# *Early Intravenous Ibuprofen Decreases Narcotic Requirement and Length of Stay after Traumatic Rib Fracture*

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**Pain control after traumatic rib fracture is essential to avoid respiratory complications and prolonged hospitalization. Narcotics are commonly used, but adjunctive medications such as nonsteroidal anti-inflammatory drugs may be beneficial. Twenty-one patients with traumatic rib fractures treated with both narcotics and intravenous ibuprofen (IVIb) (Treatment) were retrospectively compared with 21 age- and rib fracture-matched patients who received narcotics alone (Control). Pain medication requirements over the first 7 hospital days were evaluated. Mean daily IVIb dose was 2070 ± 880 mg. Daily intravenous morphine-equivalent requirement was 19 ± 16 *vs* 32 ± 24 mg ($P < 0.0001$). Daily narcotic requirement was significantly decreased in the Treatment group on Days 3 through 7 ($P < 0.05$). Total weekly narcotic requirement was significantly less among Treatment patients ($P = 0.004$). Highest and lowest daily pain scores were lower in the Treatment group ($P < 0.05$). Hospital length of stay was 4.4 ± 3.4 *versus* 5.4 ± 2.9 days ($P = 0.32$). There were no significant complications associated with IVIb therapy. Early IVIb therapy in patients with traumatic rib fractures significantly decreases narcotic requirement and results in clinically significant decreases in hospital length of stay. IVIb therapy should be initiated in patients with traumatic rib fractures to improve patient comfort and reduce narcotic requirement.**

MORE THAN 300,000 patients are treated for traumatic rib fractures each year in the United States with approximately one-third requiring hospital admission.[1] Rib fractures account for more than half of all blunt thoracic injuries.[2] Rib fracture-related pain may cause respiratory splinting, atelectasis, pneumonia, respiratory failure, need for prolonged mechanical ventilation, and even death.[1–5] These adverse events are especially prominent among elderly patients in whom seemingly minor rib fractures can significantly increase the risk of respiratory complications and death.[3–5] Inadequate pain control, resulting in increased pulmonary complications and hospital length of stay, appears to be a major factor in rib fracture-related morbidity and mortality.[1–3, 5] Early pain management, before respiratory compromise develops, is essential to improving patient outcome from acute traumatic rib fractures.

Pain management for traumatic rib fractures can be challenging.[1, 6–8] Narcotic analgesics remain the core of pain management therapy for rib fracture-related pain.[1] These medications can result in multiple side effects, however, including respiratory depression, delirium/confusion, dizziness, hypotension, seizures/convulsions, bradycardia, and constipation.[9] Narcotic-induced respiratory depression can be especially problematic in the presence of rib fracture-related pulmonary comorbidities such as pulmonary contusion, hemothorax, and pneumothorax.

A variety of adjunctive therapies have been proposed to augment the pain relief afforded by narcotic medications including nonsteroidal anti-inflammatory drugs (NSAIDs), epidural analgesia, intermittent intercostal nerve blocks, continuous intercostal nerve block infusion catheters, and surgical fixation.[1, 5–9] The use of these adjunctive therapies, intended to both improve pain control and reduce the need for narcotics, varies widely from hospital to hospital.

Oral NSAIDs are used as an adjunctive therapy in approximately 25 per cent of patients with traumatic

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rib fractures.[1] These medications are typically not administered to the patient who is without oral intake and their use as an adjunctive pain therapy may therefore be delayed for several days postinjury. An intravenous formulation of ibuprofen (IVIb) (Caldolor®; Cumberland Pharmaceuticals, Nashville, TN) has recently become available and a multicenter, randomized, double-blind, placebo-controlled trial has demonstrated the safety of IVIb, administered alongside narcotic analgesics, in reducing postoperative pain.[8] This intravenous formulation may be administered early in the patient's hospital course potentially affording improved pain control when the patient is at greatest risk for respiratory compromise. We hypothesized that the use of adjunctive pain medications such as IVIb would improve pain control in patients with traumatic rib fractures and reduce the need for narcotic pain medications.

