Outpatient Parenteral Antimicrobial Therapy: Who, Why and How?

R. Andrew Seaton
Brownlee Centre,
Gartnavel General Hospital
The Burden of Inpatient IV Antibiotic Therapy

- 1/3 hospital admissions receive antibiotic treatment\(^1\)
- 1/10 receive i.v. antibiotics
  - \(\sim 24,000\) per million population/yr
- All specialties
  - Integrated part of hospital care
  - Necessitate hospital admission
  - Prolong admission
  - Some could be discharged if they do not require i.v. antibiotic therapy\(^2\)

Infection types in acute admissions receiving i.v. antibiotics (n=381)\(^1\)

- RTI 36%
- UTI 7%
- SSTI 16%
- IAI 14%
- Other 5%
- Deep-seated 9%
- Unknown 9%
- Not documented 4%

Outpatient parenteral antimicrobial therapy (OPAT)

- Parenteral (i.v. or i.m.) antimicrobial administered on different days without an overnight hospital stay\(^1,2\)
  - If no oral agent available or appropriate
  - Assures absorption, compliance and rapid achievement of therapeutic concentrations

- Proven effectiveness in:\(^1\)
  - SSTIs
  - Osteomyelitis
  - Endocarditis
  - Meningitis

2. Buxton ILO. In: Goodman & Gilman’s The Pharmacological Basis of Therapeutics 11th edn. Brunton LL et al. (editors). 2006;1–39
Patient benefits of OPAT

- Quality of life\textsuperscript{1,2}
  - Family and familiar surroundings
  - Sleep and privacy
  - Nutrition, clothing
  - Mental health
- Increased education and training in self-care\textsuperscript{2}
- Lower out-of-pocket costs
- Return to their daily activities (work, school)\textsuperscript{1,2}
- Reduced risk of complicating infections and antimicrobial resistant organisms\textsuperscript{3}

Organisational Benefits of OPAT

- Efficiency in admissions
  - Avoided admission
  - Reduced length of stay
  - More effective use of resources
  - Impact on elective and acute work
- Lower rate of HCAI
- Specialists managing infection
- Financial savings relate to reimbursement / efficiencies
OPAT Evidence, Experience and Consensus

- OPAT, CoPAT since early 80s in USA
  - OPAT registry until c2002
- Hospital at the home in Australia (1990s-)
- O(H)PAT, NIPIV in Italy, UK, Netherlands, Austria developing 1990s-
  - UK consensus statement 1998
  - European consensus 2000
  - Good Practice Recommendations 2012

OPAT Evidence, Experience and Consensus

- **Standards** for infusion therapy, RCN 2005 and 2007
- Disease–specific *guidance* (Endocarditis)
- *Patient Group Directions* (UK, SSTI)
- 2 *RCTs*: 1999 and 2004 (SSTI, total 300 pts)
- *RCTs* of new antimicrobials includes OPAT Rx pts
- Hospital care at home *systematic review* (total 1327 patients) 2009

OPAT* in clinical trials: Complicated S. aureus bacteraemia

52% received OPAT (mean 14.9 days (1-49))

Proportion of patients, %

<table>
<thead>
<tr>
<th></th>
<th>MRSA</th>
<th>IE</th>
<th>Completed</th>
<th>Success</th>
<th>Deaths</th>
<th>Readmission</th>
<th>SAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPAT</td>
<td>36%</td>
<td>9%</td>
<td>90%</td>
<td>45%</td>
<td>56%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>IPAT</td>
<td>41%</td>
<td>19%</td>
<td>86%</td>
<td>47%</td>
<td>19%</td>
<td>18%</td>
<td>54%</td>
</tr>
</tbody>
</table>

***Daptomycin or vancomycin or semi-synthetic penicillin

Good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults in the UK: a consensus statement

1. OPAT team and service structure
2. Patient selection
3. Antimicrobial management and drug delivery
4. Monitoring of the patient during OPAT
5. Outcome monitoring and clinical governance
Good Practice Recommendations

• **Team** (doctor, infection specialist, nurse, pharmacist) with **Medical Lead**

• Agreed management plan and Clear documentation

• Inclusion/ exclusion criteria agreed
  – Infection-related and Patient suitability criteria

• **Initial assessment by a competent member of the OPAT team**

• Out of hours/ emergency plan agreed
Good Practice Recommendations

• The treatment should include choice and dose, frequency and duration. Should take into account flexibility based on clinical response.

• Antimicrobial choice within OPAT should be subject to review by the local antimicrobial stewardship programme.

• Weekly MDT/virtual ward round.

