Tanderil[R] in rhinoplasty a double-blind between patient trial

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SUMMARY

A double-blind, between patient trial was done in patients undergoing a rhinoplasty, with the purpose to investigate the anti-inflammatory effect of oxyphenbutazone (Tanderil[R]).

The results indicate that Tanderil[R] has a favourable influence on the post-operative symptoms after rhinoplasty.

INTRODUCTION

OPERATIONS on the face may cause considerable edema and ecchymosis, particularly when osteotomies have been performed. This postoperative swelling is unpleasant for the patient and it may even give him a forbidding appearance. It is also probable that there is a relationship between the amount of swelling and the degree of postoperative pain.

Consequently it is understandable that methods have been sought of limiting the postoperative edema and ecchymosis. This can be achieved in a number of ways:

1. By an accurate and relatively atraumatic surgical technique.
2. By infiltration of the surgical field with epinephrine or, if general anaesthesia is being used, by the application of controlled hypotension.
3. By the application of a pressure dressing immediately after surgery.
4. By the administration of certain anti-inflammatory drugs.

The purpose of the following double-blind between patient trial has been to investigate the effect of the anti-inflammatory agent oxyphenbutazone (Tanderil[R])* in patients on whom a rhinoplasty had been carried out.

Several papers have been published concerning the use of Tanderil[R] in nasal surgery. Harter (1962) and Meunier and Roux (1964) found a considerable decrease of swelling in 13 and 90 patients respectively undergoing nasal surgery. Bailey and Nahum (1965) performed a double-blind study in 42 patients who had nasal operations, involving osteotomies. They found that Tanderil[R] was not effective in preventing postoperative edema in such operations, nor in promoting more rapid resolution of postoperative edema, although it did appear to enhance

* Registered Trade Mark.

the clearing of postoperative periorbital ecchymosis. Durrani et al. (1965) compared the effectiveness of Tanderil® with that of Chymoral® and a placebo. Both anti-inflammatory agents were effective, but Tanderil® proved considerably more effective than Chymoral® in reducing the postoperative tissue reaction and narcotic requirement. Josuran and Melik (1966) found in a double-blind trial in 96 patients that Tanderil® significantly reduced edema, temperature and sedimentation rate, particularly after moderate and major surgery of the paranasal sinuses and the facial bones. Finally Elner and Jacobsson (1966) studied the effect of Tanderil® in 108 patients who underwent osteotomies and reduction of the nasal bones, or bone grafting to the nose. Tanderil® was not found to have any effect on the resolution of postoperative edema and hematoma.

MATERIAL AND METHODS

48 patients have been included in this trial; treatment with Tanderil® or placebo was randomly allocated.

	Subsample Tanderil®	Subsample placebo
Male	18, average age 29 years (17-48)	16, average age 25 years (16-49)
Female	6, average age 23 years (20-27)	8, average age 25 years (16-43)

Figure 1. Distribution according to sex and age.

In all patients an extensive rhinoplasty, including submucous reconstruction of the septum and reconstruction of the cartilaginous and bony pyramid, with medial, lateral and transverse osteotomies, was done; all operations were done personally by the senior author. The operations were performed under general anaesthesia with controlled hypotension; immediately after the procedure, and before the blood pressure was allowed to return to normal, an intranasal pack, an adhesive tape dressing, a stent, and a pressure dressing were applied. The pressure dressing was removed after 16-20 hours; the adhesive tape dressing and the intranasal pack were first changed after 4-6 days.

	Subsample Tanderil®	Subsample placebo
4th postop. day	6	6
5th postop. day	15	17
6th postop. day	3	1
TOTAL	24	24

Figure 2. First change of dressing.

