PAPER

# Preemptive Pain Control in Patients Having Laparoscopic Hernia Repair

## *A Comparison of Ketorolac and Ibuprofen*

*Charles G. Mixter III, MD; Loren D. Meeker, PhD; Thomas J. Gavin, RPh, MS*

**Objectives:** To determine if nonsteroidal anti-inflammatory drugs provide adequate pain control for patients having laparoscopic hernia repair and to compare the effectiveness of ketorolac tromethamine with ibuprofen in reducing postoperative laparoscopic hernia pain.

**Design and Setting:** Prospective double-blind randomized study at a 100-bed community hospital.

**Patients:** Seventy patients ranging in age from 16 to 83 years scheduled for elective laparoscopic inguinal hernia repair.

**Interventions:** Patients undergoing laparoscopic hernia repair were enrolled in a double-blind randomized study to compare the 2 treatments. Group 1 received a placebo capsule 1 hour before surgery and ketorolac tromethamine, 60 mg intravenously, at the time of trocar insertion. Group 2 received ibuprofen, 800 mg an hour before surgery, and isotonic sodium chloride solution, 2 mL intravenously, at the time of trocar insertion. In addition, all patients received local infiltration of 30 mL of bupivacaine hydrochloride into their trocar sites. All patients were discharged within 5 hours of the operation and were instructed to take 400 mg of ibuprofen orally every 4 hours for 24 hours whether or not they were experiencing pain. A 24-hour supply of ibuprofen was provided to all study patients. Pain was assessed using the Visual Analog Pain Scale with a maximum pain rating of 100. Assessments were done at the time of and 18 hours after discharge.

**Main Outcome Measure:** Postoperative pain 18 and 24 hours after discharge was assessed using a standardized questionnaire in a telephone interview by a registered nurse from the Outpatient Surgical Unit.

**Results:** There was no significant difference in the level of pain experienced by 35 patients who received ketorolac intravenously and 35 who received ibuprofen orally. There was no significant difference between the 2 treatment groups in the amount of pain experienced at discharge and 18 hours after discharge.

**Conclusions:** Pain relief from ibuprofen, 800 mg, administered orally an hour before laparoscopic hernia repair was not statistically different from that obtained with intravenous ketorolac, 60 mg, administered intraoperatively when comparing the hospital discharge pain score and the mean and highest pain scores 18 hours after discharge. Ibuprofen offers equivalent pain control at a lower cost and reduced potential for adverse drug events compared with intravenous ketorolac in patients having laparoscopic hernia repair. No patient required narcotic supplementation, and pain control was judged satisfactory by all the patients.

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*From the Department of Surgery, Exeter Hospital, Exeter, NH (Dr Mixter and Mr Gavin), and the Department of Mathematics, University of New Hampshire, Durham (Dr Meeker).*

PREEMPTIVE PAIN control remains controversial, even though numerous studies have suggested a benefit from the administration of analgesic medications in the perioperative period.[1,2] Pain control by infiltration with local anesthesia at the operative sites reduces postoperative requirements for narcotic medications.[3,4] The combined use of both intravenous ketorolac tromethamine (Toradol, Syntex International, Ltd, Palo Alto, Calif) and bupivacaine hydrochloride (Marcaine, Sterling Winthrop, Inc, New York, NY) infiltrated into the trocar sites has been shown to have a synergistic effect in reducing the need for narcotic medications in the postanesthesia care unit (PACU).[5,6] Most reports, however, have been of preemptive analgesia administered only during the perioperative period. Preliminary studies at our institution have suggested that the continuation of "preemptive management" is essential for at least 24 hours postoperatively if effective pain control after laparoscopic and open surgical procedures is to be achieved.

