

## Systemic Corticosteroid and Isotretinoin Treatment in Cystic Acne

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Prednisolone combined with erythromycin was given to 6 patients with cystic acne. The treatment responses were compared to those in 6 patients with cystic acne receiving isotretinoin and erythromycin and also to those in 3 patients with acne fulminans treated with prednisolone and erythromycin. During the first 4 weeks cystic acne showed a clear improvement in 5 out of 6 patients in both treatment groups. A similar improvement occurred in all 3 patients with acne fulminans. When corticosteroid was stopped, 2 out of 5 patients with cystic acne had a relapse and needed isotretinoin for complete control. In the isotretinoin-treated group, one patient with cystic acne needed prednisolone because the acne worsened to an ulcerative form. Slightly elevated liver enzymes, possibly due to erythromycin treatment, were observed in 2 patients with cystic acne and in one patient with acne fulminans. The present results show that prednisolone combined with erythromycin is an effective treatment during the early stages of cystic and febrile acne, but isotretinoin is needed for long-term control. **Key words:** Prednisolone-isotretinoin; Erythromycin; Liver enzymes; Acne fulminans.

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Isotretinoin is the drug of choice in cystic acne (1), as are systemic steroids in acne fulminans (2-4). Intralesional steroids have been used in severe inflammatory acne for short periods (5, 6) and topically if excessive granulation tissue formation has occurred during isotretinoin therapy (7). We have previously reported good results with systemic corticosteroid treatment in acne fulminans (3, 8), but the question remains whether systemic steroids offer some benefit in cystic acne.

The purpose of the present study was to compare the effectiveness of systemic steroids and isotretinoin combined with erythromycin in the initial treatment of non-febrile cystic acne.

### MATERIAL AND METHODS

#### Patients

The patients were 12 consecutive outpatients with cystic acne (CA) from the University Hospitals of Tampere and Oulu. The patients had several nodulocysts (diameter  $\geq 5$  mm) and 6 of them had been unresponsive to previous antibiotic therapy. All patients had papules and pustules on the face and/or chest and back and 3 of them also had a few ulcerations. Simultaneously with CA patients we treated 3 patients with acne fulminans (AF), who had ulcerative lesions with musculoskeletal symptoms, fever, leukocytosis and/or elevated ESR or CRP.

The study was approved by the Ethics Committee of Tampere University Hospital and the University of Oulu.

#### Treatments

**Cystic acne.** Prednisolone and isotretinoin were used in initial treat-

ment of CA, and according to the protocol the duration of prednisolone treatment had to be 4 weeks. The treatments were randomized, so that every other consecutive patient was given isotretinoin (group 1) and every other patient prednisolone (group 2). If no clinical improvement occurred during 4 weeks the steroid treatment had to be changed to isotretinoin and vice versa. Because systemic corticosteroids are usually combined with antibiotics in AF (8), and tetracycline is not recommended with isotretinoin (9, 10), we combined erythromycin with both treatments.

**Group 1.** The dose of isotretinoin was 40-80 mg/d, i.e. 0.7 mg-1.0 mg/kg (mean 0.88 mg/kg). This dose was given for at least 4 weeks, after which it was optimized for each patient according to the treatment response. Erythromycin acistrate (800 mg/d) was withdrawn after 4 weeks. There were 5 males and one female, aged 13-24 years, mean 18.3 years.

**Group 2.** The dose of prednisolone was 40 mg/d and erythromycin acistrate 800 mg/d. The steroid dose was reduced by 10 mg weekly. After cessation of the steroid therapy at 4 weeks, erythromycin was continued for the next 12 weeks. This group included 3 females and 3 males, aged 18-29 years, mean 22.2 years.

**Acne fulminans.** This group included 3 males aged 15, 15 and 16 years. They received prednisolone 50 mg/d and erythromycin acistrate 800 mg/d. The dose of prednisolone was reduced according to the treatment response.

#### Methods

Clinical improvement was evaluated by counting the papules, pustules, nodulocysts and ulcerations on face, back and chest mainly by the same investigator (S-LK) at the beginning of the study and at weeks 2, 4, 8 and 16 during the treatment. Non-inflamed lesions (comedones) were not counted.

