

SHORT COMMUNICATION

Respiratory viral infections are not uncommon in neonatal intensive care units

A-M Kujari (anna-maija.kujari@utu.fi)¹, M Waris², L Lehtonen¹, O Ruuskanen¹

1. Department of Paediatrics, Turku University Hospital, Turku, Finland

2. Department of Virology, University of Turku, Turku, Finland

Correspondence

A-M Kujari, Department of Paediatrics, Turku University Hospital, FIN-20520 Turku, Finland.
Tel: +358 400 784160|
Fax +358 2 3131460|
Email: anna-maija.kujari@utu.fi

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Full-term and preterm infants admitted to neonatal intensive care units (NICUs) face a high risk of infections, due to the immaturity of their innate and adoptive immune systems, inadequate protection through maternal immunity and the need for repeated invasive procedures (1). In recent years, our knowledge of viral infections in neonates has increased, due to multiplex polymerase chain reaction (PCR)-based techniques. It is now possible to screen for as many as 17 viruses from a single mucus sample (2). However, the role of viral respiratory tract infections in the symptoms of infants admitted to NICUs at birth is still poorly understood.

In a recent review, 32 respiratory viral outbreaks in NICUs were reported (3). These were caused by several different respiratory viruses, including respiratory syncytial virus (RSV) (89 patients in 11 outbreaks), enteroviruses (101 patients in 10 outbreaks) and adenovirus (79 patients in six outbreaks). In addition, outbreaks of coronavirus, rhinovirus, influenza A virus and parainfluenza virus infections have been reported (4–7). An epidemic may result in the temporary closure of a NICU. Recently, a NICU was closed for 28 days after adenovirus type 19 caused an outbreak of keratoconjunctivitis, which affected 12 NICU infants, two NICU staff members, two relatives of patients and two members of the ophthalmologic team (8).

We report on an observational study on the use of a multiplex PCR in a NICU in Finland. The study was carried out at Turku University Hospital, the only tertiary level NICU in south-west Finland, which serves a population of about 750 000. An average of 600–700 infants are admitted to the NICU annually, resulting in approximately 6000 patient care days per year. About one-third of the infants are preterm, and 50–85 very low birth weight infants are

treated annually. Two to four patients are treated in one room. Parents are encouraged to stay with their infant and provided with unlimited access. Visitors with respiratory tract infection symptoms are not allowed into the NICU, and siblings under school age cannot visit if there is an RSV outbreak in the community. Otherwise, healthy siblings are allowed access.

During the study period from 1 January 2009 to 30 June 2011, 1589 infants were admitted to the unit and 76 (5%) were evaluated for respiratory viruses. A nasopharyngeal aspirate was taken from infants if they presented with symptoms of respiratory infection, such as rhinorrhoea, sneezing, increased bronchial secretions, episodes of bradycardia and/or desaturations, or if they had been exposed to someone with a respiratory infection. We collected and analysed 139 samples from 76 infants for this study. Nasopharyngeal aspirates were collected in sterile tubes and analysed on the same or following day. Nucleic acids were extracted from the aspirates using Nuclisense easyMag extractor (Biomérieux, Boxtel, the Netherlands). Respiratory virus genomes were detected using Seeplex RV12 multiplex PCR assay for adenovirus, influenza A and B viruses, parainfluenza types 1–3 viruses, RSVa, RSVb, rhinovirus, human metapneumovirus, and coronaviruses 229E/NL63 and OC43/HKU1 (Seegene, Seoul, Korea). In addition, specimens were tested in a real-time PCR assay for enteroviruses, rhinovirus and RSV (9).

