Uso di antibiotici in ospedale: epidemiologia e misure di controllo

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ANTIBIOTIC PRESSURE: EFFECT on COLONIZATION BURDEN

Shentag, Crit Care Med 2001

Cefazolin  Ceftazidime  Glycopeptides

10^5 MSSA → 10^3 MSSA BSSA MRSA → 10^6 MRSA → 10^6 VRE Candida HRSA GISA

community  hospital
Prevalence and Patterns of Antibiotic Prescribing in Italian Hospitals

- INF-NOS → 15 hospitals (2001), size 384-1809 beds

- Pharmacy records for the year 2000 were used to describe and compare antimicrobial usage density and costs

- DDD, as defined by the WHO, were used (treatment days/100 pts days/year)

Porretta A et al. Infection 2003:31(S2):16-21
Prevalence and Patterns of Antibiotic Prescribing in Italian Hospitals - Intervention for the Control of Antibiotic Prescriptions -

• In 13 hospitals→ hospital drug formulary committee had been instituted;
• in only 4 hospitals it met >3t in 2000

• Periodic drug usage review with data feedback to the wards in 13 hospitals (10 of them performed a quarterly review)

Porretta A et al. Infection 2003:31(S2):16-21
Prevalence and Patterns of Antibiotic Prescribing in Italian Hospitals

- Intervention for the Control of Antibiotic Prescriptions
  - In 7 hospitals → a cycling protocol
  - In 4 hospitals → reporting of antimicrobial susceptibility testing results
  - In 6 hospitals → prescription of 2nd line or high cost antimicrobials was allowed on the basis of susceptibility testing results (in 4 upon the advice of ID consultant)
  - Automatic stop order (absence of active intervention by clinician or ID consultant)

Porretta A et al. Infection 2003:31(S2):16-21
Prevalence and Patterns of Antibiotic Prescribing in Italian Hospitals - Data on Annual Antibiotic Consumption -

Density of prescription $\rightarrow$ 55.3 DDDx100 pt/d

Porretta A et al. Infection 2003:31(S2):16-21
Prevalence and Patterns of Antibiotic Prescribing in Italian Hospitals

- Data on Annual Antibiotic Consumption -

ICU - 2 or > AB
- DDD : 232.8

Porretta A et al. Infection 2003:31(S2):16-21
Prevalence and Patterns of Antibiotic Prescribing in Italian Hospitals
- Data on Annual Antibiotic Consumption -

Surgery  DDD: 37.9

Porretta A et al. Infection 2003:31(S2):16-21
Prevalence and Patterns of Antibiotic Prescribing in Italian Hospitals
- Data on Annual Antibiotic Consumption -

Porretta A et al. Infection 2003:31(S2):16-21
Prevalence and Patterns of Antibiotic Prescribing in Italian Hospitals - Data on Annual Antibiotic Consumption - Infectious Diseases

Porretta A et al. Infection 2003:31(S2):16-21
Prevalence and Patterns of Antibiotic Prescribing in Italian Hospitals

- Difference in prescription by ward (%) on the day of the survey-

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Surgery</th>
<th>ID</th>
<th>ICU</th>
</tr>
</thead>
</table>

ES cephal. + β-lactam inhib.  
Fquin  
Glyco  
Carbap  
Aminog

Porretta A et al. Infection 2003:31(S2):16-21
Prevalence and Patterns of Antibiotic Prescribing in Italian Hospitals - Survey -

- Of 2,165 pts → 985 (45.5%) were receiving at least 1 antibiotic (76% single – 24% combo)

- Reasons:
  - 36%
  - 27%
  - 22%
  - 15%

Porretta A et al. Infection 2003:31(S2):16-21
La politica antibiotica

Dati INFNOS

• 1/3 circa dei pazienti senza infezione è in trattamento antibiotico

• Di questi il 5% è in trattamento con glicopeptidi e il 3,5% con carbapenemici

• Il giorno dello studio sono registrati più di 60 antibiotici usati

• In Chirurgia nel 50% dei casi di IO non è stato utilizzato il laboratorio
Antibiotic usage in intensive care units: a pharmaco-epidemiological multicentre study

