MANAGEMENT OF HOSPITALISED PATIENTS WITH INFECTION AND IMPLICATIONS FOR ANTIMICROBIAL STEWARDSHIP

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Welcome to London
AIM

- Clinical Decision Making in managing hospitalised patients with potentially resistant infections
- Implications for hospital stewardship
Method?

Patient and organisational case study with Q & A
PRESENTATION
1/2011

- 62 year old admitted to acute medical admissions unit with 3 day history of "flu like illness" followed by chills, vomiting, diarrhoea and increasing confusion. Incontinent of urine for 24 hours.

- Discharged from hospital 3 weeks earlier. Mainly tired & some sweats

- Type 2 DM, hypertension, peripheral vascular disease and PUD
Recent History

- 3rd hospitalisation in 12 months
- 4th course of antibiotic therapy in 12 months - 2 UTI’s & 2 LRTI/s [FQ’s and aminoglycoside and cephalosporins]
- Recent colonisation with MRSA
- Urinary catheter whilst in hospital recently
- 24 months ago removal of L renal calculus

- TB 30 years ago
- Smoker
- Co-amoxiclav started by GP
- Lisinopril
- Omeprazole
- Aspirin
- Glipizide
- Metformin
- Statin
EXAMINATION

- 39°C
- 28 breaths/minute
- 110 beats/min
- Confused MSQ = 4/10
- Dehydrated
- Lower back tenderness
- Chest: spare basal crepitations
- Systolic murmur “all areas”
- Normal rectal examination
LABORATORY

- WCC 22.4
- PLT 98
- UREA 14.8
- Cr 196
- BG 23 mmol/l
- Po2 8.8
- Lactate 4.2
- CRP 345
- Glycosuria, ketonuria +, pyuria and nitrites
What other laboratory information would you like?
RECENT MICROBIOLOGY

- MRSA colonisation
- *K. pneumoniae* in urine and blood 4 weeks earlier when in hospital
- *E. faecalis* in urine 6 months earlier

Undertaken:
- Blood and urine cultures
Q1: Differential diagnosis?
How do you recognise a true Scotsman?
ANSWER 1
Severe Sepsis 2\textsuperscript{nd} ry to

- Urinary Tract Infection
- + previous UTI
- + diabetes mellitus
- + recent catheterisation
- + ?BPH
- + previous calculus
- + nitrite positive
ENDOCARDITIS

- "-ve murmur not localised"
- "-ve no previous valvular heart disease"
+ recent hospitalisation
+ intravenous catheters recently
+ MRSA colonisation
ANSWER 1

- LOWER RESPIRATORY TRACT INFECTION
  - ve cXR normal
  - ve minimal chest findings
  + recent hospitalisation
  + Smoker
  + MRSA colonisation
Q2: Is the infection hospital, healthcare or community acquired?
Community Acquired Infection

- An infection that was present at the time of infection to hospital or presented within 48 hours of admission
Hospital acquired infection

- An infection that arose > 48 hours or or more after admission to hospital which was not incubating at the time of admission
Healthcare Acquired Infection

- History of hospitalisation, surgery, dialysis or residence in LTCF within a year of contracting the infection, or the presence of a permanent indwelling catheter or percutaneous medical device e.g. gastrostomy, tracheostomy or Foley catheter.
Q3: What is the likely microbiological epidemiology of the likely syndromes?
# Aetiology of clinically significant bacteraemia (bloodstream infection)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Hospital (HA) or community (CA) acquired</th>
<th>Incidence (% of total cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>HA = CA</td>
<td>29</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>HA &gt; CA, 2:1</td>
<td>19</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>CA &gt; HA, 10:1</td>
<td>13</td>
</tr>
<tr>
<td><em>Klebsiella</em> spp.</td>
<td>HA &gt; CA, 3:1</td>
<td>7</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>HA &gt; CA, 10:1</td>
<td>5</td>
</tr>
<tr>
<td>‘Viridans’ streptococci</td>
<td>CA &gt; HA, 3:1</td>
<td>4</td>
</tr>
<tr>
<td>Coagulase-negative</td>
<td>HA &gt; CA, 20:1</td>
<td>4</td>
</tr>
<tr>
<td>staphylococci</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Varies with organism</td>
<td>19</td>
</tr>
</tbody>
</table>
Likely source of clinically significant bacteraemia (bloodstream infection)

