Antimicrobial Stewardship within an OPAT Service

Andrew Seaton
ID Consultant,
Queen Elizabeth University Hospital
Lead Doctor Antimicrobial Management Team, NHS GGC
@raseaton66
What is the role of OPAT?

• To improve quality and efficiency of care and reduce risk of harm in patients with infection who would otherwise be hospitalised for IV antibiotic therapy
  – Infection team influence in the broader patient population
  – Essential component of the modern integrated, interdisciplinary infection service
  – More efficient and appropriate use of inpatient resource – part of the Antimicrobial Stewardship strategy
What OPAT is not

• An alternative to thoughtful person-centred medical care (or a good debridement)
• An easy or cheap option (long term implant failure)
• Safer (than oral Rx)
• Better (than oral Rx all the time)
ANTIMICROBIAL STEWARDSHIP

Systematic approach to safe and effective use of antibiotics – optimising outcome, minimising harm and preserving future therapies
Aims of an AMS Programme

- Optimise antibiotic use
  - Route, dose, interval and duration
- Optimise infection-related outcome
  - Survival
  - Speed of recovery / Length of stay
- Minimise inappropriate antimicrobial use
- Minimise risk (unintended consequences)
  - ADRs (AKI and other antimicrobial-related toxicity)
  - AMR
  - *C. difficile*
  - Vascular device-related infection
- Promote cost-effective prescribing
OPAT is part of an Antimicrobial Stewardship (AMS) Strategy

• Start SMART then FOCUS
  – Review the clinical diagnosis + continuing need for antibiotics at 48*-72 hours
  – Document a clear plan of action:
    • Stop antibiotics if there is no evidence of infection
    • Switch antibiotics from IV to oral
    • Change antibiotics: narrower spectrum or broader if required
    • Continue + document next review / stop date

• OPAT

Start Smart - Then Focus Antimicrobial Stewardship Toolkit for English Hospitals, PHE, Updated March 2015
Key AMS Considerations within OPAT

1. Is IV Rx (OPAT) appropriate?
2. Choice of IV antimicrobial agent
3. Monitoring and follow up
4. IVOST during OPAT
5. Duration of therapy
6. OPAT-AMS Governance
1. Is IV Rx (OPAT) appropriate?

• **Stewardship at the OPAT “gate”**
  – Requires a systematic infection specialist team-led approach
    • Correct diagnosis (e.g. Cellulitis Vs Varicose eczema)
    • Correct interpretation of microbiology (e.g. DFI)
    • Proper source control (metal work removal, drain abscess)
    • Planned (or completed) antibiotic Rx
    • **ARE THERE IVOST OPTIONS?**
OPAT “Gate-keeping”

OPAT2016 posters: Hederwick and Peirse
“High consequence infections”

• IV Rx is the current management strategy when evidence supporting oral antibiotic therapy is lacking
  – Bacterial Central Nervous System Infection (except Lyme, TBM)
  – Bacterial Endocarditis (except R sided in IVDU)
  – S.aureus bacteraemia (first 2 weeks)
  – Bone and joint infection?
Osteomyelitis: OVIVA STUDY

• Equipoise in published literature reflected in variation in clinical practice UK/Ireland/Global

• 1054 adults with OM randomised to either IV or oral Rx within 1 week of initiation of IV Rx
  – PJI, other orthopaedic, Spinal, DFI.....
  – SABs excluded

• **Primary Treatment success (all comers) 86% @ 1 year**
  – Shorter hospitalisation/costs in oral Rx
  – Less line-related complications in oral Rx

Scarborough et al, ECCMID, 2017
OVIVA - Important caveats

• Patients with SAB were excluded
• If no oral (or IV) regimen available - excluded
• MDR infections (Gram positive and negative) and significant potential DDIs likely to have limited oral options and led to some exclusions
• Carefully constructed oral regimens with close monitoring (ECGs, Bloods) and other drug modification by specialists supervising Rx
## Oral Antibiotics in BJI - Considerations

<table>
<thead>
<tr>
<th>Oral Antibiotic</th>
<th>MRSA</th>
<th>CNS</th>
<th>Bone Penetration</th>
<th>Biofilm activity</th>
<th>QTc prolong</th>
<th>Other DDIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillins</td>
<td>✗</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifampicin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na fusidate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quinolones</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pristinamycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## BJI – Antibiotic DDIs