Table 1. Antibiotic prescriptions

<table>
<thead>
<tr>
<th>Type of patient/reason for treatment</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with sepsis/empirical prescription (n = 143)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vancomycin</td>
<td>43</td>
<td>30.1</td>
</tr>
<tr>
<td>ceftazidime</td>
<td>38</td>
<td>26.6</td>
</tr>
<tr>
<td>ciprofloxacin</td>
<td>37</td>
<td>25.9</td>
</tr>
<tr>
<td>gentamicin</td>
<td>36</td>
<td>25.2</td>
</tr>
<tr>
<td>amikacin</td>
<td>34</td>
<td>23.8</td>
</tr>
<tr>
<td>piperacillin + tazobactam</td>
<td>30</td>
<td>21.0</td>
</tr>
<tr>
<td>teicoplanin</td>
<td>27</td>
<td>18.9</td>
</tr>
<tr>
<td>metronidazole</td>
<td>27</td>
<td>18.9</td>
</tr>
<tr>
<td>imipenem + cilastatin</td>
<td>25</td>
<td>17.5</td>
</tr>
<tr>
<td>meropenem</td>
<td>23</td>
<td>16.1</td>
</tr>
<tr>
<td>Medical patients without sepsis/prophylaxis (n = 119)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>24</td>
<td>20.2</td>
</tr>
<tr>
<td>cefazolin</td>
<td>15</td>
<td>12.6</td>
</tr>
<tr>
<td>ceftazidime</td>
<td>13</td>
<td>10.9</td>
</tr>
<tr>
<td>cefotaxime</td>
<td>13</td>
<td>10.9</td>
</tr>
<tr>
<td>cefoxitin</td>
<td>10</td>
<td>8.4</td>
</tr>
<tr>
<td>Medical patients without sepsis/unknown reason (n = 78)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ceftazidime</td>
<td>15</td>
<td>19.2</td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>14</td>
<td>17.9</td>
</tr>
<tr>
<td>cefazolin</td>
<td>11</td>
<td>14.1</td>
</tr>
<tr>
<td>cefotaxime</td>
<td>11</td>
<td>14.1</td>
</tr>
<tr>
<td>piperacillin + tazobactam</td>
<td>9</td>
<td>11.5</td>
</tr>
<tr>
<td>Surgical patients without sepsis/prophylaxis (n = 299)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cefazolin</td>
<td>44</td>
<td>14.7</td>
</tr>
<tr>
<td>ceftazidime</td>
<td>37</td>
<td>12.4</td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>35</td>
<td>11.7</td>
</tr>
<tr>
<td>metronidazole</td>
<td>23</td>
<td>7.7</td>
</tr>
<tr>
<td>cefuzoxime</td>
<td>23</td>
<td>7.7</td>
</tr>
<tr>
<td>Surgical patients without sepsis/unknown reason (n = 86)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cefazolin</td>
<td>19</td>
<td>22.1</td>
</tr>
<tr>
<td>ceftazidime</td>
<td>11</td>
<td>12.8</td>
</tr>
<tr>
<td>cefoxitin</td>
<td>10</td>
<td>11.6</td>
</tr>
<tr>
<td>teicoplanin</td>
<td>10</td>
<td>11.6</td>
</tr>
<tr>
<td>metronidazole</td>
<td>10</td>
<td>11.6</td>
</tr>
</tbody>
</table>

979 pts in 43 ICU

153 had sepsis

3rd gen. cephal. 42%
Mean duration 4.6d

Combination 31%
Mean duration 3d

164 pts (20.9%)
Hospital-acquired infections in Italy: a region wide prevalence study

- Between October and December 2000, a region-wide prevalence study of HAI was conducted in all public hospitals (59 facilities with ca. 16 000 beds; 560 000 admission yearly) in Piemonte Region, Italy, and in the one hospital of the neighbouring autonomous region of Valle d’Aosta.

- The study population comprised a total of 9467 patients.

- The prevalence of HAI was 7.84%.

