al-Kindy teaching hospital during the period from January 2007 through august 2011. A total of 40 patients were included in the study; 22(55%) males and 18(45%) females. Their ages ranged from 8-50 years with a mean 27.65±13.11.

Patient's selection

The following criteria were used for selecting patients in this study:

1. Paitients with bilateral symmetrical distribution of lesions were chosen; one side was considered as a treatment side and the other side as the control side (to be injected after finishing the study). All patients had between 2-8 lesions except one patient who had seven lesions in the trunk; three of them were injected and the other four lesions were used as a control.
2. Only patients with chronic recalcitrant, stable plaque psoriasis who were treated for two months with topical calcipotriol ointment and clobetasol propionate, and either showed no improvement or relapsed immediately after discontinuation of therapy were

enrolled in the study after stopping therapy for two months.

3. Patients with preexisting chronic illness such as diabetes and hypertension and patients on systemic immunosuppressive medications were excluded from the study.
4. A written consent and agreement was taken from the patients or their parents (if they were children) that one side will be injected during the study period and the other side will be injected after finishing the study. The developments of side effects (atrophy, pigmentary changes and infection) were also discussed with the patients or their parents.

Clinical assessment: The surface area of each plaque was measured separately pre and post injection by measuring the maximum length and width.

Statistical analysis: for determination of the statistical significance among different variables descriptive statistics (like mean and standard deviation) were used together with analytic statistics which is t-test between two dependent means.

MATERIALS & TECHNIQUES

All patients received one single session of triamcinolone acetonide intralesional treatment.

Triamcinolone acetonide suspension was used in a dilution of 15-20 mg/ml (20 mg/ml were used only for very thick hyperkeratotic lesions in palms and soles) using a small insulin syringe with a needle gauge 29, firmly locked so that it won't disengage. For the pediatric age group (8-16 years old) a total dose not exceeding 1mg/kg is used; for adult patients a total dose not exceeding 80mg is used. Lesions were injected intradermally with 0.1-0.2ml of the diluted material in adjacent areas so as the whole lesion was infiltrated. Blood pressure and fasting blood sugar levels were measured before initiation of therapy and after one week of treatment. Follow up on a monthly basis for up to 6 months was done to monitor the clinical response, development of complications and to report side effects.

RESULTS

Of the 40 patients enrolled in this study; 22(55%) were males and 18(45%) were females. Their age ranged from 8-50 years with a mean of 27.65±13.17 [table 1]. All patients continued the 6 months period time of the study. Most of the patients had 4 lesions (16 patients) [table2].

TABLE 1: showing age and gender distribution of patients.

		No	%
Age (years)	<10years	3	7.5
	10--	10	25.0
	20--	9	22.5
	30--	8	20.0
	40--	9	22.5
	=>50years	1	2.5
	Mean±SD (Range)	27.65±13.17	8-50
	Gender Male	22	55.0
	Female	18	45.0

TABLE 2: showing distribution of lesions

Site of lesion	No	%
Ear	1	1.2
Elbow	13	15.5
Dorsum of hand	5	6.0
Palm	15	17.9
Trunk	7	8.3
Knee	19	22.6
Ankle	9	10.7
Dorsum of foot	6	7.1
Sole	9	10.7

TABLE 3: showing total number of lesions.

Total number of lesions	No. of patients	%
2	12	30.0
4	16	40.0
6	8	20.0
7	1	2.5
8	3	7.5

The total number of lesions was 167, distributed mainly in palms and on knees [table3] and only one patient had lesions in both external ears (choncae). Eighty four lesions were used as a control group and 83 lesions as a treatment group. The mean lesions size for the control group was 13.00±10.52 (1-40cm) and, after 6 months was 13.00±10.52 (1-40cm). The mean lesion size in the treatment group was 12.05±10.05 (1-42cm) and 6 months after treatment was 1.97±5.09 (0-30), with a P value 0.0001 which is highly significant. The P value between

the control and treatment groups in the beginning of the study was 0.076 which is not significant & it became 0.0001 after 6 months which is highly significant [table4 and figure1]. The mean and the standard deviation were also measured for each site alone [table 5, figure 2 and 3].The P value for each site prior to the injection session was not significant between the two groups (treatment and control), where as it was highly significant for each site in the treatment group pre and post injections for lesions on the elbows, knees, palms and soles, dorsum of the hands and ankles.

TABLE 4: showing means lesion size of the control and treated groups pre and post injection.

