

LONG-TERM TREATMENT OF ROSACEA WITH ORAL TETRACYCLINE

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Long-term treatment of rosacea with a small daily dose of a tetracycline by mouth is entirely empiric. It might be looked at as a by-product of the relatively early introduction in Britain and the U.S.A. of long-term tetracycline therapy in acne vulgaris. Williams (4) was certainly among the first to emphasize that tetracyclines were far more effective in rosacea than in acne. Little was published on the subject, however, until Sneddon (3) in 1966 presented the results from his controlled clinical trial, demonstrating clearly that the benefit of tetracycline was statistically significant and was successful in controlling rosacea in 87% of patients.

At the out-patient clinic of the Department of Dermatology, Rikshospitalet, Oslo, oral tetracycline medication became the routine measure against rosacea as from the end of the year 1965.

Material and Methods

During the period 1. January 1966-1. April 1968, long-term tetracycline medication was given to 95 patients with rosacea of the face. Twenty-one of these did not return for adequate follow up, by reason of geographical circumstances. Hence, they have been excluded from the series, although, according to mail correspondence, they responded favourably. Thus, the present material comprises 74 patients (56 women and 18 men) followed through more than 4

weeks of treatment. Fifty-one of them were followed for more than 8 weeks.

All patients have been instructed to take one capsule or tablet with a tetracycline by mouth each morning before breakfast. In few cases only was higher dosage given during the first week or so; this was soon found to be quite unnecessary. During the very first period of the investigation methyl-L-lysine tetracycline¹ was used in a daily dose of 150 mg because it was less expensive for the patient. Later on, a daily capsule of 250 mg of tetracycline chloride was employed. Temporarily, tablets with 300 mg of oxytetracycline chloride made by the hospital dispensary were introduced, but they seemed to be less effective than 250 mg capsules of tetracycline chloride.²

At the outset the rather costly tetracyclines made it difficult for some of the patients to undergo long-term medication. The later important fall in tetracycline prices have now almost completely eliminated this obstacle.

In order to compensate for a possible vitamin-B deficiency induced by the tetracycline altering the intestinal flora, most of the patients have been given additional supply of the vitamin-B complex in moderate doses. Nearly all of them had also previously taken vitamin-B tablets which had not improved their rosacea.

Patients were told to stop tetracycline medication in case of diarrhoea and to take iodochlorohydroxyquinoline tablets for a

¹ Tetralysal.

² Manufacturer: Arco S.A., Lugano, Switzerland.

Table 1. Oral Tetracycline (250 mg daily) in Rosacea, followed for 4 weeks or more

Improvement	F	M	F + M
Excellent	21	7	28
Good	29	4	33
Moderate	3	6	9
Unchanged or worse	3	1	4
Total	56	18	74*

Table 2. Oral Tetracycline (250 mg daily) in Rosacea, followed for 8 weeks or more

Improvement	F	M	F + M
Excellent	16	5	21
Good	24	1	25
Moderate	0	4	4
Unchanged or worse	1	0	1
Total	41	10	51

Table 3. Oral Tetracycline (250 mg daily) in Rosacea

Side effects	F=56	M=18	F+M=74
Diarrhoea	5 (5)	2	7 (5)
Anal irritation	1	1	2
Abdominal cramps	1	0	1
Dyspnoea	1 (1)	0	1 (1)
Total	8 (6)	3	11 (6)

() = treatment stopped because of side effect

week, in order to inhibit *Candida* or resistant strain of bacteria in the intestine.

Women in the fertile age group were told to stop tetracycline treatment at once if pregnancy was suspected.

The diagnosis of rosacea was made clinically. Differentiation from acne vulgaris in pustular cases was based on the occurrence of teleangiectasia and lack of comedones.

Eleven female patients presented marked perioral and/or periorbital lesions reminding of the entity "perioral dermatitis" de-

scribed by Hjorth *et al.* (1), but displayed simultaneously changes consistent with the diagnosis of rosacea. Cases of perioral dermatitis in women without additional signs of rosacea have not been included in this series.

Improvement during treatment has been graded as 1) *excellent*, i.e. full clinical normalization of the skin, 2) *good*, i.e. almost full normalization, but with persistence of a few papules or inconspicuous erythema, 3) *moderate*, i.e. improvement, but with persisting non-acceptable papules/pustules or conspicuous erythema.

Results

The results after 4 weeks of tetracycline medication are outlined in Table 1. Excellent or good improvement was noted in 61 patients, i.e. 82%. Among the 51 patients who had been followed for more than 8 weeks of treatment, excellent or good improvement was noted in 46 cases, i.e. 90% (Table 2).