Essential to our pain management program has been the avoidance of the use of narcotic medications, thereby eliminating many of the deleterious



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## PATIENTS AND METHODS

Between August 19, 1994, and December 26, 1996, 70 patients ranging in age from 16 to 83 years were enrolled in a prospective randomized study to determine the efficacy of NSAIDs in the control of postoperative pain in patients undergoing laparoscopic transperitoneal inguinal herniorrhaphy. This operation is elective, is relatively standardized, is performed in a wide range of patients, and can be done on an outpatient basis. All procedures were performed by a single surgeon (C.G.M.). Only patients with contraindications to NSAIDs were excluded from the study. Not all patients undergoing the procedure during this time period agreed to enter the study. After agreeing to participate in the study, patients were then randomly assigned to 1 of the 2 treatment groups by choosing a card from a group of 100 cards, 50 of which contained 1 treatment protocol, and the other 50 contained the second treatment protocol. After 18 months, the accrual of patients was terminated. Seventy persons had participated in the trial and, coincidentally, each group contained 35 patients. The study was reviewed and approved by the Exeter Hospital Institutional Review Board, Exeter, NH, and patients signed a consent form before the procedure.

All patients received general anesthesia provided by 1 of 6 staff anesthesiologists; this person was also responsible for the administration of narcotic medications in the PACU. Although no attempt was made to standardize anesthetic management, a review of the medical records after the study had been closed indicated that the anesthetic management was sufficiently uniform so as to not affect the results. The Visual Analog Pain Scale had not been used at Exeter Hospital before this investigation. We wanted to assure ourselves that the group of patients receiving ketorolac and bupivacaine were treated similarly to patients in a previous study,[5] in which the synergistic effects of these drugs in reducing the need for perioperative analgesics were demonstrated. Each patient's study medications were provided by the hospital pharmacy and were labeled with only the patient's name. Every patient received a capsule an hour before the surgical procedure (either ibuprofen, 800 mg orally, or a placebo medication). To provide a reproducible time for the administration of the study drug and to assure ourselves that the patient had no bleeding tendencies, each patient was given an intravenous injection (ketorolac tromethamine, 60 mg, or isotonic sodium chloride, 2 mL) by the anesthesiologist following the placement of two 12-mm trocars lateral to the umbilicus and a single 12-mm trocar at the umbilicus. After the repair was completed and the skin closed, 10 mL of 0.5% bupivacaine hydrochloride was administered to each wound.

Early ambulation was encouraged, and most patients walked immediately after discharge from the PACU. Patients were allowed an unrestricted diet before discharge. They were not required to urinate before leaving the hospital. No restrictions regarding postoperative activities were given to patients.

Before being discharged, each patient was provided with packets containing 200-mg tablets of ibuprofen and was instructed to take 400 mg of ibuprofen every 4 hours for the first 24 hours after the operation, including during the night. In addition, patients were instructed to walk at least every 4 hours even during the night. All patients were treated as outpatients and discharged directly from the short-term stay unit. Although patient compliance was only randomly evaluated, most of our patients apparently complied with the postoperative instructions.

Pain was assessed by the Visual Analog Pain Scale and was recorded on discharge from the PACU, on discharge from the short-term stay unit, and whenever pain medication was given. Pain intensity was recorded on a horizontal line with 10 divisions and was graded on a scale from 0 to 100 (0 indicates no pain; 100, unbearable pain). Pain location was also recorded.

A postdischarge assessment was performed by trained interviewers as part of the normal postdischarge activities of the short-term stay unit personnel, who used a standardized postoperative telephone interview form. Patients were asked to describe the maximum severity of their pain during the previous 24 hours; the average level of their pain during the previous 24 hours; the locations of their pain; whether they had had any nausea or vomiting; whether they had dry mouth, dizziness, drowsiness, or unusual symptoms; and, at the end of the interview, whether they had had any shoulder pain during the postoperative period.