<table>
<thead>
<tr>
<th></th>
<th>RIF</th>
<th>FUSID</th>
<th>QUIN</th>
<th>TMP</th>
<th>LINEZ</th>
<th>DOXY</th>
<th>CLINDA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RIF</strong></td>
<td><img src="color" alt="RIF" /></td>
<td><img src="color" alt="FUSID" /></td>
<td><img src="color" alt="QUIN" /></td>
<td><img src="color" alt="TMP" /></td>
<td><img src="color" alt="LINEZ" /></td>
<td><img src="color" alt="DOXY" /></td>
<td><img src="color" alt="CLINDA" /></td>
</tr>
<tr>
<td><strong>FUSID</strong></td>
<td></td>
<td><img src="color" alt="FUSID" /></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>QUIN</strong></td>
<td></td>
<td></td>
<td><img src="color" alt="QUIN" /></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TMP</strong></td>
<td></td>
<td></td>
<td></td>
<td><img src="color" alt="TMP" /></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LINEZ</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><img src="color" alt="LINEZ" /></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DOXY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><img src="color" alt="DOXY" /></td>
<td></td>
</tr>
<tr>
<td><strong>CLINDA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><img src="color" alt="CLINDA" /></td>
</tr>
</tbody>
</table>
Subset analysis suggests IV Rx may be preferred/ more evidence required when

- SAB-related
- One stage revision
- No positive microbiology
- Organisms where there are limited oral options
  - Pseudomonas, Cipro R GNs
  - MDRGPos infections
2. Choice of IV agent: The OPAT-AMS dilemma

- **AMS**: Most effective, safe and narrow-spectrum agent with least capacity for collateral effects (AMR, HCAI) for specific indication

- **OPAT**: As above BUT choice and dosing of agent to optimize early hospital discharge/admission avoidance may take precedence over an agent’s spectrum of activity
AMS Challenges in OPAT

• Lack of drug stability data for many narrow spectrum antimicrobials
• Lack of narrow spectrum antimicrobials with easy (once daily) administration
  – Ceftriaxone, Teicoplanin, Daptomycin and Ertapenem
• Lack of antimicrobials with rapid speed of administration
  – Daptomycin
• *C. difficile* risk of commonly used OPAT agents
SOME REASSURANCE......
Antibiotic Administration Routes Significantly Influence the Levels of Antibiotic Resistance Microbiota

Lu Zhang, Ying Huang, Yang Zhou, Timothy A. Drutz

ABSTRACT

This study investigated the influence of antibiotic administration routes on the levels of antibiotic-resistant bacteria and the propagation of antibiotic resistance (AR) gene pools in the gastrointestinal (GI) tracts using C57BL/6J mice. Enterococci or E. coli were inoculated with a mixture of tet(M)-carrying Escherichia coli or tet(O)–carrying Enterococcus faecalis and treated with different doses of tetracycline hydrochloride (Tet) or ampicillin sodium (Amp) and delivered by oral or i.v. injection. Exposure to Tet was observed by both oral and i.v. injection routes. Together, these data suggest that oral administration of antibiotics has a prominent effect on AR amplification and development in gut microbiota, which may be minimized by alternative drug administration approaches, as illustrated by i.v. injection in this study and proper drug selection.
Antibiotic Choice & Admin Route and Clostridium difficile (CDI) Risk in OPAT

- Cephalosporin use restricted in hospitals due to high risk of CDI...... but not in OPAT

- Despite higher use of IV cephalosporins in OPAT, UK OPAT cohort studies suggest much lower rates of *Clostridium difficile* (0.05 per 1000 OPAT days) compared to hospitalised patients.