Hospital-acquired infections in Italy: a region wide prevalence study - the day of the survey -

- 3456 pts (36.5%) received at least one antibiotic

Hospital-acquired infections in Italy: a region wide prevalence study - the day of the survey -

Hospital-acquired infections in Italy: a region wide prevalence study - inappropriate use -

- Glycopeptides: enterobacteria, Ps. aeruginosa, MSSA
- 3rd and 4th gen. cephalosporins: enterococci
- 3rd generation cephalosporins: 35% in surgical prophylaxis
- Glycopeptides: 5% surgical prophylaxis (only 26.4% - prosthetic device - complied with GL)
- Clean surgery: 512 pts (30.9%) received prophylaxis
- Mean duration of surgical prophylaxis: 3.1 d (31% more than 4 d)

Antibiotic policy in the hospital setting

d. Implementation, with human and economic resources, of an antibiotic restriction programme, and identification of antibiotic molecules that need restriction;

e. Adoption of antibiotic cycling strategies, for empiric therapy, in “hot” hospital zones and based on local antibiotic resistance surveillance system programmes, better defining the molecular basis of antibiotic resistance;

f. Establishment of cost-effective surveillance systems using existing laboratory generated data.

Petrosillo & Struelens, ESCMID 2002
Antibiotic policy in the hospital setting

a. Implementation of educational programmes on use of antimicrobial agents (including pharmacokinetics and pharmacodynamics);

b. Establishment of guidelines and antibiotic audits for an evidence-based and standardized use of antimicrobials;

c. Identification of those procedures that need and do not need antimicrobial prophylaxis either for surgical or non-surgical purpose (select the drugs for prophylaxis which are not needed for subsequent therapy);

Petrosillo & Struelens, ESCMID 2002
Education
There is a large body of evidence from databases such as the Cochrane database which indicates that the following interventions have a significant effect on healthcare provider behaviour:

- Education
- Guidelines
- Outreach visits and academic detailing
- Audit and feedback

**Controversies on the effect of educational programs on antimicrobial use in hospitals**

There is a need of continuous reinforcement, supplemented by the feedback of audits of antibiotic use within a specific hospital setting.
Prophylaxis
Diffusione di protocolli scritti

# Incidence of SSI in Italian Surgical Settings

Table V. Characteristics of surgical antibiotic prophylaxis

<table>
<thead>
<tr>
<th>Onset day of antibiotic prophylaxis</th>
<th>#</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>previous days before operation</td>
<td>271</td>
<td>6.7</td>
</tr>
<tr>
<td>the day of the operation</td>
<td>3746</td>
<td>92.0</td>
</tr>
<tr>
<td>the day following the operation</td>
<td>45</td>
<td>1.1</td>
</tr>
<tr>
<td>Timing of administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>more than 30 min’ before of the induction of anaesthesia</td>
<td>1413</td>
<td>37.6</td>
</tr>
<tr>
<td>within 30 min’ of the induction</td>
<td>2035</td>
<td>54.2</td>
</tr>
<tr>
<td>after the operation</td>
<td>279</td>
<td>7.4</td>
</tr>
<tr>
<td>Duration of prophylaxis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>one dose, one day</td>
<td>1765</td>
<td>43.4</td>
</tr>
<tr>
<td>more doses, one day</td>
<td>940</td>
<td>23.0</td>
</tr>
<tr>
<td>more than one day</td>
<td>1339</td>
<td>33.0</td>
</tr>
<tr>
<td>Days of administration (median, range)</td>
<td>4</td>
<td>(1-40)</td>
</tr>
<tr>
<td>Number of antibiotics administered</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3593</td>
<td>88.0</td>
</tr>
<tr>
<td>2</td>
<td>405</td>
<td>9.9</td>
</tr>
<tr>
<td>3</td>
<td>69</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Petrosillo N, et al. ECCMID 2004
Restriction
Restriction of hospital formulary through pharmacy and therapeutics committee

Methods

- Cyclic rotation of antimicrobials within a class
- Antibiotic order forms
- Antibiotic stop orders – therapeutic use
  - prophylactic use
- Restriction of use
- Removal of specific agents
- Review of medical records by pharmacists
- Usage feedback to physicians
- Computerized review
- Group purchasing practices
- Generic substitution

Shlaes et al. CID 1997;25:584-99
Effectiveness of a vancomycin restriction policy in changing the prescribing patterns of house staff

- Intervention to reduce the rise in VRE infections

- 1995: Encouraging house staff to follow hospital guidelines had little impact.

