Profilassi Antibiotica e Trattamento
delle Infezioni in Chirurgia
Ricostruttiva Mammaria

Elda Righi, MD PhD
Clinica Malattie Infettive
ASUIUD - Udine
SSI and Breast Surgery

• The rates of SSI in breast surgery including axillary procedures vary from 1.4% to 38.3%

• SSI reported 1.5% for wide excision and up to 38% for mastectomy

• Risk factors: obesity, chemo-radiotherapy, drainage >20 days, radical surgery

SSI and Breast Surgery: high rates?

- British ALMANAC trial: SSI in axillary dissection versus sentinel lymph node biopsy (SLNB) were 14% and 11%.
- American College of Surgeons Oncology Group Z0011 trial: SSI higher in breast cancer patients with axillary dissection (8%) than SLNB (3%).
- Rates 5x higher without Abx compared to other types of “clean surgery” usually < 2.5% (around 1.5%).
- 2/3 acute postoperative, 50%> 1 month.
- Risk of prosthetic implant infections.

Efficacia della Profilassi Antibiotica

• Cochrane review di 7 RCT con 1984 pts sottoposti a chirurgia mammaria per ca ha mostrato differenza nella percentuale di SSTI (8% profilassi vs 10.5% senza profilassi) per chirurgia non ricostruttiva

• Assenza consenso condiviso sulla profilassi antibiotica nella chirurgia mammaria elettiva

• Antibiotici perioperatori usati per ridurre incidenza infezioni del sito chirurgico con risultati variabili

Bunn F et al Cochrane Database Syst Rev 2006
Turkish Survey n=245 response
25% > 100 breast surgery per year
70% preferred single-dose antibiotics
58% *S. aureus*, 29% *S. epidermidis*

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Percentage of respondents</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>The presence of diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>83.5%</td>
<td></td>
</tr>
<tr>
<td>no</td>
<td></td>
<td></td>
</tr>
<tr>
<td>receiving immunosuppressive drug</td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>58.8%</td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>41.2%</td>
<td></td>
</tr>
<tr>
<td>the use of drain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>55.5%</td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>44.5%</td>
<td></td>
</tr>
<tr>
<td>additional dose if operation duration &gt; 2hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>23.2%</td>
<td></td>
</tr>
<tr>
<td>no</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*: not significant.

Fattori di rischio come il diabete favoriscono scelta verso profilassi, mentre drenaggi non la influenzano.
Type of intervention

Prophylaxis frequent in mastectomy, not in wide local resection

Principi di Profilassi

➢ **Antibiotici con buona copertura sui Gram-positivi**
  - Cefazolina (o ampicillina/sulbactam – amoxicillina/clavulanato)
  - Alternative: clindamicina (o vancomicina ± aztreonam, gentamicina or FQ)

➢ **Considerare copertura più ampia (Gram -) se fattori di rischio o procedure pulito-contaminate**

➢ **Se contaminazione cutanea da MRSA, copertura specifica da considerare** *(no consenso)*

ASHO Guidelines Bratzler 2013
Duration and doses

- Limited to the shortest duration possible even if drain or catheter or implant in place
- 30-60 minutes before skin incision
- Purpose is to limit adverse events and resistance
- Single dose similar to multiple doses (cefazolin 2 g or 3 g > 120 kg; ampicillin/sulbactam 3g)
- Redosing if necessary (after 4 hours)

ASHO Guidelines Bratzler 2013
Da Evitare...

- Antibiotici ad ampio spettro o usati in terapia (e.g., ceftriaxone)
- Profilassi prolungate (rischio selezione resistenze o *C. difficile*)
- *C. difficile* frequente in anziani e immunodepressi
Infections in Breast Surgery

- Contaminated implant/saline
- Surgery or environment
- Implants/drainage
- Reoperation
- Endogenous flora (CoNS, *Bacillus* spp., *Streptococci*, anaerobes)
- Seeding of implant from remote infection sites
- Preop chemotherapy

- Cellulitis
- Chronic wound infections
- Implant failure
- Sepsis
- Biofilm/capsular contracture
- Rib osteomyelitis
- Delay in oncological treatments

Patogeni

- *S. aureus*
- CoNS (*S. epidermidis* >>> biofilm)
- Streptococchi
- Gram-negativi (*Pseudomonas* in DM)
- Patogeni meno frequenti (ricordarsi micobatteri e funghi se fattori di rischio, scarsa risposta agli antibiotici, decorso subacuto)
TTS

- Fever, rash, liver enzyme increase, hypotension, GI symptoms
- Early onset (12-24 h from surgery)
- MRSA toxic shock syndrome

