Secondary and Tertiary Peritonitis

Portuguese guideline

Eduardo Melo
Intra-Abdominal Infections

• Proper empiric antimicrobial therapy has an enormous effect on the morbidity and mortality rates of patients suffering from IAI, especially those who are critically ill (IAI represent 25% of cases of severe sepsis and septic shock)

• Inappropriate treatment may result in poor patient outcome
Selection of Antimicrobial

- Optimizing empirical therapy!
- Addressing the resistance of target agents
- Reducing unnecessary antimicrobial use
- Avoiding the emergence of multiresistance

Delicate Balance
Selection of Antimicrobial

- Challenge due to the heterogeneity of IAI and the emerging resistances of target pathogens to commonly prescribed antimicrobials
- Guidelines are developed to outline therapeutic protocols and help clinicians to better treat IAI but the antimicrobial treatment must be customized to the local pattern and the individual patient
Classification

- IAI results from invasion and multiplication of enteric bacteria in the wall of a hollow viscus or beyond.
- **Intraperitoneal**: peritonitis, abscess.
- **Visceral**: liver, spleen, kidney, pancreas, tuboovarian
- **Perivisceral**: gallbladder, appendix, colon
- **Interloop**
Uncomplicated IAI Definition

Infection involves a single organ and does not extend to the peritoneum

- Surgical approach
  - Excision, drainage
  - Perioperative prophylaxis 24h (Altemeier class II clean-contaminated surgery)

- Medical approach
  - Antimicrobial therapy ≥ 7 days

Complicated IAI Definition

Extends beyond the hollow viscus of origin into the peritoneal space, either with abscess formation or peritonitis

- Source control
  - Requires either operative or percutaneous intervention to resolve

- Antimicrobial therapy
  - (Altemeier class III contaminated or class IV infected)

Source control

- “Single procedure or series of procedures that eliminate infectious foci, control factors that promote ongoing infection, and correct or control anatomic derangements to restore normal physiologic function.”
- Failure to achieve adequate source control is associated with a worse clinical outcome.
- Inadequate antimicrobial therapy doubles mortality
1. Adjuvant to source control
2. Start soon (first hour of diagnosis in case of severe sepsis or septic shock)
3. Additional administration just before the surgical procedure if there is a delay > 60 min from the first administration
4. Use adequate and appropriate antibiotics
5. Send blood cultures and intra-abdominal fluid for microbiology if the peritonitis is community-acquired with severe sepsis or healthcare-associated
6. Consider Polymicrobial coverage
   - Community acquired, normal host, no prior antibiotics: think Enterobacteriaceae, Streptococci and Bacteroides (lower GI)
   - Healthcare-associated, prior antibiotics, immunocompromised host: also think of Pseudomonas, Enterococcus, Yeast, Staphylococcus
## Classification of Peritonitis

<table>
<thead>
<tr>
<th>Type</th>
<th>Definition</th>
<th>Microbiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Due to bacterial translocation or hematogenous seeding. No break in integrity of GI tract</td>
<td>Monomicrobial; coliforms or streptococci</td>
</tr>
<tr>
<td>Secondary</td>
<td>Microscopic or macroscopic perforation</td>
<td>Polymicrobial; coliforms, gram-positive cocci and enteric anaerobes</td>
</tr>
<tr>
<td>Tertiary</td>
<td>Persistent or recurrent peritoneal infection developing after treatment of secondary peritonitis</td>
<td>Nosocomial organisms; enterococci, staphylococci; resistant gram negative bacilli and yeast</td>
</tr>
</tbody>
</table>
### Microbiology of Peritonitis

<table>
<thead>
<tr>
<th>Location</th>
<th>Colony counts</th>
<th>Flora</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroduodenal</td>
<td>( \leq 1.000 \text{ CFU/ml} )</td>
<td>Gram positive, oral flora</td>
</tr>
<tr>
<td>Biliary and Upper small gut</td>
<td>( \leq 1.000-10.000 \text{ CFU/ml} )</td>
<td>Same + Coliforms</td>
</tr>
<tr>
<td>Distal small gut</td>
<td>1-100 million CFU/ml</td>
<td>Coliforms + Enterococcus + Anaerobes</td>
</tr>
<tr>
<td>Colon</td>
<td>10-100 billion CFU/ml</td>
<td>Coliforms + Enterococcus + Anaerobes + Streptococci</td>
</tr>
</tbody>
</table>
Microbiology of Peritonitis