During the two-and-a-half-year study period, no outbreaks of viral respiratory tract infection occurred in the NICU. Of the 139 samples taken from 76 infants, 28 samples (20%) from 15 infants (20%) were positive for one or more viruses. Six babies were positive for rhinovirus, five for parainfluenza type 3 virus, one for parainfluenza type 2

Table 1 Clinical characteristics of 14 neonates with confirmed respiratory virus infections

Patient/sex	Gestational age, weeks	Birth weight, g	Virus (log ₁₀ copies/mL)*	Age at infection, weeks	Symptoms	CPAP, weeks	Mechanical ventilation, weeks	Duration of symptoms, days	Miscellaneous
1/M	26 + 5	925	Rhinovirus (10.2)	8	Rhinorrhoea, desaturation	9	2	ND	Virus shedding 2 weeks
2/F	27 + 0	900	Rhinovirus (8.6)	15	Rhinorrhoea	6	4	4	Virus shedding 5 weeks
3/M	29 + 6	1440	Rhinovirus (8.4)	3.5	Congestion, desaturation	5	0.5	4	Neutropenia, IVGG, virus shedding 2 weeks
4/M	30 + 1	2110	Rhinovirus, RSVa, coronavirus	6.5	Bronchial secretion	4	No	2	Interstitial pulmonary disease
5/M	30 + 4	1540	Rhinovirus*	2	Bronchial secretion	2.5	No	1	Hirschsprung disease
6/F	30 + 5	1135	Parainfluenza type 3 virus	3.5	Bronchial secretion	2.5	No	8	
7/M	31 + 3	1315	Parainfluenza type 3 virus	1.5	Congestion	1	No	3	
8/F	31 + 5	1480	Parainfluenza type 2 virus	3	Sneezing, congestion	0.5	No	3	
9/M	32 + 0	1540	Rhinovirus (8.9)	17	Bronchial secretion	No	28	10	BPD, pulmonary hypertension
10/M	32 + 1	1210	Parainfluenza type 3 virus	5	Pneumonia, pleural effusion	No	56	10	Diaphragmatic hernia, anomalies
11/F	32 + 3	985	RSVb	4	Congestion	0.5	No	4	
12/F	32 + 4	1880	Parainfluenza type 3 virus	1	Congestion	0.5	No	2	
13/F	37 + 0	3700	Parainfluenza type 2 virus	2	Rhinorrhoea, congestion	No	No	1	
14/M	40 + 3	4095	Rhinovirus (11.6)	0.5	Rhinorrhoea	No	No	3	Parents had upper respiratory infection

CPAP, Continuous positive airway pressure; RSV, Respiratory syncytial virus; ND, Not defined; IVGG, Intravenous gammaglobulin; BPD, Bronchopulmonary dysplasia. *Copy number was determined when the specimen was positive for rhinovirus by real-time PCR.

virus and one for RSVb. One infant presenting with congestion was simultaneously positive for rhinovirus, coronavirus and RSVa. Another with rhinorrhoea tested positive for parainfluenza type 2 virus on the first day of symptoms, borderline positive for coronavirus 5 days later and parainfluenza type 3 virus on three consecutive screenings during the next 11 days, after the mild symptoms had completely subsided. One child remained positive for rhinovirus for 5 weeks, until discharge.

Fourteen of these 15 virus-positive infants had rhinorrhoea or increased bronchial secretions, and one was asymptomatic. The clinical characteristics of the 14 symptomatic patients are summarised in Table 1. Two were full-term infants: one rhinovirus-positive infant was born to parents experiencing clear signs of the common cold, and another parainfluenza type 2 virus-positive infant was admitted to the NICU on the third day of life due to dehydration and feeding problems. All 12 preterm infants (gestational ages 26–32 weeks and birth weights from 900 to 2110 grams) had required ventilatory support at birth, ranging from brief nasal continuous positive airway pressure to prolonged mechanical ventilation. At the time of the respiratory infection, the chronological age of the preterm infants was one to 17 weeks. Five infants had twin siblings, none of whom experienced symptoms of respiratory infection. No infants died of a viral respiratory tract infection, and most made a prompt recovery. One child with diaphragmatic

hernia, hypoplastic lungs and several congenital anomalies developed severe pneumonia with pleural effusions in conjunction with parainfluenza type 3 virus infection. He needed mechanical ventilation throughout his life and died at the age of 13 months from causes unrelated to his past respiratory infection.

Of the 61 infants with negative PCR tests, 35 presented with rhinorrhoea, nine with lower respiratory symptoms and nine with symptoms of septicaemia. Five were screened because of contact with a family member with a respiratory infection, namely three mothers and two twin siblings.

