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Diclofenac for pain after hip surgery

Sixty-eight patients were studied during the day after hip replacement for arthrosis. No pain reliever was allowed within 4 h prior to initial assessment of pain. An injection of diclofenac 75 mg, pethidine 50 mg, or placebo was given intramuscularly, and a second injection was usually given after 3.5 h. Pain was recorded before and for 3 h after these injections. Ten patients in the placebo group demanded rescue drug because of insufficient pain relief. Four patients discontinued the study due to side effects: nausea (one patient in the placebo group) and somnolence or nausea (three patients in the pethidine group). Assessed both by visual analogue scale (VAS), and by the investigator's assessment, the diclofenac group had less pain than the pethidine and placebo groups. Side effects were least frequent in the diclofenac group. This study demonstrates that at the doses used here, compared with pethidine, diclofenac is more effective in relieving postoperative pain and has fewer side effects.

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Diclofenac is a derivative of phenylacetic acid and in animal models it has shown a high degree of anti-inflammatory, analgesic, and antipyretic activity (Menassé et al. 1978). It is a potent inhibitor of prostaglandin synthesis both *in vitro* and *in vivo*, which explains at least one of its mechanisms of action. Diclofenac has been in clinical use, notably in the rheumatic field, since 1973, generally administered orally or rectally (Brogden et al. 1980). Recently, encouraging results in management of severe pain have been reported with diclofenac given intramuscularly, e.g. in renal colic (Lundstam et al. 1982, Vignoi et al. 1983). By means of a double-blind comparison of diclofenac, pethidine and placebo in a homogeneous patient population, we evaluated the potential of diclofenac in the management of postoperative pain.

Patients and methods

Sixty-eight patients who underwent total hip replacement for arthrosis were studied on the day following surgery; they were evenly distributed among the treatment groups with regard to sex, age, body weight, and pain, according to the investigator's assessment before the first injection (Table 1). They had all been informed about the nature of the study and had given their consent. No patient with bronchial asthma, mental disease, serious liver or kidney disease, gastric or duodenal ulcer, bleeding disorder, or known or suspected allergy against salicylates or other NSAIDs was included in the study. No patient had received analgesics during the 4 h preceding the beginning of the study. The hospital pharmacy supplied ampules with either placebo (saline), 75 mg of diclofenac sodium (Voltaren® (Voltarol®) Ciba-Geigy Ltd.), or 50 mg of pethidine (meperidine) hydrochloride. All ampules contained 3 ml of solution and were identical in appearance. At the time when the patient needed an analgesic, pain was assessed and recorded. After this, the analgesic was injected intra-

Table 1. Patient characteristics in each treatment group.

Treatment group	Number			Age (years)	Body weight (kg)	Assessment of pain before treatment					
						Investigator					Patients
						1 (slight)	2	3	4	5 (severe)	VAS (0–100)
	Men	Women	Total	Mean±SD	Mean±SD	Number of patients					Mean±SD
Placebo	10	13	23	65± 9	75±12	8	5	4	6	0	42±28
Diclofenac 75 mg	11	11	22	67± 8	72±12	8	4	8	2	0	40±27
Pethidine 50 mg	11	12	23	66±10	72±16	6	6	7	4	0	42±27

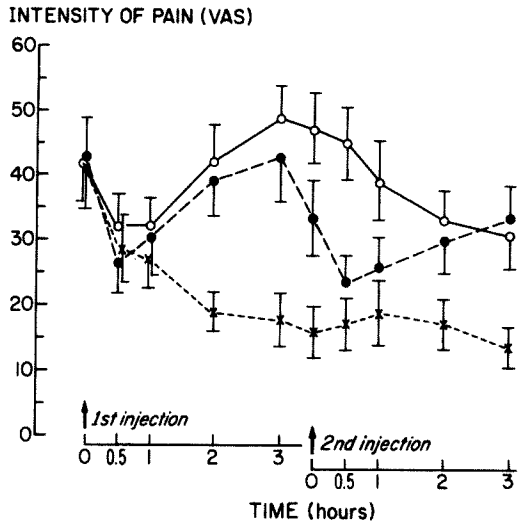

Figure 1. Mean values and standard error of pain intensity assessed in groups of patients treated with diclofenac ×, pethidine ●, or placebo ○.

muscularly in the upper gluteal region. A second injection with the same substance was as a rule given after 3.5 h. If severe pain was present within 3 h after the first injection, a second injection was given. If satisfactory pain relief had not been obtained within 30 min after the second injection, a standard therapy of 50 mg of pethidine was given, and the patient was withdrawn from the study. No other analgesic or anti-inflammatory drug was given during the observation period. All patients started weight-bearing and walked a few steps with the aid of crutches under the supervision of a physiotherapist during the first part of the observation period.

