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Viral Infections in a Neonatal Intensive Care Unit

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Abstract

Background and aims: The incidence of neonatal viral infections is probably underestimated. Our objective was to assess the incidence of viral infections among hospitalized infants in a level III neonatal intensive care unit, the associated clinical manifestations and outcome.

Material and methods: We conducted an observational retrospective study of patients admitted to the neonatal intensive care unit over a ten year period (2000-2009), analyzing data of patients with laboratory confirmed viral infection.

Results: A viral infection was diagnosed in 1.7% (n=68) of infants admitted to the NICU: 32.3% respiratory syncytial virus, 17.9% metapneumovirus, 17.9% influenza H1N1 and 13.4% cytomegalovirus. Other less found virus were rotavirus, adenovirus, enterovirus, parainfluenza, herpes simplex and varicella zoster. The medium length of stay was 30 days and most infants were not inborn. In the inborn infants the most common virus were influenza H1N1, cytomegalovirus and metapneumovirus. In 48.5% these infections occurred in preterm. The overall mortality was 4.5%.

Conclusion: In our study the respiratory infections were the most common viral infections and the overall mortality was not negligible. It's our responsibility to prevent viral infections, as well as help in their early detection and treatment.

Keywords: NICU; Viral infection

Introduction

The incidence of viral infections in patients treated in the neonatal intensive care unit (NICU) is not well-known. Some studies suggest an incidence between 1-5.7% [1,2]. This incidence is probably underestimated because viral studies are not routinely obtained in neonates [3]. Many viral diseases in NICU infants are undiagnosed or appreciated only late in the course of a disease. This happens because of subtle or asymptomatic presentation, confusion with bacterial disease, and failure to consider viral disease. There are not many publications on this theme, with the majority reporting outbreaks of viral infections in NICUs [4-6] that certainly do not reflect the real impact of these infections. Our objective was to assess the incidence of viral infections among hospitalized infants in a level III neonatal intensive care unit, the associated clinical manifestations and outcome. If applicable, we analyzed the pharmacologic agents used for prophylaxis and treatment of such diseases.

Materials and Methods

We conducted an observational retrospective study of patients admitted to the NCIU over a ten year period (from January 1st 2000 to December 31st 2009). We analyzed clinical records data of those with laboratory confirmed viral infection obtained by polymerase chain reaction and/or viral culture. All the cases interpreted as contaminants were excluded. The statistical analysis was made with SPSS® statistics 18.

Results

General data: A viral infection was diagnosed in 68 (1.7%) of 3907 infants admitted to the NICU, 50% (n=34) for each gender. The mean age at admission was 4.7 ± 3.5 days. The medium length of stay (MLS) was 30 days (minimum 5, maximum 107 days) and in 57.4% (n=39) of cases the infants were admitted from their home or another hospital. The viral infection was the cause of admition in 24 (35.3%) infants; all others were already hospitalized for other reason when a viral infection was diagnosed (Table 1).

Pathogens: Twenty two (32.3%) had a respiratory syncytial virus (RSV) infection, 12 (17.6%) a metapneumovirus infection, 12 (17.6%) an influenza virus infection and 9 (13.2%) a cytomegalovirus (CMV) infection. Also identified infections were 4 rotavirus, 3 adenovirus, 2 enterovirus, 2 parainfluenza, 1 herpes simplex virus and 1 varicella zoster virus. In the inborn infants the virus that caused the higher number of infections were influenza H1N1 (29.6%), CMV (22.2%) and metapneumovirus (25.9%).

Presentation: In the CMV cases 55.5% (n=5) of the infants had symptomatic infections (all presented with hepatosplenomegaly, 2 with cholestatic jaundice and 1 with purpuric nodules). In these cases ganciclovir was used. In 2 cases the infection was detected in utero by amniocentesis, in all others only detected after delivery. There were 2 cases of asymptomatic CMV infection. The other 2 were cases of CMV pneumonia that progressed respectively to chronic lung disease and pulmonary hypertension. The MLS of all CMV cases was 20 days.

The respiratory infections were the vast majority of the viral infections found (72%) and generally presented with apnea, respiratory distress or cyanosis.