The day before the operation the patients were started on ampicillin (Penbritin®) 500 mg t.i.d. and on dextrochlorfeniramin (Polaramine®) 2 mg t.i.d., both drugs

being continued until the sixth postoperative day. Both Tanderil® and placebo were given in the form of sugar-coated tablets of identical appearance, which were contained in bottles numbered 1-48. The distribution of Tanderil® and placebo among the bottles was randomly allocated; the key to the distribution was kept in a sealed leter in the hospital's pharmacy so that it would be available in case of drug intolerance. It was, however, not necessary to unseal this letter before the end of the experiment. The patients were given two tablets of Tanderil® or of placebo t.i.d. on the day before the operation, two tablets on the morning of the day of operation, two tablets t.i.d. on the 1st, 2nd and 3rd postoperative day and one tablet t.i.d. on the 4th, 5th and 6th postoperative day. Three quarters of an hour before operation all patients received a standard premedication, adjusted to their respective weights. The operation was begun between 2 and 3 p.m. and had an average duration of 2 hours. Postoperatively Pethidine® 75 mg i.m. was administered at 11 p.m. No further analgesics were administered routinely. The patients were instructed that they could request an analgesic if they had pain; in this case they were given glafenine (Glifanan®) 200 mg p.o. Glifanan® was selected as it is supposed to have no anti-inflammatory action. In one patient one tablet of 100 mg of butobarbital (Soneryl®) was administered on one single occasion because of insomnia. Apart from the medication mentioned above no other drugs were administered during the trial period. The patients were assessed for facial swelling and discoloration early on the morning of the first six postoperative days; they were also asked whether they experienced any pain, and if so, to what degree. The assessment was done by

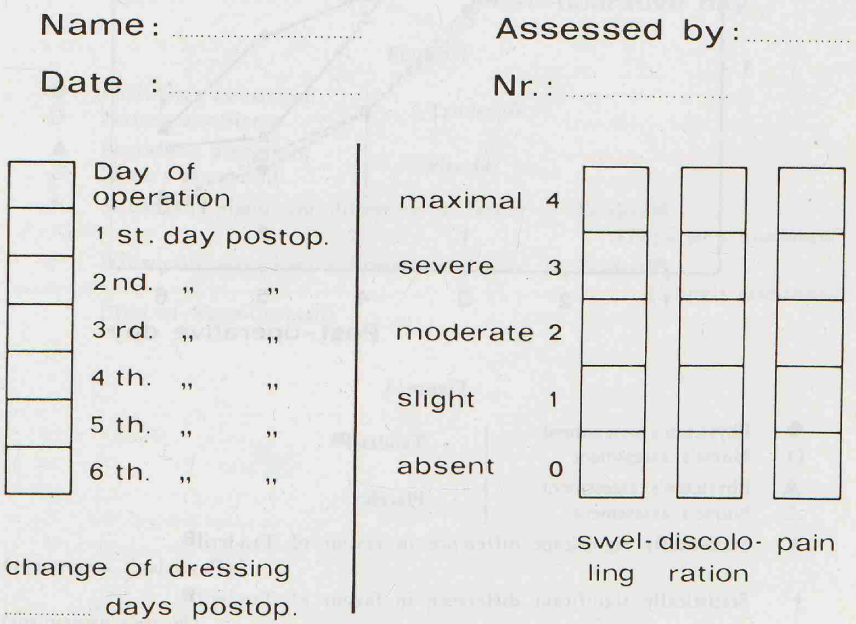

Figure 3

the authors and, independently, by one out of three members of the nursing staff. The results of the assessment were noted daily on specially designed cards (Figure 3), which were filed immediately after completion.

RESULTS

The results with regard to swelling, discoloration and pain are shown in Figures 4-6. These figures are self-explanatory.

