THERAPY

INDICATIONS AND DOSAGES IN LONG RANGE THERAPY OF CORTISTEROIDS IN DERMATOLOGY

by
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INTRODUCTION

No treatment is more impressive than the use of Cortisteroids, especially, in Dermatology inspite of the fact that they are not specific therapeutic agents. This is so, not only because the reversal of the lesions, which are visible, is rapid, but alse because of the fact that there are quite a number of chronic dermatoses for which even satisfactory management till now has not been possible.

INDICATIONS

The beneficial effect of Cortisteroids is based on their capacity to suppress evidence of the disease. But, unfortunately, this effect is temporary and lasts only till it is being administered. As it does not cure the disease but just suppresses its signs and symptoms this effect of Corticosteroids has been termed by Sulzberger as "Morbidostatic." This morbidostatic anti-inflamatory effect even though non-specific, limited, and temporary, has been utilised in a wide range of dermatologic diseases. Various diseases in which it has to be used over a long period can be divided into three groups.

1. Serious, often fatal diseases, in which there is no choice but to use the steroids. Diseases included in this group are :—
   (a) Pemphigus.
   (b) Systemic Lupus Erythematosus.
   (c) Dermatomyositis.
   (d) Scleroderma.

   Corticosteroids have not only provided the clinician with a more rational method for management of these diseases but also, according to some, it has prolonged the span of life.

2. Chronic incapacitating and distressing dermatoses in which corticosteroids have been found useful. These include :—
   (a) Severe atopic dermatitis (of children, adolescents and adults).
   (b) Nummular eczema.
   (c) Eczematous eruption of the hands,
   (d) Exudative discoid and Ch. lichenoid dermatoses.
   (e) Erythrodermia.

   These disorders, as a rule, do not cause death but, all the same, they can wreck the social and family life of the sufferer. Their use

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is, therefore, justified especially when other measures have failed to control the disease.

3. Dermatoses in which they are still under study and may be useful. They are :—
   (a) Psoriasis.
   (b) Sarcoidosis.
   (c) Seborrhoeic dermatitis.
   (d) Dermatitis herpetiformis.
   (e) Alopecia areata.
   (f) Lichen planus.

CHOICE OF CORTICOSTEROID

This has assumed importance lately because of the newer analogues coming into the field. The choice should be based on the following three considerations:—

1. Its specific therapeutic effect.
2. Its cost.
3. Its side effects.

1. *Spocific therapeutic effect.* Even if pharmacologic effects of the various preparations which are available are similar, the therapeutic results obtained in a malady with a particular preparation may not be achieved by therapeutically equivalent or even higher doses of other corticosteroids. Notable example of this is triamcinolone in psoriasis. Recently certain workers have claimed better results with this analogue in certain varities of pemphigus also. Again, under particular circumstances in the same disease it may be more advantageous to use one preparation in preference to others, for instance in rapidly spreading systemic lupus erythematosus or pemphigus one may choose to give ACTH by I. V. drip infusion rather than an oral preparation.

2. *Expense.* of the treatment is high and many a time poses a serious problem. One is often at one's wits ends on account of this and does not know how to continue the treatment.

3. *Side Effects.* Only a few facts will be mentioned in this connection.

Firstly, prednisolone, because of its lesser effect upon electrolytes, has virtually replaced earlier preparations of cortisone or hydrocortisone, especially, in prolonged therapy. Secondly, the side effects of the newer analogues (triamcinolone and dexamethasone), no doubt, are less in degree as compared to prednisolone, it is not to be forgotten that these newer analogues have added some of their own side-effects e. g. muscle weakness, increased gastric irritation. Moreover, it is as yet, too early to pass one's judgement on them especially from this point of view. Further, they have done nothing to solve the problem of expense.

DOSAGE

What Sutton remarked in his book about the dosage of corticosteroids is very apt, and will be good to recall here. He remarks "the right dose is good, wrong dose is not; for underdosage accomplishes nothing and overdosage does harm." This quotation emphasises sufficiently the importance of finding out the correct controlling dose. This has to be determined in each and individual case, and there cannot be a set dosage schedule. The procedure for finding out the correct controlling dose has varied from worker to worker. However certain important facts some of them still controversial have emerged and have to be kept in mind. They are as under :—

1. It is only after a preliminary study, thorough examination and proper evaluation of each patient for evidence of hypertension, renal insufficiency, gastric ulcers, glycosuria, pulmonary tuberculosis past, persent or occult, or evidence of any other infection, has been made that treatment with corticosterodis should be instituted. Even when these are absent at the start of the treatment, patients should be carefully, watched for their development during prolonged therapy.

