Prednisolone-21-stearoylglycolate in scleritis

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Scleritis is one of the collagen diseases. It is a serious condition often accompanied by severe pain and the disabling ocular complications of keratitis, uveitis, glaucoma, macular oedema, complicated cataract, retinal detachment, and even perforation of the globe. In its characteristic form the disease is recurrent, eventually becoming quiescent. Adequate treatment should be given at an early stage, aimed at suppression of the condition until natural remission occurs; otherwise there may be marked reduction in vision and loss of the eye.

In the Scleritis Clinic of the Professorial Unit at Moorfields Eye Hospital, the effects of oxyphenbutazone (Tanderil), Indomethacin, and systemic and local prednisolone have been compared. The present study is concerned with the effect of prednisolone-21-stearoylglycolate (Sintisone).

No satisfactory classification of scleritis exists in the literature. We have recently classified it as follows (Watson, Hayreh, Awdry, 1968a, c):

(1) Anterior scleritis

- (i) Nodular scleritis
- (ii) Diffuse scleritis
- (iii) Necrotizing scleritis, which includes scleromalacia perforans.

(2) Posterior scleritis

Further subdivision of this classification is not justified, as it is not related to the aetiology.

Materials

The study was carried out on 27 patients with lesions shown in Table I. Their ages ranged from 16 to 84 years (Table II), and there were thirteen women and fourteen men. Thirteen had some associated systemic disease or precipitating factor (Table III).

All but two of these patients had been treated with other drugs (Table IV), but these were discontinued during the trial. In mild cases of scleritis, local steroids were used. If the condition did not respond or was very severe, systemic anti-inflammatory drugs were given: Tanderil, Indomethacin, or prednisolone. Sintisone was given to 25 patients in whom there was no improvement, or a recurrence. Out-patients were assessed at weekly intervals.

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Table I *Nature of lesions*

Type of Lesion	No. of cases
Nodular scleritis	7*
Anterior diffuse scleritis	5
Sclero-keratitis	11**
Necrotizing scleritis	1
Posterior scleritis with retinal detachment	1
Diffuse anterior and posterior scleritis with uveitis and macular oedema	1
Bilateral diffuse episcleritis	1***
Total	27

* = One had episcleritis in the other eye

** = One had a marked uveitis

*** = This patient's condition did not respond to local steroids or to any systemic anti-inflammatory drugs other than steroids

Table II *Age distribution*

Age (yrs)	No. of cases
10-19	2
20-29	1
30-39	1
40-49	10
50-59	7
60-69	3
70-79	2
80-89	1
Total	27

Table III *Cases with associated systemic disease*

Systemic disease	No. of cases
Rheumatoid arthritis	5
Osteoarthritis	2*
Herpes zoster ophthalmicus	2
Enteritis (most probably ulcerative colitis)	1
Sensitivity to industrial solvents	1
Raised ESR with no other systemic abnormality	1
Xanthomatosis	1
Total	13

* = In one of these there was a persistently raised ESR

Table IV *Treatment given before Sintisone trial*

Treatment	No. of cases
Local steroids	12
Local steroids and Tanderil	2
Local steroids and Indomethacin	1
Local steroids and systemic prednisolone	2
Local steroids, Tanderil, and Indomethacin	1
Local steroids, Tanderil, Indomethacin, and systemic prednisolone	4
Local steroids, Tanderil, Indomethacin, systemic prednisolone, and ACTH	3
No treatment	2
Total	27

Dosage

One tablet of prednisolone-21-stearoylglycolate contains 6.65 mg. and is equivalent to prednisolone 3.5 mg. The period of maximum dosage (Table V, overleaf) depended upon the response of the lesion: this dose was continued for 7 to 14 days, in three cases for 21 days, and in one for 28 days (these four patients received eight tablets per day). Once the response was satisfactory, as judged by the disappearance of pain and inflammation, the dose was reduced gradually. In most patients the reduction in dosage was to 6, 4, 3, 2, and 1 tablet a day, at intervals of about 4 to 7 days. The drug was then withdrawn. In patients in whom the disease tended to recur on the above regime of reduction of dosage, it was necessary to reduce the dose in half-tablet steps. There were some, however, who needed a maintenance dose and the drug could not be withdrawn completely.

Table V Dosage of Sintisone during initial period

<i>No. of Sintisone tablets per day (expressed as prednisolone in mg.)</i>	<i>No. of cases</i>
12* (42 mg.)	1
8 (28 mg.)	17
6 (21 mg.)	6
4 (14 mg.)	3
Total	27

*One tablet of Sintisone (6.65 mg.) is equivalent to prednisolone 3.5 mg.

Table VI Complete resolution of scleritis with Sintisone

<i>Time of onset</i>	<i>No. of cases</i>
2 days	1
4 days	7
5 days	3
6 days	1
1 wk	6
2 wks	1
4 wks	2
Total	21

Table VII Incomplete resolution of scleritis with Sintisone

<i>Time of onset</i>	<i>No. of cases</i>
2 days	1
4 days	1
2 wks	2
4 wks	1
Total	5

Results

The result was assessed as complete resolution of the lesion, incomplete resolution, or no response. The last was recorded in only one patient, who stopped taking the drug after one week because the symptoms were not relieved. 21 cases showed complete resolution of the scleritis (Table VI), and in five the condition improved but there was incomplete resolution over a period of 4 weeks (Table VII).

