methohexitone the peak level in cord blood was maintained for up to seven minutes. In the present study the considerable difference between the two groups of infants strongly suggests a greater residual barbiturate effect in the high-dose group. The results also show that within the currently acceptable clinical usage of methohexitone the dose used to induce anaesthesia for caesarean section may be a significant factor in the aetiology of some cases of neonatal depression.

It would seem rational to relate the induction dose of methohexitone to the physical status of the mother, and the maternal weight before delivery is the most readily accessible measurement. We recommend that the dose of methohexitone used to induce anaesthesia for caesarean section should be of the order of 1 mg/kg.

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Fenoprofen in Treatment of Osteoarthritis of Hip and Knee

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Summary

Two studies on 41 patients with osteoarthritis of the hip or knee have shown fenoprofen—a compound with analgesic and anti-inflammatory properties—to be an effective addition to the drug treatment of these conditions. It was found to be superior to paracetamol but no statistically significant difference was shown in a comparison with phenylbutazone.

Introduction

Fenoprofen (DL-2-(3-phenoxyphenyl)propionic acid) has demonstrable analgesic, anti-inflammatory, and antipyretic properties in animals (Nickander *et al.*, 1971). Recently it has been shown to be effective and well tolerated in patients with rheumatoid arthritis (Fries and Britton, 1973; Huskisson *et al.*, 1974). We have assessed its value in osteoarthritis of the hip and knee.

Study 1

A total of 24 patients with osteoarthritis of the hip or knees were admitted to a double-blind crossover study of single doses of fenoprofen 600 mg, paracetamol 990 mg, and placebo. Treatments were given in pairs, each patient comparing every possible pair. A patient might therefore receive fenoprofen on day 1 of the study, paracetamol on day 2, fenoprofen on day 4, placebo on day 5, paracetamol on day 7, and placebo on day 8. On the third and sixth days no trial analgesics were given. The com-

pounds were supplied in pink or white capsules so that each of a pair of treatments appeared to be different; one patient might compare pink fenoprofen with white placebo, while another compared white fenoprofen with pink placebo. The order of administration was randomized in a latin square design balanced for order and colour of the capsules. No other medication was allowed for six hours after administration of the test analgesics.

The analgesics were taken at about the same time each day when pain was either severe or moderately severe. After taking the capsules the patients were asked to record pain relief hourly for six hours using a simple scale consisting of no pain relief and slight, moderate, and complete pain relief. After each pair of treatments preference was recorded.

The results are shown in the chart.

Study 2

Fenoprofen 2 g daily was compared with phenylbutazone 300 mg daily on a double-blind crossover basis, each drug being given for 14 days, with an intercalated double-blind crossover

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study of Distalgesic (dextropropoxyphene hydrochloride and paracetamol) eight tablets daily and paracetamol 4 g daily, each being given for seven days. The treatment programme was as follows: week 1, paracetamol or distalgesic tablets; weeks 2 and 3, fenoprofen or phenylbutazone capsules; week 4, distalgesic or paracetamol tablets; and weeks 5 and 6, phenylbutazone or fenoprofen capsules.

Out of 18 patients who entered the trial 17 completed it satisfactorily; one was withdrawn for domestic reasons. Twelve of the patients were women and five were men and their mean age was 58.8 years.

All the patients had established osteoarthritis of one or both hips with pain of at least one month's duration, the character and severity of which were subject to only little variation. Patients with a history of peptic ulceration or of allergy or intolerance to analgesic/anti-inflammatory drugs were excluded.

Patients were seen on the last day of each period of study and their appointments were made for the same time in the morning on each of their five visits. The results of the following were recorded: (1) patients' assessment of pain severity at the time of each examination (visual analogue scale 0-20); (2) patients' assessment of the overall pain severity during each period of treatment (visual analogue scale 0-20); (3) quality of sleep during each treatment period (visual analogue scale 0-20); (4) intermalleolar distance (cm); (5) walking time, 15 m (sec.); (6) patient's opinion of the trial drug at the end of each period of study—excellent, good, fair, poor, useless; and (7) patients' drug of preference at the end of the trial. In addition the patients were asked to state which of the two one-week periods of therapy they preferred and also to give their order of preference for all four periods of treatment.

All side effects were noted and laboratory studies consisting of urine analysis, full blood count (including platelets), haemoglobin estimation, and transaminase and alkaline phosphatase estimations were performed before admission to the trial and at the end of each of the two-week periods of treatment.

When the two one-week periods of therapy were compared there was a slight preference for Distalgesic but the results were not statistically significant. When the order of preference for all

four treatment periods was considered significant preference was shown for the fenoprofen or phenylbutazone periods as opposed to the Distalgesic or paracetamol periods.

The results are summarized in tables I to III.

TABLE II—Study 2. Drug Preference of 17 Patients with Osteoarthritis of Hip

	No. in Favour of Fenoprofen	No. in Favour of Phenylbutazone	No. noting No Difference	P
Patients' opinion at end of each treatment period	6	8	3	N.S.
Patients' final preference	6	10	1	N.S.

TABLE III—Study 2. Side Effects noted by 17 Patients during Treatment

	No. of Patients taking Fenoprofen	No. of Patients taking Phenylbutazone
Epigastric discomfort	1	2
Abdominal fullness	2	0
Constipation	2	1
Tiredness	0	2
Headaches	0	2
Drowsiness	1	2
Dry mouth	0	1
Rash on forehead (acneiform eruption)	1	0
Total	7	10

Discussion

The single-dose study shows that in terms of pain relief in osteoarthritis fenoprofen is superior to paracetamol, which is in turn superior to placebo.

In the second study no significant difference was found between fenoprofen 2 g daily and phenylbutazone 300 mg daily, though the results were marginally in favour of phenylbutazone. There was a similarly marginal preference for Distalgesic over paracetamol but a significant subjective preference for the fenoprofen and phenylbutazone periods as opposed to the two weeks with the other drugs.

Side effects were minor and presented no problems and laboratory tests showed nothing abnormal.

Fenoprofen should prove a useful addition to the drug treatment of osteoarthritis.

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TABLE I—Study 2. Subjective and Objective Assessments in 17 Patients with Osteoarthritis of Hip at End of Each Treatment Period. Results are expressed as Means $\pm$ S.E.

	Fenoprofen	Phenylbutazone	P
Pain severity at time of examination (visual analogue scale 0-20)	10 $\pm$ 1	8 $\pm$ 1	N.S.
Overall pain severity during each treatment period (visual analogue scale 0-20)	12 $\pm$ 1	13 $\pm$ 1	N.S.
Quality of Sleep during each treatment period (visual analogue scale 0-20)	12 $\pm$ 1	14 $\pm$ 2	N.S.
Intermalleolar distance (cm)	57.2 $\pm$ 3.0	55.2 $\pm$ 2.2	N.S.
Walking time, 15 m (sec.)	20.8 $\pm$ 2.8	21.1 $\pm$ 3.0	N.S.