Assessment of the Analgesic Efficacy of Intravenous Ibuprofen in Biliary Colic

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BACKGROUND

Biliary colic (BC) is a common and painful symptom in patients with gallbladder disease. Often presenting to the emergency department (ED), patients with BC frequently require rapid analgesia with NSAIDs or opioids.

Intravenous (IV) ibuprofen has recently been approved for fever and pain in adults, and until now has not been utilized in the treatment of BC.

In this double-blind, randomized, controlled trial we aim to assess the analgesic efficacy of IV ibuprofen given in the ED for the treatment of BC.

MATERIALS AND METHODS

- Adults presenting to the ED with right upper quadrant pain and meeting enrollment criteria were asked to participate in the study.
- Participants were randomized to IV ibuprofen therapy (800mg) or a saline-only control group after receiving an initial dose of morphine in triage.
- Analgesic efficacy was evaluated using a visual analog scale (VAS) to assess for a decrease in pain scores on a scale of 0-10. Subjects completed a VAS every 15 minutes in the first hour and every 30 minutes in the second hour.
- A VAS score decrease of 33% compared to time 0 was considered a minimum clinically important difference (MCID) in patient-perceived pain. Two-way ANOVA and summary statistics were also performed.

TABLE 1. *Enrollment criteria.*

Inclusion Criteria
1. Patient age 18-55
2. Present to ED with right upper quadrant abdominal pain
3. Suspected diagnosis of biliary colic
4. Negative pregnancy test for women of childbearing potential
5. No history of cholecystectomy

RESULTS

FIGURE 2. *Change in mean VAS scores over time for ibuprofen and control groups*

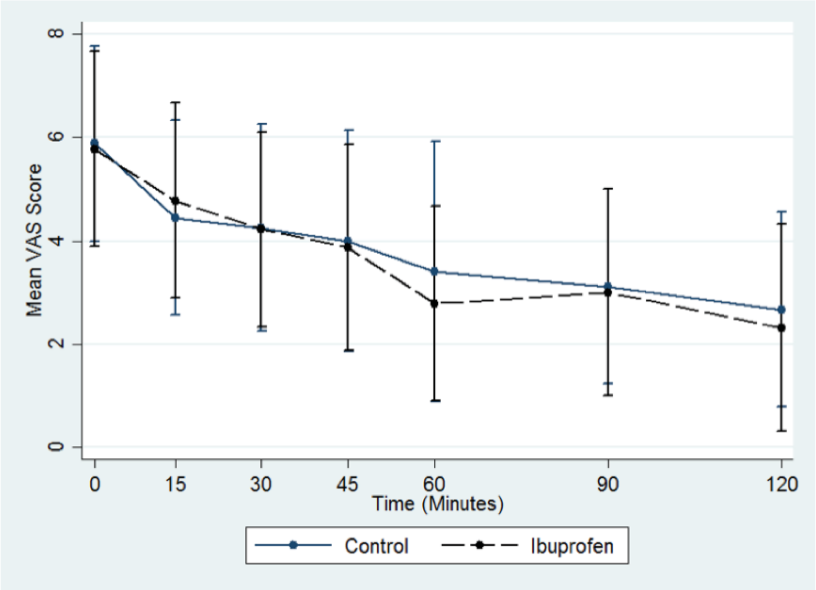

TABLE 2. *Two-Way ANOVA*

Variables	P-Value[1]
Treatment Status	0.93
Time	0.031
Treatment * Time Interaction	0.90

[1]P-values calculated using Two-way ANOVA.

TABLE 3. *Mean VAS values*

Time	*Mean VAS score*
Ibuprofen	
0 minutes	5.78
MCID threshold[1]	3.85
120 minutes	2.31
Control	
0 minutes	5.89
MCID threshold	3.92
120 minutes	2.67

[1]Minimum clinical difference (MCID) threshold defined by 33% decrease in initial t=0 VAS score

N = 22 patients
9 ibuprofen, 9 placebo
4 excluded

- **No statistically significant difference in treatment status of ibuprofen vs. placebo (p = 0.93)**
- **Statistically significant decrease in measured VAS scores over time in both ibuprofen and placebo groups (p = 0.031)**
- **Average decrease of -3.2 VAS units seen in both arms (p = 0.026)**
- **Clinically significant decrease in average VAS scores (>33%) seen in both ibuprofen (60%) and placebo (55%) groups at 120 minutes**
- **No difference in time to clinically significant reduction in pain between groups: 45-60 minutes to reach >33% VAS reduction in both arms (MCID threshold).**

DISCUSSION & CONCLUSION

- Sample size was inadequate to fully assess the efficacy of IV ibuprofen vs. placebo.
- No significant difference in treatment status was seen in our analysis group (n=18), however there was a statistically and clinically significant decrease in pain in both groups.
- Two potential confounding factors may have affected our results.
  - IV morphine was administered on initial assessment as standard-of-care and for ethical considerations; it has an analgesic duration of up to 7 hours. We cannot rule out that the observed VAS reduction was a result of morphine administration, masking any potential effects of ibuprofen.
  - Similarly the decrease in both groups' pain may be related to the inherent episodic and self-limited nature of biliary colic, especially given the potentially extended time-course of patient presentation to treatment.
- Ketorolac (NSAID) is currently used in BC with success. As biliary spasm is in-part prostaglandin-mediated, unclear if selective inhibition of COX-1 by ketorolac vs. non-selective inhibition of COX1&2 by ibuprofen affects analgesic outcome.
- Further studies are indicated to better elucidate the role of IV ibuprofen in the treatment of BC.

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