In several cases, particularly in some of those with perioral and/or periorbital lesions, 3-5 months of therapy was needed before the skin had cleared completely. In 2 cases, bilateral long-lasting keratitis disappeared concomitantly with the clearance of the skin. These were the only keratitis cases observed.

The history of rosacea before treatment varied from 2 months to 25 years with an average of 35 months in women and 30 months in men. The duration of tetracycline medication per 1. April 1968 ranged 1-30 months with an average of 8 months. Six patients, all women, had then taken tetracycline for more than 20 months, and 18 patients, among whom were only 2 men, had been on tetracycline for more than a year.

Complication occurred in 11 cases (14.9%) and are outlined in Table 3. However, only in 6 cases, did the complication result in permanent stopping of the medication, i.e. 8% of the cases treated. Two patients with diarrhoea were able to continue the tetracycline medication after a temporary stop and an intermittent course

* Mean age: 43 years (range: 17-79).

Table 4. *Tetracycline in Rosacea.—Results from Stopping Treatment*

	F	M	F+M
Relapse	18	4	22 (Reiteration of treatment successful in all cases)
No relapse	4	2	6

of oral icdochlorohydroxyquinoline treatment, without recurrence of diarrhoea or any other complication.

With the exception of the case with dyspnoea (allergy?) and one of the cases with anal irritation (Table 3), the effect on rosacea was good or excellent also in these patients with complications. Thus, the 5 patients who had to discontinue tetracycline medication because of recurrent diarrhoea were very unhappy as their rosacea promptly relapsed after having been well controlled on tetracycline.

In none of the cases, complicating pyogenic infection with tetracycline-resistant strains has been noted in the patients or in their environment.

During the period of observation tetracycline medication was stopped in 28 cases after satisfactory control of the rosacea had been achieved. This was followed by prompt relapse in 22 of them. Readministration of treatment was successful in all. Only in 6 patients, the skin remained clear of lesions, after the medication had been stopped. The history of rosacea in these cases ranged from 6 months to 2 years with an average of 13 1/2 months, and the duration of medication from 1 month to 9 months with an average of 5 1/2 months.

It is a general impression that the chances of a lasting cure increases somewhat with the duration of treatment after clinical normalization of the skin. Some patients are able to control their rosacea with a very low maintenance dose after the skin has been clear for a while, so that, in a few cases, the dose might ultimately be reduced to 250 mg every other day or even less, while full stoppage will result in a relapse.

Discussion

The mechanism by which tetracycline controls rosacea remains unknown. Chronic rosacea as well as more acute forms, erythematous as well as papulopustular cases, respond equally well. It has been doubted that the effect is an antibacterial one, because of the small doses required and the very subsequent and often delayed improvement occurring over weeks or months.

The present author has made the experience that rosacea of the face usually is more easily controlled with oral tetracycline if a hexachlorophene-containing emulsion is used with water for daily cleansing instead of ordinary soap. If this is a reality it seems to support the idea that local bacterial factors are implicated, after all, in the pathogenesis of rosacea. However, the nicely performed studies by Marks (2) to test the validity of six different concepts in the pathogenesis of rosacea did not show evidence of local bacterial infection playing a role.

It might be speculated whether tetracyclines influence rosacea indirectly by an antibiotic action within the intestine, and hereby alters intestinal absorption; or is the effect in rosacea caused by an entirely non-antibiotic still unknown pharmacological quality of the tetracycline group?

The therapeutic efficacy of tetracycline in long-lasting and incapacitating rosacea is today among the most fascinating and enjoyable experiences for the skin therapist, as well as for his patients whose occupational and social adaptation has sometimes for years been severely disturbed because of their skin disorder. Certainly, the effect from tetracyclines is much more impressive in rosacea than in acne vulgaris which according to the present author's experience is better treated otherwise.

SUMMARY

Seventy-four patients with rosacea were given long-term oral treatment with tetracycline chloride in daily doses of 250 mg before breakfast. At the end of 4 weeks excellent or good improvement was noted in 61 cases (82 %). Fifty-one patients were

followed for more than 8 weeks of treatment and in this group satisfactory control of rosacea was achieved in 46 cases (90%). Tetracycline medication had to be stopped permanently because of complications in 6 cases (8%).

A small daily dose of oral tetracycline will control almost every case of rosacea. However, 3-5 months of treatment may occasionally be needed to clear the skin completely. When the skin has cleared, some patients can be maintained on an even smaller dose, e.g. 250 mg every other day, while full stoppage will usually result in relapse. However, in 6 cases of the present series, more lasting remission occurred when tetracycline medication was stopped after 1-9 months of treatment.

The mechanism by which tetracycline controls rosacea is unknown.

REFERENCES

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