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ORIGINAL ARTICLE

Missed opportunities for antimicrobial stewardship in pre-school children admitted to hospital with lower respiratory tract infection

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Aim: To describe the usage of multiplex polymerase chain reaction on nasopharyngeal swab (NPS) samples in pre-school children presenting with lower respiratory tract infection (LRTI) at Christchurch Hospital, and its impact on the use of antibiotics empirically and at discharge.

Methods: This retrospective cohort study included 237 children, ages 3 months to 5 years, admitted to hospital during the winter months of 2012–2015 with a diagnosis of community-acquired LRTI. Children were identified by discharge coding and their notes reviewed.

Results: A significantly larger proportion of children who had a NPS sample taken (42/146, 36%) received no empiric antibiotics compared with children who did not have a sample taken (7/91, 7.7%, $P < 0.001$). Of those who did have a NPS sample taken 17 of 146 (11.6%) had their antibiotics discontinued prior to or at the time of discharge compared with only 3 of 91 (3.3%) of those who did not have a NPS sample ($P < 0.025$). Children with influenza detected were more likely to receive no antibiotics or have their antibiotics discontinued prior to or at discharge. Only a small proportion of children with other viruses identified had their antibiotics discontinued.

Conclusions: It appears that clinicians were generally reluctant to stop antibiotics prior to discharge in young children with LRTI in whom influenza or other viruses were identified. In our view, it makes sense to stop antibiotics when the clinical presentation and NPS testing is consistent with a viral aetiology. Not stopping antibiotics at or before discharge in these children represents a missed opportunity for antimicrobial stewardship.

Key words: antimicrobial stewardship; lower respiratory tract infection.

What is already known on this topic

1 Viruses are responsible for the great majority of pre-school lower respiratory tract infection (LRTI).
2 Respiratory syncytial virus is the most common virus causing LRTI in hospitalised pre-school children.
3 Pre-school children have the highest rates of hospitalisation due to influenza-related respiratory disease in New Zealand.

What this paper adds

1 In our hospital, a higher proportion of children have antibiotics discontinued when influenza is identified on a nasopharyngeal swab compared with other viruses.
2 A high proportion of pre-school children admitted with LRTI have antibiotics continued beyond discharge even when a viral aetiology is highly likely.
3 94% of children presenting with LRTI who had an NPS sample taken had at least one viral pathogen identified.

The development of multiplex polymerase chain reaction (PCR) assays have allowed clinicians to identify a large range of viruses and other pathogens in children with lower respiratory tract infection (LRTI). One or more viruses were identified in 66% of children admitted to hospital with radiologically proven LRTI in a recent study in the USA, with respiratory syncytial virus (RSV) most commonly detected.[1]

Interpretation of PCR results from nasopharyngeal samples can be challenging, however, as viruses can frequently be identified in the upper airways of asymptomatic children.[2]

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The 2011 Infectious Diseases Society of America (IDSA) guidelines for the management of community-acquired pneumonia (CAP) in children[3] have recommended that 'antimicrobial therapy is not routinely required for pre-school aged children with CAP, because viral pathogens are responsible for the great majority of clinical disease'. In addition, they state that 'antibacterial therapy is not necessary for children, either outpatients or inpatients, with a positive test for influenza virus in the absence of clinical, laboratory, or radiological findings that suggest bacterial coinfection'. In New Zealand, pre-school children have been shown to have highest rates of hospitalisation due to influenza-related respiratory disease.[4]

This study aimed to describe the usage of multiplex PCR on nasopharyngeal swab (NPS) samples in children presenting with LRTI during the winter months in our hospital, with particular emphasis on its impact on the use of antibiotics empirically and at discharge.

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Methods

Christchurch Hospital is the largest hospital in the South Island of New Zealand, providing tertiary level paediatric care for most sub-specialties. Children from the community with LRTI may be admitted under the care of a General Pediatrician, after either being referred by their General Practitioner or through the Emergency Department. First-line antibiotics in our department for community-acquired LRTI in children <5 years of age are either oral amoxycillin or intravenous penicillin.