The incidence of recurrence of the scleritis in 26 patients of this series was recorded during a follow-up period which varied from one month to 2 years (Table VIII). In sixteen cases cessation or reduction of the dosage was followed by a recurrence of scleritis, and the initial regime had to be repeated. Thirteen patients required a maintenance dose to keep them free from recurrent attacks (Table IX).

Table VIII Incidence of recurrence of scleritis

<i>Follow-up period (mths)</i>	<i>Recurrence</i>	
	<i>Absent</i>	<i>Present</i>
1	—	1
2	1	1
3	2	—
4	—	1
6	—	1
8	1	1
12	1	1
13	1	—
14	1	—
16	1	1
18	1	3
24	1	6
Total no. of cases	10	16

Table IX Maintenance dose of Sintisone

<i>Dose (tablets)</i>	<i>No. of cases</i>
1 alternate days*	1
1 daily	2
1½ daily	1
2 daily	7
4 daily	2
Total	13

*Equivalent to prednisolone 3.5 mg.

In four patients Sintisone was withdrawn, for the following reasons:

(1) Acute psychosis with suicidal tendencies developed in two women aged 52 and 54 years. In the first, the psychosis started towards the end of the first week of treatment with eight tablets per day,

and became severe during the second week (six tablets per day). The drug was tailed off to a complete stop in 48 hours and recovery was dramatic. The scleritis in the meantime had resolved completely. In the second patient, the psychosis developed 4 weeks after treatment with eight tablets per day and there was complete recovery when the drug was discontinued. This patient showed no evidence of psychosis on prolonged treatment with prednisolone before and after the Sintisone. The scleritis had resolved partially with Sintisone, but was completely suppressed by prednisolone.

(2) In one patient showing sensitivity to industrial solvents there was no response to Sintisone during the first week. He stopped taking it and asked to return to prednisolone, of which he now requires a maintenance dose of 40 mg. which just controls the scleritis.

(3) In one woman aged 84 with scleromalacia perforans, Sintisone achieved only incomplete resolution of scleritis over a 4-week period and the lesion flared up when the dose was reduced to less than six tablets daily. Suppression was achieved with prednisolone 80 mg. daily.

The associated systemic conditions (Table III) also improved whilst the patients were receiving Sintisone. In one patient, enteritis of long duration, probably ulcerative colitis, responded very satisfactorily, and this patient is symptom-free on a maintenance dose of two tablets daily. All the patients with rheumatoid arthritis noticed an improvement.

Side-effects

Noticeable side-effects were recorded in only three patients. As mentioned above, acute psychosis with suicidal tendencies was seen in two. One patient, a woman of 57, complained of hot flushes on the initial dosage. No significant gastrointestinal symptoms were reported. In one patient, who had a tendency to "indigestion", this was slightly more marked. In another, however, with a history of gastric ulceration, there were no symptoms on a maintenance dose of two tablets per day for 8 months; and during two further periods of treatment with larger doses because of recurrence of scleritis, there has been no clinical or x-ray evidence of gastric ulceration.

There was no significant gain in weight in these patients. In fact, some who had gained in weight on treatment with prednisolone commented that they lost weight on changing to Sintisone.

No other side-effect was noticed in this series, though no detailed systemic examination was carried out and reliance was placed on the patients' own statements.

Discussion

All but two of the patients in this series had received treatment for scleritis before they were given Sintisone (Table IV). In our experience of the response of scleritis to different drugs (Watson, Lobascher, Sabiston, Lewis-Faning, Fowler, and Jones, 1966; Watson and others, 1968b, c), we have found that local steroids are effective in only a minor proportion of the patients with mild scleritis, oxyphenbutazone 600 mg. per day in about 50 per cent., Indomethacin 100 mg. per day in about 50 per cent., and systemic prednisolone 60 to 120 mg. per day in 100 per cent. In the present series Sintisone was found to be as effective as prednisolone in all except the two mentioned above (Nos. 2 and 3). On comparing the dosage of Sintisone with that of prednisolone in scleritis, we have found that initially the effective dose is the equivalent of prednisolone 28 to 42 mg. as compared to prednisolone 60 to 120 mg. per day. The response of scleritis to Sintisone and prednisolone is, in the majority of cases, dramatic; but systemic steroids are suppressive

and not curative, and when the drug is stopped the symptoms recur (Table IX). The rate of recurrence with Sintisone as compared with prednisolone cannot be assessed accurately. Apart from the acute psychosis in two patients in this series, no significant side-effects, and none of those commonly associated with other systemic corticosteroid therapy (particularly fluid retention), were noticed. The absence of fluid retention and glaucoma with Sintisone was also reported by Sharma, Hayreh, and James (1968).

Thus it can be concluded that, in the treatment of scleritis, Sintisone is as effective as any other steroid and more effective than Tanderil or Indomethacin. It has fewer side-effects than prednisolone. The effective initial dose is usually eight tablets daily, reducing gradually as soon as a response has been obtained. Patients who require a high maintenance dose of prednisolone also require a high maintenance dosage of Sintisone but, in view of the very similar therapeutic response with a comparatively lower dose and fewer side-effects, it would seem reasonable that Sintisone should be used in preference to prednisolone.

Summary

A clinical trial of systemic Sintisone was carried out in 26 patients with scleritis and one with marked episcleritis. It was as effective in these cases as any other corticosteroid. The only major side-effect noticed was acute psychosis in two patients, which promptly disappeared on cessation of treatment. The initial effective dose was eight tablets daily, equivalent to prednisolone 28 mg., reducing gradually as soon as a clinical response was obtained.

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