

Oral Ibuprofen Versus Paracetamol Plus Codeine for Analgesia After Ambulatory Surgery

Johan C. Ræder, MD, PhD*, Siri Steine, MD, PhD†, and Tor T. Vatsgar*

Departments of *Anesthesia and †General Practice Medicine, Ullevaal University Hospital, Oslo, Norway

The combination of oral codeine and acetaminophen is often used for postdischarge pain control after ambulatory surgery. However, frequently reported side effects include sedation, constipation, and nausea (1). Furthermore, drugs containing codeine may be abused (2) and may result in serious side effects when combined with alcohol or benzodiazepines. Nonsteroidal antiinflammatory drugs are a nonprescription alternative to these drugs.

The aim of this study was to compare ibuprofen with codeine/acetaminophen for pain control during the first 72 h after ambulatory surgery.

Methods

The study was approved by the Regional Ethical Committee, and adult patients scheduled for elective hernia repair, hemorrhoidectomy, or varicose vein resection were included after informed, written consent was obtained. Exclusionary criteria included a history of allergic reactions or side effects with aspirin, acetaminophen, or nonsteroidal antiinflammatory drugs, and opioid-containing oral analgesic use.

After IV premedication with 1–2 mg midazolam, anesthesia was induced with fentanyl 1.5 $\mu\text{g}/\text{kg}$ IV and a propofol target control infusion of 4 $\mu\text{g}/\text{mL}$ IV. Anesthesia was maintained with a propofol target control infusion of 2.0–2.5 $\mu\text{g}/\text{mL}$, 66% nitrous oxide in oxygen, and alfentanil 10 $\mu\text{g}/\text{kg}$ IV as needed. The patients had spontaneous or assisted ventilation with a laryngeal mask airway with standard intraoperative monitoring. Before the end of the anesthesia, all patients received ketorolac 30 mg IV in addition to local anesthesia with 10–20 mL of lidocaine 10 mg/mL at the incision site and paracetamol 1 g rectally. On the recovery ward, the patients received fentanyl 0.5 $\mu\text{g}/\text{kg}$ IV for pain control and metoclopramide 10 mg

for nausea. According to a double-blinded, randomized study design, the patients received identical-appearing tablets for analgesia at home; these tablets contained either ibuprofen 800 mg or paracetamol 800 mg and codeine 60 mg and were to be taken three times a day for 3 days.

The patients received a written questionnaire, which was to be completed 24 and 72 h after surgery, about their pain experience, general functioning, and side effects. The patients were asked to grade their pain experience from 1 (no pain) to 10 (worst pain possible); average pain and worst pain experienced; and pain during defecating, sitting, coughing, and moving. The patients were asked about their general functioning at home (1 = all their time in bed to 5 = full normal activity) and whether the global experience of the postoperative period was worse, similar, or better compared with what they had expected. The patients were also asked specifically about side effects such as nausea, vomiting, dizziness, constipation (i.e., absence of defecation), nightmares, or anxiety.

The two groups were compared with Student's *t*-test for parametric variables and the Mann-Whitney *U*-test or χ^2 test for nonparametric variables, with *P* values < 0.05 considered statistically significant.

Results

Although 116 patients were enrolled in the study, 12 patients did not answer the questionnaire; therefore, only 104 patients were used in the analyses. There was no difference between the groups in demographic data, surgical characteristics, drugs given, pain experience, or side effects during the hospital stay or time to discharge eligibility (data not shown), except for more nausea in the recovery ward in the Ibuprofen group (19% vs 4%).

There was no statistically significant difference between the two groups with respect to pain control during the 3-day postoperative observation period (Table 1). There were no significant differences between the groups in postoperative side effects except for significantly more constipation (i.e., absence of

This study was supported with a research grant from Weiders Pharmaceuticals, Norway.

Accepted for publication February 14, 2001.

Address correspondence to Johan C. Ræder, MD, PhD, Department of Anaesthesia, Ullevaal University Hospital, N-0407 Oslo. Address e-mail to johan.rader@ioks.uio.no.

Table 1. Postdischarge Pain in the Two Treatment Groups

Variable ^a	Ibuprofen (n = 51)	Paracetamol plus codeine (n = 53)
4-24 h after surgery		
Strongest pain experienced (mean ± SD)	5.4 ± 2.5	5.2 ± 3.0
Score >3 (%)	72	79
Score >5 (%)	43	49
Score >7 (%)	23	34
Average pain experienced (mean ± SD)	3.8 ± 2.1	3.7 ± 2.3
Score >3 (%)	43	38
Score >5 (%)	23	24
Score >7 (%)	12	17
24-72 h after surgery		
Strongest pain experienced (mean ± SD)	4.7 ± 2.7	4.8 ± 2.8
Score >3 (%)	58	57
Score >5 (%)	39	41
Score >7 (%)	14	24
Average pain experienced (mean ± SD)	3.2 ± 2.7	3.1 ± 1.8
Score >3 (%)	37	35
Score >5 (%)	13	12
Score >7 (%)	2	0

^a 1 = none; 10 = strongest possible. There were no significant differences between the groups.