## Methods

This study is a retrospective chart review analyzing the pain management of patients 18 years of age or older who sustained rib fractures and were treated in a Level I trauma center. All patients were managed according to an evidence-based clinical guideline instituted in November 2011 that advocated a multimodality approach to the treatment of rib fracture-related pain.[9] Patients were included in the review if they sustained at least one rib fracture, required inpatient admission, and received narcotics with or without IVIb for pain management. Patients were excluded if they were admitted to the intensive care unit, were intubated or unable to verbally relate their pain level, received ketorolac or any other NSAID, received any type of intercostal nerve block, reported a history of narcotic addiction or dependence, had major associated injuries that would significantly increase their narcotic requirement, or did not receive IVIb during the first 48 hours of hospital admission. This study was approved by the Orlando Health Institutional Review Board (10.104.09) and the University of Central Florida College of Medicine Institutional Review Board (SBE-11-07695).

Rib fractures were identified using either plain radiographs or computed tomography of the chest. Each patient's radiographic studies were evaluated by one of the authors (M.L.C., C.P.S.) and compared with the attending radiologist's interpretation. Rib fractures were further classified as simple, segmental, or displaced. The presence of bilateral rib fractures was noted.

Pain was assessed and documented at least every 4 hours by the patient's nurse. A patient's level of pain was determined used a self-reported numeric scale from 0 (no pain) to 10 (worst possible pain). Pain medication was titrated to achieve patient comfort rather than a predetermined numerical score. Narcotics were initially administered intravenously beginning in the emergency department and subsequently converted to an oral narcotic formulation once patient comfort had been achieved and an oral diet was appropriate. No patients in the study received epidural or paracostal anesthetic injections or infusion catheters.

IVIb was dosed at 600 to 800 mg intravenously every 6 hours and initiated as soon as possible after rib fracture diagnosis. Contraindications to IVIb therapy included long-bone fracture (as a result of concern for malunion), allergy, history of gastrointestinal bleeding/ulcer, or acute intracranial hemorrhage. Unless contraindicated, patients received IVIb for at least 48 hours after admission before conversion to oral ibuprofen.

Patients receiving both IVIb and narcotics for pain control (Treatment group) were matched to contemporaneous patients from the trauma registry who received narcotics alone (Control group). Patients were matched by admission date (within 1 year), gender, age (±5 years), number of rib fractures (±1 rib fracture), and similarity of overall injury (Injury Severity Score [ISS] ±5).

Patient demographics, number and type of rib fractures, mechanism of injury, thoracic Abbreviated Injury Score, ISS, admission unit, hospital length of stay, pharmacy cost, and hospital charges were collected. Patient-reported pain assessment scores and medication requirements during the first 7 days of hospitalization (or until hospital discharge if sooner) were reviewed. All narcotics (morphine, fentanyl, hydromorphone, oxycodone) were converted to their intravenous (IV) morphine-equivalent to facilitate comparison and data analysis (10 mg IV morphine = 100 μg IV fentanyl = 20 mg oral oxycodone = 1.5 mg IV hydromorphone). Oral ibuprofen dosages were converted to their IVIb equivalent (680 mg oral = 800 mg IV). Both narcotic and ibuprofen-related complications were noted.

Data were analyzed using standard descriptive statistics and are reported as either percentage or mean ± standard deviation. Statistical analysis was performed using Fisher's exact test (for categorical data), Student's *t* test (for parametric continuous data), or Mann-Whitney *U* test (for nonparametric continuous data) as appropriate. Statistical significance was defined as $P < 0.05$.

