APPENDIX

Effectiveness and safety of a disposable elastomeric continuous infusion pump for outpatient parenteral antimicrobial therapy (OPAT) in a UK setting

**SUPPLEMENTARY DATA**

**Supplementary Table S1.** BSAC NORS Definitions of OPAT Outcomes.16

|  |  |
| --- | --- |
| **Infection outcomes** |  |
| Cure | Completed OPAT therapy +/- oral step down for defined duration with resolution of infection and no requirement for long term antibiotic therapy (usually relates to less severe infections e.g., SSTI, UTI unless prosthetic material removed). |
| Improved | i. Completed OPAT therapy +/- oral step down with partial resolution of infection but need for further follow up OR ii. Completed OPAT therapy but required escalation of antimicrobial therapy during OPAT (without admission) +/- oral step down with ultimate cure or partial improvement (as above) e.g., osteomyelitis, any infections where prosthetic material has not been removed. |
| Failure | Progression or non-response of infection despite OPAT, required admission, surgical intervention or died for any reason. |
| **OPAT outcomes** |  |
| Success | Completed therapy in OPAT with no change in antimicrobial agent, no adverse events, cure or improvement of infection and no readmission |
| Partial Success | Completed therapy in OPAT with either change in antimicrobial agent or adverse event not requiring admission |
| Failure of OPAT | Readmitted due to infection worsening or due to adverse event. Death due to any cause during OPAT |
| Indeterminate | Readmission due to unrelated event e.g., chest pain |

BSAC, British Society for Antimicrobial Chemotherapy; NORS; national outcomes registry system; OPAT, outpatient parenteral antimicrobial therapy; SSTI, skin and soft tissue infection; UTI, urinary tract infection.

**Supplementary Table S2.** Description of patient outcomes

|  |  |  |  |
| --- | --- | --- | --- |
| **Patient Outcome** | **Flucloxacillin** **(*n* = 131)** | **Piperacillin/tazobactam****(*n* = 301)** | **Total** **(*n* = 432)** |
| Cure | 5 (3.8) | 27 (9.0) | 32 (7.4) |
| Improved | 99 (75.6) | 233 (77.4) | 332 (76.9) |
| Failure | 27 (20.6) | 41 (13.6) | 68 (15.7) |
| Progression or non-response of infectiona  | 1 (0.8) | 1 (0.3) | 2 (0.5) |
| Death | - | 2 (0.7) | 2 (0.5) |
| Readmissionb | 26 (19.8) | 38 (12.6) | 64 (14.8) |
| Non-OPAT related | 8 (30.8)\* | 19 (50.0)\* | 27 (42.2)\* |
| Worsening of infection/no improvement | 8 (30.8)\* | 8 (21.1)\* | 16 (25.0)\* |
| New infectionc | 6 (23.1)\* | 4 (10.5)\* | 10 (15.6)\* |
| Vascular access related complications | 2 (7.7)\* | 4 (10.5)\* | 6 (9.4)\* |
| Adverse drug reaction  | 2 (7.7)\* | 3 (7.9)\* | 5 (7.8)\* |

Data are presented as *n* (%).

OPAT, outpatient parenteral antimicrobial therapy.

\* As a percentage of number of readmissions.

a Not requiring hospital readmission.

b Readmission resulting in early termination of OPAT therapy.

c New infection included bacteria pneumonia (*n* = 5), COVID-19 infection (*n* = 4) and urinary tract infection (*n* = 1).

**Supplementary Table S3.** Reasons for 30-day unplanned readmissiona (*n* = 117)

|  |  |  |  |
| --- | --- | --- | --- |
| **Reason for readmission** | **Flucloxacillin (*n* = 31)** | **Piperacillin/tazobactam (*n* = 86)** | **Total** **(*n* = 117)** |
| Non-OPAT related | 12 (38.7) | 37 (43.0) | 49 (41.9) |
| Worsening of existing infection/no improvementb | 8 (25.8) | 34 (39.5) | 42 (35.9) |
| New infection | 8 (25.8) | 7 (8.1) | 15 (12.8) |
| Vascular access-related complications | 2 (6.5) | 4 (4.7) | 6 (5.1) |
| Adverse drug reaction | 1 (3.2) | 4 (4.7) | 5 (4.3) |

Data are presented as *n* (%).

OPAT, outpatient parenteral antimicrobial therapy.

a Defined as unplanned inpatient admission for any reason during or within 30 days of OPAT discharge.

b Worsening infection by diagnosis: endocarditis (*n* = 1), discitis (*n* = 2), necrotising otitis externa (*n* = 3), prosthetic joint infection (*n* = 4), diabetic foot osteomyelitis (*n* = 6), and recurrent infective exacerbation of bronchiectasis/chronic obstructive pulmonary disease (*n* = 26).