Conditions which can change the expected microbioma

- Hospitalization or interaction with healthcare facilities
- Prior exposure to antibiotics
- Obstruction and stasis of the gut
- Think of: Pseudomonas, MDR gram negatives, Enterococcus, Yeast, Staphylococcus
EM DISCUSSÃO PÚBLICA

ASSUNTO: Tratamento antimicrobiano das Infeções Intra-abdominais

PALAVRAS-CHAVE: Antibióticos; cirurgia;

PARA: Hospitais

CONTACTOS: Departamento da Qualidade na Saúde (dgs@dgs.pt)

Nos termos da alínea a) do n.º 2 do artigo 2º do Decreto Regulamentar nº 14/2012, de 26 de janeiro, a Direção-Geral da Saúde, por proposta conjunta do Departamento da Qualidade na Saúde e do Programa de Prevenção e Controlo de Infeções e das Resistências Antimicrobianas, emite a seguinte Norma, na área da qualidade organizacional.
Antimicrobial resistance surveillance in Europe

2012
Klebsiella with resistance to Cephalosporins, Fluoroquinolones and Aminoglycosides
Klebsiella with resistance to Carbapenems
Escherichia coli with resistance to Cephalosporins
Escherichia coli with resistance to Cephalosporins, Fluoroquinolones and Aminoglycosides
### Consumption of Antibacterials Community 2011

<table>
<thead>
<tr>
<th>Country</th>
<th>DDD per 1 000 inhabitants and per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Netherlands</td>
<td></td>
</tr>
<tr>
<td>Estonia</td>
<td></td>
</tr>
<tr>
<td>Latvia</td>
<td></td>
</tr>
<tr>
<td>Romania (b)</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td></td>
</tr>
<tr>
<td>Sweden</td>
<td></td>
</tr>
<tr>
<td>Slovenia</td>
<td></td>
</tr>
<tr>
<td>Austria</td>
<td></td>
</tr>
<tr>
<td>Hungary</td>
<td></td>
</tr>
<tr>
<td>Norway</td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td></td>
</tr>
<tr>
<td>Czech Republic</td>
<td></td>
</tr>
<tr>
<td>United Kingdom</td>
<td></td>
</tr>
<tr>
<td>Lithuania (a)</td>
<td></td>
</tr>
<tr>
<td>Bulgaria</td>
<td></td>
</tr>
<tr>
<td>Finland</td>
<td></td>
</tr>
<tr>
<td>Spain (b)</td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td></td>
</tr>
<tr>
<td>Iceland (a)</td>
<td></td>
</tr>
<tr>
<td>Ireland</td>
<td></td>
</tr>
<tr>
<td><strong>Portugal</strong></td>
<td></td>
</tr>
<tr>
<td>Malta</td>
<td></td>
</tr>
<tr>
<td>Slovakia (a)</td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td></td>
</tr>
<tr>
<td>Luxembourg</td>
<td></td>
</tr>
<tr>
<td>France</td>
<td></td>
</tr>
<tr>
<td>Belgium</td>
<td></td>
</tr>
<tr>
<td>Cyprus (a)</td>
<td></td>
</tr>
<tr>
<td>Greece</td>
<td></td>
</tr>
</tbody>
</table>

Legend:
- Penicillins (J01C)
- Cephalosporins and other beta-lactams (J01D)
- Tetracyclines (J01A)
- Macrolides, lincosamides and streptogramins (J01F)
- Quinolones (J01M)
- Sulfonamides and trimethoprim (J01E)
- Other 101 classes
Consumption of Antibacterials
Hospital 2011
Consumption of Antibacterials Hospital 2011

Distribution of antimicrobial consumption of Antibacterials For Systemic Use (ATC group J01) in the hospital sector in Portugal, reporting year 2011

- J01A Tetracyclines
- J01B Amphenicols
- J01C Beta-lactam antibacterials, penicillins
- J01D Other beta-lactam antibacterials
- J01E Sulfonamides and trimethoprim
- J01F Macrolides, lincosamides and streptogramins
- J01G Aminoglycoside antibacterials
- J01M Quinolone antibacterials
- J01X Other antibacterials
Consumption of Beta-Lactam Hospital 2011

Distribution of antimicrobial consumption of Other Beta-Lactam Antibacterials (ATC group J01D) in the hospital sector in Portugal, reporting year 2011

- J01DB First-generation cephalosporins
- J01DC Second-generation cephalosporins
- J01DD Third-generation cephalosporins
- J01DE Fourth-generation cephalosporins
- J01DF Monobactams
- J01DH Carbapenems
Consumption of Carbapenems
Hospital 2011
SURVEILLANCE REPORT

Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals

2011–2012
Use of Carbapenems 2012
Use of Antibacterials in Surgery community-acquired infections

- J01A Tetracyclines 0%
- J01B Amphenicols 0%
- J01C Beta-lactam antibacterials, penicillins 30%
- J01D Other beta-lactam antibacterials 30%
- J01E Sulfonamides and trimethoprim 1%
- J01F Macrolides, lincosamides and streptogramins 5%
- J01G Aminoglycoside antibacterials 9%
- J01H Quinolone antibacterials 9%
- J01I Combinations of antibacterials 0%
- J01X Other antibacterials 17%
Use of Beta-Lactams in Surgery community-acquired infections

- J01DB First-generation cephalosporins 5%
- J01DC Second-generation cephalosporins 11%
- J01DD Third-generation cephalosporins 30%
- J01DE Fourth-generation cephalosporins 11%
- J01DF Monobactams 0%
- J01DH Carbapenems 54%
- J01DI Other cephalosporins and penems 0%
Use of Antibacterials in Surgery
hospital-acquired infections
Use of Beta-Lactams in Surgery
hospital-acquired infections

- J01DB First-generation cephalosporins 4%
- J01DC Second-generation cephalosporins 3%
- J01DD Third-generation cephalosporins 22%
- J01DE Fourth-generation cephalosporins 0%
- J01DF Monobactams 0%
- J01DH Carbapenems 72%
- J01DI Other cephalosporins and penems 0%
Algorithm

Secondary Peritonitis

- Extra-biliary
- Community acquired

Mild to Moderate

- No risk ESBL
- With risk ESBL

Severe

- No risk ESBL
- With risk ESBL
Community-acquired Peritonitis extra-biliary

- Coverage of the usual enteric microbiome
  - Gram-negative
    - *Enterobacteriaceae*
  - Gram-positive
    - *Streptococcus*
  - Anaerobes
    - *Bacteroides fragilis*
- No coverage
  - *Pseudomonas, Staphylococcus, Enterococcus, Yeasts*
High Risk community peritonitis

- Advanced age (>70)
- High severity of illness (APACHE II score >15)
- Delay in initial intervention (>24H)
- Comorbidity and degree of organ dysfunction
- Low albumin level
- Poor nutritional status
- Degree of peritoneal involvement
- Failure of source control
- Underlying malignancy

The Sepsis Continuum

- A clinical response arising from a nonspecific insult, with ≥2 of the following:
  - T >38°C or <36°C
  - HR >90 beats/min
  - RR >20/min
  - WBC >12,000/mm³ or <4,000/mm³ or >10% bands

SIRS with a presumed or confirmed infectious process

Sepsis with organ failure

Refractory hypotension

SIRS = systemic inflammatory response syndrome

High Risk community peritonitis

- Coverage of the usual enteric microbiome
  - Gram-negative
    - Enterobacteriaceae
  - Gram-positive
    - Streptococcus + Enterococcus
  - Anaerobes
    - Bacteroides fragilis
- Increased risk of therapeutic failure and higher severity in presentation
ANTIBIOTIC RESISTANCE THREATS in the United States, 2013

EXTENDED SPECTRUM β-LACTAMASE (ESBL) PRODUCING ENTEROBACTERIACEAE

- 26,000 drug-resistant infections
- 1,700 deaths
- 140,000 enterobacteriaceae infections per year

$40,000 in excess medical costs per year for each infection

THREAT LEVEL
SERIOUS

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.
Examples of How Antibiotic Resistance Spreads

- Animals get antibiotics and develop resistant bacteria in their guts.
- Drug-resistant bacteria can remain on meat from animals. When not handled or cooked properly, the bacteria can spread to humans.
- Fertilizer or water containing animal feces and drug-resistant bacteria is used on food crops.
- Drug-resistant bacteria in the animal feces can remain on crops and be eaten. These bacteria can remain in the human gut.
- George gets antibiotics and develops resistant bacteria in his gut.
- George stays at home and in the general community. Spreads resistant bacteria.
- George gets care at a hospital, nursing home or other inpatient care facility.
- Resistant germs spread directly to other patients or indirectly on unclean hands of healthcare providers.
- Resistant bacteria spread to other patients from surfaces within the healthcare facility.
- Patients go home.
Risk factors for ESBL + Enterobacteriaceae

- Recent antibiotic usage (Cephalosporins in the past 30 days)
- Residency or recent travel in a country with high incidence of MDR-Enterobacteriaceae
- Interaction with healthcare facility with endemic MDR-Enterobacteriaceae
- Advanced age
- Dialysis
- Residency in long-term care facilities or nursing homes