## Results

Over a 6-month period, 21 patients received both IVIb and narcotics for traumatic rib fracture-related

TABLE 1. *Demographics: All Patients*

| | Treatment | Control | *P* Value |
|---|---|---|---|
| No. of patients | 21 | 21 | |
| Age (years) | 52 ± 14 | 53 ± 16 | 0.83 |
| Gender (male) | 62% | 81% | 0.31 |
| Thoracic AIS score | 3 ± 1 | 3 ± 1 | 0.93 |
| ISS | 12 ± 3 | 16 ± 8 | 0.27 |
| Mechanism of injury | | | |
| Motor vehicle crash | 43% | 19% | 0.10 |
| Motorcycle crash | 24% | 33% | 0.50 |
| Fall | 19% | 29% | 0.47 |
| Automobile *vs* pedestrian | 14% | 19% | 0.68 |
| Rib fractures | | | |
| Type | | | |
| Simple | 78% | 82% | 0.55 |
| Segmental | 3% | 9% | 0.08 |
| Displaced | 22% | 17% | 0.43 |
| Bilateral | 14% | 5% | 0.29 |
| Number (per patient) | | | |
| Total | 5 ± 3 | 4 ± 2 | 0.40 |
| Simple | 4 ± 3 | 4 ± 2 | 0.46 |
| Segmental | 3 | 4 ± 0 | NC |
| Displaced | 2 ± 1 | 3 ± 1 | 0.16 |
| Stepdown unit admission | 52% | 52% | 1.0 |
| Hospital LOS (days) | 4.4 ± 3.4 | 5.4 ± 2.9 | 0.32 |

AIS, Abbreviated Injury Score; ISS, Injury Severity Score; LOS, length of stay; NC, not calculable (single patient).

pain management (Treatment group). These were compared with 21 severity of illness-matched patients who received narcotics alone (Control group). The Treatment and Control groups were well matched (Table 1). Rib fractures were identified by computed tomography of the chest in 86 per cent of Treatment patients and 90 per cent of Control patients ($P = 0.63$). One-third of patients in each group had rib fractures as their only injury, whereas the remaining two-thirds sustained additional blunt injuries including splenic laceration, pulmonary contusions, vertebral column fractures, pelvic fractures, and extremity fractures. There was no difference in the need for operative intervention to repair other injuries (0 *vs* 14%; $P = 0.23$). No patient in either group underwent operative stabilization of their rib fractures. Eleven patients (52%) in each study group were admitted to a stepdown unit, whereas the remaining 10 patients were admitted to a regular floor bed. Incentive spirometry volumes were incompletely documented to allow reliable analysis.

Hemo/pneumothorax (71 *vs* 62%; $P = 0.74$), clavicle fracture (19 *vs* 14%; $P = 0.68$), scapula fracture (14 *vs* 29%; $P = 0.45$), atelectasis (62 *vs* 52%; $P = 0.53$), and pulmonary contusion (29 *vs* 29%; $P = 1.0$) were similar between groups. No patient in either group developed pneumonia, gastrointestinal hemorrhage, or renal dysfunction. One patient in each group required transfer to a stepdown unit for pulmonary insufficiency. One patient in the Treatment group with eight rib fractures required transfer to the intensive care unit for acute respiratory failure and mechanical ventilation. There were no mortalities in either group.

The need for tube thoracostomy for traumatic hemothorax or pneumothorax was similar between groups (33 *vs* 43%; $P = 0.75$). Patients who require tube thoracostomy are at increased risk for pain. A sensitivity analysis was therefore performed evaluating the subset of patients in each group who required tube thoracostomy (Table 2). In this analysis, the Treatment group had significantly more patients who sustained their rib fractures as a result of a fall and one fewer patient with displaced rib fractures.

Treatment patients received an average IVIb equivalent of 2070 ± 880 mg daily. Mean daily morphine-equivalent requirement over the first 7 days of hospitalization was significantly lower in the Treatment group (19 ± 16 mg *vs* 32 ± 24 mg; $P < 0.0001$). Total mean pain medication requirements for the first 7 days of hospitalization for both the overall study and tube thoracostomy analyses are depicted in Table 3. In the overall study analysis, total weekly morphine-equivalent requirement was significantly decreased in Treatment patients ($P = 0.007$). The daily morphine-equivalent requirement did not differ between the study groups on Day 1 or Day 2; however, narcotic requirement was significantly decreased in Treatment patients on each subsequent day of therapy (Days 3