Statistical analyses involved the $\chi^2$ test for independence and the nonparametric Mann-Whitney rank sum test (modified for the occurrence of ties) for the comparison of group medians.[14]

effects seen with the administration of opioids, such as nausea, ileus, urinary retention, excessive sedation, and diminished respiratory function.[7-9] Because ketorolac can be readily administered either intravenously or intramuscularly, it has become an agent of choice for preemptive pain control in surgically treated patients. Unfortunately, ketorolac is expensive—no generic intravenous form is available—and its use has been associated with significant adverse effects, including gastrointestinal bleeding, generalized perioperative bleeding, and acute renal failure, and this has caused concern regarding its routine use as an analgesic agent in the perioperative period.[10,11] Although many of these side effects can be avoided through proper patient selection, dosing, and short-term administration,[12] the drug is still not recommended for intraoperative use. Studies had suggested that indomethacin administered rectally might be an effective substitute for ketorolac in these patients.[13]

We selected laparoscopic herniorrhaphy as our study model for the evaluation of our preemptive pain control program. It is a standardized procedure that is elective and has predictable outcomes. We designed the study with the following objectives:

- determine whether oral ibuprofen (Motrin, Pharmacia & Upjohn, Inc, Kalamazoo, Mich) would be as effective as intravenous ketorolac in reducing pain medicine requirements in the PACU;
- determine the effectiveness of nonsteroidal anti-inflammatory drugs (NSAIDs) alone in providing satisfactory pain control in the postoperative period; and
- determine the effectiveness of our program in preventing severe shoulder pain commonly associated with laparoscopic surgery.



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**Table 1. Patient Characteristics**

| | Study Group | |
|---|---|---|
| | Ketorolac Tromethamine | Ibuprofen |
| Patients, No. | 35 | 35 |
| Mean (range), y | 47 (19-76) | 50 (18-83) |
| Median postoperative stay, h* | 4.1 (1-8) | 3.8 (2-7) |
| Type of herniorrhaphy, No. | | |
| Unilateral | 19 | 21 |
| Bilateral | 13 | 11 |
| Recurrent | 1 | 2 |
| Sliding | 2 | 1 |

*The numbers in parentheses indicate the combined time in the postanalgesia care and short-term stay units.

**Table 2. Work Characteristics of Groups**

| | Study Group | |
|---|---|---|
| | Ketorolac Tromethamine | Ibuprofen |
| Median return to work (range), d | 4.0 (2-17) | 5.5 (1-14) |
| Type of work, No. of patients | | |
| Sedentary | 5 | 2 |
| Sedentary light | 2 | 5 |
| Light duty | 3 | 6 |
| Medium duty | 7 | 6 |
| Heavy labor | 9 | 10 |
| Student | 2 | 0 |
| Retired | 4 | 1 |
| Unknown | 3 | 5 |

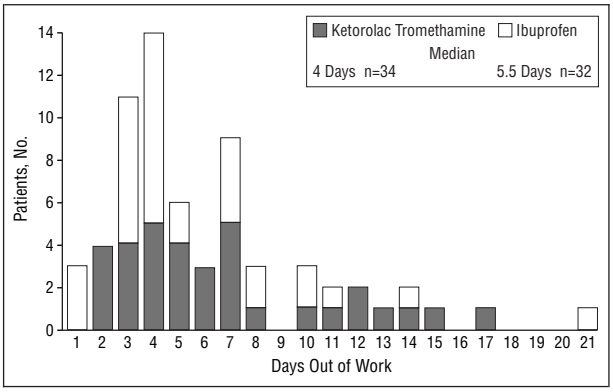


**Figure 1.** *Total number of days that patients remained out of work, including the day of the surgical procedure. Return-to-work data were indeterminable in 4 patients.*

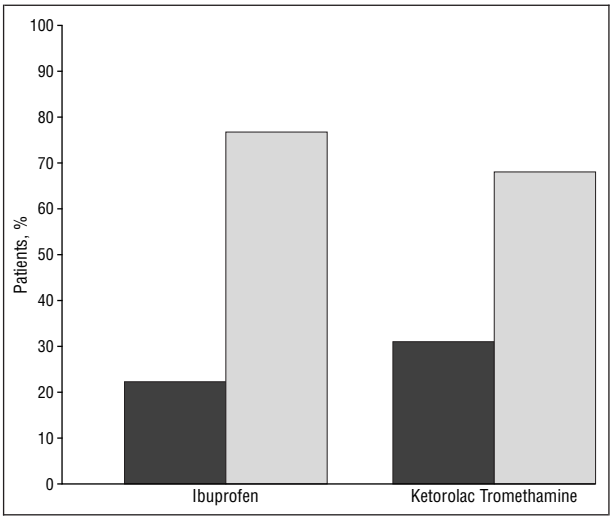


**Figure 2.** *Percentage of patients requiring narcotic medications (fentanyl citrate) in the postanesthesia care unit. Dark bars indicate those who received fentanyl; light bars, those who did not.*