Table 2. Postdischarge Side Effects, Functioning, and Global Experience in the Two Treatment Groups

Variable	Ibuprofen (n = 51) ^a	Paracetamol plus codeine (n = 53) ^a
4-24 h after surgery		
Nausea (%)	30	38
No defecation (%)	32	70*
General function (1-5) (mean ± SD)	2.7 ± 0.9	2.7 ± 1.2
Global experience compared with expectation (worse/similar/better) (%)	20/38/42	20/56/24
24-72 h after surgery		
Nausea (%)	18	23
No defecation (%)	6.3	22†
General function (1-5) (mean ± SD)	3.3 ± 1.0	3.3 ± 1.0
Global experience compared with expectation (worse/similar/better) (%)	21/35/44	22/67/11‡

^a No significant differences were found between the groups, unless noted.

* $P = 0.0002$.

† $P = 0.05$.

‡ $P = 0.002$.

defecation) in the Paracetamol plus Codeine patients, both at Day 1 and Day 3 (Table 2). At 72 h after surgery, significantly more patients in the Ibuprofen group rated the global postoperative experience as better than expected (Table 2).

Discussion

In this study, we found equivalent postdischarge analgesic effects with ibuprofen 800 mg orally (po) and paracetamol 800 mg plus codeine 60 mg at identical eight-hour intervals. Whereas ibuprofen 800 mg three times daily (TID) is the maximum recommended dose of this drug, further analgesic effect may possibly be achieved by increasing the dose of paracetamol from 800 to 1000-1500 mg TID

(3). However, the equianalgesic effect observed is compatible with the results of previous investigations involving single-dose use. In a study of pain after orthopedic surgery, Heidrich et al. (4) found a better analgesic effect with ibuprofen 400 mg compared with paracetamol 300 mg plus codeine 30 mg. A comparable analgesic effect and an increased incidence of nausea and drowsiness with codeine was confirmed in the study by Breivik et al. (1), who compared codeine (60 mg po) with or without paracetamol (1 g po) to diclofenac (100 mg po) after dental extractions.

An important issue is whether the results are applicable to a wider population of outpatients with postoperative pain. In our study, 6.4% of the patients declined to participate in the study because they had had a previous bad experience (i.e., side effects) with

paracetamol plus codeine medication. It is interesting to note that more patients in the Ibuprofen group experienced nausea in the recovery ward before receiving any study medication. It would seem that short-term treatment with NSAID is relatively free of side effects unless there is a preexisting contraindication to using these nonopioid analgesic drugs (5,6). The most significant side effect in this study was constipation resulting from codeine. This complication may add to the patients' feeling of discomfort and explain why the total experience was significantly better in the ibuprofen-treated patients.

In conclusion, oral ibuprofen 800 mg is equianalgesic to paracetamol 800 mg plus codeine 60 mg when given every eight hours for three days after ambulatory surgery. Use of ibuprofen also results in better global satisfaction and significantly less constipation.

References

1. Breivik EKD, Barkvoll PP, Skovlund EP. Combining diclofenac with acetaminophen or acetaminophen-codeine after oral surgery: a randomized, double-blind single-dose study. *Clin Pharmacol Ther* 1999;66:625-35.
2. Sproule BA, Busto UE, Somer G, et al. Characteristics of dependent and nondependent regular users of codeine. *J Clin Psychopharmacol* 1999;19:367-72.
3. Korpela R, Olkkola KT. Paracetamol: misused good old drug? *Acta Anaesthesiol Scand* 1999;43:245-7.
4. Heidrich G, Slavic-Svircev V, Kaiko RF. Efficacy and quality of ibuprofen and acetaminophen plus codeine analgesia. *Pain* 1985;22:385-97.
5. Souter A, Fredman B, White PF. Controversies in the perioperative use of non-steroidal antiinflammatory drugs. *Anesth Analg* 1994;79:1178-90.
6. Kellstein DE, Waksman JA, Furey SA, et al. The safety profile of nonprescription ibuprofen in multiple-dose use: a meta-analysis. *J Clin Pharmacol* 1999;39:520-32.