CHAPTER **18**

THE EFFECT OF INTRAVENOUS KETOROLAC ON PCA USE IMMEDIATELY FOLLOWING MAJOR FOOT AND ANKLE SURGERY

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INTRODUCTION

A delicate balance between providing adequate postoperative analgesia with minimization of adverse medication effects must exist to provide the most comfortable postoperative experience for the patient. Nonsteroidal anti-inflammatory medications (NSAIDs) are used commonly along with opioid analgesics in the immediate postoperative period following major foot and ankle surgery. NSAIDs acting peripherally in the body combined with the centrally acting opioids work synergistically to reduce pain.

Ketorolac tromethamine (Toradol®) is a non-narcotic analgesic with both anti-inflammatory and anti-pyretic properties. Ketorolac is a pyrrolo-pyrolle derivative chemically related to the anti-inflammatory agent indomethacin. The tromethamine salt in ketorolac contributes to its solubility. Ketorolac is known to be an effective analgesic agent due to its ability to inhibit the synthesis of prostaglandin synthetase and consequently prostaglandin production.[1] This may by itself greatly reduce the severity of postoperative pain by decreasing edema formation. The postoperative requirement for narcotic pain medication may be significantly reduced with concomitant administration of intravenous ketorolac because prostaglandins are thought to be a modulating factor in postoperative pain.

It has been reported that postoperative intramuscular administration of ketorolac may reduce morphine consumption by 33%.[2] This reduction in narcotic usage may result in fewer side effects commonly associated with opioid analgesics such as nausea, vomiting, pruritis and constipation. This decrease in side effects could potentially reduce the length of postoperative hospital stays, as increase patient satisfaction with pain control measures. There have been many studies performed and cited in the literature pertaining to PCA narcotic usage and ketorolac administration either preoperatively or postoperatively for general, gynecologic and orthopedic surgery. However, no studies focusing on foot and ankle surgeries have been executed. It is the purpose of this study to primarily examine the percentage of reduction of PCA usage in the first 24 hours postoperatively with concomitant ketorolac administration for major foot and ankle surgery performed at Northlake Medical Center. It is the secondary aim of this study to examine the reported levels of patient discomfort and the occurrence of narcotic related side effects or adverse ketorolac events.

LITERATURE REVIEW

A randomized, double-blind study was constructed by Stouten and colleagues in 1992 to compare intramuscular ketorolac with morphine in patients with moderate to severe pain after major surgery.[3] They examined a total of 117 patients and rated their pain intensity utilizing a 5-point verbal scale. The patients were administered either intramuscular (IM) 10 mg ketorolac, 30 mg ketorolac, or 10 mg morphine for pain control. They also monitored vital signs and blood gases before and after medication administration. Overall efficacy comparisons showed that intramuscular 30 mg ketorolac was more effective than 10 mg ketorolac, and both doses of ketorolac were more effective than 10 mg intramuscular morphine for pain control.

A similar randomized, double-blind study by Yee et al in 1986 looked at 245 patients categorized into either major or general surgery groups.[4] These patients were given either 10, 30, or 90 mg IM ketorolac, or 6 or 12 mg IM morphine for postoperative pain and asked to rate their discomfort based on a visual analog scale. The general surgery patients were those undergoing tendon or ligament repairs or other orthopedic procedures and major surgery patients included mostly abdominal or gynecologic procedures. The general surgery

patients showed superior efficacy rankings for all ketorolac dosages compared with the morphine treated groups. They also found that the length of pain relief was longer for the ketorolac compared with the morphine groups.

In a 1996 study performed by Nitschke et al,[5] 92 patients were randomized to PCA IM ketorolac or IM morphine groups for postoperative pain control following colon resections. A mini-mental status exam (MMSE) was administered pre-operatively and daily for the first 5 days following surgery. They found that the ketorolac group had significantly lower pain scores and less post-operative confusion than the morphine groups. In the same study, the mean length of hospital stay for the ketorolac group was 7 days compared with 8.7 days for the PCA morphine group and the duration of ileus following surgery was shorter. It was concluded from this study that ketorolac provided a better postoperative course than IM or PCA morphine in respect to pain control, postoperative confusion, and length of stay. However, they stated that there was a strong patient preference for PCA and recommended that ketorolac be administered via PCA because of the decrease in side effects.

