

CZĘŚĆ II.

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INFECTIONS REPORTED IN NEWBORNS WITH VERY LOW BIRTH WEIGHT WHO REQUIRED SURGICAL TREATMENT. DATA FROM THE POLISH NEONATOLOGY SURVEILLANCE NETWORK

ZAKAŻENIA U NOWORODKÓW Z BARDZO MAŁĄ MASĄ URODZENIOWĄ, WYMAGAJĄCYCH WYKONANIA ZABIEGU OPERACYJNEGO. DANE POLSKIEJ SIECI NEONATOLOGICZNEJ

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Abstract

Aim: To determine the risk of various forms of infections appearing in very low birth weight newborns (VLBW) during the period of 30 days after surgical treatment in hospitals which have perinatal care departments with neonatal intensive care units that form the Polish Neonatology Surveillance Network (PNSN).

Material and methods: Continuous prospective monitoring of infections was carried out from January 1st to December 31st 2009 in six neonatal intensive care units which form the Polish Neonatal Surveillance Network. (PNSN).

910 newborns with very low birth weight (VLBW) were included in the study programme. 91 (10%) of this group underwent 118 surgical interventions. 12 newborns needed two or more surgeries. The most common procedure was the closure of persistent ductus arteriosus (PDA) and photocoagulation of vascular damage in the eye fundus.

Results: In the period of 30 days after surgery the following were diagnosed: in 3 newborns – necrotizing enterocolitis (NEC), in 22 newborns – sepsis (BSI) and in 54 newborns – pneumonia (PNEU). Symptoms of BSI and PNEU were on average observed on the 10th day after surgical intervention, while in the case of NEC on the 17th day. The highest incidence of infection (148.4%) was observed after PDA closure and in connection with introducing a drain into the pleural cavity through the intercostal space. The incidence of PNEU (37.3%) was twice as high as the incidence of BSI (18.6%).

Surgical procedure was a factor significantly increasing the risk of infection and morbidity (RR 2.1, $P < 0.001$) In our investigations there was no case of the local infection of a surgical site.

11 newborns died (mortality was 12.1%).

The most common bacterial strains found in our investigation were coagulase-negative *Staphylococcus* and *Escherichia Coli*.

Conclusions: Taking into consideration the fact that surgical procedure in VLBW-newborns significantly increases the risk of pneumonia and to a minor degree the risk of NEC and BSI, further detailed investigation in the field of perisurgical epidemiology is needed in order to elaborate a more deeply oriented and more effective strategy of infection prevention in the group of VLBW newborns.

Key words: neonatal surgical, infections, surveillance of infections

Streszczenie

Celem pracy było określenie ryzyka wystąpienia w okresie 30 dni po zabiegu operacyjnym różnych form zakażeń u noworodków z bardzo małą masą urodzeniową (VLBW) hospitalizowanych w oddziałach objętych Polską Siecią Neonatologiczną (PSN).

Materiał i metody: Ciągły prospektywny nadzór nad zakażeniami prowadzono w okresie od 1 stycznia do 31 grudnia 2009 r. w sześciu oddziałach intensywnej terapii noworodka szpitali świadczących opiekę perinatalną i tworzących PSN. Badaniami objęto 910 noworodków z VLBW.

W badanej grupie u 91 (10% badanej populacji) noworodków przeprowadzono ogółem 118 zabiegów operacyjnych, (u 12 konieczne było przeprowadzenie dwóch lub więcej operacji). Zabiegiem wykonywanym najczęściej było zamknięcie przetrwałego przewodu tętniczego oraz fotokoagulacja zmian naczyniowych na dnie oka.

Wyniki: W grupie dzieci operowanych rozpoznano, w okresie do 30. doby po operacji 3 przypadki martwiczego zapalenia jelit (NEC), 22 przypadki sepsy (BSI) oraz 54 zapalenia płuc (PNEU).

Pierwsze objawy obserwowane były średnio w 10 dobie po operacji w przypadku BSI i PNEU oraz w 17 dobie po zabiegu z powodu NEC. Najwyższą zachorowalność związaną z zakażeniami (148,4%) obserwowano po zamknięciu przetrwałego przewodu tętniczego oraz w związku z wprowadzeniem drenu do jamy opłucnowej przez międzyżebrze. Zachorowalność na PNEU (37,3%) była 2 razy wyższa, niż zachorowalność na BSI (18,6).

Zabieg był czynnikiem istotnie zwiększającym ryzyko zakażenia i wystąpienia (RR 2,1, $p < 0,001$). W badanej grupie noworodków nie stwierdzono żadnego zakażenia miejsca operowanego. W grupie dzieci operowanych 11 noworodków zmarło (śmiertelność wynosiła 12,1%).