2. The initial controlling dose for a particular patient no doubt, is the judgement of an individual physician but the following has to be kept in consideration by him :—

(a) The dermatologic condition of the patient,

(b) Severity of the inflammatory process.

and (c) the type of the steroid used.

3. The necessity and importance of hitting hard with an adequate high dose at the very beginning has been emphasised by Baer and Witten (1957), It is felt from our experience that a dose of 40 mg. to 80 mg. of prednisolone or equivalent of other derivatives would serve this purpose in majority of cases in our country.

4. The dose of corticosteroid required to suppress the disease in small children is by no means as small as one might expect considering child's lesser weight and size.

5. At times of stress e. g. accident, acute infection, surgical emergencies, it is recommended that the dosage of the steroid be increased.

6. A severe "Rebound phenomenon" i. e. severe aggravation of the dermatoses usually occurs if the dose is stopped or dropped too rapidly. There may, also, be recurrnces or flare-ups during the reduction of the dose even when lowering of the dose is gradual. This requires increase in dosage, but this elevation is almost always transient.

7. Steroides are usually given in more or less, evenly-spread 4 to 6 doses. But George V. Reckling and Albert. M. Kligman (1961) gave two days' total-dosage in a single dose every other day to their patients and have claimed that the response to this alternate day therapy was quite comparable to that occuring with conventional four-dosage daily treatment. They further feel that by reducing the duration of high blood levels of steroids by this method, adverse side effects might be minimised. It is felt that this intermittent scheduling of corticosteroids needs further study and should be given a trial.

8. It was previously recommended that during long-range therapy cortisone or prednisolone should be interrupted at regular intervals and short course of ACTH instituted to stimulate the adrenal cortex. But our attempts to substitute prednisolone with ACTH during treatment, even when done gradually, caused on the other hand further deterioration of the condition. Baer and Witten, editors of the Year Book of Dermatology and Syphilology (1956–1957), also feel that this periodic administration of ACTH during long-range therapy with corticosteroids is not necessary.

9. Exudative dermatoses allow many avenues for entrance of bacteria. Keeping this as well as the results obtained by Rimbaud and Duntze (1959) in view, combined anti-biotic and anti-inflammatory treatment was tried in a few cases of pemphigus. The antibiotic after culture and sensitivity test, usually in doses considerably higher than those customarily employed, was started first, and then corticosteroid was added after nearly 24 to 36 hours. Results, in cases in which this regimen was adopted, has been very gratifying.

10. Incidence of folliculitis has been very high in our cases in whom long range therapy was employed. It was especially so, in those cases who were prescribed an ointment for local use as well. This or any other evidence of infection should not be ignored and suitable therapy instituted at once.

Lastly it may be mentioned that facial rounding, buffalo hump, hirsutism, acne etc. may be encountered during the long-range therapy but these are not serious complications and should be ignored. This is perhaps the price which a patient has to pay for this long-range therapy.

OUR EXPERIENCE

Our experience with this long-range therapy of corticosteroids in some of the skin disorders at V. J. Hospital, Amritsar is as under.

Pemphigus:– total number of cases of this disease treated during the year 1962 is 17. Of these, 2 were of pemphigus foliaceus, one of pemphigus erythematodes, and the remaining 14 were of pemphigus vulgaris. The data regarding dosage employed to centrol the disease and minimum dosage required to maintain this controlled state is given in Table I.

TABLE I.

Corticosteroids in Pemphigus At V. J. Hospival, Amritsar (1962).

