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OXYPHENBUTAZONE (TANDERIL®) IN SURGERY FOR HERNIATED DISCS

A Double Blind Trial

By

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Many follow-up results have been reported of lumbar disc surgery performed for disc herniation, but it is also stated that even if 90–95 per cent of the patients go back to work, only 15–50 per cent of them claim that they are completely free from pain (2, 5, 7, 9, 16, 17). Some of the poor results have been explained in terms of post-operative scarring (14).

Since Oxyphenbutazone (Tanderil®) is said by many authors to reduce post-operative inflammation and connective tissue adhesions and oedema (3, 4, 6, 11, 13, 15, 19) a double blind study on the effect of this drug in lumbar disc surgery was performed and is reported here, in order to evaluate its effect on the post-operative course.

MATERIAL

Fifty-four consecutive cases of surgically proved herniated discs were studied. All operations were performed by the author. The pre-operative diagnosis was determined by the clinical examination and confirmed by a positive myelogram using a water soluble contrast (abrodil) (1, 8). The same operative technique was used in all cases, *i.e.* infiltration with a weak adrenaline-solution down to the arches, a midline incision with the patient prone on the operating-table, chiseling off the musculature with a broad chisel and performing a narrow hemi-laminectomy, followed by excision of the ligamentum flavum and extirpation of the prolapsed material. No attempt was made to evacuate the entire disc. Control of bleeding was routine. Sponges and suction bottles were weighed and the amount of bleeding during surgery was recorded in grams. The time in minutes from the opening of the skin until closure was noted.

All patients were out of bed and standing the day following operation.

Tanderil® or the blind tablet in the dosage of 200 mg three times a day were given

to the patients for one day pre-operatively. On the day of operation 200 + 200 mg given to be followed by 200 mg × 3 for 8 more days and then 100 mg × 3 for another 4 days.

Post-operatively the patients were given some analgesics according to a present program. A weak drug was given at first, followed by progressively stronger drugs. The analgesic effect was divided into five groups according to pharmacological strength, ranging from aspirin to morphine and one tablet from each group was given a score of 1–5 respectively.

The amount of reaction around the wound was noted and this was scored on a 0–3 scale. (No reactions 0, minimal reaction 1, definite redness and swelling 2, discharge from wound and burying of the sutures 3.

Emesis was watched for as a possible indication to discontinue the drug.

Prior to pre-operative administration of the drug, a haemoglobin determination, white blood cell-count and thrombocyte count were performed. This was repeated three days post-operatively and two weeks post-operatively in all cases.

The clinical history of the patients was carefully noted pre- and post-operatively until they regained employment. All cases were followed personally by the author, the average number of visits after discharge from hospital was four times.

The final follow-up was made exactly one year following surgery, in each case by personal interviews. The patients were asked if they had any pain either in the leg, in the back or in both, if they could return to their previous work or if they had to change to less strenous work. In the examination the movements of the back were noted, the scar was inspected and palpated for tenderness and a thorough neurologic examination was performed. The patients were asked if they thought they were perfectly well and symptom free and if they regarded themselves as nearly perfect, the same as before, or worse, following the surgery (Table 1).

Table 1. Follow-up Scheme.

The numbers in (brackets) refer to the points given to each answer.
The sum is the follow-up score.

A. Any symptoms like tiredness, strain, stiffness: every day (3), once a week (2), once a month (1), never (0).
B. Pain in back every day (3), once a week (2), once a month (1), never (0).
C. Pain in leg every day (3), once a week (2), once a month (1), never (0).
D. Occupation postoperatively;

heavy work	(0)
middle (housewife)	(1)
light work	(3)

E. Mobility of low back: same as prior to illness (0), somewhat less (1), definite restriction (2).
F. Increase of neurologic loss post-operatively (2).
G. Lasègue's sign: negative (0), 60–80° (1), <60° (2).
H. Any need of analgesic (2).
I. Are you: perfectly well (0), nearly perfectly well (1), improved (2), the same as preoperatively (3), worse than before the operation (4).

After the completion of the investigation, the code of the tabletes used was opened and it was found that of the 54 patients 27 had received Tanderil® and 27 the placebo.

All 54 cases were utilized in the evaluation of the early post-operative course. Four were excluded from the one-year follow-up, one in each group for each of the following: recurrence of sciatica with re-operation within a year and superimposed concomitant illness. In both of the latter instances, the patients stated that the result was good.