<table>
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<tr>
<th>Organism</th>
<th>Common source</th>
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<tr>
<td><em>Escherichia coli</em></td>
<td>GU, biliary, peritoneal</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>IV, skin, respiratory, B&amp;J</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>Respiratory (CNS)</td>
</tr>
<tr>
<td><em>Klebsiella</em> spp.</td>
<td>GU, biliary, peritoneal</td>
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<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Respiratory, GU</td>
</tr>
<tr>
<td>Viridans' streptococci</td>
<td>Respiratory, cardiac, skin</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>IV, skin, prosthesis</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>GU, IV</td>
</tr>
</tbody>
</table>

Weinstein M, et al CID 1997; 24: 584-602
What is your clinical diagnosis?
What is your microbiological diagnosis?
What empiric treatment would you instigate?
ANSWER 3

- Site of infection
- Geographical location
  - Home v hospital (where in hospital) v healthcare facility etc
- Recent travel
- Outbreaks
- Co-morbidities
- Recent colonisation
- Recent antibiotics
EMPIRIC MANAGEMENT

- Probable health-care acquired UTI
- Worried about endocarditis also
- Started on Tazocin and Vancomycin
CASE UPDATE

- BLOOD CULTURE
  - *K. pneumoniae* – ESBL

- CONTINUING MANAGEMENT
  - Switch to meropenem. Continue vancomycin just in case.
What happened to our patient?
OUTCOME

- Cure after meropenem but develops CDI diarrhoea! Needed treatment with oral vancomycin.
- Microbiology concerned as 4th patient in 2 weeks with ESBL bacteraemia from same ward
- You are a member of the antimicrobial management team and have been asked by the infection prevention lead to support the investigation of an outbreak
- What do you want to do from a stewardship perspective?
WHAT DATA [INTELLIGENCE] DO YOU NEED?
What data do you need
Ward based, hospital based, national
data on epidemiology?

- Microbiology
  - Surveillance data - blood, urine
  - IC practice review: Hand hygiene, CVC-PVC, Catheters, etc
- Environment
- Consumption data on high risk antibiotics – cephalosporins, fluoroquinolones, etc
- Compliance with local policy
- Compliance with antibiotic review
- Patient flow and movement data
- Clinical data from case notes - risk factors e.g antibiotics, invasive interventions etc
National ESBL epidemiology

<table>
<thead>
<tr>
<th></th>
<th>E. coli</th>
<th>K. pneumoniae</th>
<th>P. aeruginosa</th>
<th>A. baumannii</th>
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<tr>
<td>2008</td>
<td>2499 (7.2%)</td>
<td>512 (8.4%)</td>
<td>196 (0.0%)</td>
<td>53 (0.0%)</td>
</tr>
<tr>
<td>2009</td>
<td>3486 (7.5%)</td>
<td>672 (8.8%)</td>
<td>269 (0.4%)</td>
<td>64 (1.6%)</td>
</tr>
<tr>
<td>2010</td>
<td>3602 (7.6%)</td>
<td>715 (8.3%)</td>
<td>295 (0.3%)</td>
<td>36 (0.0%)</td>
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The resistance (and number of isolates tested) in E. coli and K. pneumoniae bacteraemias in 2008-2010

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| 2008       | i.r.     | i.r.           | i.r.           |
| 2009       | i.r.     | i.r.           | i.r.           |
| 2010       | i.r.     | i.r.           | i.r.           |

Note: i.r. - data not available.
LOCAL ESBL DATA

Number of New ESBL Patients per Month Jan 2009 onwards

Number of ESBL Patients and ESBL Isolates (New and Recurrent) per Month Ninewells Hospital January 2009 onwards
NHS Scotland: use of “high risk” C. diff genic antibacterials in secondary care* DDD/1000/day 2008-2010.

