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Late onset perinatal sepsis in the neonatology intensive care unit – risk factors

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ABSTRACT

The lowest-birth-weight premature is very susceptible for nosocomial infections. These infants require the most invasive therapeutic interventions and the longest exposure to environment conductive for microbial colonization. Incidence of nosocomial infection and risk factors in premature has been compared over two years, 2010 and 2015. We examined the effects of common procedures on the incidence of nosocomial sepsis. Birth weight, distribution of pathogens and the therapeutically procedures had been analysed. We tried to find strategies to minimise the risks for acquiring sepsis. Hospital documentation from neonatal intensive care unit (NICU) has been analysed retrospectively during two different years in the University Hospital Osijek. Incidence of nosocomial sepsis among hospitalised premature has been 8.9% in 2010, and 4.8% in 2015. The highest rate of affected infants weighed below 1,500 g in both periods. Statistically significance in these two periods has been found in the percentage of pre-term infants with umbilical vein catheter (UVC), and in the number of pre-term on invasive mechanical ventilation. The most common pathogen in 2010 was methicillin-resistant Staphylococcus epidermidis (MRSE), and in 2015 coagulase negative Staphylococci (CONS). The percentage of Candida parapsylosis was higher in 2015. Lowering the incidence of late-onset sepsis has been accomplished by using peripherally inserted central catheters (PICCs) and non-invasive mechanical ventilation. Invasive procedures must be avoided as much as possible.

Key words: low-birth-weight pre-term infants, nosocomial infections, risk factors, umbilical venous catheters, NICU, PICC, mechanical ventilation, high-flow nasal cannula

INTRODUCTION

Infection rates are standard indicators of quality and safety in all healthcare settings all over the world. (1) Hospital acquired infections continue to be a serious and common complication of hospitalisation. (2) Monitoring them is increasingly regarded as an important contributor to safe and high-quality healthcare. (3) According to various studies the incidence of infections varies based on birth weight, underlying diseases, medical facilities, and mode of care in different centres.

Recent technological advances have improved the neonatal survival rate. Ratio of pre-term deliveries is about 10% of all born. In recent years this ratio has been higher (because perinatal care is at a much higher level than it was before, and many tiny premature survived, many more babies have been born after "in vitro fertilization", many more pregnancies have been "pathological" and there were many more Caesarean sections on "request"). As long as we continue to have deliveries of preterm of very low gestation, we shall struggle with nosocomial infections.

This is associated with the use of invasive procedures and long term admission in the NICU and a higher risk of complications. (4, 5) Premature infants are more susceptible to nosocomial infections because of poor skin integrity and immature immune systems (they have inefficient mucous and cutaneous barriers). They are exposed to a variety of therapeutic interventions. They have many risk factors: use of broad spectrum antimicrobial drugs, steroids, tracheal tubes. The digestive tract is an important reservoir of all kinds of pathogens and subsequent sepsis in pre-term infants. (6)

Complications of prematurity associated with an increased rate of nosocomial infections included prolonged mechanical ventilation and prolonged intravenous access, prolonged parenteral nutrition, invasive mechanical ventilation. Late-onset sepsis remains an important risk factor for mortality and morbidity especially among VLBW pre-term. Reported incidence is very high regardless of the improvements in the quality of neonatal assistance. (7, 8)

One-third of nosocomial infections would be preventable if we have effective infection control protocols. (4) Strategies to reduce their incidence are very important for every NICU. Many procedures can help us in the battle with nosocomial infection. That includes: promotion of enteral feeding with fresh human milk, antibacterial in-line filters, and enteric microbiota composition enhancement with the use of probiotics, specific and anti-fungal prophylaxis. Some of the important points in prevention includes: continuous care and monitoring of the infection and type of micro-organisms, insisting on careful hand washing, minimal use of central veins catheters, low use of empiric antibiotic therapy and adequate nursing. (9,10)

The use of antibiotics in the NICU should be carefully monitored. Many factors were connected to poor hand hygiene, such as under staffing, overcrowding and work overload. Nurse patient ratios and nursing skills mix, significantly affect inpatient mortality.

MATERIALS AND METHODS

This study was retrospective and all premature infants admitted to the NICU in two periods, year 2010 and 2015, were included. In the year 2010, 201 premature infants were included and in 2015 250. The diagnosis of nosocomial infection was made by clinical and laboratory findings, as well as by positive haemoculture. Samples for microbiological analyses had been taken from blood, gastric aspirate and from the trachea. Clinical findings included hypo and hypertermia, apnoea, bradycardia and tachycardia, circulatory disorders, hypotonia, feeding difficulty and lethargy. Laboratory findings were leucocytosis, leucopenia, thrombocytopenia, a ratio of immature/mature neutrophils >0,2 and C-reactive proteins value of >5 mg/l. Data were analysed using SPSS, 22.0.0.0, IBM Corp., Armonk, NY, SAD. Univariate analysis methods were used at 5% level of significance. Differences between groups were analysed using chi2 test.