RESULTS

A. *The Effect of Oxyphenbutazone on the Early Post-Operative Course*

This period lasted from the day of operation to the return to work. During this period the following variables were noted: 1. Haemoglobin, white blood-cell and thrombocytes counts, pre- and post-operatively. 2. Duration of the operation. 3. Amount of bleeding. 4. Total score of analgesic drugs given to the patients (according to a 1–5 point scale). 5. Total increase in temperature (increases above 37.0 in the morning and 37.5 in the afternoon were summed up). 6. Oedema and reaction around the scar. 7. Return to work in weeks post-operatively. 8. Return of pre-operative neurologic loss. 9. Straight leg raising test 3 months post-operatively.

The patients examined are separated into two groups of the same size, one group of patients receiving Tanderil® and the other group receiving the placebo.

No cases of post-operative thrombosis, urinary tract infections or other complications occurred.

The χ^2-test or Student's t-test were used to ascertain if the two groups could be regarded as equal with respect to the following variables: age, sex, pre-operative symptoms in number of months and straight leg raising test (Lasegue's sign) pre-operatively. No significant differences were found with respect to these four variables. Thus the Tanderil®- and placebo groups can be regarded as completely comparable (Level of Significance: 5 per cent).

The mean difference between the pre-operative and post-operative values for the variables: grams of haemoglobin, number of white blood-cells and number of thrombocytes showed that Tanderil® did not affect any of these variables differently from the placebo (Level of Significance: 5 per cent).

In Table 2 the results of Student's t-test are shown for the variables nos. 2–5 mentioned earlier. The test was used to find out if the differ-

ence between the mean value of the Tanderil®-group and the mean value of the placebo-group can be regarded as statistically sufficient or in other words if any significant difference exists.

As shown in Table 2 Tanderil® has a sufficient statistically reducing effect on the three variables: A) the amount of bleeding at operation, B) total score of post-operative analgesic and C) post-operative added temperature rise.

Table 2.

Variable	Tanderil® Mean	Varians	No.	Placebo Mean	Varians	No.	Result
Duration of oper., min.	42	170	27	45	227	27	not signif.
Bleeding, gm	164	19623	27	273	47506	27	*signif.*
Total score of analges.	17	116	27	24	205	27	*signif.*
Total incr. in temp. °C	1.2	0.7	27	1.9	1.9	27	*signif.*
Incapac. post op. weeks	12	23	27	12	43	27	not signif

On the other two variables shown in the Table, Tanderil® can be said to have no statistical effect.

It can also be shown (with F-test) that the variability in the results for total post-operative temperature rise and bleeding are significantly less within the Tanderil®-group than within the placebo-group.

Regarding the variables oedema and reaction around the sutures no difference was found using χ^2-test.

B. *The Effect of Oxyphenbutazone in the Follow-up Results*

For evaluation on the late effect 50 patients were available, 25 in each group. All were examined by personal interview.

As in most other follow-up series presented, not all the patients were absolutely free from any symptoms, although all regarded themselves as cured and were back working. 26 patients were absolutely free from residual pain or stiffness, 15 in the placebo-group and 11 in the Tanderil®-group.

Table 3.

Variable	Tanderil® Mean	Varians	No.	Placebo Mean	Varians	No.	Result
Follow-up score	3.6	10.5	25	3.5	7.0	25	not signif.

Table 4.

Bleeding ml.	Analg. score ≥ 20 p	< 20 p	
≥ 250	3	3	6
< 250	7	14	21
	10	17	27

$\chi^2_{obs} < 1.$

Table 5.

Bleeding ml.	Raise in temp. ≥ 1.2	< 1.2	
≥ 250	2	4	6
< 250	9	12	21
	11	16	27

$\chi^2_{obs} < 1.$

A standard form was used in each case (see Table 1). Each answer or positive finding was given a point as indicated. The total score was added for each patient and subjected to a statistical analysis. (Table 3).

There was no difference between the Tanderil® and placebo groups in the amount of residual symptoms.

The χ^2-test was also used to find out whether Tanderil® had any effect on the return of pre-operative neurologic loss and on Lasegue's sign or whether any difference existed between the two groups regarding return to heavy or less heavy work. No such difference was found.

DISCUSSION

From the statistical evaluation presented it is clear that Tanderil® in the dosage given in this double blind trial has no effect on late residual symptoms following surgery for herniated discs.

However, the patients in the Tanderil®-group needed less analgesics post-operatively and the temperature reaction following surgery was

less. *Mathies & Scholze* (12) stated that the effect of Tanderil® post-operatively could be explained by an anti-hyaluronidase effect that lessens the inflammatory exudation. *Wilhelmi* (18) showed that Tanderil® is not a real analgesic drug per se.