Do najczęściej stwierdzanych w hodowli bakterii należały: Koagulazo-ujemne, gronkowce i *Escherichia coli*.

Wnioski: Biorąc pod uwagę fakt, że zabieg operacyjny u noworodków z VLBW znacząco zwiększa ryzyko rozwoju zapalenia płuc, a także w mniejszym stopniu martwicze zapalenie jelit (NEC) i posocznicę (BSI), konieczne są dalsze pogłębione badania nad epidemiologią zakażeń okołoperacyjnych. Umożliwi to opracowanie skuteczniejszej strategii profilaktyki w grupie noworodków z bardzo małą urodzeniową masą ciała.

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INTRODUCTION

Progress in science and technology has made it possible to save the lives of newborns who had no chance of survival some decades ago. In the last 20 years there has been a significant increase in the number of newborns requiring hospitalization in neonatal intensive care units. Newborns with very low birth weight (<1500 grams) constitute (both in Poland and around the world) about 1% newborns born alive (1, 2). Some of them require surgical intervention. Surgical treatment became possible both due to the development of surgical techniques, modern anesthesia, better knowledge of newborn pathophysiology and progress in therapy (such as parenteral feeding, introduction of modern techniques of intensive care, mostly mechanical ventilation) (3). Due to the fact that infections still constitute one of the main threats to newborns' life and health in the perinatal period, an important element of improving the newborns' condition and limiting mortality in the post surgery period is infection prophylaxis and

effective antibacterial therapy. So far there has been a lack of well-documented research on the population of VLBW newborns after surgical intervention.

MATERIAL AND METHODS

Continuous prospective monitoring of infections was conducted from January 1st to December 31st 2009 in six neonatal intensive care units in hospitals with perinatal care departments and Neonatal Intensive Care Departments forming PNSN.

Targeted monitoring was carried out according to the PNSN's research protocol. The protocol was developed at the Department of Microbiology of Collegium Medicum of Jagiellonian University in Kraków in cooperation with members of the Neonatal Network Board. The participation criteria were: newborns hospitalized in cooperating centers, born after 22 weeks of gestation whose birth weight was lower than 1500 g or did not

exceed 1800 g on admittance to the unit in case of infants who were born outside the centre.

Registration was carried out upon filling in a questionnaire containing the basic data from the medical history of the infant and the obstetric history of the mother.

NEWBORN POPULATION

910 newborns were included in the study. 166 (18.2%) were newborns with the birth weight of up to 750 grams, 250 (27.5%) with birth weight 751-999 grams and 494 newborns (54.3%) with birth weight 1000-1500 grams. 223 newborns were from multiple pregnancies. Female newborns constituted 46.9% of the research group and among the newborns who reached the weight of 1800 grams – 53%.

812 deliveries were analysed. Among the newborns studied 68.5% were delivered via a caesarean section. Neither the gender percentage nor that of c-sections differed significantly between centres.

The newborns' condition after delivery was assessed with the Apgar score and the CRIB (Critical Risk Index for Babies). Scoring in CRIB was on a two-point scale. Most newborns were qualified into the 0-4 point group: 70.2% of the population, then, by stratification: 20.5% – 5-10 points, 7% – 11-15, 2.3% – 16-22. The participation of newborns in specific groups was statistically significantly different in the above mentioned units. In the Apgar score, 8 and more points in the first minute were given to 17.5% of the newborns in the group, 5-7 points to 45.7%, and 4 points or less to 36.8% of the newborns. The Apgar score of 8 points and more in the 5th minute was given to 27.6% newborns, 5-7 points – 48.8%, and 4 or less to 24.1% of newborns in the study group. Premature rupture of membranes (PROM) was observed in 25.1% of the cases.

Differences between centres were statistically significant (tab. I).

Infections were diagnosed and qualified on the basis of infection definition, developed and accepted by the Network Board, as well as on the basis of experience and the data of National Nosocomial Infections Surveillance (NNIS), Centers for Disease and Prevention (CDC) in the USA (4), including modifications of the Neo-KISS [5] German programme.

Epidemiological analysis was conducted using: – Cumulative incidence rate, describing the risk of infection with respect to the size of the population, i.e. the number of patients admitted for hospitalization and the number of new cases of infection expressed as a percentage,

– Mortality rate, describing the risk of death of the person with the given illness,

– Prevention of microorganisms, i.e. the frequency of isolating bacterial etiological factors.

Statistical analysis:

For the assessment of the lack of differences between the means for the studied groups of newborns (the group with no symptoms of infection vs. newborns with infections), the research used the univariate analysis of variance (One-way ANOVA). The level of the significance of differences was measured with the least significant difference test and Tukey's test; for assessing the occurrence of infections in

different groups of newborns the independent test sample chi-square was used.