Measurement of pain was done immediately before and 0.5, 1,2, and 3 h after the injection. The patients estimated the intensity of pain using a visual analog scale (VAS), ranging from 0 ("no pain") to 100 ("pain as bad as could be"). The investigator's assessment of the pain was recorded according to a 5-grade scale. Side effects were recorded at each time of pain assessment. Three hours after each injection the patients were specifically asked about the following symptoms: somnolence, vertigo, nausea, headache, abdominal pain, dry mouth, and other symptoms.

Statistical analysis

Comparisons between means were performed with Student's t-test, and contingency tables were analyzed according to Fisher's "exact probability method." To ordinal data, the Wilcoxon signed mid-rank test or Wilcoxon mid-rank sum test was applied, depending on whether the observations were related to each other or not. Ties were compensated for, and significance levels of $P < 0.05$ were accepted (two-tailed).

Results

Ten patients were withdrawn from the study because they had to be given the rescue drug. All of these belonged to the placebo group. One patient in the placebo group and three patients in the pethidine group were withdrawn from the study because of side effects. These were dizziness (one, placebo group), drowsiness (one, pethidine) and vomiting (two, pethidine).

There was better pain relief with diclofenac as compared to pethidine, and a high correlation between the investigator's and the patient's assessment (Figure 1, Table 2).

A second injection of the same substance was given within 3 h after the first if severe pain recurred. For five patients in the placebo group and four in the pethidine group, the second injection was given within 3 h after the first injection, whereas all the second injections in the diclofenac group were given after 3.5 h.

Side effects were noted most frequently in the pethidine group and least frequently in the diclofenac group (Table 3).

There was no significant difference in the

Table 2. Average pain intensity 0.5–6.5 h after drug administration. Mean ± SD.

Treatment group	Investigator's assessment (1–5)			Patient's assessment (0–100)		
Placebo	2.2±0.9	p<0.001	p>0.10	42.4±17.6	p<0.001	p<0.10
Diclofenac 75 mg	1.3±0.4	p<0.01		19.3±15.4	p<0.05	
Pethidine 50 mg	1.8±0.6			32.1±19.6		

Table 3. Symptoms during treatment for pain.

Symptom	Placebo	Diclofenac	Pethidine
Drowsiness	6	2	10
Dizziness	0	0	1
Vomiting	5	6	12
Dry mouth	11	11	9
Headache	2	0	3
Abdominal pain	2	0	1
Confusion	1	0	0
Total	27	19	36

postoperative blood loss between the groups. Wound healing was assessed 7 days postoperatively. A slight serous discharge of short duration was found in two cases from the placebo group, in two cases from the diclofenac group, and in one case from the pethidine group. No case of deep infection occurred.

Discussion

It is difficult to obtain large enough patient groups with the same type of severe pain and it is also difficult to measure pain. By studying patients during the day after hip replacement, we could observe a large number of patients, allowing us to compare two types of analgesics and a placebo under very similar conditions. Thus, the whole study was completed during 6 months in patients treated by the same team. On the VAS scale with 100 for maximal pain, the initial pain level in all groups was slightly over 40. Following injection of 75 mg of diclofenac intramuscularly, there was remarkably good relief of pain as assessed both from the visual analog scale and by the investigator. The duration of pain relief was more than 3.5 h in all patients given this compound.

Pethidine, as expected, also diminished pain. Although, at the dosage used, the pain relief was less than in the diclofenac group, the largest number of symptoms listed as side effects were observed after pethidine. Since "side effects" were also frequently recorded in the placebo group, it is obvious that many of these symptoms were not true side effects and would be expected to be suppressed by the anxiolytic effect of pethidine. This, and the fact that 22 reports of side effects in the pethidine group were caused by drowsiness or vomiting, make it apparent that 50 mg pethidine did indeed cause a signficant number of true side effects which probably would be even more apparent with a higher dosage. In the diclofenac group, recorded side effects were less frequent than in the placebo group, which may be related to the relative sense of well-being associated with adequate pain relief.

Our results suggest that NSAIDs routinely should be preferred to opiates in the early postoperative period. This conclusion is supported by earlier studies of ketoprofen and zomepirac (Forest 1980, Wollheim 1981). Since the effect is seen almost instantly, analgesia does not seem to be a secondary effect from decreased edema. In view of the good results on pain of various etiology with NSAIDs, it would seem that these drugs rather have a universal direct action affecting the pain mechanism either centrally or peripherally (Vignoi et al. 1983, Hultin & Olander 1978).

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