S. No. & particulars	Diag.	Acantho-lysis.	Steroid used.	Cont. dose.	Mainte-nance dose.	Duration of treatment	Remarks.
1. R. K. 40F	P. V.	POS.	PRED.	40 mg.	15 mg.	3¼ months.	
2. S. S. 30M	P. V.	POS.	PRED.	60 mg.	10 mg.	5 months.	
3. R. N. 36M	P. V.	POS.	PRED.	50 mg.	15 mg.	2 months.	
4. C. S 50M	P. V.	POS.	PRED.	40 mg.	20 mg.	3½ months.	First admission
			PRED.	20 mg.	20 mg.	1 months.	2nd admission.
5. S. S. 60M	P. V.	POS.	PRED.	(40 mg. in-effective, substituted with			
			ACTH.	100 I. U., I/M. but condition deteriorated rapidly.			
6. K. K. 50F	P. V.	POS.	PRED.	30 mg.	15 mg.	2¾ months.	First admission
			PRED.	40 mg.	15 mg.	1½ months.	2nd admission, after 4 months.
7. K. D. 15F	P. F.	POS.	PRED.	20 mg.	10 mg.	3½ months.	
8. H. S. 65M	P. V.	POS.	PRED.	20 mg.	17½ mg.	25 days.	
9. G. D. 50F	P. V.	POS.	PRED.	50 mg.	40 mg.	5½ months.	Left against medical advice.
10. B. K. 25M	P. E.	Not done	D. M.	6.0 mg.	1.0 mg.	1½ month.	
11. D. 18F	P. V.	POS.	PRED.	20 mg.	15 mg.	1½ month.	Flare up after 1¾ M.
			PRED.	20 mg.	15 mg.	2 month.	inspite of taking maint. dose.
12. L. 42F	P. V.	POS.	D. M.	5 mg.	1.25 mg.	3 months.	
13. G. K. 25F	P. F.	POS.	PRED.	50 mg.	being worked out.	10 months.	Still in hospital.
14. S. D. 45M	P. V.	POS.	PRED.	40 mg.	20 mg.	2¾ months.	
			D. M.	8.0 mg.	(still on cont. dose.	3½ months.	Still in hospital.
15 P. 50F	P. V.	POS.	PRED.	50 mg.	being worked out.	3 months.	Still in hospital.
16. H. K 25F	P. V.	POS.	PRED.	80 mg.	(still on cont. dose.	4½ months.	Still in hospital.
17. S. S. 19M	P. V.	POS.	PRED.	80 mg.	being worked out	4 2/3 months	-do-

Cont. dose stands for controlling dose. D. M. stands for Dexamethazone and Pred. for Prednisolone.

One case (No. 5) aged 60, was first treated with prednisolone 10 mg. 6 hourly and then with ACTH 25 I. U., intramuscularly 4 times a day for 7 days. His condition did not improve with this dose. As he was taken away from the hospital against medical advice, we lost touch with this patient.

If the dosage required for the treatment of the remaining 16 cases is converted into prednisolone dosage equivalents we find that the controlling dose in this series was 80 mg. in two, 60 mg. in one, 50 mg. in five, 40 mg. in four, 30 mg. in one and 20 mg. in three cases. It varied from the maximum dose of 80 mg. to as low a dose as 20 mg. The average of the series works out to be 45 mg. According to the western literature, controlling dose in pemphigus may be as large as 750 mg. (Andrews, 1955), 1000 mg. (Pilsbury, 1956) or even 1500 mg. (Mackenna, 1954;

Nelson et al, 1955) of cortisone which is equivalent to 150 mg. 200 mg. 300 mg. of prednisolone respectively. But this does not seem to be our experience. Dose required initially by us is comparatively considerably less.

Maintenance Dose: five patients are still in the hospital though the disease has been brought under control even in them. Whilst reduction in doses has been started in three cases (No. 13, 15 and 17) it has not been possible to lower the controlling dose till now in the remaining two cases. The maintenance dose of this series has varied from 6.5 mg. to 40 mg. average being 15.6 mg. There does not seem to be much difference between the maintenance dose of ours and that of western countries.

Case No. 13 who is in the hospital for last 10 months and who required 80 mg. of prednisolone for control of the disease. is that of pemphigus foliaceus. In contrast to this we have another case (Case No. 7) of pemphigus foliaceus in whom we could control the disease in 1½ month with 20 mg. of prednisolone only and whose maintenance dose worked out to 10 mg. of prednisolone only. Therefore our experience with treatment of pemphigus foliaceus is not very very consistent.

In one case of pemphigus erythematodes that we happened to treat with dexamethasone, we obtained quite gratifying results.

It may also be added that mucosal lesions were much more resistant to treatment than the skin lesions.

Erythrodermia:—total number of cases of erythrodermia treated in the year 1962 as eight. Seven of these were of symptomatic variety but in one cause could not be determined. The dosage of prednisolone employed in these cases of erythrodermia is summarised in Table II.

TABLE II.

Corticosteroids in Erythrodermia at V. J. Hospital, Amritsar (1962)

S. No. & particulars	Steroid used.	Cont. dose.	Maintenance dose.	Duration of treatment.	Remarks.
1. R. D. 40F	PRED	30 mg.	20 mg.	2 months.	First admission.
	PRED	20 mg.	15 mg.	1¾ months.	Second admission.
	PRED	30 mg.	15 mg.	2½ months.	Third admission.
2. H. S. 55M	PRED	15 mg.	10 mg.	1½ months.	
3. R. L. 53M	PRED	15 mg.	5 mg.	3 weeks.	
4. I. S. 40M	PRED	17.5 mg.	10 mg.	1½ months.	
5. R. P. 55M	PRED	30 mg.	15 mg.	1½ months.	First admission.
	PRED	40 mg.	20 mg.	3 months.	Second admission.
6. A. S. 30M	PRED	40 mg.	20 mg.	2 month.	
7. P. S. 42M	PRED	20 mg.	10 mg.	1½ months.	
8. K. K. 42F	D. M.	4.0mg.	Not on any steroids since 5½ months.	4 months.	