RESULTS

Table 1 shows the incidence rate of nosocomial sepsis in relation to birth weight of the studied premature infants, which was found as the most important factor in its occurrence. In the year 2010, 201 premature has been hospitalised in our NICU. Almost 24% of them are pre-term and of low birth weight. Late onset sepsis occurred mostly in those infants (73% of all pre-term with sepsis). A relatively high percentage of sepsis occured in prematures between 2,001-2,500 g (16.7% of all infected infants). Incidence of late-onset sepsis was highest in low birth weight infants; almost 27 % of them had been infected. About 73% of all infected infants were those of low birth weight.

In the year 2015, the percentage of low birth weight infants was nearly the same. The percentage of all infected pre-term infants was the highest again in those bellow 1,500 g (83. 4%). This has been higher than in the year 2010, but the onset of sepsis was in the third or fourth week of life and in 2010 it was in the second week. In the group of infants from 2,001 to 2,500 g, the percentage of infants with late-onset sepsis in the total number of those with sepsis was more than three times less. The incidence of nosocomial infections in all birth weight groups of premature infants has been lowered over the last five years.

Table 2 shows bacteriological profile of isolated pathogens. In the year 2010, 23 samples from 18 infants were isolated. The most frequently isolated organism was methicilin resistant Staphylococcus epidermidis (almost 40%). The percentage of it has been lowered in the year 2015. Same happened with Klebsiella pneumoniae ESBL (two times lower percentage in the year 2015). Candida albicans which was found in 2010, was never found in the year 2015, but Candida parapsylosis has been found in more than a quarter of samples in that year. The percentage of Pseudomonas aeruginosa has been lowered in 2015.

Therapeutically interventions are shown inTable 3. More than one third of all premature infants had been ventilated in the year 2010, and about one fourth of them in 2015. The main difference in those two periods has been the way of mechanical ventilation; one half of premature infants in 2015 underwent non-invasive mechanical ventilation. Umbilical venous catheter has been put five times more often in the year 2010, and we started to put PICCs in 2015. There was a significant difference in therapeutical interventions in those two periods. We change our way of thinking, and our way of taking care of pre-term infants.

Table 1. Incidence of nosocomial infection in premature infants (by birth weight) in two periods

	2010			2015			
		Infected	Incidence		Infected	Incidence	
Birth weight (g)	No (%)	No (%)	%	N (%)	No (%)	%	p
<1000	15 (7.5)	6 (33.3)	40	19 (7.6)	6 (50)	31.6	>0.05
1000-1500	33 (16.4)	7 (38.8)	21.2	44 (17.6)	4 (33.4)	9.1	>0.05
1501-2000	48 (23.9)	1 (5.6)	2.1	62 (24.8)	1 (8.3)	1.6	>0.05
2001-2500	51 (25.4)	3 (16.7)	5.9	62 (24.8)	1 (8.3)	1.6	>0.05
>2500	54 (26.8)	1 (5.6)	1.8	63 (25.2)	0	0	>0.05
Total	201 (100)	18 (100)	8.9	250 (100)	12 (100)	4.8	

Table 2. Isolated pathogens in premature infants

	2010	2015	
Pathogen	N (%)	N (%)	p
MRSE	9 (39.1)	5 (22.7)	>0.05
Klebsiella pneumonia ESBL	5 (21.7)	2 (9.1)	>0.05
Pseudomonas	4 (17.4)	3 (13.6)	>0.05
CONS	4 (17.4)	6 (27.3)	>0.05
Candida albicans	1 (4.4)	0	
Candida parapsilosis	0	6 (27.3)	

Total No of isolates	23 (100)	22 (100)

ESBL - Extended spectrum beta-lactamase
CONS - Coagulase-Negative Staphylococcus
MRSE - Methicillin-resistant Staphylococcus epidermidis

Table 3. Therapeutically interventions in premature infants in two periods

	2010	2015	
Intervention	No (%)	No (%)	p
Invasive mechanical ventilation	69 (34.3)	33 (13.2)	<0.05
Non-invasive mechanical ventilation	2 (1)	31 (12.4)	<0.05
UVC	40 (19.9)	10 (4)	<0.05
PICC	0	35 (14)	
Total	201	250	