## RESULTS

### STUDY GROUP

Seventy patients were enrolled in the study. At the termination of the study, 35 patients each had been assigned to receive either ibuprofen or ketorolac. The study groups were similar in age, type of procedure performed, and the average length of their postoperative hospital stay (**Table 1**). As expected, there were no differences noted in pain levels between patients undergoing either a bilateral or a unilateral repair and, therefore, these patients were grouped with patients undergoing a unilateral repair. There was no difference between the groups when work characteristics (**Table 2**) and the total length of time out of work (**Figure 1**) were evaluated, suggesting that the groups were similarly motivated regarding recovery and postoperative activity.

### COMPARISON OF IBUPROFEN AND KETOROLAC

No statistical differences were observed between the patients who had received ibuprofen orally and those who had received ketorolac intraoperatively. The percentage of patients receiving narcotic medication in the PACU was similar in both groups (**Figure 2**) and was similar to the results recorded in a previously published study[5] that demonstrated the synergistic effect of the use of ketorolac and ibuprofen in reducing the need for narcotic medication in the PACU. There were no statistically significant differences in the postoperative Visual Analog Pain Scale scores between the 2 groups at the time of discharge from the hospital (**Table 3**). There was no statistically significant difference in the length of time spent in the PACU or the short-term stay unit between the groups (**Table 4**). All patients localized their discomfort to the abdominal wall and trocar sites. No patients had groin pain even if they had undergone bilateral repairs.

### ADEQUACY OF NSAIDs IN PROVIDING PAIN CONTROL DURING HOSPITAL STAY

The median maximum Visual Analog Pain Scale score for the group receiving ketorolac was 35 (scale, 0-100), and for the group receiving ibuprofen, it was 30. This represents the worst pain that the patients experienced during their hospital stay. No patient required narcotic medications following discharge from the PACU. At the time of discharge from the hospital, the median pain level was



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**Table 3. Pain Levels in the Hernia Study Group**

| Pain Level | Median VAS Score* in Study Group: Ketorolac Tromethamine | Ibuprofen | *z* Score Based on Ranks† |
|---|---|---|---|
| Maximum hospital | 35 | 30 | 0.18 |
| At discharge | 20 | 25 | 0.26 |
| Maximum as outpatient | 35 | 30 | 0.15 |
| Average as outpatient | 20 | 20 | 0.80 |
| Average during 24 h | 20 | 17 | 1.02 |

*VAS indicates Visual Analog Pain Scale. Scoring is 0 to 100, with 100 being unbearable pain.
†None of the differences in z scores between the groups were statistically significant.

**Table 4. Length of Stay in the Hospital and Days to Return to Work***

| | Median Time in Study Group: Ketorolac Tromethamine | Ibuprofen | *z* Score Based on Ranks† |
|---|---|---|---|
| Time in PACU, min | 56 | 68 | 1.51 |
| Time in STS unit, min | 192 | 165 | 0.33 |
| Postoperative hospital stay, min‡ | 247 | 230 | 0.06 |
| Out of work, d§ | 4.0 | 5.5 | 1.17 |

*PACU indicates postanalgesia care unit; STS, short-term stay.
†None of the differences in z scores between the 2 treatment groups were statistically significant.
‡Includes time in both the PACU and the STS unit.
§Includes the day of the surgical procedure.