TABLE 2. *Demographics: Tube Thoracostomy Patients*

| | Treatment | Control | *P* Value |
|---|---|---|---|
| No. of patients | 7 | 9 | |
| Age (years) | 58 ± 11 | 56 ± 16 | 0.79 |
| Gender (male) | 57% | 78% | 0.38 |
| Thoracic AIS score | 3 ± 1 | 3 ± 1 | 0.67 |
| ISS | 13 ± 5 | 18 ± 6 | 0.14 |
| Mechanism of injury | | | |
| Motor vehicle crash | 29% | 33% | 0.84 |
| Motorcycle crash | 14% | 22% | 0.69 |
| Fall | 43% | 0% | 0.03 |
| Automobile *vs* pedestrian | 14% | 44% | 0.20 |
| Rib fractures | | | |
| Type | | | |
| Simple | 64% | 81% | 0.10 |
| Segmental | 9% | 11% | 0.81 |
| Displaced | 27% | 16% | 0.26 |
| Bilateral | 0% | 11% | 0.36 |
| Number (per patient) | | | |
| Total | 5 ± 3 | 4 ± 2 | 0.61 |
| Simple | 4 ± 2 | 4 ± 2 | 0.65 |
| Segmental | 3 | 4 | NC |
| Displaced | 2 ± 0 | 3 ± 0 | 0.004 |
| Stepdown unit admission | 71% | 89% | 0.38 |
| Hospital LOS (days) | 6.1 ± 2.8 | 7.0 ± 2.8 | 0.53 |

AIS, Abbreviated Injury Score; ISS, Injury Severity Score; LOS, length of stay; NC, not calculable (single patient).

TABLE 3. *Daily Narcotic Requirements*

| | Treatment | Control | *P* Value |
|---|---|---|---|
| All Patients (no.) | 21 | 21 | |
| Day 1 (mg) | 23.5 ± 18.2 | 16.9 ± 14.9 | 0.21 |
| Day 2 (mg) | 23.5 ± 15.9 | 34.9 ± 21.0 | 0.06 |
| Day 3 (mg) | 20.0 ± 14.6 | 36.5 ± 25.7 | 0.02 |
| Day 4 (mg) | 15.5 ± 14.6 | 36.7 ± 25.4 | 0.01 |
| Day 5 (mg) | 10.7 ± 12.4 | 40.0 ± 27.7 | 0.003 |
| Day 6 (mg) | 11.1 ± 9.6 | 33.3 ± 29.4 | 0.04 |
| Day 7 (mg) | 9.0 ± 8.2 | 28.4 ± 18.0 | 0.03 |
| Total (mg) | 82.6 ± 54.3 | 169.8 ± 115.3 | 0.004 |
| Tube thoracostomy patients (no.) | 7 | 9 | |
| Day 1 (mg) | 19.7 ± 21.1 | 22.4 ± 18.9 | 0.79 |
| Day 2 (mg) | 24.0 ± 15.7 | 39.8 ± 21.5 | 0.11 |
| Day 3 (mg) | 24.3 ± 18.9 | 33.5 ± 8.7 | 0.27 |
| Day 4 (mg) | 20.9 ± 17.8 | 26.1 ± 8.8 | 0.53 |
| Day 5 (mg) | 13.6 ± 13.7 | 27.9 ± 13.8 | 0.10 |
| Day 6 (mg) | 13.5 ± 9.9 | 25.3 ± 13.3 | 0.13 |
| Day 7 (mg) | 10.0 ± 9.1 | 35.0 ± 17.1 | 0.03 |
| Total (mg) | 111.2 ± 81.3 | 183.0 ± 64.6 | 0.10 |

through 7) (Table 3; Fig. 1). In the tube thoracostomy analysis, the daily morphine-equivalent requirement of the Treatment patients was decreased, although not significantly, for each day of the study except for Day 7.