UVC, umbilical vein catheter
PICC, peripherally inserted central catheters

DISCUSSION

Late-onset sepsis is primarily a problem for premature infants of low birth weight with disorders requiring prolonged hospitalization. Despite intensive surveillance and prophylactic procedures, late-onset sepsis in NICUs remains a large world problem. We included in the study all admitted preterm babies in the year 2010 and 2015. The incidence of nosocomial infection in the year 2010 was 8.4%, and in the year 2015 it was 6%. The incidence differs from 6 to 25% of the NICU populations. (11-14)

The incidence of late-onset sepsis is lowered because of using non-invasive mechanical ventilation (nasal CPAP and high-flow nasal cannula). The same is done by using PICC catheters instead of umbilical venous catheters. It is visible especially in pre-term infants bellow 1,500 g. The same results are seen in bigger infants who needed parenteral nutrition. The percentage of very low birth weight among all infants with sepsis has also been lowered.

The vast majority of infections were caused by Gram-positive organisms according to literature -70%, 10%. (14,15) In our study the percentage of these infections has been about 39% in 2010 and was lowered in 2015 to 22.7%. It was accomplished by putting PICCs instead of umbilical venous catheters and peripheral lines. Infections with coagulase-negative staphylococci accounted for 48% of infections. (4, 16, 17) The better the NICU is, it appears that the percentage of CONS in nosocomial infections will be higher. Infections with CONS develop when the pre-term is very tiny and has been on total parenteral feeding for a very long period. According to the literature Klebsiella is found in 34% of nosocomial infections. (18, 16, 11) Invasive mechanical ventilation was identified as significant risk factor (15). In our investigation the incidence of Klebsiella was lower, especially in the year 2015. By using non-invasive mechanical ventilation, Klebsiella became a slightly smaller problem. The same is with Pseudomonas. We lowered the incidence of pseudomonas also by using a less aggressive type of mechanical support. When umbilical venous catheters have been used frequently, the incidence of Candida albicans has been higher. Candida albicans appears when venous catheters were used for a longer period of time, and when prophylaxis is insufficient. By using PICCs and prophylaxis with fluconazole, C. albicans disappears, but a new problem arises, Candida parapsylosys. It seems that it is not preventable in very tiny pre-term infants who need extended intra venous support. The rate of infection was inversely related to birth weight. (19) Complications of prematurity with an increased rate of late-onset sepsis included prolonged ventilation, prolonged intra vascular access, especially central venous umbilical catheters. (20)

The most common intervention associated with infection was the use of central intra vascular catheters. We are trying to keep the smallest and the sickest babies alive. , Nosocomial infections in NICU are only partially preventable. We must look for procedures to reduce the risk of infections in NICU. Intravenous access is a necessity in the NICU either through the use of percutaneous inserted central catheters. PICCs have become essential in the NICU for long-term venous access to deliver medications and parenteral nutrition. A major disadvantage is that it may require multiple IV sticks, and that can increase the incidence of nosocomial infections. (2)

The proactive management of percutaneously inserted central catheters results in decreased incidence of infection in the ELBW population. (21) The use of "in line filters" is also very useful. (6) Paediatric intensive care unit stays and duration of mechanical ventilation were also significantly reduced. Preventive interventions include early extubation strategies and switching to non-invasive respiratory support. In our study, as well as in the others, using non-invasive high-flow nasal cannula resulted in decreased rates of late-onset sepsis. (22-25) Results differ in developed countries and in developing countries. (26) High-flow nasal cannula can be used in very tiny infants, even among those bellow 1,500 g. Heated, humidified air has similar efficacy and safety to nCPAP when applied immediately post extubation or early on as an initial non-invasive support for respiratory dysfunction. (22) Use of NHF oxygen therapy includes maintaining airway potency, decreased work of breathing, reduced energy expenditure and improved mucociliary function. (25) The incidence of adverse events including pneumothorax, gastric distension and mucosal injury does not occur. (23) Early use of HFNC oxygen therapy is not associated with increased duration of mechanical ventilation or NICU stay. (24)

CONCLUSION

Very low birth weight infants must be handled very carefully. Minimal handling is the best way for their support. By changing the way of care, we can change their morbidity and mortality. Long lasting intra venous catheters (PICCs) are very good, and the risk of nosocomial infections by using them is very low. Non-invasive mechanical ventilation can help premature infants to become stable and enables them maximal comfort and help. Very low birth weight infants take a lot of time and care, and great efforts must be done to achieve the best results in neonatology.

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