Intra-Abdominal Infections

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Select guidelines


  • IDSA: “Update in Progress”
Intra-abdominal infection (IAI)

- Infection of any of the organs or organ spaces in the abdominal cavity
  - Lower part of the esophagus
  - Stomach
  - Intestines (small and large)
  - Colon
  - Rectum
  - Gall bladder
  - Spleen
Intra-abdominal infection

<table>
<thead>
<tr>
<th>Uncomplicated</th>
<th>Complicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Infection contained within a single organ (stomach, gallbladder, intestines, etc) without anatomic disruption</td>
<td>• Infection extends beyond the organ with spillage of microorganisms into normally sterile space</td>
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<tr>
<td>• May or may not require surgical management</td>
<td>• Primary management is oftentimes source control</td>
</tr>
</tbody>
</table>
Common pathogens

• Most common
  • *E.coli*
  • *Bacteroides* species

• Other common pathogens
  • Other Enterobacteriaceae
  • *Streptococcus* species
  • Clostridial species

• Hospital-associated or tertiary peritonitis pathogens
  • *Pseudomonas aeruginosa*
  • *Enterococcus* species

Empiric treatment of community-onset IAI should target these organisms

Empiric treatment of hospital-onset IAI should target these organisms
Management of intra-abdominal infections

- Expeditious diagnosis
- Early resuscitation
- Timely and appropriate source control
- Antimicrobial Therapy
SOURCE CONTROL
DRAIN IT OUT, CUT IT OUT, OR CUT IT OFF

• What is it?
  • Drainage of infected fluid
  • Debridement of necrotic tissue
  • Definitive measure to control contamination and restore normal gastrointestinal anatomy and function

• What is the goal?
  • Reduce bacterial and toxin load
  • Transform the local environment such that further microbial growth is impeded and host defenses can be optimize

Arguably, the most important aspect of treatment.
**IV antimicrobials for empiric therapy**

<table>
<thead>
<tr>
<th></th>
<th>Mild to Moderate IAI or Lower-Risk Patients</th>
<th>Severe IAI or High-Risk Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferred</strong></td>
<td>(Ceftriaxone or cefotaxime) PLUS metronidazole</td>
<td>Piperacillin-tazobactam</td>
</tr>
<tr>
<td><strong>Alternative</strong></td>
<td>Ertapenem</td>
<td>Cefepime PLUS metronidazole OR Anti-pseudomonal carbapenem</td>
</tr>
<tr>
<td><strong>Severe Beta-lactam allergy</strong></td>
<td>Ciprofloxacin PLUS metronidazole (only for mild or very-low risk)</td>
<td>Aztreonam PLUS metronidazole PLUS vancomycin</td>
</tr>
</tbody>
</table>
Antibiotics that are not recommended

- Not recommended for empiric therapy in community-onset IAI

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin-sulbactam</td>
<td>E.coli resistance</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>If E.coli resistance is a concern at your facility</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Anaerobe resistance</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>Anaerobe resistance</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>Anaerobe resistance</td>
</tr>
<tr>
<td>Antifungals</td>
<td>Yeast is a rare pathogen</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Staphylococcal and enterococcal species are rare pathogens</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>Inferior efficacy and increased toxicities</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>Lower efficacy and higher deaths</td>
</tr>
</tbody>
</table>
Circumstances where *antibiotics are not indicated*

- Low-risk uncomplicated acute colonic diverticulitis
  - 2017 SIS Guidelines
  - 2015 Diverticulitis Guidelines
- Severe or necrotizing pancreatitis
  - 2010 IDSA Guidelines
  - 2017 SIS Guidelines
Circumstances where ultra-short durations are indicated

- Antibiotic therapy should be limited to 24 hours post-operatively in the following patient populations:
  - Traumatic bowel perforations operated on within 12-hours
  - Gastroduodenal perforations operated on within 24-hours
  - Acute or gangrenous appendicitis in the absence of perforation
    - Some studies suggest only a single pre-operative dose is needed
  - Acute or gangrenous cholecystitis in the absence of perforation
    - Some studies suggest only a single pre-operative dose is needed
  - Ischemic, non-perforated bowel
What about everything else?

“Antimicrobial therapy of established infections should be limited to 4 to 7 days, unless it is difficult to achieve adequate source control. Longer durations of therapy have not been associated with improved outcomes.”