**Table 5. Postdischarge Patient Complications**

| Complication | Study Group*: Ketorolac Tromethamine (n = 30) | Ibuprofen (n = 29) |
|---|---|---|
| Urinary retention | 0 | 0 |
| Excessive bleeding | 0 | 0 |
| Nausea | 2 | 2 |
| Dry throat | 10 | 12 |
| Readmission | 0 | 0 |
| Shoulder pain | 0 | 0 |

*At the end of the postdischarge interview, patients were specifically asked about postoperative shoulder pain. One patient in the ketorolac group and 5 additional patients in the ibuprofen group stated that they had experienced transient discomfort (Visual Analog Pain Scale [VAS] score on a scale of 0-100; median, 10; range, 3-80) during the postoperative period.

20 for the group receiving ketorolac and 25 for the group receiving ibuprofen. All patients were ambulatory.

## POSTDISCHARGE EVALUATION

Following discharge, patients were asked to rate their average pain level for the previous 24 hours. The median 24-hour pain score for both groups was 25. Postdischarge data were not collected on 11 patients. These patients were evenly distributed between both study groups (ketorolac, 5; ibuprofen, 6), and all of these patients had low pain scores at the time of discharge from the hospital. During their postoperative visit, these patients stated that they had either returned to work or left the house on errands and therefore had been unavailable for a telephone interview.

No patient complained about groin pain even if they had undergone bilateral repairs. Only 1 patient spontaneously complained about shoulder pain (pain score, 50) during the postoperative telephone interview. Five additional patients acknowledged that they had had some mild (average score, 40) shoulder pain when they were specifically asked about it by the interviewer. Although more patients in the group receiving ibuprofen noted shoulder pain, these results were not statistically different, and the severe postoperative shoulder pain frequently observed in many patients following laparoscopic procedures was virtually eliminated. A dry mouth was a common complaint (**Table 5**). The median maximal Visual Analog Pain Scale level after discharge was 35 for the group receiving ketorolac and 30 for the group receiving ibuprofen, and the median pain level after discharge was 20 in both groups, demonstrating excellent pain control. It is likely that this score would have been lower if the 11 patients who were unavailable for telephone interviews had been included. There were no statistically significant differences in pain levels between these 2 groups (Table 3).

## COMMENT

Many authors have evaluated the efficacy of laparoscopic procedures by comparing the length of stay in the hospital, complication rates, and morbidity data following discharge. The postoperative management of the patients having laparoscopic surgical repair is only occasionally discussed, and most of the data published are conflicting. This is most likely due to the difference in management protocols, rather than in differences in surgical technique. Numerous publications have demonstrated the effectiveness of preemptive analgesia in both open and laparoscopic procedures, but the results have been variable.[15] Surprisingly, the actual time of administration of a preemptive analgesic medication appears to be of little importance.[16] In a 6-year period, we have used intravenous ketorolac and local infiltration of bupivacaine in about 1000 patients having laparoscopic procedures. Several principles of management have been developed that we think have been responsible for our reduced length of stay and early return of our patients to their normal activities. Paramount to our management program has been preemptive analgesia with NSAID analgesic medications and local infiltration of anesthetic agents into the wounds. Early ambulation while the effects of bupivacaine are maximal is important because active walking appears to play an important role in reducing wound discomfort in the postoperative period and, in addition, may reduce the amount of postoperative adhesions.

Educating the nursing staff and patients regarding the effectiveness of NSAIDs is an essential element of our program. When medical personnel do not subscribe to the effectiveness of these medications, they often advo-



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cate the administration of narcotic medications in patients who, when objectively evaluated, have adequate pain control. Avoiding the use of narcotic drugs is extremely important in preventing many postoperative complications such as atelectasis, urinary retention (especially common in patients having hernia repair), nausea, and ileus. It has also become apparent that if the postoperative discomfort of patients is to be minimized, we must *continue* to treat them preemptively for pain at least 24 hours after a surgical procedure.

An additional benefit of this medication program has been the virtual elimination of substantial shoulder pain in our patients. This effect has also been noted in our patients having laparoscopic procedures who were not included in this study. The use of NSAIDs apparently can prevent this reaction to laparoscopy, and although not statistically significant, the data suggest that ibuprofen may be less effective than ketorolac in preventing this complication. A larger study is needed to confirm these observations.