1. Swelling

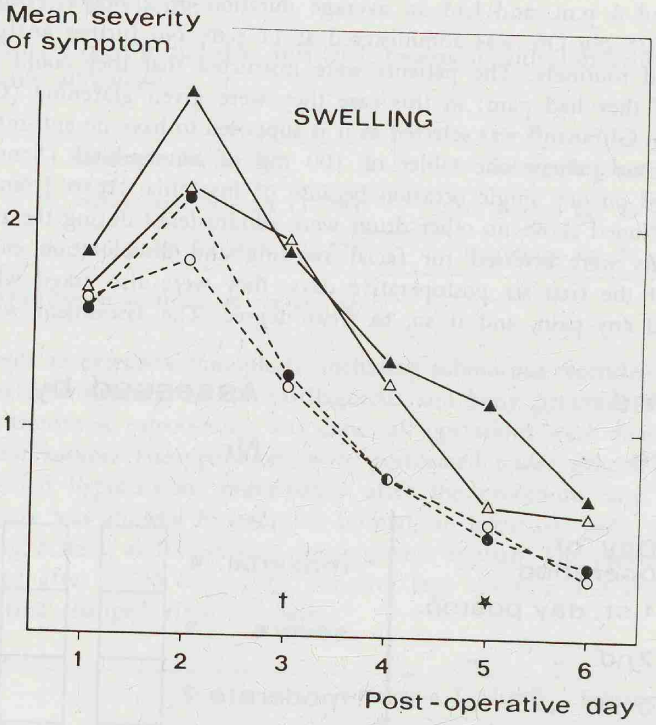

Figure 4

● Physician's assessment
○ Nurse's assessment
} Tanderil®

▲ Physician's assessment
△ Nurse's assessment
} Placebo

★ Statistically significant difference in favour of Tanderil® (Physician's assessment)

† Statistically significant difference in favour of Tanderil® (Nurse's assessment)

(Test of Yates-Cochran)

2. Discoloration

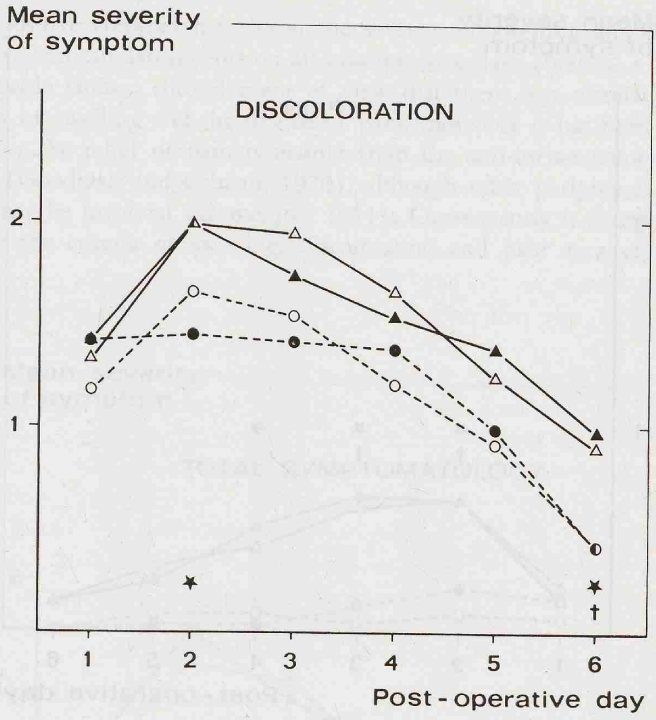

Figure 5

● Physician's assessment
O Nurse's assessment
} Tanderil®

▲ Physician's assessment
△ Nurse's assessment
} Placebo

★ Statistically significant difference in favour of Tanderil® (Physician's assessment)

† Statistically significant difference in favour of Tanderil® (Nurse's assessment)

(Test of Yates-Cochran)