P value	After 6 months	Before	Size of lesion (cm)
-	13.00±10.52 (1-40)	13.00±10.52 (1-40)	Control group
0.0001*	1.97±5.09 (0-30)	12.05±10.05 (0-42)	Treated group
	0.0001*	0.076	P value

-Data were presented as Mean±SD (Range)

*Significant using Students-t-test for difference between two dependent means

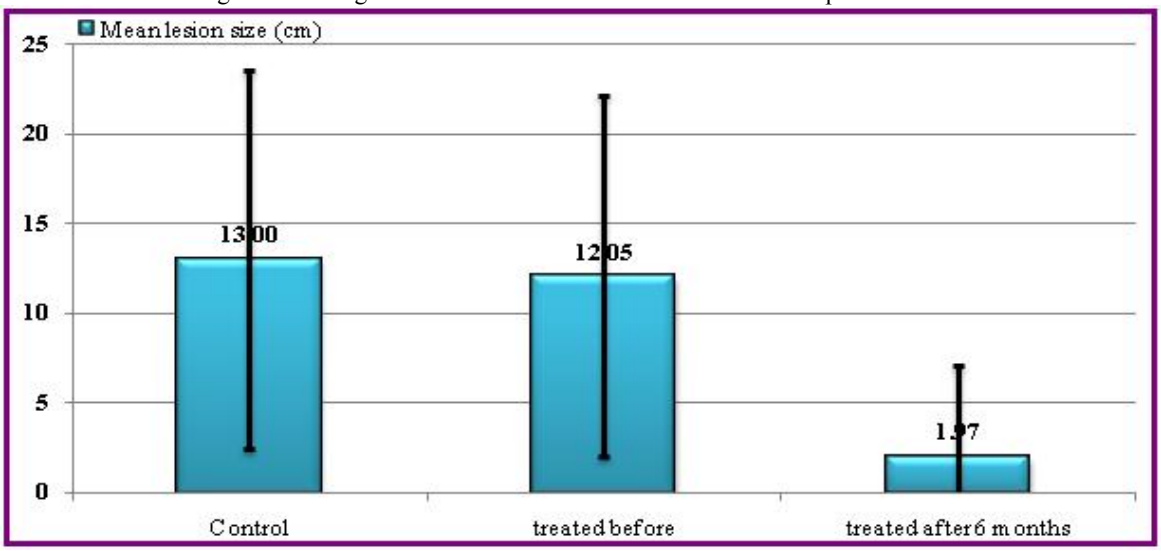

FIGURE1: showing mean lesion size of control and treated group pre and postinjection.

TABLE 5: showing mean lesion size of each site pre and post injection and control group.

P value		Size of lesion (cm)			Site of lesion
Treat before X treat after	Cont X treat before	treated after 6 months	treated before	Control	
-	-	0±	7.00±	1.00±	Ear
0.0001*	0.053	0.92±3.33	7.86±2.98	9.58±4.53	Elbow
0.007*	0.629	0±	2.14±0.95	2.48±1.43	Dorsum of hand
0.0001*	0.247	1.33±5.16	17.41±8.17	19.79±11.65	Palm
0.356	0.547	8.03±10.48	9.10±9.89	7.83±5.72	Trunk
0.0001*	0.073	2.77±5.82	13.97±9.87	16.03±8.91	Knee
0.048*	0.674	0.22±0.44	5.04±6.68	4.22±2.91	Ankle
0.070	0.415	1.18±1.59	2.83±2.14	3.33±3.20	Dorsum of foot
0.0001*	0.999	1.72±1.46	26.65±7.52	26.64±7.53	Sole

-Data were presented as Mean±SD

*Significant using Students-t-test for difference between two dependent means

However, the P value was not significant for lesions on the trunk and dorsum of the foot. There was only one patient who had lesions in both external ears (ear conchae) and it showed complete resolution after 6 months of one injection session. [Figure 4and 5]. All patients complained from pain and discomfort at the site of injections mainly in the palms and soles. Ten patients (25%) and seven patients (17.5%) developed atrophy and hypo pigmentation respectively. Atrophy and hypo pigmentation were temporary and resolved in a few months. Only two patients (5%) developed secondary infection in form of abscess formation in the sole region 10-14 days after the injection. Hypersensitivity reactions or panniculitis were not recorded [table6]. Most of the patients were satisfied with the outcome of the injection; (60%) showed full satisfaction, (27.5%) were partially satisfied and only (12.5%) were not satisfied [table7].