3. Monitoring and Follow up

- At each patient encounter (including case discussion/virtual ward round) the following are reviewed
  - The patient’s clinical and social picture
  - Previous and current microbiology, including antibiograms
  - Radiological imaging as appropriate
  - Need for surgical intervention/source control as appropriate
  - Lab markers and antimicrobial therapeutic monitoring
  - Tolerability/ effectiveness of the antimicrobial regimen
  - **Opportunities for intravenous to oral switch considered.**
4. IVOST DURING OPAT

• **Patient** - Functional gastrointestinal tract
• **Infection** - Absence of infection where few data support oral therapy (e.g. bacterial meningitis, brain abscess, infective endocarditis, SAB). Clinical improvement
• **Organism** - Susceptible to oral agent(s)
• **Antibiotic** - Good oral bioavailability and penetration to infection site at appropriate concentrations, lack of DDIs, allergy and other CIs (QTc)
OPAT IVOST scenarios

Scheduled/Fixed Duration IV
- e.g. Endocarditis, CNS, some BJI, some GNB/UTI

Anticipated IVOST
- e.g. Cellulitis,

Unplanned IVOST
- e.g. Toxicity or line infection
OPAT IVOST scenarios

Anticipated

Based on improvement in clinical signs e.g. Cellulitis, Wound infection
4.1 Patients with superficial skin and soft tissue infection should be reviewed daily by the OPAT team to optimize speed of intravenous to oral switch.

4.2 There should be a weekly multidisciplinary meeting/virtual ward round to discuss progress (including safety monitoring and outcome) of patients receiving OPAT.

4.3 Patients receiving in excess of 1 week of antimicrobial therapy should be regularly reviewed by the OPAT specialist nurse and physician, in addition to discussion at the weekly multi-disciplinary team meeting. The frequency and type of review should be agreed locally.

4.4 Patients should have blood tests performed at least weekly if OPAT <1 month or at least twice monthly if OPAT >1 month. Blood tests should include full blood count, renal and liver function, C-reactive protein (CRP) and therapeutic drug monitoring where appropriate. Other tests may be required for specific indications or therapies.

4.5 The OPAT team is responsible for monitoring clinical response to antimicrobial management and blood investigations, and for reviewing the treatment plan, in conjunction/consultation with the referring specialist as necessary.

4.6 There should be a mechanism in place for urgent discussion and review of emergent clinical problems during therapy according to clinical need. There should be a clear pathway for 24 h immediate access to advice/review/admission for OPAT patients agreed with the referring clinician, and this should be communicated to the patient both verbally and in writing.
Good Practice Recommendations

• **SSTI should be reviewed daily** by the OPAT team to optimize speed of intravenous to oral switch.
Skin and Soft Tissue Infection
OPAT Patient Group Direction for SSTIs: empiric antibiotic Rx

History of MRSA or Beta-lactam allergy?

- Yes
  - Teicoplanin ▼ Clindamycin*
  
  *If Beta-lactam allergy or sensitive MRSA

- No
  - Ceftriaxone ▼ Clindamycin or Flucloxacinil

Review Daily To Optimise IVOST
Nurse-led Mx for OPAT SSTIs

Comparison of patients pre- and post-introduction of a nurse-led management protocol

- Protocol management was associated with reduced duration of outpatient i.v. therapy (from 4 to 3 days, $P=0.02$)

SSTI: Median duration of OPAT (days)

Linear time trend in log (OPAT days)
Estimate 0.904 (0.886-0.922)
p<0.0001

Seaton RA et al, IJAA, 2011
OPAT IVOST scenarios

Scheduled/ Fixed Duration IV

Either exclusive IV Rx e.g. Endocarditis, meningitis or Planned switch (poorly evidence based) e.g. certain BJI
Scheduled / Fixed Duration IV Rx

• Patient Considerations
  – Clinical improvement (usual at time of OPAT referral)
  – Able to swallow (usual)

• Antimicrobial Considerations
  – Absorbed and penetrates to site of infection
  – Organism (if known) is sensitive
  – Allergy
  – Host and DDIs
Gram negative infections

• Minimal evidence base & limited oral options in MDRGNB
• Pivmecillinam and Fosfomycin not recommended for uUTI or bacteraemia and short duration Rx for Lower UTI –limited OPAT use
• Opportunities for IVOST in liver abscess/ other intra-abdominal based on radiological & biochemical improvement (Quinolones, Co-amoxiclav, Metronidazole)
Duration of OPAT in days (median, IQR) by year for non-SSTI cases by year of OPAT

Spearman's coefficient of rank correlation = -0.17, p < 0.0001

Barr et al IJAA, 2012
(Common) IVOST OPAT Barriers in BJI

• **Enterococcal infection**
  – High dose Amox (bone penetration)
  – Linezolid (DDIs + Toxicity)

