Evaluating Adverse Consequence of Routinely Prescribing Adult Patients Antibiotics After an Uncomplicated ERCP Procedure

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Overview of Project

• Review guidelines for surgical prophylaxis in setting of uncomplicated ERCP Procedures

• Evaluate surgical prophylaxis prescribing patterns locally at the University of Iowa Hospitals & Clinics.

• Determine if prolonged surgical prophylaxis has any benefits or potential adverse consequences

• Propose future directions
Background

• ERCP is an elective surgery to treat issues of the gallbladder and pancreatic ducts
  ▫ There is the risk that microbial flora can be transferred into the bloodstream leading to infection (e.g. cholangitis)
  ▫ Antimicrobial prophylaxis is generally not necessary for uncomplicated ERCP; but may be considered for select high risk elective ERCP cases
    • Prophylaxis should be limited to 24 hours

ERCP = Endoscopic retrograde cholangiopancreatography
The Iowa City VAMC started an antimicrobial stewardship program in September 2015.

Findings during first year of the program:
- Recurring antibiotic misuse has been the routine use of antimicrobial prophylaxis to patients after an ERCP.
- Antibiotics were often prescribed even in the absence of an infection.
- Most common antibiotic: Ciprofloxacin.
  - FDA Warning
- Practice goes against practice guidelines.
Objectives of Study

• Primary objective
  ▫ evaluate antimicrobial prophylaxis and guideline concordance among patients who received an uncomplicated ERCP procedure

• Secondary objectives
  ▫ evaluate differences of guideline concordant and discordant cases
    • demographics
    • antimicrobial duration
    • antibiotic associated diarrhea
    • *C. difficile* infection
    • resistance
    • mortality
    • post-procedure infection rates
Methods

- **Design**
  - Multi-center retrospective cohort study

- **Study Period**
  - 01/01/2015 – 06/20/2016

- **Data Source**
  - Electronic medical record chart review

- **Population**
  - Adults with uncomplicated ERCP procedure at UIHC Exclusion Criteria: cholangitis, extra-biliary infection, repeat ERCP

- **Definitions**
  - Post-ERCP cholangitis defined a-priori and independently reviewed by an infectious disease physician
Inclusion & Exclusion Criteria

• Include:
  • Adult patients undergoing ERCP

• Exclude:
  ▫ Patients with:
    ▪ symptomatic cholangitis
    ▪ asymptomatic cholangitis (cholestasis with purulent bile noted during ERCP)
    ▪ infection of a non-biliary source requiring antibiotics during index hospitalization
  ▫ Episodes of repeat ERCP if occur within 3 mo. of index procedure
Methods

• **Statistical Analysis**
  ▫ Descriptive statistics were used to summarize patient demographics and antimicrobial prescription patterns
  ▫ Fisher exact or Chi squared test (2-tailed) was used to compare binary data.
  ▫ Student’s-T test was use to evaluate continuous data
  ▫ Multivariate step-wise regression analysis used to evaluate for variables independently associated with select outcomes
    • Corresponding ORs and CIs were determined
    • A p-value < 0.05 was considered statistically significant
Results

- During the study period 1459 cases were evaluated of which 813 met inclusion criteria with an overall guideline concordance rate of 47.2%.
- The most common reason for exclusion was repeat ERCP within three months of the index procedure.
- The mean duration of antimicrobial prophylaxis was 5.1 days (SD 6.2) which varied significantly between groups (p < 0.001).
Results: Study Cohort

Eligible for chart review
N = 1459

Excluded from Analysis*

- Repeat ERCP within 3 months (n = 455)
- Symptomatic cholangitis (n = 217)
- Extra-biliary infection (n = 86)
- Asymptomatic cholangitis (n = 47)

Included
n = 813

* Patients may have had more than one exclusion criteria
Results

- Guideline concordant cases appeared to be of lower acuity
  - Lower incidence of cholecystectomy/cystostomy ($p < 0.001$), lower albumin levels ($p < 0.001$) and repeat ERCP within three months of the index procedure ($p < 0.001$)

- Among evaluable cases ($n=813$) guideline concordant cases had less antibiotic associated diarrhea ($p < 0.001$)
  - Trend towards lower post-ERCP cholangitis ($p = 0.13$) and combined $C. diff$ infection and/or resistance ($p = 0.12$)