All children aged 3 months to 5 years admitted to hospital during the winter months (June/July/August) of 2012–2015 with a diagnosis of community-acquired LRTI were included in this study. Children were identified by discharge coding (ICD-10 codes J12–J18) and the discharge letter on each patient was reviewed to confirm the diagnosis. Radiological confirmation was not required.

During the winter months, PCR respiratory virus testing is available daily, including weekends. For samples arriving in the laboratory in the morning, a result was generally available by 4 pm. Canterbury Health Laboratories uses the Fast-track Diagnostics Kit multiplex PCR[5] which tests for the following organisms: adenovirus, bocavirus, coronaviruses 229E, OC43, HKU1 and NL63, human metapneumovirus (hMPV), influenza viruses A and B, parainfluenza viruses 1–4, picornavirus, RSV and mycoplasma pneumoniae.

For the purposes of this study, children with multiple viruses detected were classified firstly according to whether they had influenza or not, as this is the only virus infection with treatment available. Then those without influenza were categorised as per Rhedin *et al.*[2] as having either RSV/hMPV/parainfluenza or rhinovirus/bocavirus/coronavirus as their primary infection in that order of preference.

No minimum length of stay was specified, so children evaluated and discharged on the same day were included in the analysis. Length of stay was calculated in days. Children coded as bronchiolitis or with a clinical description fitting bronchiolitis in their notes were excluded, along with children who were immunocompromised or had cystic fibrosis. Readmissions that occurred within 2 weeks of a previous admission for LRTI were excluded.

Clinical notes and laboratory records were reviewed on each child to determine the treatment and investigations each child received. The use of empiric antibiotics was recorded, as well as whether antibiotics were stopped at discharge or continued in the community. The total length of antibiotics prescribed for individual children at discharge was not able to be determined.

Contingency table analysis was used to compare the proportions of children with specific outcomes. A χ^2 test with a probability value of <0.05 was considered statistically significant.

Results

Two hundred and thirty-seven pre-school children with LRTI were admitted in the winter months of 2012–2015. The average length of stay was 1.6 days with 188 of 237 (79.3%) in hospital for 2 days or less. The mean age of the children was 26 months, 67% of children were New Zealand European, 11% Maori and 9% of Pacific Island decent.

An NPS sample was obtained on admission in 146 (62%) children as part of their initial investigations. At least one pathogen was detected by multiplex PCR testing in 137 (94%), 68 children had either Influenza A or B detected and 60 had one of either RSV/hMPV/parainfluenza virus.

A significantly larger proportion of children who had an NPS sample taken (42/146, 36%) received no empiric antibiotics compared to children who did not have a sample taken (7/91, 7.7%, $P < 0.001$). Of those who did have an NPS sample taken 17 of 146 (11.6%) had their antibiotics discontinued prior to or at the time of discharge compared with only 3 of 91 (3.3%) of those who did not have an NPS sample ($P < 0.025$).

Table 1 shows the antimicrobial management used in the children who had an NPS in relation to the NPS results. Children with influenza detected were more likely to be treated with oseltamivir but were also more likely to receive no antibiotics or have their antibiotics discontinued prior to or at discharge. Only a small proportion of children with other viruses identified had their antibiotics discontinued.

In total, 145 children (61%) had an admission lasting >12 h. Of this subgroup, 104 (71%) had an NPS sample taken compared with only 41 (29%) of those children admitted for a shorter time period. Only 12% of children who did not have an NPS received no antibiotics on admission compared with 44% of those who had an NPS on admission ($P = < 0.003$).

No children during the study months were readmitted following discharge with LRTI.