Although this study was carried out in an attempt to document our observations in a controlled group of patients, we have applied this plan of pain management to patients undergoing a large variety of laparoscopic and a limited number of open procedures. These data appear to confirm our observations regarding the efficacy of preemptive pain control in our patients. Although none of the adverse reactions commonly associated with ketorolac administration occurred during the study, it appears that the administration of ibuprofen preoperatively is equally effective, and therefore, ketorolac administration can be avoided in many cases. Pain management of the patients was satisfactory, and they enjoyed a rapid return to their normal activities.

Preemptive analgesia with the use of perioperative NSAIDs, local infiltration of wounds with bupivacaine, and continued routine postoperative administration of NSAIDs by the clock has the potential to substantially reduce postoperative complications in patients. This regimen provides excellent pain control and improved outcomes at a decreased cost. These principles of care can be applied to a wide variety of surgical procedures.

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*C. David London, MD, chief of anesthesia at Exeter Hospital, reviewed the anesthesia records and assisted during the implementation of this study.*

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## DISCUSSION

**Joseph Amaral, MD, Providence, RI:** The reduction of postoperative pain seems to be a critically important issue in an era of health care cost containment as it can lead to a reduction in the length of hospitalization and number of complications. The authors have explored the issue of preemptive analgesia and demonstrated no difference in postoperative pain between orally administered preoperative ibuprofen and intraoperatively administered ketorolac. It is of note that all wounds were infiltrated at the end of the procedure with a locally acting anesthetic, bupivacaine. Unfortunately, in this study there is no control group, and so it is not clear if either modality was truly effective. Dr Mixter presents us with retrospective data looking at this issue and to support his premise. I could add that Dr Forse and colleagues have reported in the *Canadian Journal of Surgery* that there seems to be more pain relief when ketorolac or indomethacin is given preoperatively, compared with a control group in which they did not receive it.

A major issue in this study is whether the authors were truly evaluating preemptive analgesia or rather evaluating continuous analgesic treatment during the period when nociceptive impulses are generated from the wound. The theory of preemptive analgesia states that the analgesia should be present before hypersensitization of the dorsal horn of the spinal cord. This then results in a decreased sensitivity of the dorsal horn and therefore less pain medication required postoperatively or less pain perception. In the present study, the oral ibuprofen was given just before the procedure, and the intravenous ketorolac was given after the cannulas were placed. Recently it has become apparent that in addition to the traditional anti-inflammatory effects that NSAIDs have, they also have potent peripheral, spinal, and central analgesic mechanisms of their own. The unresolved question for me from the study, then, is whether or not we are looking at preemptive analgesia as the authors have used the term or just continuous analgesia—more pain medicine is better.

Finally, I would like to ask the authors some specific questions. First, is it possible that infiltration of the wounds with bupivacaine provided most of the pain relief observed, that is,



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is there any added benefit to having the ketorolac or indomethacin around? Studies by Alexander in the *British Journal of Surgery* noted a Visual Analog Pain Scale score at rest of 10 and with motion of 30 after just bupivacaine infiltration. These data are similar to his with both modalities.

Second, since the patients did not receive oral narcotics to take at their discretion, is it not possible that their relief would have been better had they been made available to them to take?

Third, since preemptive analgesia requires that the analgesic be present before hypersensitization of the dorsal horn, would it have been better to have given the ketorolac at the onset of anesthesia rather than after the cannulas were placed?

Fourth, during his presentation, Dr Mixter emphasizes the complications of narcotics and would raise the issue that those probably are related to parenteral use. Given the fact that after laparoscopic procedure we require narcotics maybe for 2 or 3 doses, are we making a big deal about a small thing?

Fifth, have you any concerns regarding the spurious occurrence of renal failure following the use of NSAIDs that has caused some people to stop their trials?

And, finally, do you have any data to suggest that the patients do better with regard to nociceptive parameters such as earlier discharge from the hospital, earlier return to activity, or earlier return to diet when NSAIDs are used compared with when they are not.