• SSTI should be reviewed daily by the OPAT team to optimize speed of intravenous to oral switch.
Antimicrobial Stewardship in OPAT

• Safe and appropriate use of antimicrobials
• DoH: “Start Smart Then Focus” specifies utilising OPAT to avoid/ reduce admission
• Appropriate use of IV therapy in OPAT
  – Antibiotics not a substitute for source control
  – Availability of oral alternatives
  – Most appropriate IV agent (spectrum)?
  – Antibiotic review:
    • Timely IV to oral switch
    • Duration of therapy / stop date
Antimicrobial Considerations in OPAT

• Is there an evidence base for the use of the agent for the condition (in OPAT)?
• Are there any specific safety or monitoring requirements?
• Is there a convenient ambulatory dosing regimen?
• The ideal OPAT agent is one that optimises outcome, minimises adverse events and is patient focussed with minimal inconvenience
Current Models of Care in UK

• Traditional: ID/ Micro led service
  – Focus on IP infection transitioning to ambulatory care e.g. Bone and joint/ device related

• Emerging:
  – Acute / Emergency Medicine
    • Focus on SSTI; admission avoidance
    • Hospital at home

  – Primary care led service
    • Usually referral from hospital specialists
    • Some SSTI pathways initiated in community
OPAT in MAU

• Ideally positioned to avoid admission

• General Medical skills and team work essential
  – Suitability for OP care
  – Co-morbidity and concomitant medication
  – Adverse events monitoring and recognition

• Mx of infections common to acute medicine
  – Cellulitis/ SSTI
  – Some UTI (ESBLs if no oral options)
  – Some OP Diabetic foot infection (importance of MD care)

• Complex infection Mx in conjunction with infection specialist
Glasgow OPAT service 2000-

• ID (GIM) led with team approach
  – Clinical Pharmacy
  – Weekly virtual ward round
  – Weekly clinic

• Nurse practitioner
  – Vetting/ assessment/ education
  – Line and logistics
  – Communication
  – IV access

• Clinical links/ referral pathway
• Prospectively maintained database
## Glasgow OPAT service 2000-2010

<table>
<thead>
<tr>
<th>Variable</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (years)</td>
<td>51 (13-95)</td>
</tr>
<tr>
<td>Referred from PC or ED</td>
<td>32.5%</td>
</tr>
<tr>
<td>Length of admission prior to OPAT</td>
<td>7.5 days (IQR, 2-17)</td>
</tr>
<tr>
<td>Clinic: Patient/carer administration</td>
<td>77% : 19%</td>
</tr>
<tr>
<td>Single use IV device</td>
<td>50%</td>
</tr>
</tbody>
</table>
Proportion of patients and duration of Rx

Episodes (n=2638) OPAT days (total= 39,038 days)

- **Other**: 22.8%, 24.5%, 52.7%
- **BJI**: 55.9%
- **SSTI**: 17.5%
Infections treated in the Glasgow OPAT service (2001-2011)
Antibiotic agents used for OPAT

Most frequently used antibiotic agents for OPAT (3183 episodes)

- Ceftriaxone: 57%
- Teicoplanin: 25%
- Other: 25%
Most common other agents (-Aug’12)
Relative frequency of first line antimicrobial agent use in Glasgow OPAT service.

SSTI = skin and soft tissue infection; BJI = bone and joint infection; CVS = cardiovascular system infections including endocarditis and intra-cardiac device infections; CNS = cardiovascular system infections; UTI = urinary tract infections; Abdo. Abscess = Intra-abdominal abscess including liver abscess.

Seaton and Barr, EJIM, 2013
# OPAT Outcomes 2001-2010

<table>
<thead>
<tr>
<th>Outcome</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure</td>
<td>1501 (67.2)</td>
</tr>
<tr>
<td>Improvement</td>
<td>562 (25.2)</td>
</tr>
<tr>
<td>No change</td>
<td>52 (2.3)</td>
</tr>
<tr>
<td>Deterioration</td>
<td>91 (4.1)</td>
</tr>
<tr>
<td>Death</td>
<td>8 (0.4)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>19 (0.9)</td>
</tr>
</tbody>
</table>

92.4% success
## OPAT Outcomes 2001-2010

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Number of events</th>
<th>Rate per 1000 OPAT days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Line-related infection</td>
<td>14 (0.6%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Other line-related complications</td>
<td>92 (4.1%)</td>
<td>2.8</td>
</tr>
<tr>
<td><em>Clostridium difficile</em> (within one month)</td>
<td>2 (0.1%)</td>
<td>0.05</td>
</tr>
<tr>
<td>ADR</td>
<td>219 (9.8%)</td>
<td>6.7</td>
</tr>
<tr>
<td>Unplanned readmission</td>
<td>201 (9.1%)</td>
<td>6.3</td>
</tr>
</tbody>
</table>
Reasons for admission from OPAT

- Deterioration in infection: 76
- Planned surgery: 63
- Adverse drug reaction: 38
- Other planned admission: 28
- Unplanned surgery: 20
- Line complication: 12
- Logistics/transport: 11
- Health care associated infection: 7
- Unrecorded reason: 7
Relative frequency of adverse drug reaction (ADR) types, in all first OPAT episodes over 10 year study period.