Calculations were conducted using Open Source SciPy; the assumed level of significance: $p < 0.05$.

The study was conducted with the consent of the Bioethical Commission of Jagiellonian University no. KBET/221/B/2011.

RESULTS

In the studied group 91 (10%) newborns underwent a total of 118 surgical procedures; 12 needed 2 or more surgeries in the period of observation of the newborns in hospital, i.e. until they reached the body weight of 1800 grams. The most common procedures were closure of PDA and photocoagulation of eye vessels (tab. I).

In the group of newborns after surgery in the period of 30 days after surgical intervention there were: 3 cases of necrotizing enterocolitis (NEC), 22 cases of sepsis (BSI) and 54 cases of pneumonia (PNEU). In the case of sepsis and pneumonia the first symptoms were observed 10 days after surgical procedure and in the case of NEC – 17 days after surgical procedure. The highest incidence of infection (148.4%) was observed after the PDA closure and in connection with introducing a drain to the pleural cavity through intercostal space (tab. III). PNEU incidence (37.3%) was twice as high as the incidence of BSI (18.6%). In the case of PNEU, surgical procedure was a factor significantly increasing the risk of the development of infection and morbidity (RR 2.1, $p < 0.001$).

In our investigation no case of the local infection of a surgical site was diagnosed. Eleven newborns (12.1%) died after surgical intervention – two newborns after PDA closure (one on the 1st, the other on the 3rd day post-operation). Symptoms of primary sepsis were observed (CVC-BSI) in eight newborns, and in one case pneumonia (2 days after the operation). Additionally, 19 days after the operation temporary ileostomy CVC-BSI was diagnosed in one newborn. All these infections were observed in babies with a birth weight of 600 grams.

DISCUSSION

The results presented come from the first Programme of Infection Control in neonatal units which was the first Polish national programme of this kind, as well as the first one in Central and Eastern Europe. In Poland 4000 VLBW newborns are born every year, which constitutes 1.1% of all live births. The programme included over 19.1% VLBW newborns born in Poland in 2009. It also constituted over half VLBW newborns born in the regions where the units constituting PSN are located. The mortality of VLBW newborns in Poland in 2009 was 24.3%, and in units constituting PSN significantly less: 19% (2).

Newborns with low birth weight, JURG or preterm newborns constitute a small group of patients undergoing surgical procedures. At the Institute of Mother and Child in Warsaw 381 were operated on in the years 2000-2006, and the studied group numbered 155 (6). So far the problem of infections in VLBW newborns after surgical procedures has not been widely discussed in the literature.

Table I. Characteristics of newborns qualified for the study in individual units.

Tabela I. Charakterystyka noworodków zakwalifikowanych do badania w poszczególnych jednostkach.

	Centre A <i>Ośrodek A</i>		Centre B <i>Ośrodek B</i>			Centre C <i>Ośrodek C</i>	Centre C <i>Ośrodek C</i>		
Number of Patients <i>Liczba pacjentów</i>	N=88		N=152			N=152	N=41		
Average 95% CL/Średnia 95% CL									
Gestational age (week) <i>Wiek ciążowy (tydz.)</i>	28.3	27.7; 28.9	27.9	27.4; 28.4	28.7	28.1; 29.1	27.7	26.7; 28.7	28.9
Birth weight (grams) <i>Masa urodzeniowa (gramy)</i>	992	928; 1057	986	939; 1033	1145	1064; 1225	953	854; 1052	1044
Participation in population/Udział w populacji liczba/%									
Female <i>Płeć żeńska</i>	42	47.7	78	51.3	72	47.4	18	43.9	105
Casarean section <i>Cesarskie cięcie</i>	60	68.2	104	68.4	121	79.6	35	85.4	178
Single pregnancy <i>Ciąża pojedyncza</i>	70	79.5	114	75.0	121	79.6	35	80.5	169
Twin <i>Bliźniacza</i>	16	18.2	34	22.4	21	13.8	8	19.5	53
Triplets <i>Trojaczka</i>	2	2.3	4	2.6	6	3.9	0	0.0	12
4 and more <i>4 dzieci i więcej</i>	0	0.0	0	0.0	4	2.6	0	0.0	0
Trophic nutrition <i>Żywnienie troficzne</i>	66	75.0	41	27.0	124	81.6	15	36.6	25
CRIB*									
0-4	b/d		95	62.5	b/d		b/d		176
5-10	b/d		35	23.0	b/d		b/d		44
11-15	b/d		15	9.9	b/d		b/d		12
16-22	b/d		7	4.6	b/d		b/d		2
Apgar (1 min)									
0-4	32	36.4	64	42.1	41	27.0	12	29.3	57
5-7	30	34.1	62	40.8	84	55.3	20	48.8	153
8-10	26	29.5	26	17.1	27	17.8	9	22.0	24
Apgar (5 min)									
0-4	42	47.7	48	31.6	14	9.2	11	26.8	47
5-7	14	15.9	65	42.8	78	51.3	18	43.9	156
8-10	32	36.4	39	25.7	60	39.5	12	29.3	31
PROM	28	31.8	44	28.9	41	27.0	11	26.8	49

*CRIB – ClinicalRisk Index for Babies – total number refers to the units using CRIB.