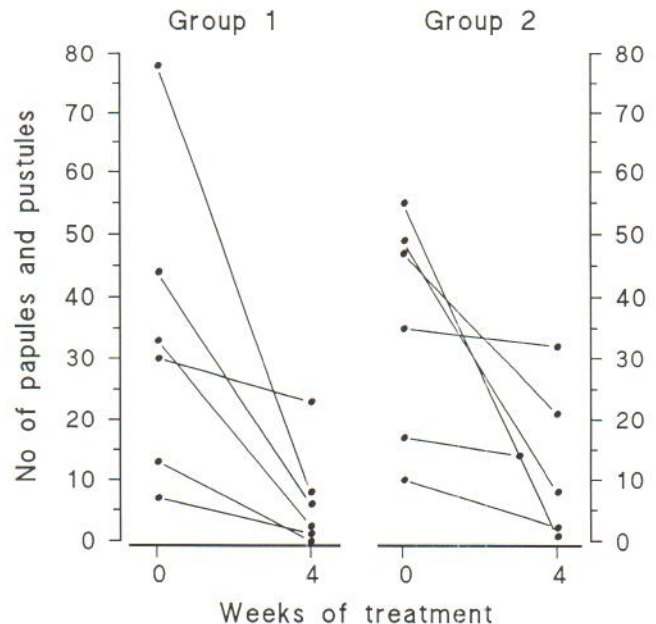


Fig. 1. Number of papules and pustules in patients with cystic acne in treatment group 1 (isotretinoin and erythromycin) and in treatment group 2 (prednisolone and erythromycin) during a 4-week treatment period.



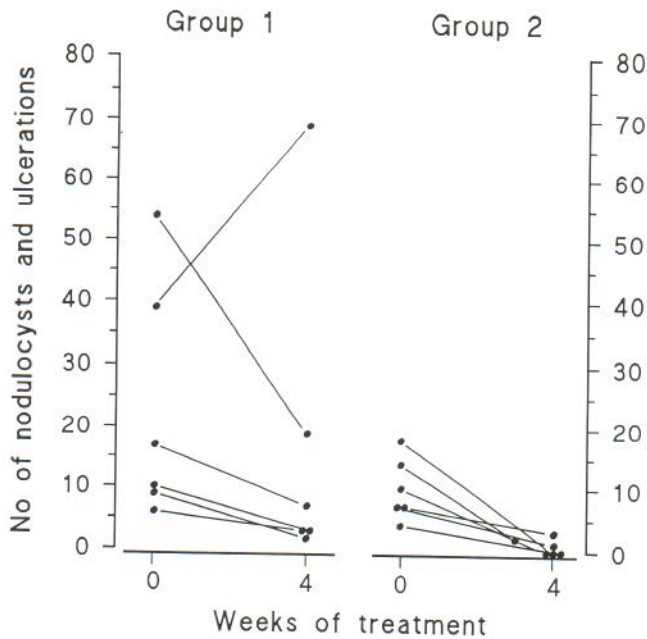


Fig. 2. Number of nodulocysts and ulcerations in patients with cystic acne.

## RESULTS

At the beginning of the study, the mean number of nodulocysts and ulcerations was higher in patients with CA in treatment group 1 than in group 2, but as for papules and pustules the groups were similar (Figs. 1 and 2, Table I).

### Clinical response during weeks 0-4

The clinical response was rather similar in both treatment groups with CA during the first 4 weeks (Table I, Figs. 1 and 2). In group 1 (isotretinoin and erythromycin) the number of papules and pustules decreased in all 6 patients, but in one male patient the number of nodulocysts increased (Fig. 2). In group 2 (prednisolone and erythromycin) all acne lesions de-

creased in all 5 patients who completed the 4-week treatment, as well as in the patient whose treatment was stopped after 3 weeks (Figs. 1 and 2).

All 3 patients with AF responded well and the number of papules, pustules, nodules and ulcerations decreased rapidly (Table I).

### Clinical response during weeks 5-16

In group 1 the acne was almost totally improved after 16 weeks in 4 patients with CA still receiving isotretinoin. In one patient isotretinoin was changed to prednisolone at week 12 because his acne turned to an ulcerative form. After this, his acne began to improve.

In group 2 the acne worsened after week 4, when prednisolone was withdrawn, in one out of 5 patients. Her treatment was changed to isotretinoin at week 6 (Table II). In another patient the number of papules and pustules began to increase slightly after week 8, but she received isotretinoin only when the study was over. The third patient in this group was dissatisfied with the treatment results, which were objectively good, and his medication was changed to isotretinoin at week 8.

The steroid treatment could be discontinued in the 3 AF patients after 13, 17 and 17 weeks. Their acne and musculo-skeletal symptoms tended to relapse if the steroid dose was reduced too quickly. One patient was given isotretinoin from week 10 after erythromycin had been stopped due to side-effects.