• **Staphylococcal infection**
  – Quinolones (QTc prolongation DDIs)
  – Rifampicin (DDIs, co-admin with Linezolid)

• **BH Streptococcal infection**
  – Clindamycin and doxycycline resistance
  – Linezolid (DDIs + Toxicity)
5. Duration of Therapy (IV and oral)

In AD 321, Roman Emperor Constantine the Great codified that there would be 7 days in a week. Even in the modern era of evidence-based-medicine, this 1695-year-old decree remains a primary reference for duration of antibiotic therapy: it leads physicians to treat infections in intervals of 7 days. Thus, it is gratifying when clinical trials challenge the standard antibiotic duration of 7 to 14 days.
Table

Infections for Which Short-Course Therapy Has Been Shown to Be Equivalent in Efficacy to Longer Therapy

<table>
<thead>
<tr>
<th>Disease</th>
<th>Treatment, Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-acquired pneumonia(^{1-3})</td>
<td>3-5</td>
</tr>
<tr>
<td></td>
<td>7-10</td>
</tr>
<tr>
<td>Nosocomial pneumonia(^{6,7})</td>
<td>≤8</td>
</tr>
<tr>
<td></td>
<td>10-15</td>
</tr>
<tr>
<td>Pyelonephritis(^{10})</td>
<td>5-7</td>
</tr>
<tr>
<td></td>
<td>10-14</td>
</tr>
<tr>
<td>Intraabdominal infection(^{11})</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Acute exacerbation of chronic bronchitis and COPD(^{12})</td>
<td>≤5</td>
</tr>
<tr>
<td></td>
<td>≥7</td>
</tr>
<tr>
<td>Acute bacterial sinusitis(^{13})</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Cellulitis(^{14})</td>
<td>5-6</td>
</tr>
<tr>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Chronic osteomyelitis(^{15})</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>84</td>
</tr>
</tbody>
</table>
6. OPAT-AMS Governance

Outpatient parenteral antimicrobial therapy and antimicrobial stewardship: challenges and checklists

M. Gilchrist* and R. A. Seaton

*Imperial College Healthcare NHS Trust, Charing Cross Hospital, London W6 8RF, UK; 2NHS Greater Glasgow and Clyde, Brownlee Centre, Gartnavel General Hospital, Glasgow G12 0YN, UK
Outpatient parenteral antimicrobial therapy and antimicrobial stewardship: challenges and checklists

M. Gilchrist1* and R. A. Seaton2

1Imperial College Healthcare NHS Trust, Charing Cross Hospital, London W6 8RF, UK; 2NHS Greater Glasgow and Clyde, Gartnavel General Hospital, Glasgow G12 9WN, UK

*Corresponding author. Tel: +44-203-311-1706; Fax: +44-203-311-1347; E-mail: mark.gilchrist@imperial.nhs.uk

Outpatient parenteral antimicrobial therapy (OPAT) is an effective agent with minimal colonisation to optimize early hospital discharge. This brief article discusses OPAT in the context of OPAT and the IDSA/Society for Healthcare Epidemiology of America where appropriate. Current US recommendations for OPAT include: initial antimicrobial therapy and the potential benefits or population. Within its limitations, the local antimicrobial stewardship committee or equivalent.

Within an OPAT service:
- All the antimicrobials currently in use are authorized by the host organization’s antimicrobial stewardship committee or equivalent.
- Does each antimicrobial prescribed fulfil the local antimicrobial prescribing standards?
- All antimicrobials administered are in accordance with locally agreed protocols.
- All antimicrobials are monitored where appropriate for toxicity or subtherapeutic concentrations.
- There is an active intravenous to oral switch programme.
- All antimicrobial adverse events are reported as per locally agreed protocols.
- Antimicrobial resistance data are reviewed and considered.