4C antibacterials in 2010
30.7% lower than 2008
Cephalosporins ↓ 54%
Co-amoxiclav ↓ 27%
Fluoroquinolones ↓ 26%
Clindamycin ↓ 13%

*10 boards, covering 58% Scottish population
Hospital: Restricted Drugs

No of DDDs

Financial Month / Financial Year

New "Antibioticman" Policy

CEFUROXIME

MOXIFLOXACIN

PIPERACILLIN, TAZ OBACTAM

MEROPENEM

LEVOFLOXACIN
Compliance data from Ward 8

![Graph showing compliance data from October 2008 to August 2009. The graph includes a line indicating overall compliance, a line showing compliance after pharmacist intervention, and a line showing the required compliance. The months are marked from October 2008 to August 2009, with the y-axis representing overall compliance from 0% to 100%. The graph demonstrates fluctuations in compliance throughout the period, with notable increases after pharmacist interventions.]
LOCAL UNIT BASED DATA

No of DDDs

Financial Year / Financial Month / Financial Month Name

Cephalosporins
Gentamicin
Quinolones
Clindamycin
Carbapenems

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How do you interpret the data?
INVESTIGATION OF TRENDS

- ESBL NATIONALLY AND LOCALLY STABLE UNTIL THIS OUTBREAK
- EMPIRIC THERAPY COMPLIANCE SEEMS TO BE GOOD;
- LOOK AT DDD DATA- GOOD BUT 4-6 MONTHS NOTE RISE IN CEPHALOSPORIN AND QUINOLONE USE
- SHARE WITH PRESCRIBING TEAM
- LOOK FOR FACTORS THAT MAY HAVE INFLUENCED THIS PRESCRIBING
- CONSIDER CASE NOTE REVIEW
- SHARE WITH INFECTION CONTROL TEAM
Actions to deal with ESBL

What would you do to support prescribing actions from this outbreak?
Actions to deal with ESBL

- Remove or restrict “high risk antibiotics-
  - Pre-authorisation approval, post-prescription review, promote carbapenem sparing agents- temocillin, tigecycline, fosfomycin, 3 day review /automatic stop order

- Educational or persuasive
  - Regular ID infection input with feedback, regular educational sessions, improvement measures [review bundles, monitoring compliance, case note review/root cause analysis, run charts]

COMBINATION OF EDUCATIONAL AND RESTRICTIVE
New recommendations for empirical intravenous antibiotic treatment were communicated to prescribers throughout the hospital by infectious diseases physicians working with Strama (the Swedish strategic programme against antibiotic resistance). No restrictive measures were used. The intervention effect was analysed with interrupted time series (ITS) regression analysis of local and national monthly antibiotic sales data.
Segmented trend lines (grey) for monthly antibiotic use at UUH during January 2000–December 2007.


THREE KEY MESSAGES

- ASSESSMENT FOR RISK OF RESISTANCE CAN BE CLINICAL VALUE AND IMPORTANT TO GUIDE THERAPY IN UNWELL PATIENTS

- A RANGE OF STEWARDSHIP TOOLS CAN SUPPORT IMPROVEMENT THE QUALITY OF ANTIBIOTIC PRESCRIBING- THEY PROBABLY NEED TO BE MULTI-FACETED

- CONSUMPTION AND SURVEILLANCE DATA, DATA, DATA………….. INTEGRATED, LOCAL AND NATIONAL
Interactive case study

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Professor of Medicine
Radboud University Medical Centre
Nijmegen The Netherlands
Once upon a time...

