Antimicrobial policies in the neonatal units of the United Kingdom and Republic of Ireland

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Objectives: To review antibiotic and antifungal policies in British and Irish neonatal units (NNUs).

Methods: A telephone survey was performed regarding empirical antimicrobial guidelines of NNUs in the UK and Republic of Ireland.

Results: The response rate was 91% (202 of 222 NNUs). The guidelines from all responding units covered group B Streptococcus and Escherichia coli, the most common causes of neonatal sepsis and meningitis. However, 19% did not cover Listeria, the cause of meningitis in 5% to 7% of cases in England and Wales. Second-line recommendations varied greatly between units, with widespread use of broad-spectrum agents. Fungal prophylaxis and treatment guidelines were generally rudimentary.

Conclusions: Empirical antimicrobial recommendations on many NNUs include broad-spectrum antibiotics without ensuring universal coverage of important pathogens. We raise concerns about the selection pressures exerted for resistant pathogens and invasive fungal disease, especially as few units specify fungal prophylaxis or treatment guidance. Development of rational guidelines for the UK and Irish neonatal units might help to optimize treatment while minimizing overuse of broad-spectrum agents.

Keywords: neonatal infection, antimicrobial agents, guidelines

Introduction

Antimicrobials are essential to help minimize mortality and morbidity from neonatal infection, yet judicious selection of agents is required if appropriate pathogen coverage is to be achieved without providing the selection pressure for antibiotic-resistant pathogens such as methicillin-resistant Staphylococcus aureus (MRSA) and fungi. Prompted by a fatal case of early onset neonatal listeriosis, we surveyed antimicrobial guidelines in all neonatal units (NNUs) in the UK and Republic of Ireland in order to evaluate current empirical recommendations. We report the first study to provide a snapshot of current antibiotic policies in British and Irish NNUs.

Methods

We carried out a telephone audit of all NNUs in the UK and Republic of Ireland between February 2006 and February 2007. Units were identified from The Directory of Critical Care (CMA Medical Data, 2005). Of the 229 units listed, 6 had closed and 1 was excluded because it was a highly specialized NNU without attached obstetric facilities. Consent was obtained from senior medical or nursing staff at each unit. A team member was asked to refer to their unit guidelines in order to report unit policy on empirical antimicrobial recommendations for specific clinical scenarios. Ethical approval was not sought as the study was a service evaluation not research.

Results

We obtained data from 202 of 222 NNUs in the UK and Republic of Ireland (91%).

The source of antimicrobial dosing was published guidelines (e.g. Children’s British National Formulary) in 69% of NNUs. The remainder used local guidelines, among which dosing varied widely, e.g. benzylpenicillin from 25 to 100 mg/kg/dose, twice to four times daily.

First-line policies for early onset (EO) sepsis

Sixty-nine per cent of NNUs (140) recommended benzylpenicillin and gentamicin. A penicillin was not included in the first-line
46% of NNUs (93), varied even more widely, with the most
widely but in over a quarter (28%, 56 units), this was a broad-
biotics regimen for LO sepsis (180); recommendations varied
Eighty-nine per cent of NNUs stated an empirical first-line anti-
porin plus a penicillin plus an aminoglycoside).

Late onset (LO) sepsis

Empirical second-line policies for LO sepsis, reported from
46% of NNUs (93), varied even more widely, with the most
common regimen (cefotaxime and vancomycin) accounting for
only 8% and other recommendations including meropenem, tei-
coplanin, piperacillin/tazobactam and aztreonam.

Line-related infections

Over one-third of the NNU policies (37%; 74 units) specified
alternative antibiotics first-line for septic episodes where central
venous catheters were in situ, most commonly vancomycin
(21%) or teicoplanin (12%).

Antifungal recommendations

Guidance for use of antifungal prophylaxis was specified in only
one-third of NNUs (32%; 64), but twice as many specified indi-
cations for antifungal treatment (65%; 131). Fluconazole and
ampoterinic were recommended equally (66 and 65 U,
respectively).

Discussion

Rational antibiotic policies for neonatal sepsis should cover the
common and important pathogens, ideally guided by local,
regional and national epidemiology, but British and Irish NNUs
currently lack systematic neonatal infection surveillance. In the
absence of this evidence base, we have examined units’ anti-
microbial recommendations on the grounds that such policies are
in place to direct empirical antimicrobial prescribing. To our
knowledge, this study provides the first snapshot of current anti-
microbial policies in UK and Irish NNUs.

