Initial treatment of biliary colic: Are NSAIDs better than opiates?

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Patient
A 45-year-old healthy male presents to urgent care clinic with acute right upper quadrant (RUQ) abdominal pain without fevers. The patient’s exam confirms a tender RUQ without rebound or guarding. He is found to have a white blood cell count of 15,000 with normal liver function and biliary tests. He is clinically diagnosed with biliary colic and an abdominal ultrasound is ordered to evaluate for acute cholecystitis. The ultrasound confirms gallstones without evidence of biliary tree dilation or obstruction.

Clinical Question
In a patient with acute biliary colic, does initial treatment with NSAIDS versus opiates prevent the development of acute cholecystitis?

How and where could you locate evidence to answer this question?

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How would you treat this patient?
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Turn to page 63 for one possible approach.
Suggested Approach for Clinical Question #2

**Search Strategy for a Therapeutic Question**

1. Using Ovid Interface, search Cochrane Database of Systematic Reviews (1st Quarter 2005):
   a. “biliary colic” or “biliary tract disease” or “acute cholelithiasis” or “cholecystitis”
   b. “nonsteroidal” or “anti-inflammatory” or “NSAIDs”
   c. combine (a) and (b)
   d. No matches relevant to the case

2. Search repeated in Database of Abstracts of Reviews of Effects (DARE), and ACP Journal Club (shown as “EBM Reviews Full Text” – Cochrane DSR, ACP Journal Club, and DARE” using the Ovid Interface):
   a. No matches relevant to the case

3. Search all years of Medline (1966 to March Week 2 2005) using Ovid interface:
   a. “exp biliary tract disease” (exploded MESH Heading)
   b. “exp cholecystitis” (exploded MESH Heading)
   c. “biliary colic” (keyword)
   d. combine (a) or (b) or (c) limited to English Language and Human studies
   e. “Anti-inflammatory Agents, Non-Steroidal” (exploded MESH heading)
   f. combine (d) and (e)
   g. “random$” (keyword) Used to limit the results to randomized trials.
   h. combine (f) and (g)
   i. 11 studies – two of which pertained to the question:

**Study Characteristics**

<table>
<thead>
<tr>
<th>Study (Authors)</th>
<th>Akriviadis et al</th>
<th>Henderson et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Type</td>
<td>Prospective, double-blind, randomized, placebo-controlled</td>
<td>Prospective, double-blind, randomized</td>
</tr>
<tr>
<td>Patients</td>
<td>53 patients with acute biliary colic and cholelithiasis demonstrated by ultrasound</td>
<td>324 patients with clinically diagnosed acute biliary colic</td>
</tr>
<tr>
<td>Intervention</td>
<td>IM diclofenac vs placebo</td>
<td>IV ketorolac vs IV meperidine</td>
</tr>
<tr>
<td>Primary End Points</td>
<td>Response to pain and development of cholelithiasis-related complications</td>
<td>Response to pain (No assessment was performed of cholelithiasis-related complications)</td>
</tr>
</tbody>
</table>

**Validity of Evidence (Akriviadis et al)**

- Properly randomized trial.
- Follow-up was at least 72 hours for all 53 patients. This is long enough to witness the progression of biliary colic to cholecystitis.
- Follow-up was also reasonably complete with only a 3.6% drop out rate.
- Intention to treat analysis was used.
- The study was “double-blinded,” though there likely was unintentional unblinding by the treatment nurses who delivered the yellow-discolored diclofenac medication.
- The diclofenac and placebo groups were similar at the start of the study and were treated equally throughout the trial other than the experimental intervention.
- Overall this study is of high methodologic quality.

**Study Results**

Akriviadis et al
1. Pain response comparing diclofenac vs. placebo

Henderson et al

1. Pain response
   a. No statistically significant difference in pain control between the ketorolac and meperidine groups at any time interval studied.

2. Side Effects
   a. Statistically significant higher incidence of nausea and dizziness in those treated with meperidine compared to ketorolac.

**Applying the Evidence to the Patient**

- The case patient is similar to those in the studies. Thus, the results should apply.
- IM diclofenac is not available in the United States, but intravenous ketorolac is readily available.

**Summary**

The well-done study by Akriviadis demonstrated that diclofenac dramatically decreased the risk of progressing to acute cholecystitis compared to placebo. The study by Henderson had some methodological flaws, but showed that ketorolac is at least as effective as meperidine in relieving the pain associated with biliary colic. Henderson also showed that patient’s had less side effects (nausea and dizziness) with ketorolac.

Unfortunately IM diclofenac is not available in the United States. It is likely that the benefits seen with diclofenac are a drug class effect. Therefore, IV ketorolac should have a similar effect on decreasing progression to acute cholecystitis.

**Conclusion**

Ketorolac may be safely used in the initial treatment of pain associated with biliary colic. It is at least as effective as meperidine for pain relief with fewer side effects. Given ketorolac’s potential role in the prevention of progression to acute cholecystitis, it should be considered first line therapy.

**Bibliography**

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