Ready et al[6] demonstrated a 25% decrease in morphine use in general, gynecologic, and orthopedic surgery when ketorolac was administered as a continuous IV infusion or as a bolus. Yee and colleagues found that a dosage of 90 mg of ketorolac was more effective than 12 mg of morphine, and that a dosage of 30 mg or 10 mg of ketorolac were equally as effective as 12 mg of morphine for pain control. Previous studies have shown that pain control utilizing ketorolac tromethamine at dosages of 10 mg and 30 mg was equal to or greater than 10 to 12 mg of IM morphine sulfate.[3,7,8]

Rogers et al[9] studied the amount of morphine use after surgery when patients were administered IV ketorolac either before abdominal hysterectomy or after surgery compared with a control group who did not receive ketorolac. They found that after 2 hours of patient-controlled analgesia with morphine, the group administered ketorolac before surgery used less morphine than that of the control group. However, median blood loss in the group given ketorolac before the operation was greater than that of the group that did not receive ketorolac preoperatively.

MATERIALS AND METHODS

Between January 2003 and April 2004, 46 patients (age range 13-73 years) who underwent major rearfoot or ankle surgery at Northlake Medical Center were examined. The surgical procedures consisted of triple, subtalar, mid-tarsal, ankle, and tarsometatarsal arthrodeses with either internal or external fixation; ankle, calcaneal, or pilon fracture repair, or other complex reconstructive procedures. Patients with a history of bleeding disorders, GERD, asthma, hepatic or renal disease, anti-coagulation use, or NSAID sensitivity or allergy were not scheduled to receive postoperative ketorolac. Patients with sensitivity or allergy to morphine sulfate received either Demerol or Dilaudid as their PCA opioid. All patients received local anesthetic blocks at some point during their surgical procedure.

Patients were divided into two groups, Group I patients received both the PCA unit with morphine sulfate and 30 mg ketorolac through an intravenous route every 6 hours for the first 24 hours following surgery; Group II patients received a PCA with only morphine sulfate for pain control. Patients who received Demerol or Dilaudid were also examined for narcotic consumption. However, due to the small number of these patients, statistical significance could not be determined.

In the recovery unit, all patients were given a PCA unit with morphine sulfate per the anesthesia department. The PCA pump was primed with morphine 1mg/mL with a lockout time of 6 minutes. There was no background infusion of narcotic. All patients received instruction on how to operate the PCA device once they had been transferred to their room. The type of surgery, type of opioid, PCA start and end time, and the amount of opioid administered by the PCA were recorded. Patients who were scheduled to receive a basal rate of narcotic infusion per the PCA unit were excluded from the study. Patient pain level was recorded on a verbal rating scale from zero to five with zero representing the absence of pain and five representing the worst pain imaginable.

The level of sedation as assessed by the nurse assigned to the patient on a scale of zero to three with zero representing the patient being awake, one being drowsy but awake, two being asleep but arousable, and thee representing the patient being unarousable. Respiratory rate, the incidence of side

effects and the length of hospital stay were also recorded. The side effects measured were nausea, vomiting, pruritis, urinary retention, decreased oxygen saturation, or constipation. The average amount of narcotic consumption, pain, sedation, respiratory rate, and length of stay was calculated for each group.

The patients were followed for the first 24 hours following surgery. A T-test was performed to determine if the values for these parameters differed significantly between the two groups. Lastly, a cost analysis for the amount of ketorolac administered as well as for the cost for the PCA unit was performed.

The hospital pharmacy at our institution was contacted and an analysis was performed to determine cost effectiveness. The flat rate for the morphine PCA unit was compared with this price plus the cost of the administered ketorolac. This was done to determine cost effectiveness of the pain treatment protocol.

RESULTS

There were a total of 46 patients examined for this study. Of the 46 patients, 12 received ketorolac and PCA morphine, and 34 received PCA morphine alone. The average narcotic consumption, pain level, sedation, respirations, length of stay, and percentage of side effects are summarized in Table 1.

Total PCA morphine consumption for the 24 hour period following surgery was decreased for Group I compared with Group II. For Group I, patients receiving ketorolac consumed 67.7% less morphine than those in Group II (33.429 ± 12.83 versus 50.618 ± 25.204 mg; $P = 0.05$) (Table 2).

Patients in Group I reported a lower verbal pain intensity than did patients in Group II in the immediate 24 hours post surgery. Pain was decreased subjectively by 52.9% in Group I compared with Group II (0.932 ± 0.635 versus 1.763 ± 0.564; $P = 0.05$) (Table 2).

