Oxyphenbutazone and Flufenamic Acid in the Treatment of Osteo-arthritis of the Knee

A DOUBLE-BLIND TRIAL COMPARISON

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SUMMARY

Patients suffering from osteo-arthritis of the knee were admitted to a double-blind trial comparing the efficacy and tolerability of oxyphenbutazone (Tanderil) and flufenamic acid. Objective and subjective parameters were measured to assess the anti-inflammatory activity of the trial medication. Tolerability and side-effects were evaluated by subjective statement.

Fifty patients entered the trial. On the 7th day of treatment oxyphenbutazone was found to be significantly superior to flufenamic acid in improving stiffness and the patient's feeling of well-being. Oxyphenbutazone significantly reduced pain on the 3rd day of treatment, compared with flufenamic acid. No serious side-effects were encountered.

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Clinical trials have shown oxyphenbutazone (Tanderil) to be orally effective in a wide variety of rheumatic disorders and other inflammatory conditions. It possesses markedly rapid anti-inflammatory and antipyretic activity. Although oxyphenbutazone has little direct analgesic action, its ability to reduce pain is thought to be due to its anti-inflammatory activity. These properties prompted this trial with oxyphenbutazone in a series of patients suffering from osteo-arthritis of the knee.

PATIENTS AND METHODS

Fifty patients suffering from osteo-arthritis of the knee were admitted to a between-patient double-blind trial, comparing the efficacy and tolerability of oxyphenbutazone and flufenamic acid. Patients with a present or past history of dyspepsia, peptic ulcer, haemorrhagic diathesis, hypersensitivity to the trial medications, and leucopenia, were excluded. Each patient was treated for 10 days with either oxyphenbutazone or flufenamic acid. Both medications were presented in identical capsules in a dose of 200 mg *t.i.d.* Objective and subjective parameters were measured to assess the anti-inflammatory activity of the trial medication. Tolerability and side-effects were evaluated by subjective statement.

Assessments were carried out, pre-treatment (after a wash-out period of 1 week for those patients on previous antirheumatic therapy), and subsequently on days 3, 7 and 10. The index of response to treatment was measured by assessing the following 5 parameters on a 5-point scale: pain, severity of stiffness, early morning stiffness and time taken to recover, mobility and over-all feeling of well-being. Tenderness was assessed using a 4-point scale. In addition the patients themselves assessed pain and feeling of well-being using a visual analogue scale.[1] Joint circumference, effusions (flexion and extension) and erythrocyte sedimentation rate were measured, the latter only before and after the trial.

RESULTS

Fifty patients completed the trial and were equally distributed in oxyphenbutazone and flufenamic subsamples, statistically homogeneous in respect to age, sex, duration and severity of illness.

Analysis of the pain scores by means of the Kruskal-Wallis[2] test showed that there was no significant difference between the subsamples pre-treatment, or on days 3, 7 and 10, as scored by the patients. However, application of this test on the investigator's scores showed that oxyphenbutazone was superior to flufenamic acid on day 3 at the 5% level, but no differences were observed pre-treatment or on days 7 and 10.

A patient's visual analogue scale was also used to estimate the response to the treatments in respect of pain. Analysis of covariance on these pain scores showed that there was no significant difference between the treatments. However, the rate of improvement was highly significant for both subsamples and followed a linear trend with time.

The effect of treatment on the severity of stiffness was measured independently by both investigator and patients. Analysis by means of the Kruskal-Wallis test showed that no statistically significant difference between the treatments was observed on days 3 and 10. A significant difference at the 5% level was found in favour of oxyphenbutazone on day 7 for both assessments.

The assessment of early morning stiffness and rate of improvement was made by the patient on rising, and subsequently every half-hour for 4 hours. The scores were

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TABLE I. SIDE-EFFECTS

Treatment group	Patient	Pre-treatment	Day 3	Day 7	Day 10
Flufenamic acid	OA 3	—	Dizziness	Dry mouth	—
Oxyphenbutazone	OA 2	—	Thick head at night	—	—
	OA 6	Mod. heartburn	Mod. heartburn	Slight heartburn	Slight heartburn
	OA 46	Epigastric fullness	—	Heartburn	Heartburn

summated for each day to give a total stiffness score, and submitted to analysis of covariance, from which it was found that both treatments produced a significant improvement over the trial period.

Analysis of the results of the investigator's assessment of tenderness, mobility, effusion, and joint size (of the worst knee), indicated that there was no significant difference between the treatments, both giving improvement.

Erythrocyte sedimentation rate readings were taken pre-treatment and on day 10. No statistically significant differences were found between the treatments at either assessment or between the assessments pre-treatment or on day 10.

An over-all assessment of efficacy was made independently by the investigator and the patient. Analysis of the results of the patient's assessment by the Kruskal-Wallis test showed that oxyphenbutazone was significantly superior on day 7 only, and analysis of the results of the investigator's assessment failed to show any significant differences.

The patients also recorded their over-all opinion of treatment effect on a visual analogue scale; analysis of covariance showed no significant difference between the treatments but a highly significant linear improvement for both with time.

Adverse Reaction and Side-Effects

No drop-outs occurred. Three patients treated with oxyphenbutazone suffered minor side-effects, although 2 of them had had these symptoms before treatment. One patient in the flufenamic acid treatment group showed minor side-effects. Table I gives details of the side-effects encountered.

CONCLUSION

Oxyphenbutazone significantly improved stiffness on day 7 (patient and observer assessment), pain (patient assessment) on the 3rd day, and over-all feeling of well-being (patient assessment) on day 7, indicating a more rapid response of these parameters to oxyphenbutazone.

Comparing oxyphenbutazone and flufenamic acid, the latter could in no way be found to be superior. No serious side-effects were encountered and of the three patients suffering from minor side-effects, 2 had shown symptoms before treatment.

REFERENCES

1. *In* Joyce, C. R. B. ed. (1968): *Psychopharmacology: Dimensions and Perspectives.* London: Tavistock.
2. Kruskal, W. H. and Wallis, W. A. (1922): J. Amer. Stat. Assoc., **47**, 583.