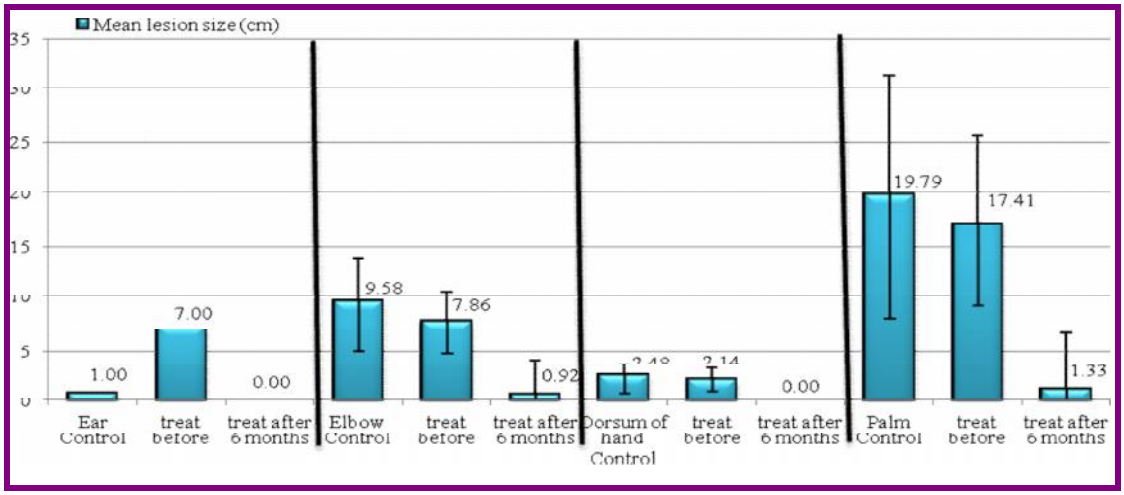

FIGURE 2: mean lesion size of each site of the control and treated pre and postinjection.

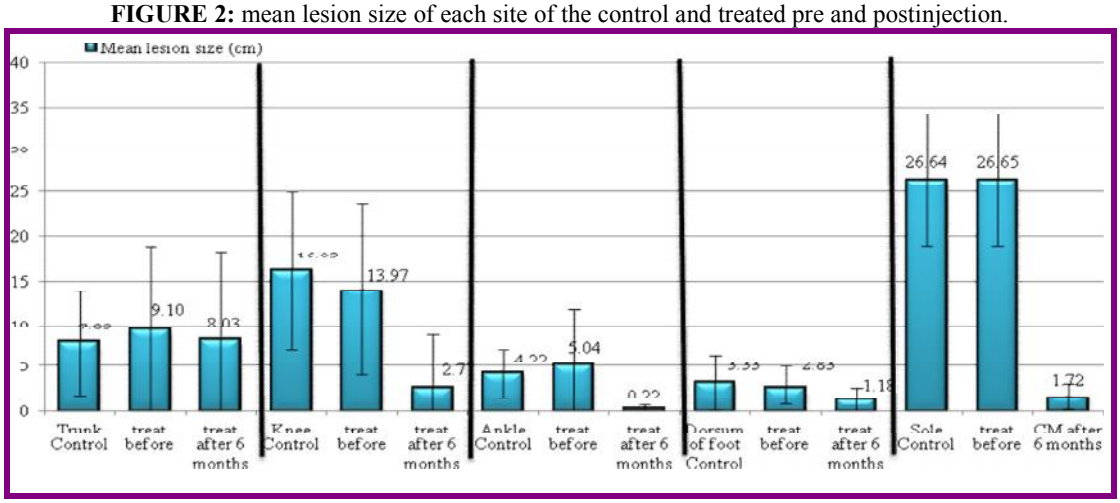

FIGURE 3: mean lesion size of each site of the control and treated group pre and postinjection.