Keywords: ambulatory care, intravenous therapy, OPAT
OPAT staffing management

Within an OPAT service:
- There is a multidisciplinary (doctor/nurse/pharmacist) component to the OPAT service.
- There is a member of the OPAT service represented at the antibiotic stewardship committee.
- Where the service is run outside of the infection team, there is a link infection specialist involved in antimicrobial therapy decisions.
- Each member of the OPAT team is up to date with current mandatory training and organizational updates around antimicrobials, infection prevention and control and vascular access.
- Each member undertakes continuing professional development around the area of OPAT.
OPAT service/organizational management

Within an OPAT service:
- An OPAT operational and governance policy exists that is approved by an appropriate healthcare committee.
- A self-administration policy exists where appropriate.
- There is a minimum of a weekly multidisciplinary review for the majority of OPAT patients.
- A more detailed review is undertaken for any patient who suffers a failed OPAT outcome.
- A healthcare-associated infection during OPAT is reported through local governance procedures.
- An annual OPAT report is published and reviewed to look for continual improvement in clinical and managerial service delivery.
- The service should endeavour to make links with other local OPAT services and contribute to data sharing and learning from peers.
SAPG Good Practice Recommendations for Hospital AMS in Scotland

• Antimicrobial Guidelines should include/ take into account:
  – Discharge Planning
    • Support early hospital discharge in suitable patients either through timely IV to oral switch or, when the facility exists, in selected patient groups through OPAT programmes
  – Where OPAT programmes exist AMTs need to ensure that they are governed by national standards and that the principles of AMS are adhered to so as to minimise the potential for inappropriate practice or unintended harm.

SAPG, December 2014
From OPAT to COPAT: The Complex OP Antibiotic Team
Expanding (Stewardship) Roles within OPAT team

• Critical role of Antimicrobial Pharmacist in decisions re antibiotic selection
• Increased focus on short term IV Rx and admission avoidance / ambulatory care
  – Cellulitis
  – Pyelonephritis/ urosepsis
• Increasingly complex MDR infections (including CROs)

• **Nursing stewardship developments**
  – IVOST
  – Nurse educators
  – Independent prescribers
  – Penicillin allergy
Conclusions

• OPAT is an important arm of AMS programme
• OPAT pre-assessment is critical must include opportunities for streamlining of Rx including IVOST + stop
• Daily review to optimise IVOST opportunity in SSTI during OPAT
• Criteria for IVOST in BJI, Intra-abdominal infections
• Organisational governance and OPAT oversight by AMS programme is essential
Acknowledgements

Mark Gilchrist
OPAT Steering Group
Tracey Guise
Carolyne Horner

NHS GGC OPAT Team
Lindsay Semple, Claire Vallance, Liz Collison, Fiona Robb, Lee Stewart, Beth White, Neil Ritchie
Risk of failure by surgical procedure and route of Rx

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>OR</th>
<th>95% CI</th>
<th>N in each group</th>
</tr>
</thead>
<tbody>
<tr>
<td>OM debrided (no implant)</td>
<td>0.93</td>
<td>(0.45, 1.94)</td>
<td>318</td>
</tr>
<tr>
<td>OM not debrided (no implant)</td>
<td>0.34</td>
<td>(0.08, 1.41)</td>
<td>76</td>
</tr>
<tr>
<td>DAIR</td>
<td>1.20</td>
<td>(0.61, 2.34)</td>
<td>237</td>
</tr>
<tr>
<td>Removal of implant</td>
<td>0.65</td>
<td>(0.34, 1.23)</td>
<td>297</td>
</tr>
<tr>
<td>1 stage revision</td>
<td>2.16</td>
<td>(0.58, 8.00)</td>
<td>87</td>
</tr>
</tbody>
</table>

Scarborough et al, ECCMID, 2017
Risk of failure by infecting pathogen and route of Rx

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>OR</th>
<th>95% CI</th>
<th>N in each subgroup</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>0.89</td>
<td>(0.49, 1.59)</td>
<td>370</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>n/a</td>
<td>n/a</td>
<td>32</td>
</tr>
<tr>
<td>Other GNR</td>
<td>1.13</td>
<td>(0.43, 2.97)</td>
<td>116</td>
</tr>
<tr>
<td>Strep. species</td>
<td>0.54</td>
<td>(0.19, 1.55)</td>
<td>81</td>
</tr>
<tr>
<td>CNS</td>
<td>0.56</td>
<td>(0.24, 1.32)</td>
<td>189</td>
</tr>
<tr>
<td>None identified</td>
<td>1.91</td>
<td>(0.77, 4.75)</td>
<td>227</td>
</tr>
</tbody>
</table>

Scarborough et al, ECCMID, 2017
Risk of failure by planned antibiotics (excluding rifampicin)

No statistically significant difference in outcome by planned antibiotic choice

Scarborough et al, ECCMID, 2017