Table 1

Results of Group I: Morphine PCA with Ketorolac

Group	# Patients	Narcotic Type	Average Narcotic Consumption (mg)	Average Pain	Average Sedation	Average Respirations	Length of Stay (hours)	% Side Effects
I*	12	Morphine	33.429	0.932	1.779	18.688	48.643	16.7%
II†	34	Morphine	50.618	1.763	1.769	18.915	49.471	67.7%

*Patients receiving Morphine PCA with Ketorolac
†Patients receiving Morphine PCA without Ketorolac

Table 2

Calculation of T-values For Narcotic Consumption and Pain Level in 12 patients

	Group I Ketorolac group n=12	Group II Non-ketorolac group n=34	T Value	DF	P
Mean ± SD mg narcotic consumption, (variance)	33.429 ± 12.83, (164.633)	50.618 ± 25.304, (635.266)	2.967	44	>0.05
Mean ± pain level, (variance)	0.932 ± 0.635, (0.403)	1.763 ± 0.564 (0.318)	3.88	44	>0.05

In Group I, 16.7% of patients reported narcotic related side effects with nausea being the most common effect. In Group II, 67.7% of patients reported side effects with nausea again being the most common. There was no significant difference between the groups in regard to sedation, respiratory rate, or length of hospital stay.

There is a flat rate charged per morphine PCA unit that is $67.75 at our institution. This price includes the narcotic supply. For each 30 mg dose of ketorolac, the charge is $12.00. As the charge for the PCA is standard, the cost for the ketorolac in addition to this is $48.00 (4 doses) for a total of $115.75. Therefore, patients receiving the morphine PCA alone (Group I) were charged $67.75 and those receiving ketorolac and the morphine PCA (Group II) were charged $115.75.

DISCUSSION

Ketorolac as well as other NSAIDs are commonly used as adjuncts to narcotic PCA devices for post-operative pain control protocols. The results of this study demonstrate that ketorolac can reduce the amount of narcotic used, the amount of post-operative pain, and the incidence of narcotic-related side effects.

All patients that had a known relative contraindication to NSAIDs are routinely excluded from receiving ketorolac postoperatively. All NSAIDs have the ability to inhibit renal function. The approved dosage of ketorolac is not to exceed 120 mg in a 24 hour period. Renal failure from ketorolac administration has been estimated to be 1:1,000–100,000 in epidemiologic studies.[16] Almost all NSAIDs including ketorolac have the potential to cause gastric irritation and can negatively affect platelet function. After ketorolac was released to the market, surveillance studies were performed and results indicated a very small risk for gastrointestinal or operative site bleeding when appropriate doses were used in healthy adult populations for less than 5 days.[17]

The decrease of 67.7% narcotic consumption in the Group I patients that received ketorolac correlates well to what exists in the literature. A range of 25 - 66% decrease in consumption has been reported in many studies where combined NSAID and narcotic therapy has been utilized.[6,14] It is highly likely that this substantial decrease in narcotic consumption by Group I patients is directly related to the relative small percentage of side effects within this group. None of the side effects reported could be attributed to ketorolac administration.

Patients receiving the morphine PCA alone (Group I) are charged $67.75 and those receiving ketorolac and the morphine PCA (Group II) are charged $115.75. It is therefore more cost effective to administer the morphine PCA alone only if there is no presence of side effects. In the presence of side effects such as nausea or pruritis that require anti-emetic or anti-pruritic medication administration, this could negatively affect the cost to the patient.

CONCLUSION

It was the hypothesis of this study that ketorolac administered simultaneously with PCA morphine would decrease the amount of narcotic used by the patient in the first 24 hours following major foot or ankle surgery. It was also hypothesized that the concomitant administration of ketorolac and PCA morphine would decrease overall pain, the incidence of side effects, and length of hospital stay. The results of this study do suggest that ketorolac administration does decrease narcotic consumption, subjective pain levels, as well as the incidence of side effects. However, length of stay was not affected to any significant degree.

Weaknesses of this study include the number of patients as well as examination of only one narcotic type. This study could be prospectively improved by creating a Demerol and Dilaudid PCA group as these patient populations become available. There seems to be a decreasing number of surgeons who prefer Demerol or Dilaudid due to either pain control levels or side effect incidence. There were many patients who were assigned to receive a basal rate of narcotic that was continuously infused throughout the postoperative period. Because the patient had no control over the dose administration, these patients had to be excluded from the study. Several patients had the PCA unit discontinued before the first 24 hours following surgery and were subsequently removed from the study. Many surgeons prefer to manage their patients without the PCA device, because they feel it is unnecessary in some cases and in certain patient populations.

In conclusion, administration of ketorolac in conjunction with PCA morphine is an effective

means of patient pain control and is more efficacious than narcotic administration alone. Decreasing the amount of narcotic medication consumed can greatly decrease side effects. Patients scheduled to receive ketorolac or any NSAID should be carefully selected keeping in mind their systemic disease status or any other factors that may be a contraindication to its usage.

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