### Side-effects

In group 2 one patient showed elevated liver enzymes (alanine aminotransferase (ALAT) 130 U/l, normal range 0-39 U/l) at week 2. Prednisolone and erythromycin treatments were discontinued after 3 weeks and the treatment was continued with isotretinoin alone (Table II). The ALAT value decreased, but remained slightly elevated. Elevated liver enzymes (ALAT 63 U/l) were detected also in another patient in group 2 at week

Table I. Treatment response in patients with cystic acne and acne fulminans

	Week of treatment		
	0	2	4
<i>Cystic acne</i>			
Isotretinoin treatment* (n = 6)			
Papules/pustules	34.2 (7-78)**	11.2 (0-20)	6.7 (0-23)
Nodulocysts/ulcerations	22.5 (6-24)	14.0 (2-47)	17.2 (2-69)
Prednisolone treatment* (n = 5)***			
Papules/pustules	39.2 (10-55)	16.2 (0-49)	12.8 (1-32)
Nodulocysts/ulcerations	9.2 (4-18)	1.6 (0-5)	0.8 (0-3)
<i>Acne fulminans</i>			
Prednisolone treatment* (n = 3)			
Papules/pustules	233.3 (112-300)	21.7 (4-33)	16.0 (4-33)
Nodulocysts/ulcerations	101.7 (91-112)	17.3 (12-25)	11.0 (7-17)

\* Combined with erythromycin.

\*\* Mean number of lesions (range).

\*\*\* One patient's results were omitted from this analysis, because his treatment was discontinued at week 3 due to side-effects.



Table II. The reasons for changing the systemic treatment in patients with cystic acne

Pre = prednisolone; Iso = isotretinoin; Ery = erythromycin.

Group*	Pat. no	Week	Drugs used	Reason for change	Drugs continued
1	1	12	Iso	Worsening of acne	Pre + Ery
2	2	6	Ery	Worsening of acne	Iso + Ery
2	6	8	Ery	Patient's dissatisfaction	Iso
2	8	3	Pre + Ery	Elevated liver enzymes	Iso
2	10	9	Ery	Elevated liver enzymes	Iso

\* 1 = isotretinoin and erythromycin; 2 = prednisolone and erythromycin.

9, while he was taking erythromycin. Due to this erythromycin was changed to isotretinoin and his ALAT values returned to normal.

One patient with AF had slightly increased ALAT values (80 U/l) when prednisolone and erythromycin were started. The ALAT value increased further (272 U/l), but it fell to normal levels when erythromycin was stopped.

## DISCUSSION

Corticosteroids are effective in controlling AF, as shown by our previous (8) and the present study, but there are only few reports on the use of systemic corticosteroids in the treatment of CA (11, 12). In the present study we compared the effectiveness of prednisolone and isotretinoin in the initial treatment of CA. Both drugs were combined with erythromycin acistrate. During the 4 weeks treatment period the number of papulopustules and nodulocysts decreased similarly in 5 out of the 6 patients in both groups. In the beginning the corticosteroids seemed to control the inflammatory cysts even better than isotretinoin. These results suggest that systemic corticosteroids combined with erythromycin can control inflammatory acne in the beginning equally well as isotretinoin combined with erythromycin. In agreement with this, we observed a good response also in 3 patients with AF treated with prednisolone and erythromycin. Whether erythromycin had any additional effect on the treatment response in the corticosteroid-treated groups is impossible to evaluate, because we had no control group treated with corticosteroids alone. The fact that 2 out of the 5 patients with CA had a relapse after prednisolone was stopped at week 4 suggests that the effect of erythromycin was only of minor importance.

There was one patient with CA treated with isotretinoin and erythromycin whose nodulocysts did not respond to treatment. His cystic acne was severe from the beginning and ulcerations developed at week 12, and prednisolone had to be given in order to control the acne. CA sometimes worsens after the beginning of isotretinoin therapy, and even AF has been reported to erupt during isotretinoin therapy (8, 13), suggesting that isotretinoin may not control severe inflammatory acne as effectively as corticosteroids.

We observed elevated liver enzymes in 2 patients with CA and in one patient with AF receiving prednisolone and erythromycin or erythromycin alone. In 2 patients the liver enzymes decreased to normal levels after these treatments were stopped, and no increase occurred when isotretinoin was

started. Similar reversible changes in ALAT values have been described previously in patients treated with erythromycin acistrate (14).

Unfortunately no data is provided concerning the relapse rates after stopping the study at week 16. It was not the intention of this study to provide long-term data. However, after several months or weeks all the patients received isotretinoin, but the clinical follow-up with scoring was not performed at this time any more.

The present study shows that prednisolone seems to be effective in the initial treatment of inflammatory CA when combined with erythromycin. However, it is evident that isotretinoin and erythromycin have a similar effect during the first weeks of therapy. CA sometimes flares after beginning of isotretinoin treatment, and especially in such cases a combination of isotretinoin and prednisolone could be beneficial. Further studies are needed to show whether this combined treatment, recently recommended for the treatment of AF (15), is effective also in the initial treatment of severe CA.

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