INDOMETHACIN IN THE MANAGEMENT OF POSTOPERATIVE PAIN

I. NISSEN, K. A. JENSEN AND J. K. ÖHRSTRÖM

SUMMARY

We have examined the analgesic effects of indomethacin in a double-blind study of 56 patients undergoing surgery for lumbar disc prolapse. The patients were allocated randomly to receive either indomethacin 100 mg i.v. before surgery, followed by 100 mg rectally 6 and 12 h after surgery and at 08:00, 16:00 and 23:00 on the next day, or placebo. Postoperative pain was assessed using a 10-cm visual analogue scale at fixed times. Side effects and consumption of supplementary analgesics were recorded. Patients receiving placebo had significantly greater pain scores and significantly more patients in the placebo group required supplementary analgesics.

KEY WORDS


Several authors have reported that patients undergoing abdominal and orthopaedic surgery derived benefit from the analgesic effect of non-steroidal anti-inflammatory drugs (NSAID) [1-4].

In our study, approved by the Regional Ethics Committee, patients underwent low back surgery for herniated intervertebral disc, and pain was therefore musculoskeletal in origin. NSAID are often used as analgesics for patients with suspected lumbar disc prolapse, but the use of NSAID after surgery for this condition has not been investigated.

Good pain relief facilitates mobility and recovery. The purpose of this study was to evaluate the analgesic effect of indomethacin in patients undergoing low back surgery, by assessing the extent of supplementary analgesia, pain scores and side effect.

PATIENTS AND METHODS

The study was a randomized, double-blind, placebo-controlled clinical investigation with two parallel treatment groups.

Informed consent was obtained from 56 patients (table I) undergoing conventional lumbar disc surgery. Exclusion criteria comprised known allergy to NSAID, history of peptic ulcer, gastrointestinal bleeding, severe cardiac, pulmonary, liver or kidney disease, malignant hypertension, haemorrhagic disorders, known or suspected pregnancy or nursing, use of an NSAID in the 24 h preceding surgery, psoriasis, concomitant treatment with lithium or severe postoperative complications within 24 h.

Patients were withdrawn from the study if any adverse effect possibly attributable to indomethacin occurred, if they received NSAID other than that specified in the study or if they did not wish to continue.

Patients were allocated randomly in blocks of four—that is, in each block two patients received treatment with indomethacin and two patients received treatment with placebo. An i.v. injection of indomethacin 100 mg or placebo was given at

<table>
<thead>
<tr>
<th>Table I. Patient data (mean (range))</th>
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<tbody>
<tr>
<td>Indomethacin group</td>
</tr>
<tr>
<td>Sex (M/F)</td>
</tr>
<tr>
<td>Age (yr)</td>
</tr>
<tr>
<td>Weight (kg)</td>
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<td>Duration of op. (min)</td>
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</table>

FIG. 1. Pain scores in indomethacin- (●) and placebo- (○) treated patients (mean, SEM).

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induction of anaesthesia, followed by indomethacin 100 mg or placebo suppositories 6 and 12 h after operation and at 08:00, 16:00 and 23:00 on the day after operation. The indomethacin and placebo preparations had the same appearance, coded numbers were used and the sealed code was kept readily accessible. Care was taken to ensure that each suppository was inserted correctly.

The patients were premedicated with pethidine 1 mg/kg body weight 0.5–1 h before surgery. After administration of pancuronium 10 μg kg⁻¹, anaesthesia was induced with thiopentone 5 mg kg⁻¹, supplemented with continuous thiopentone 3.6 mg kg⁻¹ h⁻¹. Tracheal intubation was facilitated with suxamethonium 1.0–1.5 mg kg⁻¹ and anaesthesia was maintained with 67% nitrous oxide in oxygen. The surgical technique was the same for all patients: lumbar midline incision, partial hemilaminectomy and removal of the herniated disc. If no hernia was found, the disc was left untouched.

Pain intensity was assessed using a 10-cm linear visual analogue scale (VAS). The first assessment was made before operation, when the patient's consent was obtained, then at 3, 6, 9 and 12 h after termination of the operation and at 08:00, 16:00 and 23:00 the next day. A sleeping patient was assessed as painless. Mobilization was started on the day after the operation.

All patients were allowed supplementary analgesics according to our routine management and there was no limitation on the type of supplementary analgesic, but NSAID were excluded. All analgesics were administered by the nurses on demand by the patients.

In the first 4 h after operation, niconorphine 10 mg i.m. was used. Subsequently, paracetamol 1 g was offered and if this was not effective, niconorphine 10 was given i.m.