Note: An ADR in an individual patient in some instances involved multiple drug reaction types (e.g. rash and fever); each ADR type is counted separately in frequency bars even where they stem from one ADR event.
ADRs, Infection Type and AB Used
# Trends over 10 yrs

<table>
<thead>
<tr>
<th>Category</th>
<th>Trend over time</th>
<th>(X^2_{\text{trend}})</th>
<th>(p) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Referral from non-local hospital</td>
<td>(\uparrow)</td>
<td>(72.92)</td>
<td>(p &lt; 0.0001)</td>
</tr>
<tr>
<td>Referral from secondary care</td>
<td>(\uparrow)</td>
<td>(26.07)</td>
<td>(p &lt; 0.0001)</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td>(\uparrow)</td>
<td>(24.07)</td>
<td>(p &lt; 0.0001)</td>
</tr>
<tr>
<td>Non-SSTI infection</td>
<td>(\uparrow)</td>
<td>(97.14)</td>
<td>(p &lt; 0.0001)</td>
</tr>
<tr>
<td>MRSA infections (as % of (S.) aureus)</td>
<td>(\downarrow)</td>
<td>(6.682)</td>
<td>(p = 0.0097)</td>
</tr>
<tr>
<td>G-ve infections (% of +ve cultures)</td>
<td>(\uparrow)</td>
<td>(10.491)</td>
<td>(p = 0.0012)</td>
</tr>
<tr>
<td>Self / carer antibiotic admin</td>
<td>(\uparrow)</td>
<td>(48.49)</td>
<td>(p &lt; 0.0001)</td>
</tr>
</tbody>
</table>
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
Skin and Soft Tissue Infection
OPAT Patient Group Direction for SSTIs: empiric antibiotic Rx

- History of MRSA or Beta-lactam allergy?
  - Yes → Teicoplanin ▼ Clindamycin*
  - No → Ceftriaxone ▼ Clindamycin or Flucloxacillin

*If Beta-lactam allergy or sensitive MRSA
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
Factors Associated with OPAT Failure* in SSTI (n=963)

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>1.65 (1.10-2.47)</td>
<td>0.016</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.02 (1.12-3.67)</td>
<td>0.020</td>
</tr>
<tr>
<td>Teico vs Ceftriaxone</td>
<td>1.87 (1.05-3.33)</td>
<td>0.033</td>
</tr>
</tbody>
</table>

*Switch of antibiotic, progression of infection or readmission

Seaton RA et al, IJAA 2011
Bone and joint Infection

- Usually IP speciality referral
- Interventions/ surgery
- Microbiological Dx
- Usually G+ve
- Often 4-6 weeks IV Rx
Multivariate odds ratio of failing initial OPAT therapy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Odds Ratio</th>
<th>95% C. I.</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic foot infection</td>
<td>5.94</td>
<td>2.14-16.48</td>
<td>0.001</td>
</tr>
<tr>
<td>MRSA infection</td>
<td>3.30</td>
<td>1.15-9.46</td>
<td>0.026</td>
</tr>
<tr>
<td>CoNS/Diptheroids</td>
<td>4.53</td>
<td>1.18-17.47</td>
<td>0.028</td>
</tr>
<tr>
<td>80-89 yrs</td>
<td>5.32</td>
<td>1.41-20.11</td>
<td>0.014</td>
</tr>
</tbody>
</table>

Goodness of fit: log likelihood -66.5, r² 0.144 P=0.0004

Kaplan-Meier survival estimate of time to treatment failure for all patients per diagnosis

Endocarditis

- **Recommendations:**
  - Stabilisation as IP 2/52
  - Relative contraindications
  - IV Rx for 6wks

- **NHS GGC (n=80)**
  - 82.5% Left sided
  - 32.5% PVE
  - 18.8% Cardiac failure
  - 16.3% Emboli
  - 13.8% CKD
## Associations with “OPAT failure”

<table>
<thead>
<tr>
<th>Variable</th>
<th>Failed n=25 (31.3%)</th>
<th>Completed n=55 (68.7%)</th>
<th>Multivariate analysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>OR</td>
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<td></td>
<td></td>
<td></td>
<td>CI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P</td>
</tr>
<tr>
<td>Cardiac failure or CKD</td>
<td>14 (63.6%)</td>
<td>8 (36.4%)</td>
<td>7.39</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.8–29.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.005</td>
</tr>
<tr>
<td>Teicoplanin</td>
<td>12 (67.7%)</td>
<td>6 (33.3%)</td>
<td>8.69</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.0–37.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.004</td>
</tr>
<tr>
<td>Specialist referral</td>
<td>17 (25.8%)</td>
<td>49 (74.2%)</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.1–1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.068</td>
</tr>
</tbody>
</table>

*Logistic regression: stepwise backwards selection; factors retained in the model if \( P < 0.1 \).

\( \chi^2 = 30.3 \), full model \(-2\) log likelihood = 63.6, \( P < 0.0001 \)

Duncan et al, J Antimicrob Chemother, 2013
Conclusions (1)

- OPAT is safe and effective for a variety of infections in selected patients
  - General medical skills and team working are fundamental
  - Clinical Governance framework for safe practice is essential: Good Practice Recommendations
  - Outcome data may guide future management strategies: patient selection, agent choice
Conclusions (2)

• OPAT programmes must include infection specialists and engage with Antimicrobial Stewardship programme
  – Choice of agent
  – Appropriateness of IV route of administration
  – IVOST and duration of therapy
  – Guidance for complex infection

• Opportunities (necessity?) for development within ambulatory care services/ MAU
Acknowledgements

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