**Supplementary Table S4.** Frequency of adverse events

|  |  |  |  |
| --- | --- | --- | --- |
| **Type of adverse event**a | **Flucloxacillin** | **Piperacillin/tazobactam** | **Total** |
| Major adverse event | 8 | 21 | 29 |
| Hospitalisation | 4 (50.0)b | 11 (52.4)b | 15 (51.7)b |
| Change in antimicrobial regimen(s) | 4 (50.0)b | 10 (47.6)b | 14 (48.3)b |
| Drug-related adverse event  | 8 | 25 | 33 |
| Drug Rash | 2 (25.0)c | 11 (44.0)c | 13 (39.4)c |
| Antibiotic induced diarrhoea | 2 (25.0)c | 8 (32.0)c | 10 (30.3)c |
| Blood dyscrasia | 2 (25.0)c | 3 (12.0)c | 5 (15.2)c |
| Hypokalaemia | - | 2 (8.0)c | 2 (6.1)c |
| Deranged liver function | 1 (12.5)c | 1 (4.0)c | 2 (6.1)c |
| Gastrointestinal disturbance | 1 (12.5)c | - | 1 (3.0)c |
| Vascular access-related adverse event | 16 | 32 | 48 |
| Line migration | 8 (50.0)d | 17 (53.1)d | 25 (52.1)d |
| Line occlusion | 6 (37.5)d | 11 (34.4)d | 17 (35.4)d |
| Allergy to dressing | - | 2 (6.3)d | 2 (4.2)d |
| Thrombus | 1 (6.3)d | 1 (3.1)d | 2 (4.2)d |
| Line infection | - | 1 (3.1)d | 1 (2.1)d |
| Damaged line | 1 (6.3)d | - | 1 (2.1)d |

Data are presented as *n* (%).

a Some patient-episodes had more than one adverse event.

b As a percentage of number of major adverse events

c As a percentage of number of drug-related adverse events

d As a percentage of number of vascular access related adverse events

**Supplementary Table S5.** Sensitivity analysis restricting the observed adverse event rates to the first OPAT encounter for each patient.

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **Flucloxacillin****(*n* = 121)** | **Piperacillin/tazobactam (*n* = 219)** | **Total****(*n* = 340)** |
| Incomplete infusiona | 42 (34.7) | 88 (40.2) | 130 (38.2) |
| OPAT-related adverse event | 22 (18.1) | 40 (18.3) | 62 (18.2) |
| Type of adverse eventb |  |  |  |
| Major adverse event, *n* (%); events per 1000 OPAT-days | 8 (6.6); 3.1/1000 days | 18 (8.2); 3.1/1000 days | 26 (7.6); 3.1/1000 days |
| Medication related, *n* (%); events per 1000 OPAT-days | 8 (6.6); 3.1/1000 days | 20 (9.1); 3.5/1000 days | 28 (8.2); 3.4/1000 days |
| Vascular access related, *n* (%); events per 1000 OPAT-days | 15 (12.4); 5.8/1000 days | 24 (11.0); 4.2/1000 days | 39 (11.5); 4.7/1000 days |
| Infection outcome |  |  |  |
| Cure and improved | 97 (80.2) | 186 (84.9) | 283 (83.2) |
| Failure | 24 (19.8) | 33 (15.1) | 57 (16.8) |
| 30-day unplanned hospitalisationc | 28 (23.1) | 64 (29.2) | 92 (27.1) |

Data are presented as *n* (%).

OPAT, outpatient parenteral antimicrobial therapy.

a Patient-episode who experienced at least one incident of incomplete infusion (emptying) of elastomeric device during course of OPAT.

b Some patient-episodes had more than one adverse event.

c Defined as unplanned inpatient admission for any reason during or within 30 days of OPAT discharge.

**STROBE Statement—checklist of items that should be included in reports of observational studies**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Item No. | Recommendation | Manuscript section |
| **Title and abstract** | 1 | (*a*) Indicate the study’s design with a commonly used term in the title or the abstract | Synopsis |
| (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | Synopsis |
| Introduction |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | Introduction |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | Introduction |
| Methods |
| Study design | 4 | Present key elements of study design early in the paper | Study design and setting |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Study design and setting, Data Collection |
| Participants | 6 | *(a) Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | Study design and setting |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | Outcomes and definitions, Supplementary Table S1 |
| Data sources/ measurement | 8 | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | Data Collection, Outcomes and definitions |
| Bias | 9 | Describe any efforts to address potential sources of bias | Outcomes and definitions |
| Study size | 10 | Explain how the study size was arrived at | Study design and setting |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | Statistical analysis |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | Statistical analysis |
| (*b*) Describe any methods used to examine subgroups and interactions | N/A  |
| (*c*) Explain how missing data were addressed | N/A (no missing data) |
| (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed | N/A (no loss to follow-up) |
| (*e*) Describe any sensitivity analyses | Statistical analysis |
| **Results** |  |  |  |
| Participants | 13 | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | Cohort characteristics |
| (b) Give reasons for non-participation at each stage | N/A |
| (c) Consider use of a flow diagram | N/A |
| Descriptive data | 14 | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | Cohort characteristics, Table 1 |
| (b) Indicate number of participants with missing data for each variable of interest | N/A |
| (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) | Cohort characteristics, Table 1 |
| Outcome data | 15 | *Cohort study*—Report numbers of outcome events or summary measures over time | Table 1, Supplementary Tables S2-S4 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | Clinical outcomes |
| (*b*) Report category boundaries when continuous variables were categorized | N/A (no such categorization done) |
| (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A – not relevant |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | Supplementary Table S5  |
| **Discussion** |  |  |  |
| Key results | 18 | Summarise key results with reference to study objectives | Discussion, first 6 paragraphs |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | Disscussion, 7th paragraph |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | Discussion, last paragraph |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | Disscussion, 7th and last paragraphs |
| Other information |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | Funding, Transparency declarations |

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.