- you were having dinner with a urologist. He is on call. During the soup, he has to answer his telephone. It is about a 72 year-old male who underwent prostatic surgery that morning, and who now having a high fever (and chills) and signs of sepsis.
- He tells the resident to start the patient the usual antibiotic treatment with Superpenem®. After the phone call (you have finished your soup), he asks whether you would agree with the treatment.
While he is eating his snails,

• you say that you wonder whether Superpenem® being a last resort drug should be used for such a simple urosepsis.

• You say that you even wonder whether Superpenem® has the optimal spectrum towards enterococci and Pseudomonas species.
Waiting for the lobster,

- he tells you that formerly they would treat all these patients with ciprofloxacin, but more and more patients appeared to have ‘these nasty cipro-resistant bugs’. They even encountered a few deaths...
- What would you like to know?
While he pours the Chablis,

• you ask him whether these patients have been exposed to cipro before they are being operated...

• He responds that that is indeed the case. You propose that you will come by next morning to study the charts of these patients that suffered from cipro-resistant microorganism...

• How would you proceed?
The next morning...

- you start looking at the chart of the patient who was given Superpenem the night before.

- While you are reading the chart, the urological resident receives a call that another patient on the ward has a positive blood culture with a Candida spp.
'Not again!'

- the resident exclaims...
  He tells this is the 3d patient with a Candida in the blood in the last 4 months.
- What would you like to know?
Indeed,

- all three cases were on a prolonged course of Superpenem
- When you ask what he means by prolonged he tells you these were very complicated cases that received more than 3 weeks of Superpenem®
Nosocomial fungaemia: a 2-year prospective study.

- 68 consecutive patients with fungaemia were studied during a period of 2 years, 81% had two or more positive blood cultures. Gastrointestinal tract (28%) and haematological diseases (17%) were the most common underlying conditions. The majority of cases had received vancomycin and/or imipenem (87%) and a central venous catheter (78%). Candida albicans (50%) and Candida parapsilosis (17%) were the most frequent isolates.

Costa et al. J Hosp Inf 2000
Infection by Candida albicans occurred in 7% of patients treated for 14 days and 22% of patients treated longer.
While you are still there,

- a sales representative of MaxiPharm comes in and offers the resident a trip to a meeting on 'Superpenem in serious infection' which will take place in Ibiza in May...

- 'By the way doc, if you are also interested, I could see what I can do for you...

- What is your response?
You return to the chart,

- and find out that the patient presented with lower urinary tract complaints and had a high PSA, in which case it is hard to tell whether it is chronic prostatitis or cancer. For that reason he was treated with ciprofloxacin 500 mg bid for 6 weeks about 2 months ago. The PSA did not fall.
Some weeks later,

- The patient underwent prostatic biopsies, for which he received 3 days of ciprofloxacin prophylaxis...

- A small prostatic cancer was found, and that was the reason to operate him yesterday, again under ciprofloxacin prophylaxis...

- What would you do next?
You decide to

• review the charts of the last 10 patients that were treated with Superpenem
• You ask the Medical Microbiology lab for the positive blood cultures over the past 6 months
• You ask the pharmacy for the deliveries of Superpenem over the past 6 months
In the meantime...

You find

- all 10 patients were males previously exposed to ciprofloxacin for weeks (and often repeatedly).
- The blood cultures reveal mostly ciprofloxacin-resistant E coli (12 x in 9 patients); many of these were susceptible to 2nd gen cephalosporins. There was one culture with Klebsiella (cipro R) and indeed 3 patients with positive cultures for Candida spp.
and

- a high expenditure on Superpenem®

So what are you going to do now?
Discuss with the urologists:

- Rethink longterm ciprofloxacin in patients with high PSA
- Rethink cipro prophylaxis for prostatic biopsies and surgery
- Rethink empiric treatment for postoperative urosepsis
- Regard Superpenem as a last resort drug