3. Pain

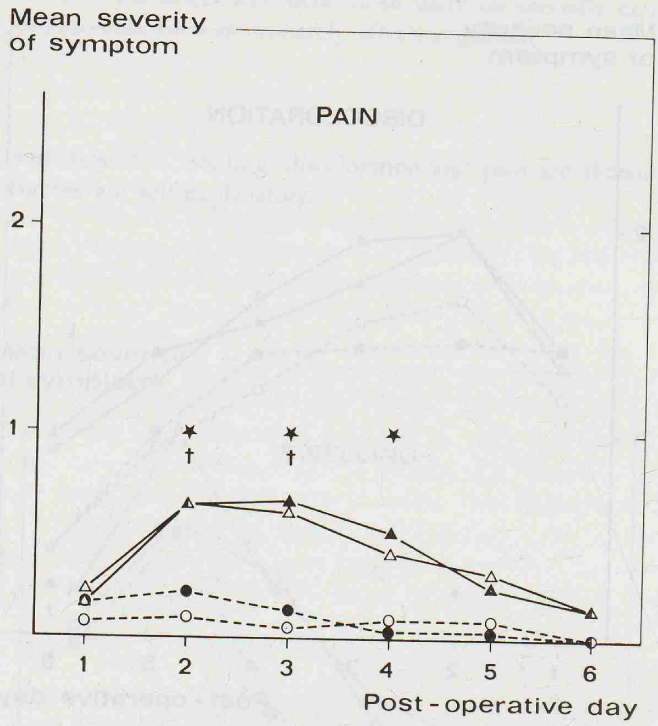

Figure 6

● Physician's assessment
O Nurse's assessment
} Tanderil®

▲ Physician's assessment
△ Nurse's assessment
} Placebo

★ Statistically significant difference in favour of Tanderil® (Physician's assessment)

† Statistically significant difference in favour of Tanderil® (Nurse's assessment)

(Test of Yates-Cochran)

4. Total symptomatology

A strong positive correlation between the severity of swelling and discoloration can be proved for all assessments on all postoperative days ($0.36 \leqslant r \leqslant 0.81$). It seems probable from a clinical point of view that there is a correlation between the severity of swelling and the degree of pain, moreover it has been shown that the basis for the relief of pain is mainly from the anti-inflammatory activity of Tanderil® (Goodman and Gilman, 1970), although other peripheral components of action may be involved (Domenjoz, 1971). Consequently it seems permissible to consider the criteria of swelling, discoloration and pain as a cluster.

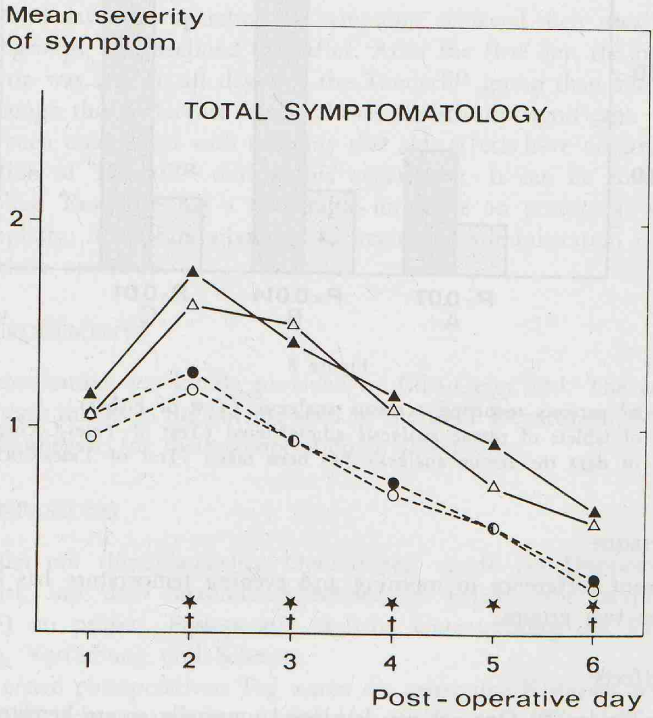

Figure 7

● Nurse's assessment
O Physician's assessment
} Tanderil®

▲ Nurse's assessment
△ Physician's assessment
} Placebo

★ Statistically significant difference in favour of Tanderil® (Physician's assessment)

† Statistically significant difference in favour of Tanderil® (Nurse's assessment)

(Test of Yates-Cochran)