The RVS cases were predominant in newborns admitted from their homes (72.7%, n=16), all presented with respiratory distress, 27.3% (n=6) also with cyanosis and 13.6% (n=3) also with fever. Only 22.7% (n=5) occurred in preterm newborns, with longer MLS and comorbilities appeared in only 4 cases. The MLS was 14 days, 45.5% (n=10) required mechanical ventilation (MV), 81.8% (n=18)

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	Number of cases	Clinical presentation	Treatment	MLS (days)	Need of MV	Outcome
CMV	9	55% symptomatic (mainly hepatosplenomegaly)	Ganciclovir in 55.5%	20	In 22.2% (CMV pneumonia)	Favorable, 2 pulmonary disease
RSV	22	Bronchiolitis in 77.3%, pneumonia in 22.7%	Bronchodilator therapy in 81.8%	14	In 45.5%	Generally favorable, 4.5% (n=1) mortality
Metapneumovirus	12	Bronchiolitis in 50%, others asymptomatic	Bronchodilator therapy in 50%	52	In 83.3%	Favorable
Parainfluenza	2	All bronchiolitis	Bronchodilator therapy	68	No	Favorable
H1N1	12	83.3% asymptomatic, others bronchiolitis, outbreak 2009	Oseltamivir	30	In 50%	Favorable
Rotavirus	4	Nosocomial, diarrhea and abdominal distention	Not specific	42	In 50%	Favorable
Adenovirus	3	Gastrointestinal and respiratory symptoms	Not specific	60	All	33.3% (n=1) mortality
Enterovirus	2	Sepsis like disease, outbreak 2007	Broad spectrum antibiotics	18	All	100% (n=2) mortality
Herpes Simplex	1	Seizure	Acyclovir	30	No	Favorable
Varicella Zoster virus	1	Varicella	Specific immunoglobulin and acyclovir	7	No	Favorable

Table 1: Presentation, treatment and outcome of viral infections.

began bronchodilator therapy and the evolution was good in 90.9% (n=20). There was 77.3% (n=17) of bronchiolitis and 22.7% (n=5) of pneumonia. The mortality was 4.5% (n=1).

The metapneumovirus cases had a favorable evolution, MLS of 52 days but 83.3% (n=10) needed MV. In 50% (n=6) a bronchiolitis was clinically detected, and kinesiotherapy was done in half of these, all other cases were asymptomatic. We reported 2 bronchiolitis due to type 3 parainfluenza virus, which had a favorable evolution without the need of IV and with MLS of 68 days.

During the year 2009 there was an outbreak of influenza H1N1 infection and 12 patients were infected, including 66.7% (n=8) of preterm newborns. All received oseltamivir in a therapeutic dosage and no adverse reactions or fatal cases were reported. In 83.3% (n=10) cases the infant was asymptomatic and the laboratorial test was only requested due to the outbreak. Although 50% (n=6) of patients needed IV during hospitalization the evolution was good in all cases. The MLS was 30 days. The rotavirus infection presented with diarrhea or abdominal distention, with MLS of 42 days. All these infants had nosocomial rotavirus infection and in 2 cases there was also adenovirus isolation on the feces.

In all cases of adenovirus infections there was also a respiratory compromise, as they all needed IV and the MLS was 60 days. One of the cases of adenovirus isolation in feces was associated with serious respiratory compromise but no respiratory isolation and this infant died because of a septic event.

The enterovirus infections occurred during another outbreak in 2007 and presented with overwhelming sepsis like disease. Treatment was tried with broad spectrum antibiotics but the mortality was 100%. These patients had MLS of 18 days. There were other similar cases that appeared at the same time in our NICU but the virus could not be identified.

The cause of admition in the only herpes simplex infection was seizures in the context of encephalitis and the infection was treated with acyclovir with favorable evolution. There was one case of varicella zoster virus infection in an infant admitted because of maternal peripartum fever and exanthema. He started specific immunoglobulin and acyclovir and developed varicella at day 11. No serious complications were observed in this case.