**Padiath Aslam, MD, Augusta, Me:** Do you change the dose of ketorolac depending on the patient's renal function, or did you take that into account? Did you have any complications as a result of it?

**Dr Mixter:** I would like to emphasize that this study was designed to provide a group of patients we could evaluate objectively. Our program of preemptive analgesia has been used in all of our laparoscopic patients and many of our open patients. Our last patient who underwent an open colectomy left the hospital on the second postoperative day. It is our strong impression that these patients do better because we avoid parenteral narcotics. My main interest has actually been this larger group of patients. It is very hard to do a double-blind controlled study when you have had such a successful program that has given good pain control without using postoperative narcotics. Because one cannot subject patients to no medication, we tried to do the next best thing. I agree with you that the study is flawed from that standpoint.

As far as infiltration of the wound providing our pain control, I think this clearly is not true. We have had several patients who had contraindications to NSAIDs, and they have considerable increase in the amount of pain. Our previous study showed that there was a synergistic effect between ketorolac and bupivacaine in the recovery room and that both drugs are necessary for pain control.

As far as oral narcotics, I agree that narcotics might provide effective preemptive analgesia. I think we have shown that continuous analgesia and early treatment avoiding narcotic complications is important in optimizing pain control. When we have delayed or eliminated the administration of these drugs, we do experience increased discomfort in our patients in the intensive care and short-term stay units. I think that if you look at the levels of pain, the return to work data, and the activity data on our patients, we demonstrate that they had excellent pain relief. Our prior experience with narcotics was not as favorable.

As far as preemptive analgesia being done before the stimulation occurs, a recent study by Dr Atkin demonstrated no difference between patients receiving bupivacaine early or late in surgery. Patients undergoing cholecystectomy demonstrated no difference in the time of administration of the analgesic. In fact, there really is not a good substantiation, with clinical studies, of the theory that preemptive analgesia prevents the establishment of pain pathways that I am aware of.

As far as renal failure goes, we have avoided giving ketorolac to patients who have significant elevations of their serum urea nitrogen level; however, recent studies have also shown that many of these patients who develop acute renal problems with NSAIDs were rendered hypovolemic during the procedure. Only 2 in 1000 patients have had acute renal problems, and they returned to normal on cessation of the drug.

## IN OTHER AMA JOURNALS

**JAMA**

**Patient-Specific Decisions About Hormone Replacement Therapy in Postmenopausal Women**

Nananda F. Col, MD, MPP; Mark H. Eckman, MD; Richard H. Karas, MD, PhD; Stephen G. Pauker, MD; Robert J. Goldberg, PhD; Elizabeth M. Ross, MD; Richard K. Orr, MD, MPH; John B. Wong, MD

**Objective.—**To examine the effect of hormone replacement therapy on life expectancy in postmenopausal women with different risk profiles for heart disease, breast cancer, and hip fracture.
**Design.—**Decision analysis using a Markov model. Published regression models were used to link risk factors to disease incidence and to estimate the lifetime risks of developing coronary heart disease (CHD), breast cancer, hip fracture, and endometrial cancer. The impact of hormone therapy on disease incidence was estimated from published epidemiologic studies.
**Setting.—**Mathematical model applicable to primary care.
**Interventions.—**Treatment with hormone replacement therapy or no hormone replacement therapy.
**Main Outcome Measure.—**Life expectancy.
**Results.—**Hormone replacement therapy should increase life expectancy for nearly all postmenopausal women, with some gains exceeding 3 years, depending mainly on an individual's risk factors for CHD and breast cancer. For women with at least 1 risk factor for CHD, hormone therapy should extend life expectancy, even for women having first-degree relatives with breast cancer. Women without any risk factors for CHD or hip fracture, but who have 2 first-degree relatives with breast cancer, however, should not receive hormone therapy.
**Conclusions.—**The benefit of hormone replacement therapy in reducing the likelihood of developing CHD appears to outweigh the risk of breast cancer for nearly all women in whom this treatment might be considered. Our analysis supports the broader use of hormone replacement therapy. *JAMA. 1997;277:1140-1147*

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