5. Administration of rescue analgesics

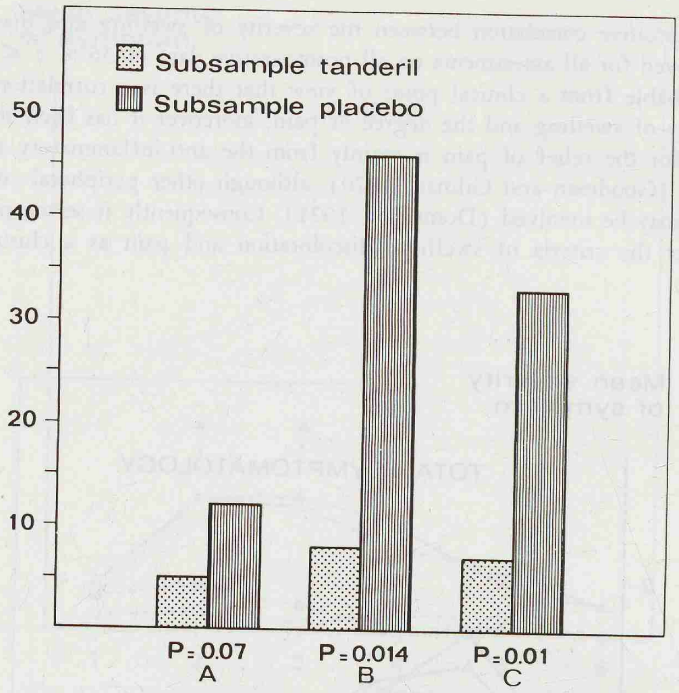

Figure 8

A. Number of patients requiring a rescue analgesic (Test of Fisher)
B. Number of tablets of rescue analgesic administered (Test of Yates-Cochran)
C. Number of days the rescue analgesic has been taken (Test of Yates-Cochran)

6. Temperature

No significant difference in morning and evening temperature has been found between the two groups.

7. Side effects

Subsample Tanderil®: One patient developed unusually severe hematomas during the operation. In one patient an urticarial exanthema appeared on the 6th post-operative day. It is not clear whether this has been caused by Tanderil® or by Penbritin®. In the 22 other patients no side effects were noted.
Subsample placebo: in 24 patients no side effects were noted.

COMMENT

At the beginning of this investigation an objective method for the assessment of swelling and discoloration was sought. Although several methods of doing this

are described, these methods did not appear practicable in the present problem and it is also doubtful if the resulting data were really more accurate than careful observation. Furthermore it has been shown that there is a strong correlation between clinical rating and measurements based on photogrammetry (Nylén and Torlegård 1966). After this trial was completed it also appeared that the entirely independent estimates of the doctors and the nurses corresponded closely.

From the figures it appears that there is no difference between the Tanderil[R] group and the placebo group on the first day after operation with respect to swelling, discoloration and pain. As regards the first two criteria, this is to be explained by the fact that the first evaluation took place immediately after removal of the pressure dressing. The almost total absence of pain on the morning of the first day after operation is to be explained by the fact that the patients received Pethidine[R] on the evening of the operation.

On the second day after operation all symptoms achieved their maximal severity in both subgroups, and declined thereafter. After the first day, the mean severity of all criteria was less on all days for the Tanderil[R] group than for the placebo group, although this difference is not always statistically significant.

It has not been established with certainly that side effects have occurred from the administration of Tanderil[R] during this experiment. It can be concluded from this study that Tanderil[R] has a favourable influence on postoperative symptoms after rhinoplasty; it appears advisable to begin the administration of Tanderil[R] the day before operation.

ACKNOWLEDGEMENTS

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ZUSAMMENFASSUNG

An Patienten mit rhinoplastischen Operationen wurde ein Doppelblindversuch durchgeführt, um den entzündungshemmenden Effekt von oxyphenbutazone (Tanderil[R]) zu prüfen. Postoperativ tägliche Untersuchung der Patienten auf Schwellung, Verfärbung und Schmerz.

Nach dem ersten postoperativen Tag waren die genannten Kriterien bei der Placebogruppe viel stärker ausgeprägt als bei den mit Tanderil behandelten Patienten, obgleich dieser Unterschied nicht ausnahmslos statistisch signifikant war.

Zusammenfassend lässt sich sagen, dass Tanderil einen günstigen Einfluss auf die postoperativen Beschwerden bei Rhinoplastiken besitzt.

RÉSUMÉ

Dans le but d'observer l'effet anti inflammatoire de l'oxyphenbutazone (Tandéril[R]), chez les patients soumis a une rhinoplastie, on effectua un double test à l'aveugle, entre les patients.

On surveilla journellement le gonflement postopératoire, la décoloration et la douleur. Après le premier jour postopératoire il apparut que l'intensité moyenne de tous les critères était moindre pour le groupe "Tanderil" que pour le groupe placebo, quoique cette difference n'ait pas toujours une signification statistique. Les résultats montrent que la Tanderil a une influence favorable, sur les symptomes postopératoires, après rhinoplastie.

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