Suga H et al, Eplasty 2016
Infezioni da MRSA - Epidemiologia

Data ECDC 2014
MSSA/MRSA

- Screening entrambi (specificare ricerca stafilococco)
- Tamponi nasali, inguinali, ascellari bilaterali
- Decolonizzazione: mupirocina nasale pomata 2-3 applicazioni/die per 5 gg
- Bagni di clorexidina 4% per 5-10 gg
- Spesso il paziente risulta nuovamente colonizzato...
Infezioni da MRSA - Terapia

- MDR – frequente terapia inadeguata
- Vancomicina: era gold standard, oggi limitazioni (incremento MIC, tossicità, lento battericida, meno efficace su MSSA)
- Nuovi farmaci in pipeline (tedizolid, oritavancina)
- Long-acting con somministrazione settimanale (dalbavancina)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daptomycin</td>
<td>8–10 mg/kg iv every 24 h (i.v.)</td>
<td>Rapid bactericidal activity</td>
<td>Only intravenous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antibiofilm activity</td>
<td>Spectrum limited to Gram-positives</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good tolerability profile</td>
<td>High costs</td>
</tr>
<tr>
<td>Ceftaroline</td>
<td>600 mg every 8 h (i.v.)</td>
<td>Broad-spectrum activity against Gram positives (including VRSA and penicillin-resistant S. pneumoniae, Enterococci not susceptible) and Gram negatives (except ESBL-producing pathogens and P. aeruginosa)</td>
<td>Only intravenous</td>
</tr>
<tr>
<td>fosamid</td>
<td></td>
<td>Good tolerability profile</td>
<td>Three daily doses, High costs</td>
</tr>
<tr>
<td>Ceftobiprole medocaril</td>
<td>500 mg every 8 h (i.v.)</td>
<td>Broad-spectrum activity against Gram positives (including E. faecalis) and Gram negatives, included P. aeruginosa (no activity against ESBL-producing pathogens)</td>
<td>Only intravenous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good tolerability profile</td>
<td>Three daily doses, High costs</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>100 mg (loading dose), followed by 50 mg every 12 h (i.v.)</td>
<td>Broad spectrum of activity against Gram positives (including MRSA and VRE) and Gram-negatives (including ESBL-producing Enterobacteriaceae)</td>
<td>Only intravenous, Bacteriostatic</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600 mg every 12 h (i.v. or oral)</td>
<td>Spectrum limited to Gram positives</td>
<td>Bacteriostatic, Limited spectrum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral formulation allows treatment of outpatients and early oral-switch</td>
<td>Drug–drug interactions, Toxicity TDM recommended</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cheap (generic)</td>
<td></td>
</tr>
</tbody>
</table>
Approccio Multidisciplinare

Same Day Surgeons & ID Specialist Approach in Breast Tissue Expander

- Inpatient vs. outpatient (clinically stable)
- Empirical antibiotics
- Ultrasound/fluid collection
- Implant removal and follow-up vs salvage therapy
- Flowchart & recommendations

* Breast Ultrasound +/- Periprosthetic Fluid Aspiration Request:

1) Submit an outpatient breast ultrasound request, and specify the reason: “Rule out periprosthetic breast fluid collection. If fluid collection to be found, please aspirate fluid, and submit for cytological analysis, as well as bacterial, fungal, acid-fast bacillus stains and cultures.”

** Antimicrobial Recommendations:

1) Antimicrobial allergies: Prior to the provision of antimicrobials, assess for any antimicrobial allergies.

2) Route of antimicrobial recommendation: Although the extend and severity of the infection should weight on the route of antimicrobial administration, the choice of either oral or intravenous antimicrobials should be left up to the treating physician.

3) Empiric antimicrobial coverage: Before the availability of the culture results, based on our historical institutional culture data, provision of adequate antimicrobial coverage, should be provided for: Methicillin-resistant staphylococcus and Gram-negative rods, including Pseudomonas.

4) Targeted antimicrobial coverage: Once the culture and antimicrobial susceptibility panel results are made available, readjust or deescalate the antimicrobial coverage to cover the offending microorganism.

5) Provision of appropriate biofilm active antimicrobials: If the tissue expander (TE) is being removed, it is not necessary to provide biofilm active antimicrobials. Nonetheless, if the device is left in place, or the intention is to salvage the TE, please provide antimicrobials with adequate biofilm penetration (see below). Lastly, the addition of rifampin should be considered to the empiric antimicrobial, or the targeted antimicrobial regimen choice, specifically if the latter reveals a rifampin sensitive staphylococci.

73% salvage

Viola G et al PRS Global Open 2016
Conclusioni

- Profilassi antibiotica utile in chirurgia ricostruttiva
- No consenso su durata, applicare principi generali profilassi
- Fattori di rischio da considerare caso per caso
- Attento follow-up post-operatorio anche per late infections
- Considerare possibile resistenza agli antibiotici
- Approccio multidisciplinare e follow-up nella salvage therapy utile