Adverse effects and the need for supplementary analgesia were noted, together with surgical complications.

**Statistical methods**

Data were analysed statistically by SAS-603, MSDOS 3.2 using an Olivetti M28 personal computer.

Age, weight and duration of operation were compared by Wilcoxon’s two-sample test (two-sided). The relative frequencies of gender in the two groups were compared by Fisher’s exact test (two-sided).

Preoperative and postoperative pain intensities and the amount of supplementary analgesics were compared using Wilcoxon’s two-sample test (two-sided). The numbers of patients not requiring supplementary analgesics were compared by Fisher’s exact test (two-sided).

A level of significance was chosen as P < 0.05.

**RESULTS**

There were 28 patients in each group. None of the 56 patients in the study had adverse reactions to the i.v. injections and none had to be withdrawn on the first day. On the day after operation one patient in the placebo group was withdrawn because of nausea.

<table>
<thead>
<tr>
<th>Time</th>
<th>Indomethacin</th>
<th>Placebo</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Day 1 (time after op.)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>0–3 h</td>
<td>22 (28)</td>
<td>17 (28)</td>
<td>0.24</td>
</tr>
<tr>
<td>3–6 h</td>
<td>23 (28)</td>
<td>13 (28)</td>
<td>0.01</td>
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<tr>
<td>6–9 h</td>
<td>21 (28)</td>
<td>15 (28)</td>
<td>0.16</td>
</tr>
<tr>
<td>9–12 h</td>
<td>22 (28)</td>
<td>13 (28)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>12 h–08:00 day 2</td>
<td>17 (28)</td>
<td>11 (28)</td>
<td>0.18</td>
</tr>
<tr>
<td>Day 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>08:00–16:00</td>
<td>17 (28)</td>
<td>4 (27)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>16:00–23:00</td>
<td>18 (28)</td>
<td>9 (27)</td>
<td>0.04</td>
</tr>
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</table>

Five patients, three in the indomethacin group and two in the placebo group, did not receive the last suppository, but the pain scores were included in the analysis.

Eight pain scores in seven patients (two in the indomethacin group and five in the placebo group) were excluded from analysis, because the patients had been given an NSAID by mistake, in addition to indomethacin.

Adverse effects were distributed evenly between the two groups and were of a minor nature, mostly nausea and diarrhoea.

The groups were comparable in sex, weight and duration of operation (table I); there were no surgical complications. There was no significant difference between the groups in the preoperative or 3-h postoperative pain scores (fig. 1). At 6 h and subsequently, the difference was significant (Wilcoxon’s two-sample test, two-sided: P < 0.05).

More patients in the placebo group than in the indomethacin group needed supplementary analgesia (table II). This difference was significant at 6 and 12 h after operation and thereafter.

The supplementary analgesics given most commonly after operation were niconorphine and paracetamol. The total amounts were niconorphine 330 mg in the indomethacin group and 850 mg in the placebo group (Wilcoxon’s two-sample test, two-sided: P < 0.001) and paracetamol 18 g in the indomethacin group and 43 g in the placebo group (P < 0.001).

**DISCUSSION**

Indomethacin was given i.v. before surgery in order to prevent an increase in prostaglandin synthesis and ensure prompt onset of analgesia. The rectal route was used after surgery, as oral therapy was thought inappropriate in the early postoperative period.

There were few adverse effects, which were minor and equally distributed between the two groups.

The hazard of bleeding has been discussed in the literature [1, 5]. In a study on patients undergoing hysterectomy, Engel and colleagues [1] found a significantly greater blood loss in the group treated with indomethacin: in another study, in which indomethacin was given only after operation, the incidence of postoperative bleeding was greater, although no link with indomethacin could be established [5]. In our study, we asked the surgeon to note if there was abnormal blood loss, but no such complication was noted, and no patient received blood transfusion.

**TABLE II. Number of patients not requiring supplementary analgesics. (Numbers in parentheses are total number of patients in the treatment group)**
Pain was recorded on the VAS at fixed times to standardize observations. We found a clear correlation between pain intensity and treatment group. The indomethacin group had a lower score and a smaller consumption of supplementary analgesics.

Rehabilitation requires a stay of 1 week in hospital, with daily physiotherapy. Rehabilitation and convalescence were not investigated in this study, as other studies have concluded that prostaglandins may play a role in mediating the surgical stress response, but that other factors are also important [5—7]. It is not clear if the preoperative injection of indomethacin affected postoperative pain or if indomethacin given only as postoperative treatment would be adequate.

ACKNOWLEDGEMENTS

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REFERENCES