Cont. dose stands for controlling dose.
Pred. stands for prednisolone

The controlling dose required in this disorder varied from 15 mg. to 40 mg. with an average of 25 mg., while the maintenance dose varied from 5 mg. to 20 mg. with an average of 12 mg.

Case No. 1 was admitted three times and case No. 5 two times, on account of relapse of their condition. Case No. 8, on the other hand, was able to dispense with her maintenance dose altogether and is without it for last 5½ months. We have lost touch with the remaining 5 cases.

Systemic Lupus Erythematosus. four cases of systemic lupus erythematosus were treated during last year. Two of them were new cases but the other two were old cases who had come back on account of relapse in their condition. Table III refers to dosage employed in this diseases.

TABLE III

Corticosteroids in Systemic Lupus Erythematosus at V. J. Hospital, Amritsar.

S. No. & particulars.	Steroid used.	Cont. dose.	Maintenance dose	Duration of treatment	Remarks.
1 W. 50 F	PRED.	40 Mg.	15 Mg.	3½ Months.	Expired.
2. R. P. 25 F	PRED.	30 Mg.	15 Mg.	1½ Months.	
3. K. 18 M	PRED.	30 Mg.	15 Mg.	2¾ Months.	Second admission.
4. P. K. 26 F	PRED.	40 Mg.	20 Mg.	9½ Months.	

Cont. dose stands for controlling dose.
Pred. stands for prednisolone.

One of the two cases died in the hospital because of kidney failure. The controlling dose of the remaining three varied from 30 mg. to 40 mg. with an average of 35 mg., while the maintenance dose varied from 5 mg. to 20 mg. with an average of 16 mg. From the above, it is quite evident that though corticosteroids are of great value in controlling the acute episodes it has no effect upon the kidney lesions. This fact was emphasised in our paper on systemic lupus erythematosus (1962) also. Hence the ultimate outcome of the disease with evidence of kidney involvement is very gloomy indeed.

Scleroderma. In one case of "Acrosclerosis" which was under our observation from 1960 to 1962, prednisolone in a dose of 15 mg. alongwith prisocol given over a period of nearly six months gave relief not only in Raynaud's phenomenon which was of much less severity at the end of treatment but also caused marked diminution in size of some and disappearance of other hypo-pigmented, sclerosed lesions present in the regions of temples, mastoid and forehead. When she visited the department in March, 1962 it was found that Raynaud's phenomenon had resumed the same severity once again though there was no increase in the scleresed areas till then. She had not taken any medicine during the last 6 months.

In three cases of generalised sclerodermia, treatment with corticosteroids produced no other benefit except that there was more mobility in the joints.

Dermatomyositis. In one case of dermatomyositis diagnosed in 1959 who had muscular pains, erythematous rash and gangeronous ulceration of the thigh, corticosteroids alongwith the antibiotic chloromycetin gave a lot of relief and seemed to arrest the progress of the disease at that time. But the patient was never seen afterwards and hence much cannot be said about this disease because of our limited experience with it.

Reticulosis. One case of chronic lymphatic leukaemia who presented and got admitted with severe generalised pruritus, lichenfication, and patchy erythema was put on certicosteroid therapy. He improved remarkably i. e. besides symptomatic relief there was also appreciable objective improvement by way of reduction in erythema and infiltration. He was, as a matter of fact, discharged from hospital as relieved. But the patient had to be readmitted after some time. True nature of the disease was discovered only at this time. Corticosteroids, now, did not give him much relief, and he succumbed to this disease subsequently in medical ward where he was transferred for treatment of lymphatic leukaemia.

Psoriasis. Corticosteroid therapy especially with triamcinolone is claimed to be useful in acute generalised exfoliative psoriasis, pustular psoriasis, psoriasis arthropathica, and for pruritus in psoriasis. But our experience with corticosteroids in psoriasis is not a very happy one except in generalised exfoliative dermatitis due to psoriasis. In cases of psoriasis arthropathica, though there was marked improvement in arthritis, we were not able to do anything to the skin lesions. This therapy was of not much help even in the relief of itching whenever it was present in cases of psoriasis as claimed by some workers.

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