The reduction of bleeding during surgery in the Tanderil®-group is at present impossible to explain. In the Tanderil®-group there was no relationship between the amount of more profuse bleeding during surgery and the need of analgesics post-operatively or the rise in temperature. (Tables 4 and 5). The amount of bleeding post-operatively, however, is impossible to evaluate.

SUMMARY

A clinical double blind trial was carried out on 54 patients to investigate the effect of Oxyphenbutazone (Tanderil®) in surgery for herniated discs.

With regard to age, sex, pre-operative symptoms in number of months and straight leg raising test pre-operatively the two groups, 27 patients in each, were completely comparable at the 5 per cent level of significance.

The statistical examination showed that Tanderil® did not affect haemoglobin, white blood-cell and thrombocytes counts post-operatively differently from the placebo. The duration of operation and the working incapacity post-operatively in weeks were the same in both groups, 45 minutes and 12 weeks, respectively.

On the variables bleeding during surgery, need of analgesics post-operatively and total increase in temperature post-operatively Tanderil® has a significantly reducing effect, (at the 2.5 per cent level).

No effect of the drug was noted on reaction around the scar or on return of pre-operative neurologic loss nor on the straight leg raising test.

For evaluation of the late effect 50 patients were available, 25 in each group. All were personally interviewed one year following surgery. There was no difference between the Tanderil® and placebo groups in the amount of residual symptoms.

RESUME

Un double essai clinique a été pratiqué chez 54 malades afin d'examiner l'effet de l'Oxyphenbutazone (Tanderil®) dans la chirurgie de l'hernie discale.

En ce qui concerne l'âge, le sexe, les symptômes pré-opératoires en nombre de mois et la force du signe de Lasègue, les deux groupes, 27 malades dans chacun, étaient entièrement comparables le rapport ne différant pas en moyenne de 5 pour cent.

L'analyse statistique a montré que Tanderil® n'affecte pas l'hémoglobine, le nombre des globules blancs at des thrombocytes ne différant pas après l'intervention du groupe du placebo. La durés de l'opération et l'incapacité de travail post-opératoire ont été les mêmes dans les deux groupes, 45 minutes et 12 semaines respectivement.

Tanderil® a un effet limitatif (en moyenne de 2.5 pour cent) sur les différentes hémorragies pendant l'opération, la nécessité d'analgésiques après l'intervention et l'élévation totale de la température.

Aucun effet du médicament n'a été noté sur la réaction autour de la cicatrice ou sur la réapparition des troubles neurologiques preopératoires ou encore sur la force du signe de Lasègue.

Pour juger des effets à plus long terme, on disposa de 50 malades, 25 dans chaque groupe. Tous ont été interrogés personlement un an après l'opération. Il n'y avait aucune différence entre le groupe Tanderil® et le groupe placebo par rapport au nombre des symptômes qui restaient.

ZUSAMMENFASSUNG

Ein klinischer, doppelter Blindversuch wurde an 54 Patienten ausgeführt, um die Wirkung von Oxyphenbutazon (Tanderil®) in der Chirurgie von hernierten Disken zu untersuchen.

Einsichtlich des Alters, Geschlechtes, voroperativen Symptomen bezüglich der Anzahl der Monate und der Lasègue'schen Probe vor der Operation, waren die beiden Gruppen, 27 Patienten in jeder, auf der „signifikanten" 5 Prozent Höhe vollkommen verglechbar.

Die statistische Untersuchung zeigte dass kein Unterschied in der Wirkung des Tanderil® auf das Hæmoglobin, die Leukozyten- und Thrombozytenzahl gegenüber den Placebo postoperativ zu finden war. Die Dauer der Operation und die postoperative Arbeitsunfähigkeit in Wochen war die gleiche in beiden Gruppen, 45 Minuten, beziehungsweise 12 Wochen.

Auf die veränderlichen Faktoren wie Blutung während des chirurgischen Eingriffes, postoperatives Bedürfnis für Analgetica und Gesamterhöhung der Temperatur nach der Operation hatte Tanderil® eine bezeichnenderweise herabsetzende Wirkung (auf der 2.5 Prozent Höhe).

Keine Wirkung des Mittels auf die Wundreaktion, dem Rückfall von præoperativen neurologischem Ausfall oder der Lasègue'schen Probe konnte beobachtet werden.

Zur Bewertung der Spätergebnisse waren 50 Patienten vorhanden, 25 in jeder Gruppe. Alle wurden persönlich ein Jahr nach der Operation befragt. Keinerlei Unterschied zwischen der Tanderil®- und der Placebogruppe hinsichtlich der Menge zurückbleibender Symptome konnte gefunden werden.

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