TABLE 6: showing side effect

%	No	Local side effects after 1 month
100	40	Pain
25	10	atrophy
17.5	7	Hypopigmentation
5	2	Abscess

TABLE 7: showing patient's satisfaction

%	No	Patient satisfaction
60.0	24	Fully satisfied
27.5	11	Partially satisfied
12.5	5	Not satisfied

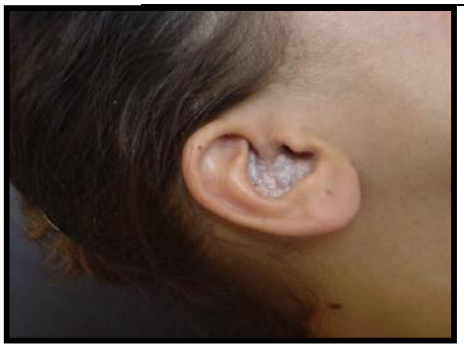

FIGURE 4: preinjection

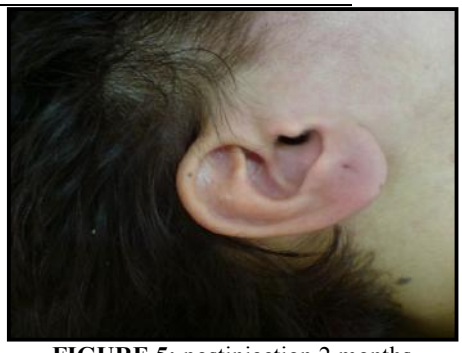

FIGURE 5: postinjection 2 months

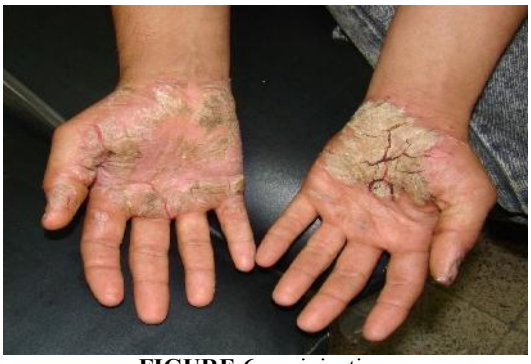

FIGURE 6: preinjection.

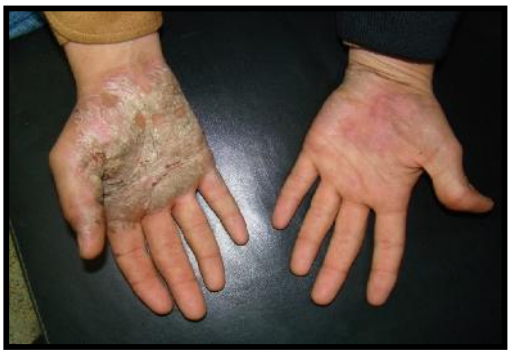

FIGURE 7: postinjection 4 months.

DISCUSSION

Psoriasis is a common, chronic, relapsing, distressing skin disease of unknown etiology that affects 2-3% of the population[1]. Recently psoriasis is thought to be an immunologically mediated disease where T-cells play an important role in its pathogenesis.[6] until now; unfortunately, there is no unique curative systemic or topical treatment. Psoriasis for most patients is more emotionally than physically disabling. It is a disease that erodes the self image, causing shame and embarrassment and forces the patient into a life of concealment and self consciousness.[7]Chronic stable psoriasis is "one of the miseries that beset mankind "; therefore even when the patient has only a few asymptomatic, chronic plaques the disease is more serious than it appears. Thus, when choosing a treatment regimen it is important to reconcile the extent and measurable severity of the disease with the patient's own perception of his or her disease. In this context it is notable that a recent study found that 40 percent of patients felt frustrated with the ineffectiveness of their current therapies, and 32%reported that treatment was not aggressive enough.[5] Intralesional injections with triamcinolone acetonide(3-10 mg/ml) is one of the known treatment options recommended for small resistant lesions for many years.[1] The mechanism of action of corticosteroid has specific and non specific effects. These different mechanisms of action, include: anti inflammatory, immunosuppressive, antiproliferative and vasoconstrictive effects.[8]

Quantitative measurements of surface areas of corneocytes from desequemative portion of psoriatic lesion showed that the surface areas of corneocyte gradually increase in size following one intralesional injection of triamcinolone acetonide.[9] From these facts and the fact that most patients accept atrophy rather than the hyperkeratotic disfiguring and disabling lesions, we decided to increase the concentration of the triamcinolone and so increase these pharmacological and clinical effects with possible increased atrophy. Usually dermatologist use10 mg/ml to avoid or minimize atrophy, and since the goal of our study was to induce atrophy so we increased the concentration of triamcinolone acetonide to (15-20) mg/ml injected at the thickened hyperkeratotic lesions mostly palms and soles, in order to induce rapid clinical improvement at these sites. The rapid, long lasting effects of intralesional steroid in comparison to other topical modalities like tar, anthraline, topical steroids…etc, which need daily application with their messy, clothes discoloring effects and rapid relapsing rate, make it a last choice when other modalities fail, or the first choice when the patient desires to have it.