While it is reassuring that empirical recommendations universal-
ly cover for group B Streptococcus (the commonest cause of
neonatal septicaemia and meningitis) and susceptible strains of
Escherichia coli, 1 in 10 NNUs do not cover the rarer but
important pathogen L. monocytogenes when treating neonatal
septicaemia empirically, and almost 1 in 5 (19%) do not cover
for this organism when empirically treating neonatal meningitis.
This is concerning in the light of the most recent data indicating
that L. monocytogenes causes 5% to 7% of neonatal meningitis
cases, and data on neonatal meningitis in England and Wales
10 years apart (1985–87 and 1996–97) show little change in
the bacterial causes of neonatal meningitis.

In the UK as elsewhere, the rising incidence of MRSA in the
paediatric population is centred largely in NNUs, and the
experience of widespread MRSA infections in Japanese NNUs
in the late 1980s is attributed in part to the overuse of broad-
spectrum antibiotics. Use of third-generation cephalosporins is
also associated with invasive fungal infections from which mor-
tality is high. We therefore question the appropriateness of
recommending broad-spectrum antibiotics such as cephalospor-
ins widely. The reasons behind individual antibiotic policies
were outside the scope of this study but, anecdotally, many units
use third-generation cephalosporins because of real or perceived
problems with aminoglycosides, including difficulties in obtain-
ing timely drug-level results. National neonatal guidelines pro-
moting the use of narrower spectrum antibiotics might
encourage hospitals to provide therapeutic drug monitoring ser-
dices routinely to NNUs. In addition, the need for therapeutic
drug monitoring would be minimized by adherence to policies
regarding the prompt cessation of antibiotics when cultures fail

Table 1. First-line antibiotic recommendations for early onset sepsis

<table>
<thead>
<tr>
<th>Antibiotic regimen</th>
<th>Number of units (n = 202)</th>
<th>Percentage of units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzylpenicillin and gentamicin</td>
<td>140</td>
<td>69</td>
</tr>
<tr>
<td>Cefotaxime monotherapy</td>
<td>17</td>
<td>8</td>
</tr>
<tr>
<td>Ampicillin/amoxicillin and benzylpenicillin</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Cefotaxime and benzylpenicillin</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Benzylpenicillin monotherapya</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Ampicillin/amoxicillin and cefotaxime</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Cefuroxime and benzylpenicillin</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Cephalosporin monotherapy</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>No formal policy</td>
<td>1</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

*Two of these units advise addition of gentamicin for specific risk factors.

Of 75% of NNU policies (151) that advised empirical change of
antibiotics for cases that failed to respond to first-line therapy,
49% (74) recommended cephalosporins second-line and 18%
(27) recommended vancomycin.

Empirical antibiotic therapy for suspected meningitis

Nearly half of the NNU’s empirical meningitis regimens included a cephalosporin (45%, 90), while a fifth did not use a
penicillin-containing regimen (19%, 39). In 12% (25), the
cephalosporin was monotherapy. A triple combination for sus-
pected meningitis was advised in 5% (11) of NNUs (a cephalos-
porin plus a penicillin plus an aminoglycoside).

Late onset (LO) sepsis

Eighty-nine per cent of NNUs stated an empirical first-line anti-
biotics regimen for LO sepsis (180); recommendations varied
widely but in over a quarter (28%, 56 units), this was a broad-
spectrum antibiotic (e.g. cefalosporin).

Empirical second-line policies for LO sepsis, reported from
46% of NNUs (93), varied even more widely, with the most
common regimen (cefotaxime and vancomycin) accounting for
only 8% and other recommendations including meropenem, tei-
coplanin, piperacillin/tazobactam and aztreonam.

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to grow pathogens (as monitoring is not required routinely until aminoglycosides are used for >48 h). Commonly recommending vancomycin for LO and line-related sepsis is also questioned given the high incidence but low morbidity and mortality from coagulase-negative *Staphylococcus* sepsis. We support the assertion from a Canadian study that vancomycin could be reserved for episodes in which the implicated organism is confirmed to be resistant to penicillins.

We propose the development of guidelines for empirical treatment of common and important neonatal infections to promote narrower spectrum antibiotic regimens such as an aminoglycoside combined with benzylpenicillin for EO neonatal sepsis, or with flucloxacillin or amoxicillin for LO sepsis. Recommendations for prophylaxis and treatment of neonatal fungaemia would further assist in managing high-risk neonates. Guidelines underpinned by epidemiological data gathered by active, neonatologist-led, systematic neonatal infection surveillance should overcome the problems of knowledge and application of antibiotic policies that have been experienced elsewhere. Future studies would usefully evaluate actual practice and adherence to recommendations of antimicrobial choice and duration, particularly in the context of negative versus positive culture results and epidemiology.

**Acknowledgements**

Our thanks are extended to Drs Mercedes A. Munteanu, Shahinul I. Khan and Sarah Wilson for assistance in data collection. We also thank all the participating neonatal units.

**Funding**

None to declare.

**Transparency declarations**

None to declare.

**References**


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