Mean highest daily pain score over the first 7 days of hospitalization was significantly lower among Treatment patients (7 ± 2 *vs* 8 ± 2; $P < 0.04$) in the overall study analysis. Mean lowest daily pain score was also significantly lower in Treatment patients (3 ± 2 *vs* 5 ± 2; $P < 0.00001$). Both the highest and lowest daily pain assessment scores were consistently lower in the Treatment group throughout the first 7 days of hospitalization (Fig. 2). On average, Treatment patients stayed in the hospital 1 day less than Control patients (4.4 ± 3.3 days *vs* 5.4 ± 2.9 days; $P = 0.17$). The hospital length of stay was also 1 day less (6.1 ± 2.8 days *vs* 7.0 ± 2.8 days; $P = 0.53$) in the tube thoracostomy analysis.

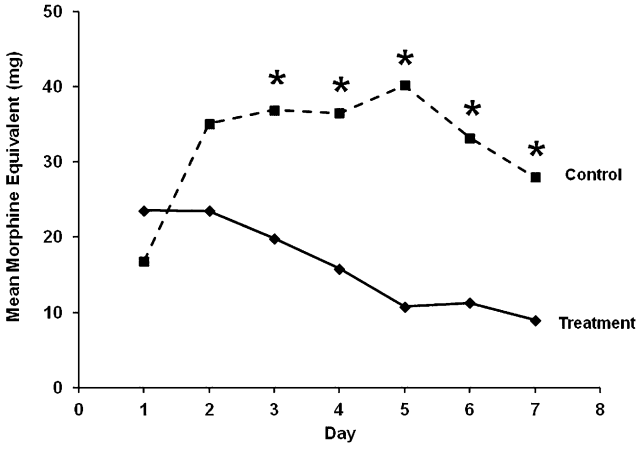


FIG. 1. Daily pain medication requirements. *$P < 0.05$ (compared with the Treatment group).

Pain medication acquisition costs are listed in Table 4. The cost of IV and total narcotic medications were both significantly decreased in the Treatment group. The cost of ibuprofen therapy in the Treatment group averaged $64.70 per hospitalization. The cost of all pain medications averaged $48.67 higher in the Treatment group. Hospital charges were similar between the two groups ($38,671 ± $28,108 *vs* $36,987 ± $14,550; $P = 0.81$).

## Discussion

Traumatic rib fracture-related pain is an underappreciated cause of morbidity and mortality. Inadequate pain control after blunt chest trauma promotes respiratory splinting, atelectasis, inadequate clearance of pulmonary secretions, pneumonia, acute respiratory failure, prolonged mechanical ventilation, need for tracheostomy, and is associated with a mortality rate of 5 to 29 per cent.[2, 5] The typical patient with traumatic rib fractures is unable to resume their normal work/daily activities for 70 days postinjury resulting in significant psychological and economic impact to patients, families, and employers alike.[1]

Appropriate management of rib fracture pain includes early mobilization, aggressive pulmonary support, and use of both narcotic pain medications and adjunctive pain therapies such as NSAIDs, epidural analgesia, intermittent intercostal nerve blocks, continuous intercostal nerve block infusion catheters, and surgical fixation.[1] Of these therapies, oral NSAIDs are arguably the simplest to administer and least expensive of the adjunctive therapies. Furthermore, NSAID therapy can be continued after discharge from the hospital and used to transition patients off of narcotic medications. Enteral NSAID administration is not always possible in the traumatically injured however.

IVIb has recently become available for clinical use. It can be initiated on patient presentation to the emergency department and facilitates early NSAID administration when adequate respiratory function is most crucial and oral administration of NSAIDs may not yet be possible or appropriate. This study demonstrates that combination therapy using both narcotics and IVIb reduces patient narcotic requirement and achieves significant improvements in pain control compared with narcotics alone. These benefits were achieved without apparent NSAID-related complications. Improved patient comfort may decrease the risk of respiratory insufficiency and failure as a result of inadequate spontaneous tidal volumes and decreased pulmonary secretion clearance and may decrease