Community-acquired Peritonitis extra-biliary

- Mild to Moderate / Low-risk
  – No risk for ESBL
    • Amoxicillin/Clavulanate
    • (Cefuroxime, Ceftriaxone, Cefotaxime) + Metronidazol
    • (Ciprofloxacin, Levofloxacin) + Metronidazol
  – Risk for ESBL
    • Ertapenem
    • Tigecycline
    • Moxifloxacin
Community-acquired Peritonitis extra-biliary

- **Severe / High-risk**
  - No risk for ESBL
    - Piperacillin+Tazobactam
    - (Ceftriaxone, Cefotaxime) + Metronidazol
  - Risk for ESBL
    - Ertapenem, Meropenem, Imipenem, Doripenem
    - Moxifloxacin
Algorithm

Secondary Peritonitis

Extra-biliary

Community acquired

Mild to moderate

With risk ESBL

Severe

With risk ESBL

Hospital acquired

Early onset

Mild to Moderate

Tertiary Peritonitis

Late onset

Severe
Hospital-acquired Peritonitis extra-biliary

- Early-onset (< 7 days)
  - Consider as community-acquired with risk for ESBL
- Late-onset (> 7 days)
  - Nosocomial secondary peritonitis (new event)
  - Tertiary peritonitis (unresolved event)
Hospital-acquired Peritonitis late-onset

- Aditioonal coverage
  - Gram-negative non-fermenting
    - *Pseudomonas, Acinetobacter*
  - Gram-positive
    - *Staphylococcus, Enterococcus*
  - Yeasts
    - Candida
  - MDR
    - *E. coli, Klebsiella ESBL +, MRSA, VRE*
    - *Depends on the local ecology*
Hospital-acquired Peritonitis late-onset

- Mild to Moderate / Low Risk
  - Tigecycline + Piperacillin/Tazobactam ± Fluconazole

- Severe / High Risk
  - (Meropenem, Imipenem, Doripenem) + Vancomycin ± (Caspofungin, Anidulafungin, Micafungin)
  - Tigecycline + Piperacillin/Tazobactam ± (Caspofungin, Anidulafungin, Micafungin)
Algorithm

Secondary Peritonitis

- Biliary
  - Mild to moderate
  - No risk ESBL
  - With risk ESBL
  - Severe
    - No risk ESBL
    - With risk ESBL
• Coverage of the usual upper small gut microbiome
  – Gram-negative
    • Enterobacteriaceae
  – Anaerobes (biliary-enteric anastomosis)
    • Bacteroides fragilis

• No coverage
  – Enterococcus
Biliary Peritonitis

• Mild to Moderate / Low Risk
  – No risk for ESBL
    • Cefuroxime, Ceftriaxone
    • Amoxicillin/Clavulanate
    • (Ciprofloxacin, Levofloxacin) + Metronidazol

  – Risk for ESBL
    • Tigecycline
Biliary Peritonitis

• Severe / High Risk
  – No risk for ESBL
    • Piperacillin+Tazobactam
  – Risk for ESBL
    • (Meropenem, Imipenem, Doripenem) ± Vancomycin
    • Tigecycline + Piperacillin/Tazobactam
Duration of antimicrobials

- **1 day**: early infection, no perforation, early removal of source
- **5-7 days**: secondary peritonitis, perforation, but good source control
- **7-14 days**: secondary peritonitis, perforation, delay in source control
- **>14 days**: abscess formation, inability to properly control source, tertiary peritonitis
Final Message

- Peritonitis is a severe polymicrobial infection with a high risk of systemic and local complications.
- Uncertainty in prognosis and difficulties in microbiologic diagnosis drives overuse of broad-spectrum antimicrobials.
- Excessive antimicrobial use contributes to emergence and spread of drug-resistant agents, jeopardizing the effectiveness of common therapeutic regimens.
Final Message

• Prudent use of antimicrobials in Peritonitis may assure the best treatment and minimize the ecological “footprint”

• Clear distinction between formularies of surgical prophylaxis and antimicrobial treatment will give a conceptual framework for the preservation of Cephalosporins of first and second generation

• Prescription of Carbapenems must be restricted to critically ill patients or healthcare associated infections
Final Message

- The empirical regimens should be chosen according to anatomical source of the peritonitis, origin of the patient (community, hospital, healthcare), severity of disease expression and risk for drug-resistant agents.
- In case of hospital acquired peritonitis the approach should be tailored to the local ecology.
- Microbiologic investigation is mandatory in critically ill patients and healthcare associated infections.
- Duration of therapy shouldn’t exceed 5-7 days.