Macgugan & co workers (1963) showed that a single injection of triamcinolone acetonide induced adrenal suppression as measured by a decrease in plasma cortisol concentration which persisted for up to 4 days; but in contrast an injection of 25 mg triamcinolone diacetate or 50 mg triamcinolone acetonide produced only an occasional transient adrenal suppression. It was concluded therefore that 25 mg or less is a safe dose.[10] So after discussion with the patients about the possibility of development of side effects, it was more acceptable for them to accept atrophy and hypo pigmentation than the daily application of topical remedies which they use for several months with only partial response and rapid relapse after discontinuation of treatment. All 40 patients who were selected for this study had bilateral chronic recalcitrant plaque psoriasis. All were treated for two months with calcipotriol and clobetasol propionate and, showed either no response or relapsed immediately after discontinuation of therapy. One side was used as a control side and other side as the treatment side. The mean lesion size in the treated side after 6 months from a single injection was significantly lower when compared with the control side, and from the mean lesion size in the same side before injection, with a P value 0.0001. P value for each site was highly significant 0.0001 for lesions on the palm and sole, elbow, and knee regions. Whereas lesions on the trunk usually relapsed within 6 months of the injection. Atrophy occurred in 25% of the patients and in most was temporary and resolved within few months.

Most of the patients were satisfied with the injection and they always asked about the next injection. Controlled trials with Excimer- laser treatment also showed effective and promising results for localized plaques[1,] but are much more costly are require repeated sessions of treatment. So intralesional triamcinolone acetonide 15-20 mg/ml is an ideal way to treat chronic plaque psoriasis resistant to other form of therapy except for trunkal lesions which showed a high relapse rate.

REFERENCES

[1]. Griffiths C.E.M, Barker J. N. W. N. Psoriasis, In: Burns DA, Breathnach SM, Cox NH and Griffiths CEM (eds). *Rook's Textbook of Dermatology*, eight edition, London; Blackwell L td; 2010, 20: 20.1-20.60.

[2]. Asha G pardasani, Steven R. Feldman: Treatment of psoriasis: An Algorithm-based primary care physicians. American Family Physicians.2000; 1; 16(3):725-733.

[3]. Al Nuamy S. Epidemiology and HLA typing of psoriasis in Iraq. A study submitted to University of Baghdad, College of Medicine. Diploma Thesis 1988; 45.

[4]. Wolff K., Johnson R.A., Psoriasis, In: Wolff K., Johnson R.A., (Eds). *Fitzpatrick's color Atlas & Synopsis of Clinical Dermatology,* sixth edition, New York ;Mc Graw Hill;2009,4: 53-71.

[5]. Gudjonsson J E, Elder JT ,.psoriasis In: Wolff Klaus, Gold Smith, Lowell A.; Katz, Stephen I.; Gilchrest, Barbara A,; Paller Amy S; Leffell David, J. (Eds). *Fitzpatrick's Dermatology in General Medicine.* Seventh edition; Mc Graw Hill. Philadelphia, 2008; 18:169-193.

[6]. T Kormeili N J, Lowe p s, Yamauchi. Psoriasis : Immunopathogenesis and Evolving immunomodulators and systemic therapies; U.S.Experience. Br J Dermatol 2004,151(1):3-15.

[7]. HabifTP,.Psoriasis and Other Papulosquamous Diseases, In:Habif T.P(eds). *Clinical Dermatology*, fifth edition, Mosby –Elsevier inc;2010,8:264-308.

[8]. Isabel C. Valencia, Francisco A. Kerdel. Topical corticosteroid, In: Wolff, Klaus; Gold Smith, Lowell A.; Katz, Stephen I.; Gilchrest, Barbara A,; Paller, Amy S; Leffell, David J(eds). *Fitzpatrick's Dermatology in General Medicine.* Seventh edition;Mc Graw Hill. Philadelphia, 2008, 216:2103-2106.

[9]. Herbert Goldschmidt: Surface area measurements of psoriatic corneocytes: effects of intralesional steroid therapy. *Journal of investigative dermatology1979, 73:558-560*.

[10]. Teik K.O, Poh F.W:Treatment of various dermatoses by intralesional injection of Triamcenolone acetonide.A clinical trial of 23 cases. *Singapore Medical journal 1965;4:* 107-109.