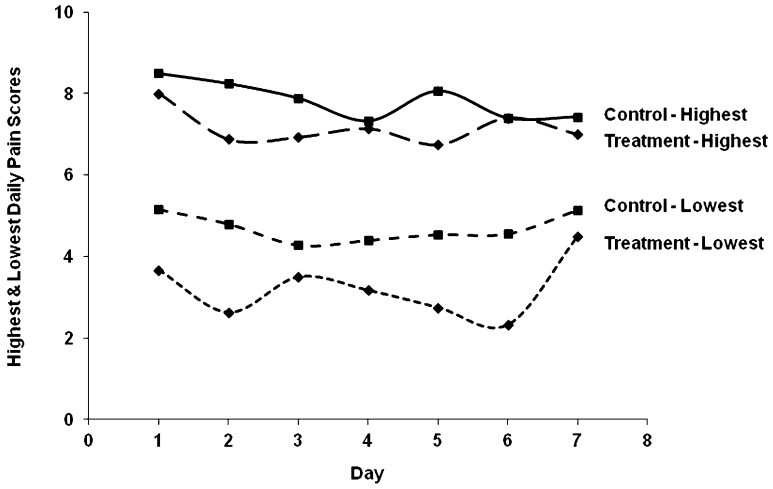


FIG. 2. Daily pain assessment scores.

TABLE 4. *Pain Medication Acquisition Cost per Patient*

| | Treatment | Control | *P* Value |
|---|---|---|---|
| IV ibuprofen ($) | 63.77 ± 39.98 | — | — |
| Oral ibuprofen ($) | 0.93 ± 2.80 | — | — |
| Total ibuprofen ($) | 64.70 ± 41.37 | — | — |
| IV narcotic ($) | 8.72 ± 5.25 | 18.28 ± 14.59 | 0.01 |
| Oral narcotic ($) | 4.08 ± 6.43 | 10.54 ± 14.30 | 0.07 |
| Total narcotic ($) | 12.80 ± 9.00 | 28.83 ± 22.07 | 0.005 |
| Total pain medication ($) | 77.50 ± 45.86 | 28.83 ± 22.07 | <0.0001 |

IV, intravenous.

hospital length of stay as a result of decreased pulmonary morbidity.

The cost of intravenous and oral ibuprofen therapy averaged less than $65.00 per patient hospitalization. The total cost for narcotic medications was significantly less in the Treatment group as a result of using adjunctive NSAID therapy. The difference in medication cost between the Treatment and Control groups was less than $50.00 per patient. This relatively minimal cost is overshadowed by the cost of an apparent additional day of hospitalization in patients who received narcotics alone. Although the potential financial benefit of early routine IVIb therapy for traumatic rib fracture may not be statistically evident in this preliminary small-scale clinical trial, the trend toward decreased hospital stay would likely be confirmed in a larger study because it was seen in both the overall study and tube thoracostomy subgroup analyses. The physiologic benefits of improved pain control and pulmonary function are more difficult to assess and will require a prospective, multicenter clinical trial.

Although a small initial study, IVIb appears to be safe and did not lead to adverse drug events. Specifically, we encountered no gastrointestinal hemorrhage or renal dysfunction in any of the study patients. A recent multicenter, placebo-controlled trial of IVIb in 406 surgical patients demonstrated no increase in medication-related complications.[8] A prospective, randomized, multicenter clinical trial is indicated to confirm the safety and efficacy of IVIb in the treatment of traumatic rib fracture-related pain.

This study has several limitations. It has a small sample size and describes our initial experience with the new formulation of a medication that has previously been demonstrated to have efficacy in oral form. Additional experience in larger numbers of patients is clearly necessary to confirm the findings of this study. The possibility of a placebo effect in the Treatment patients must be considered as well as a Type II error resulting from the small study size. Our findings, however, suggest that patients with traumatic rib fracture can achieve improved pain control and possibly reduced hospital length of stay with decreased narcotic requirement through the use of this seemingly safe and cost-effective adjunctive pain medication. Early administration of IVIb should be considered in patients with traumatic rib fractures to improve pain control. A prospective study to evaluate the efficacy of IVIb therapy in patients with traumatic rib fracture is warranted.

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