- 2010 IDSA Guidelines
STOP-IT Trial, NEJM 2015

Prospective, randomized, open-label multi-center study in adult patients with complicated intra-abdominal infection and adequate source control

4 days of antimicrobial therapy after source control

VS

Antimicrobial until 2 days after the resolution of the physiological abnormalities related to SIRS

260 patients in intention to treat analysis
Median DOT: 4 days

189 patients in per protocol analysis

257 patients in intention to treat analysis
Median DOT: 8 days

211 patients in the per protocol analysis
STOP-IT Trial, NEJM 2015

• **No difference in the primary outcome** of composite surgical site infection, recurrent intra-abdominal infection, and death
  • Approximately 20% had an event regardless of treatment group

• The major differences:
  • Increased time to event with longer antibiotic therapy (10 vs 15 days)
  • Infection with a resistant infection trended toward an increase with longer antibiotic therapy

**Longer post-operative antibiotic therapy for IAI only delays the inevitable**
Duration of therapy for percutaneous drained IAI

• Surgical intervention vs percutaneous drainage
  • Difference in the ability to remove gross pathologic tissue
• STOP-IT Post hoc subgroup analysis of patients that received percutaneous drainage as source control (J Trauma Acute Care Surg 2016)
  • 72 received a short course (4 days) and 57 received a long course (7 days)
  • No difference in primary outcomes
  • Except time to recurrent IAI (12.7 days with short course vs 21.3 with long course, P = 0.015)
How about patients with risk factors for complication?

• STOP-IT post hoc subgroup analysis of patients with risk factors (American Surgeon 2016)
  • 210 received a short course and 189 received a long course
  • No difference in primary outcomes regardless of risk factor
    • Obesity, diabetes, obesity plus diabetes, and APACHE II ≥ 15
    • Patients with APACHE II ≥ 15 had significantly short time to diagnosis of recurrent IAI and extra-abdominal infection

• Similar findings in another STOP-IT post-hoc subgroup analysis (Surgical Infections 2017)
  • Corticosteroid use, hospital-acquired infection, and/or colonic source
Is the STOP-IT Trial generalizable to critically ill patients?

• Evaluation of a short course of antimicrobial therapy for complicated IAI in critically ill surgical patients (Surgical Infections 2017)
  • Single-center, retrospective, cohort study at Vanderbilt
  • Only patients admitted to the SICU with complicated IAI with source control
  • 103 patients received a short course and 137 received a long course
    • Median 5 vs 14 days of therapy, respectively
  • After logistic regression, long duration of therapy was associated with treatment failure but not mortality
In summary, if there is adequate source control....

No more than 4 days after source control (this includes percutaneous drainage)
What about inadequate source control?

“We suggest that no more than 5-7 days of antimicrobial therapy be provided to patients with established IAI in who definitive source control is not performed. We suggest that clinical parameters, including fever, leukocytosis, and adequacy of gastrointestinal function, be assessed periodically to determine whether antimicrobial therapy can be discontinued sooner. We suggest that patients that do not respond fully to antimicrobial therapy within 5-7 days be reassessed for a potential source control intervention.”

- 2017 SIS Guidelines
How about patients with bacteremia?

“We suggest that most patients with secondary bacteremia because of IAI who have undergone source adequate source control and are no longer bacteremia can have antimicrobial therapy discontinued after seven days.”

- 2017 SIS Guidelines

Major exception: *Staphylococcus aureus* bacteremia should be treated for a minimum of 14 days with IV antibiotics.
Case, Part 1

- 66 y.o. male seen in the ED with RLQ pain.
- WBC 15.3K, vital signs WNL
- CT Abd/pelvis: acute appendicitis not complicated by free air or abscess
- Assessment: acute appendicitis

What is the treatment of choice?
Case, Part 1

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- WBC 15.3K, vital signs WNL
- CT Abd/pelvis: acute appendicitis not complicated by free air or abscess
- Assessment: acute appendicitis

What is the treatment of choice?

Consult surgery
Start antibiotics
- Mild to moderate infection (not septic)
- Other than his age, he is consider low-risk
- Ceftriaxone + metronidazole
- Piperacillin-tazobactam is also an option

Assuming there is no perforation, antibiotics can be discontinued post-operatively or within 24-hours after surgery
Case, Part 2

• In OR, patient found to have “rupture in the mid-appendix with phlegmon cavity and partially necrotic appendix.”
  • No other complications noted

• How does this change your treatment plan?
Case, Part 2

• In OR, patient found to have “rupture in the mid-appendix with phlegmon cavity and partially necrotic appendix.”
  • No other complications noted

• How does this change your treatment plan?

- Continue antibiotics up to 4 days after the procedure
- If there was a culture done, antibiotics may be tailored to the isolated organisms
- IV to PO when patient is ready for discharge to complete 4 days of treatment
Summary

• No antibiotics for pancreatitis and low-risk uncomplicated acute diverticulitis

• Discontinue within 24-hours after surgery for unperforated cholecystitis and appendicitis

• Complicated intra-abdominal infections:
  • The rule is 4 days with adequate source control
  • Exception is 7 days with inadequate source control
  • Longer durations may be indicated if source control cannot be achieve or patient is immunosuppressed
Conclusion

• There will be failures regardless of the duration of antibiotic therapy

• Failures are not from an antibiotic deficiency, but rather, inadequate source control

• Longer durations delay the inevitable, whether it be clinical cure or failure requiring additional source control
References