- 1996: Review of vancomycin orders and one-to-one discussion with the house staff regarding the rationale for the order.

- Decrease of inappropriate use (39% to 16.8% p.005)
  This change was primarily due to a decrease in vancomycin prophylaxis in cardiosurgery.

- VRE infections decreased from 0.29/100 pts to 0.13/100 pts.
Impact of antibiotic changes in empirical therapy on antimicrobial resistance in ICU-acquired infections

MRSA 93%   MRSE 79%   PIP/TZ res Ps aerug. 67%

PIP/TZ $\rightarrow$ Carbapenem in nosocomial pneumonia  
PIP/TZ $\rightarrow$ cefepime+metronidazole in peritonitis  
No antibiotic at admission without fever  
AM/CL $\rightarrow$ TMP/SMX

MRSA 73% (p=0.003)   MRSE 64% (p=0.09)  
PIP/TZr-Ps aer 29% (p<0.001) Carb-r Ps aer $\uparrow$ 41% (p=0.06)

Impact of an antimicrobial formulary and restriction policy in the largest hospital in Italy

- Therapeutic Committee for Hospital Formulary (TCHF) handbook, with reasons for antibiotic choice

- 31 antibiotics without restricted use

- Tazobactam/piperacillin, ceftazidime, cefepime, meropenem -> restricted (ID specialist or microbiology)

- 22 antibiotics erased

- 10.5% decrease of costs for antibiotics
Impact of an antimicrobial formulary and restriction policy in the largest hospital in Italy

Table 4
Daily defined dose for 100 hundred patients per day

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tazo/piperacillin</td>
<td>0.043</td>
<td>0.142</td>
<td>0.108</td>
</tr>
<tr>
<td>Meropenem</td>
<td>0.41</td>
<td>0.56</td>
<td>0.58</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>2.6</td>
<td>3</td>
<td>1.33</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>4.21</td>
<td>4.06</td>
<td>4.9</td>
</tr>
<tr>
<td>Ceftizoxime</td>
<td>1.2</td>
<td>1.84</td>
<td>3.17</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>0.78</td>
<td>0.85</td>
<td>1.68</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>0.67</td>
<td>0.42</td>
<td>1.1</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1.1</td>
<td>1.1</td>
<td>1.01</td>
</tr>
<tr>
<td>Teicoplanin</td>
<td>1.35</td>
<td>1.34</td>
<td>1.73</td>
</tr>
<tr>
<td>Clavulanic acid amoxyccillin</td>
<td>0.5</td>
<td>1.18</td>
<td>2.24</td>
</tr>
<tr>
<td>Mezlocillin</td>
<td>0.004</td>
<td>0.014</td>
<td>0.5</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>0.2</td>
<td>0.32</td>
<td>0.45</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>0.28</td>
<td>0.27</td>
<td>0.14</td>
</tr>
<tr>
<td>Imipenem</td>
<td>1</td>
<td>0.8</td>
<td>0.18</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>1.6</td>
<td>1.25</td>
<td>0</td>
</tr>
</tbody>
</table>
ESBL-producing Klebsiella pneumonia outbreaks during a third generation cephalosporin restriction policy

In spite of the adoption of 3rd generation cephalosporin restriction policies, two independent outbreaks by ESBL-producing Klebsiella pneumonia occurred in two different wards (NICU and neurosurgery).

Antibiotic Policies in Italian Hospitals: Still a Lot to Achieve

- Questionnaire survey (2000): response rate $\rightarrow$ 80% (428/535)

- Hospital formulary $\rightarrow$ 89%
- Hospital pharmacy committee $\rightarrow$ 73.1%
  (50% met at least one in 1999)
- Written justification for a list of AB $\rightarrow$ 41.4%
  (No. of antibiotics in the list $\rightarrow$ 7 [1-49])
- Hospitals with periodical pharmacy reports $\rightarrow$ 54%
- Data on DDD $\rightarrow$ 12%
- Written protocols for surgical prophylaxis $\rightarrow$ 37%

YOU'RE OBVIOUSLY IN PAIN, MR. JETER. MAYBE YOU SHOULD TALK TO SOMEBODY.