Infections in preterm newborns: These infections occurred in preterm newborns in 32 cases (47.8%), predominantly respiratory illness like infections by RSV (18.8%, n=6), metapneumovirus (25%, n=8) and influenza H1N1 (25%, n=8). In all these cases the viral infection was not the condition responsible for the infant's clinical state because at least one bacterial septic event occurred during hospitalization.

Outcome: The outcome of CMV infections was in general favorable in congenital infections. CMV pneumonia had relevant associated morbidity. In the respiratory infections reported is remarkable the favorable outcome of all the parainfluenza and the influenza H1N1 virus infections. RSV seems to be the most aggressive virus in our study, with all newborn being symptomatic, and this infection the principal isolated cause of admition in our NICU. It also had a more exuberant presentation. However, the need for IV was higher in the metapneumovirus group. The overall mortality was 6.0%, 2 cases with enterovirus infection (mortality of 100%), 1 with adenovirus infection and 1 with RSV infection.

Discussion

Viral diseases are undiagnosed or appreciated only late in the course of an illness among infants requiring care in the NICU. These infections are leading causes of mortality and morbidity in newborns [7].

In our study we found a vast majority of respiratory viral infections. These infections predominated in cold months and the clinical picture with respiratory distress associated or not with cyanosis, cough or other respiratory signs was responsible for the search of a viral infection.

Multiple studies of respiratory tract infection in newborns report the favorable course of the viral respiratory disease [8,9], even when the infections are observed in preterm infants [10].

RVS infection appears to be rare in the neonatal period [11], often with mild presentation that may not include respiratory clinical signs [12]. However the serious complications are fearsome in this age group [11], especially in preterm newborns. In our study, infants were mostly symptomatic and, unlike other studies [5,13], RSV was rare in preterm infants. The incidence of RVS pneumonia was relevant.

Parainfluenza virus cases are rarely reported in the neonate [14] and the few reports of these infections describe them as indolent and without complications [15] as we observed in our study.

A recently discovered virus, metapneumovirus, is not very commonly cited in literature [16], especially in neonates. As reported in our study, seems to be a mildly aggressive virus, similar to RSV [17], but with greater need for MV.

In 2009 an outbreak of influenza H1N1 infection was responsible for 17.9% of our cases. This particular situation required specific isolation measures and even the closure of our NCIU. Similar cases were reported at the same time in other NICUs, with milder and nonspecific course that resulted in a favorable outcome [18,19]. Since oseltamivir was never used before in this age group, special attention was paid to its eventual side effects, which did not occur as we previously reported [20]. The same was also reported in a recent study [21].

As described before [22,23], symptomatic congenital CMV infection occurred in more than half of newborn with infection. As it seems to be the most sensitive method [23], polymerase chain reaction was the diagnostic tool used and ganciclovir the antiviral therapy of choice [24]. It is peculiar that we have found two CMV pneumonias in newborns that did not had a congenital CMV infections nor were preterm, which is not very common [25,26].

Rotavirus infection had clinical features similar to the literature [27,28] but we found less clinical impact, without cases of mortality or necrotizing enterocolitis.

In the neonate, as in other age groups, adenovirus infection can produce severe disease and even death. The typical presentation, as we reported, is the respiratory compromise [29,30].

Enterovirus infections are other feared group of infections in this age, being associated with significant morbidity and mortality [31,32] and, also as we found in our study, outbreaks have been described [33].

Because of the overlap with comorbilities it is difficult in a retrospective study to define the morbidity associated with each viral infection and the associated increase in MLS and health costs. In future it could be useful to continue this study in a prospective perspective. For example, premature infants had longer MLS but this fact cannot be associated solely with the associated viral infection.

Conclusion

In our study the respiratory infections were the most common and the overall mortality was not negligible. Infants in a NICU who develop respiratory signs must always be tested for RSV and other common respiratory viruses, especially during winter season.

The outbreaks in general are of great impact on health care delivery, outcomes and costs and so the appropriated preventive measures must be reminded, to avoid situations like the outbreak of influenza H1N1 virus.

It is necessary to prevent these infections but also to consider them in a sick neonate. With the improvement of diagnostic tools such as antigen detection techniques, molecular technology and viral culture the diagnosis is now easier. The treatment options often are limited, but improving with the increasing knowledge.

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