- Cefoxitin was the most common antimicrobial agent prescribed for surgical prophylaxis
  - Ciprofloxacin was the most common antimicrobial agent prescribed at discharge
## Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>GL concordant (n=384)</th>
<th>GL discordant (n=429)</th>
<th>Total (N=813)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, std dev)</td>
<td>63.0 (16.9)</td>
<td>59.8 (17.9)</td>
<td>61.7 (17.4)</td>
<td>0.0112</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>176 (45.8%)</td>
<td>196 (45.7%)</td>
<td>372 (45.7%)</td>
<td>1</td>
</tr>
<tr>
<td>Biliary or pancreatic Malignancy</td>
<td>121 (31.5%)</td>
<td>124 (28.9%)</td>
<td>245 (30.1%)</td>
<td>0.4442</td>
</tr>
<tr>
<td>Site of Obstruction</td>
<td></td>
<td></td>
<td></td>
<td>0.2098</td>
</tr>
<tr>
<td>Inferior to hilum</td>
<td>329 (85.6%)</td>
<td>380 (88.6%)</td>
<td>709 (87.2%)</td>
<td></td>
</tr>
<tr>
<td>Superior to hilum</td>
<td>38 (9.9%)</td>
<td>28 (6.5%)</td>
<td>66 (8.1%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>17 (4.4%)</td>
<td>21 (4.9%)</td>
<td>38 (4.7%)</td>
<td></td>
</tr>
<tr>
<td><strong>Cholecystectomy or Cholecystostomy</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Prior to ERCP</td>
<td>145 (37.8%)</td>
<td>205 (47.8%)</td>
<td>350 (43.1%)</td>
<td></td>
</tr>
<tr>
<td>During same hospitalization</td>
<td>13 (3.4%)</td>
<td>62 (14.5%)</td>
<td>75 (9.2%)</td>
<td></td>
</tr>
<tr>
<td>Albumin levels (mean, std dev)</td>
<td>3.74 (0.56)</td>
<td>3.53 (0.61)</td>
<td>3.63 (0.59)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Frequency of patient receiving antimicrobial prophylaxis</td>
<td>379 (98.7%)</td>
<td>428 (99.7%)</td>
<td>807 (99.3%)</td>
<td>0.106</td>
</tr>
<tr>
<td><strong>Frequency of patient receiving antimicrobials on discharge</strong></td>
<td>2 (0.5%)</td>
<td>336 (78.3%)</td>
<td>338 (41.6%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mean Duration of antibiotics (mean days, std dev)</td>
<td>0.99 (0.11)</td>
<td>8.8 (6.6)</td>
<td>5.1 (6.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cases with follow-up note within 3 months</td>
<td>282 (73.4%)</td>
<td>294 (68.5%)</td>
<td>576 (70.8%)</td>
<td>0.1419</td>
</tr>
<tr>
<td>Post-ERCP cholangitis^</td>
<td>7 (2.5%)</td>
<td>15 (5.1%)</td>
<td>22 (3.8%)*</td>
<td>0.1282</td>
</tr>
<tr>
<td>Post-ERCP readmission^</td>
<td>74 (26.2%)</td>
<td>68 (23.1%)</td>
<td>142 (24.7%)</td>
<td>0.4392</td>
</tr>
<tr>
<td>**Post-ERCP testing for C. difficile: Antibiotic associated diarrhea^</td>
<td>14 (4.9%)</td>
<td>41 (14.0%)</td>
<td>55 (9.5%)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Post-ERCP C difficile infection or documented antibiotic resistance^</td>
<td>10 (3.6%)</td>
<td>19 (6.5%)</td>
<td>29 (5.1%)</td>
<td>0.129</td>
</tr>
<tr>
<td>Blood cultures drawn within 3 months of ERCP^</td>
<td>30 (10.6%)</td>
<td>42 (14.3%)</td>
<td>72 (12.5%)*</td>
<td>0.2083</td>
</tr>
<tr>
<td>Repeat ERCP within 3 months^</td>
<td>75 (26.6%)</td>
<td>118 (40.1%)</td>
<td>193 (33.5%)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Post-operative all-cause mortality^</td>
<td>19 (6.7%)</td>
<td>24 (8.2%)</td>
<td>43 (7.5%)</td>
<td>0.5306</td>
</tr>
</tbody>
</table>

* 5 (0.9%) were considered early and 17 (2.9%) late onset  
^ Among evaluable cases (n = 576)
Results: Antimicrobial Surgical Prophylaxis (n=807)
Results: Discharge Antibiotics (n=336)
Results

- Variables independently associated with selected outcomes upon multivariate regression analysis are displayed below:

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeat blood cultures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin</td>
<td>0.45 (0.29-0.68)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Repeat ERCP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, sex, cholecystectomy, malignancy, and albumin were included in the model, but non met statistical significance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause 30-day mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholecystectomy or Cholecystostomy</td>
<td>0.41 (0.19-0.89)</td>
<td>0.024</td>
</tr>
<tr>
<td>Biliary/pancreatic malignancy</td>
<td>5.88 (2.70-12.80)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.35 (0.19-0.62)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
Discussion

• Guideline discordant therapy exceeded 50% of which was higher than reported in other published studies.

• Post-ERCP antibiotic-toxicity (antibiotic associated diarrhea) was more common in the guideline discordant group.

• Cipro was the most common antibiotic prescribed at discharge which may have contributed to more toxicity.

• Post-ERCP cholangitis/infection rates were low and similar to that reported in other published studies.

• Prolonged antimicrobial prophylaxis did not impact post-ERCP infection rates.
Limitations

This study was not without limitations including:

- Retrospective study
  - Reviewer bias and confounding variables
- May not be generalizable outside of UIHC
- Did not evaluate for baseline comorbidities that may complicate ERCP or influence prescribing
- Significant number of patients (n = 237) were lost to follow-up which may have impacted our findings
Future Directions

• The findings of this QI project will be shared with the surgeons who perform ERCPs with the goal of improving antibiotic use

• Local ERCP surgical prophylaxis guidelines and fluoroquinolone restriction policies may be developed based on the study findings

• Future prospective studies are needed to evaluate the impact of guideline discordant therapy on adverse consequences.
Acknowledgements

• This material is the result of work supported with resources and the use of facilities at the Iowa City VA Health Care System and UIHC.

• Other key members on the project:
  ▫ Daniel Livorsi and Brian Hoff
  ▫ Megan Adamsick, Rachel Groolmus, Tyler Nichols, Kristen Peterson, Addy Rickels
References

• IDSA/ASHP Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery; AJHP 2013:582-667
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