Five previous studies discussed how PCR was used to detect respiratory viruses in premature or full-term infants during their hospital stay after birth (2,10–13). Van Piggelen et al. (10) studied 62 infants presenting with signs of respiratory infection and found respiratory viruses in 41% of the cases, with rhinovirus (n = 11) and RSV (n = 8) being the most common viruses. All infants with rhinovirus infections recovered, but four patients subsequently developed recurrent lower respiratory tract infections. Steiner et al. (11) studied 106 symptomatic infants and detected respiratory viruses in 16% of the cases, with rhinovirus (n = 16) being the most common virus. The clustering of rhinovirus infections in this study suggested a major role for nosocomial transmission. Rhinovirus shedding lasted up to 44 days (mean 19 days) potentially contributing to nosocomial transmission. Kiszun et al. (13) studied 60 patients

with suspected bacterial sepsis in the NICU. A respiratory viral infection was detected in six cases, with one RSV and five picornaviruses. Bennett et al. (2) described the viral screening of all 50 prematurely born infants admitted to two NICUs over a 12-month period. The infants were screened regularly, twice weekly. Interestingly, 52% of the infants tested positive (66 of 708 specimens) and 28% of the positive swabs included more than one virus. The most common viruses were RSV (n = 20), parainfluenza viruses (n = 15) and human metapneumovirus (n = 9). The presence of a virus was significantly associated with a prolonged need for ventilatory support and longer hospitalisation. On the other hand, 30% of the premature infants who tested positive for a virus did not show any deterioration, leaving their respiratory virus infection clinically unrecognised. There was a higher rate of bronchopulmonary dysplasia in the virus-positive population. Smit et al. (12) detected respiratory viruses in 334 neonates admitted to a neonatal medium care unit. A virus was found in 10% of the newborns, most commonly parainfluenza viruses (n = 15), rhinovirus (n = 7) and RSV (n = 6). Older age and rhinorrhoea contributed to the detection of a virus. It is of note that neonates with higher viral copy numbers were clinically ill more often than those with lower copy numbers.

Our observations suggest that viral respiratory tract infections are not uncommon in NICUs. However, in contrast to three earlier studies (2,11,12), community epidemics did not spread into our NICU during the study period. During the H1N1 pandemic and seasonal influenza epidemics, no cases of influenza were detected, and there was only one case of RSV during the two-and-a-half-year follow-up period. No outbreaks of viral respiratory tract infections occurred. During our previous 10-year follow-up using antigen detection from nasopharyngeal aspirate, we recorded two outbreaks of parainfluenza virus infections. In 2000, there were five cases of parainfluenza type 3 virus infection, and in 2004, there were five cases of parainfluenza types 1-3 virus infection within 12 days (unpublished observations). Careful hygiene and restricting visitors who displayed symptoms of viral infections seem to be sufficiently effective in controlling the viral spread into our NICU.

Our study has some limitations. It was an observational retrospective study, and all infants who deteriorated were not included. No attempts were made to find the index cases. Furthermore, it is well known that multiplex PCR tests are not as sensitive as PCR tests that aim to detect a single virus (14). Also, recent evidence indicates that the use of nasal swabs is comparable with, or even superior to, nasopharyngeal aspirate, both in terms of specimen quality and patient comfort (15). With increasing sensitivity, very low copy numbers yield positive results, but the clinical relevance of these results remains unclear. In the case of the rhinovirus, viral shedding can persist for several weeks after the clinical disease has resolved (11,16).

In conclusion, our observations, and those of others, suggest that infants in neonatal units should be evaluated for respiratory viruses if they present with respiratory

symptoms or deterioration. Simple flocked nasal swabs are recommended as well as multiplex PCR for screening. Unfortunately, opportunities to use specific antivirals are currently limited. Infection control measures should be implemented to avoid transmission. Virus-positive patients should be strictly isolated and cared for by nurses who are not responsible for the care of babies without the virus. It is advisable to monitor the duration of virus shedding, although it is unclear how contagious asymptomatic virus-positive patients are. The role that family and staff members play in transmission still needs to be studied.

COMPETING INTERESTS

The authors have no competing interests to report.

FINANCIAL DISCLOSURE

None.

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