Discussion

Children in our hospital admitted with community-acquired LRTI commonly have a NPS sample taken. In this study, those who subsequently had influenza identified were significantly more likely to not receive antibiotics or have their antibiotics stopped

Table 1 Pathogen detection and antimicrobial management in relation to nasopharyngeal swab results

Pathogen	Full course†	Initiated then discontinued	Oseltamivir prescribed	None	Grand total
Influenza A/B	16	10	11‡	31	68
RSV/hMPV/parainfluenza	43	5	2	10	60
mycoplasma pneumoniae	2			1	3
Rhinovirus/bocavirus/coronavirus	5	1			6
None	7	1	1		9
Grand total	73	17	14	42	146

†Antibiotics continued beyond discharge from hospital. ‡One child received a full course of antibiotics and oseltamavir and was included in the 'Full course' category and not the oseltamivir category. hMPV, human metapneumovirus; RSV, respiratory syncytial virus.

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prior to discharge. However, a substantial proportion continued with antibiotics even if influenza was identified. It also appears that clinicians were reluctant to stop antibiotics prior to discharge in children in whom other viruses were identified, even when these provide a plausible aetiological explanation for the child's LRTI. In our view, these represent missed opportunities for antimicrobial stewardship and many children are receiving courses of antibiotics that are too long.

Rhedin *et al.*[2] recently reported that in children with acute respiratory tract infection hMPV, parainfluenza viruses and RSV were highly over-represented in children with respiratory tract symptoms compared with asymptomatic controls, suggesting that in a child with compatable symptoms and signs they are likely to be the cause of the LRTI. This association is less certain for other viruses such as human rhinovirus, adenoviruses, human bocavirus and human coronaviruses. In our population, children with RSV, hMPV or parainfluenza viruses almost uniformly had antibiotics continued beyond 5 days.

Overall, the proportion of children in our population who had antibiotics stopped following receipt of the multiplex PCR testing results was low (11.6%). A NPS in a pre-school child is an invasive test, and performing a multiplex PCR routinely for such a common clinical presentations may be expensive. The benefits include a better understanding of the changes in prevalence of particular viruses in LRTI in the community, the ability to provide more definitive information for the parents on the aetiology of the child's infection and the potential to reduce the amount of antibiotics children receive. In our hospital, obtaining a NPS sample is adding valuable information for clinicians but is not being used effectively for antimicrobial stewardship.

There is evidence to suggest that in pre-school children viruses are important in the aetiology of the majority of LRTIs.[6–8] The IDSA guidelines clearly try to direct clinicians away from using antibiotics empirically in this population. Many clinicians may feel uncomfortable not prescribing antibiotics in children with LRTI, particularly those severe enough to need hospitalisation, and start empiric antibiotics routinely. Diagnostic tests for bacterial infections of the lower respiratory tract are limited and insensitive in young children which may contribute to this practice. However, it makes sense to stop antibiotics when the clinical presentation is consistent with infection by a virus identified on NPS sample.

In this study, a multiplex PCR was used for the detection of all the pathogens. No other rapid point-of-care testing for influenza was used. There would have been no differences in the turnaround time for results to explain the discrepancy between the rates of antibiotic prescribing between children with influenza and other pathogens. The proportion of children for whom the PCR test result was available prior to discharge is unknown so it is difficult to know if this contributed to the ongoing use of antibiotics following discharge. Ensuring NPS results are available rapidly will be an essential part of any antimicrobial stewardship programme.

The retrospective nature of this study meant we were unable to determine the decision making processes involved in each prescription of empiric antibiotics. Equally decisions around stopping antibiotics are seldom documented adequately. It is possible that aspects such as clinician preference and beliefs may have contributed significantly to the outcomes but this is beyond the scope of a study like this to determine.

Conclusion

Effective antimicrobial stewardship involves not only choosing appropriate antibiotics but also ensuring that antibiotics are stopped when they are not required. We have identified a cohort of children with significant respiratory disease in whom molecular diagnostic techniques are frequently being used to diagnose viral infection. In our hospital, the introduction of this routine diagnostic paradigm has unfortunately not been accompanied by a change in clinical practice to include the early cessation of antibiotics. The next challenge is to educate the clinicians to encourage them to stop antibiotics early in pre-school children with LRTI where a clinically compatable viral pathogen has been detected.

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