Table I. Cd.

Tabela I. Cont.

	Centre D <i>Ośrodek D</i>		Center E <i>Ośrodek E</i>		Total <i>Ogółem</i>	P-value
Number of Patients <i>Liczba pacjentów</i>	N=234		N=241		N=910	
Average 95% CL/Średnia 95% CL						
Gestational age (week) <i>Wiek ciążowy (tydz.)</i>	28.4; 29.3	28.0	27.6; 28.4	28.3	28.1; 28.6	0.018
Birth weight (grams) <i>Masa urodzeniowa (gramy)</i>	1009; 1079	1034	997; 1071	1024	1004; 1044	0,0144
Participation in population/Udział w populacji liczba/%						
Female <i>Płeć żeńska</i>	44.9	111	46.1	427	46.9	<0.001
Casarean section <i>Cesarские cięcie</i>	76.1	125	51.9	623	68.5	<0.001
Single pregnancy <i>Ciąża pojedyncza</i>	72.2	168	69.7	676	74.3	<0.001
Twin <i>Bliźniacza</i>	22.6	49	20.3	181	19.9	<0.001
Triplets <i>Trojacza</i>	5.1	13	5.4	37	4.1	<0.001
4 and more <i>4 dzieci i więcej</i>	0.0	1	0.4	5	0.5	<0.009
Trophic nutrition <i>Żywnienie troficzne</i>	10.7	65	27.0	336	36.9	<0.001
CRIB*						
0-4	75.2	b/d		197	21%	<0.001
5-10	18.8	b/d		83	9%	<0.001
11-15	5.1	b/d		27	2%	<0.001
16-22	0.9	b/d		9	0%	<0.001
Apgar (1 min)						
0-4	24.4	128	53.1	335	36.8	<0.001
5-7	65.4	66	27.4	416	45.7	<0.001
8-10	10.3	47	19.5	159	17.5	<0.001
Apgar (5 min)						
0-4	20.1	57	23.7	219	24.1	<0.001
5-7	66.7	107	44.4	440	48.4	<0.001
8-10	13.2	77	32.0	251	27.6	<0.001
PROM	20.9	53	22.0	228	25.1	<0.001

*CRIB – ClinicalRisk Index for Babies – total number refers to the units using CRIB.

Table II. Surgical procedures performed in the study population.

Tabela II. Zabiegi operacyjne jakim poddano noworodki w badanej populacji.

Surgery performed/Przeprowadzone zabiegi		
Description of procedure/Opis zabiegu	Number of/Liczba	%
PDA closure <i>Zamknięcie przetrwałego przewodu tętniczego</i>	49	49.5
Laser photocoagulation of choroid/retina <i>Laserowa fotokoagulacja zmiany naczyniówki/siatkówki</i>	20	19.2
Temporary ileostomy <i>Czasowa ileostomia</i>	9	9.1
Introduction of Holter valve <i>Wprowadzenie zastawki Holtera</i>	5	5.1
Introduction of drain to pleural cavity through intercostal space <i>Wprowadzenie drenu do jamy opłucnowej przez międzyżebrze</i>	5	5.1
Percutaneous drainage of abdominal cavity <i>Przezskórny drenaż jamy brzusznej</i>	3	3.0
Closure of atrioventricular canal <i>Zamknięcie kanału przedsionkowo-komorowego – inne</i>	2	2.0
Other permanent tracheotomy <i>Inna stała tracheotomia</i>	1	1.0
Pneumothorax <i>Odma opłucnowa</i>	1	1.0
Intrathoracic esophageal anastomosis <i>Śródpiersiowe zespolenie przełykowo-przełykowe</i>	1	1.0
Local excision of lesion or tissue of small intestine, excluding duodenal lesions <i>Miejscowe wycięcie zmiany lub tkanek jelita cienkiego, za wyjątkiem zmian w dwunastnicy</i>	1	1.0
Partial resection of the small intestine – other <i>Częściowa resekcja jelita cienkiego – inne</i>	1	1.0
Laparotomy – other <i>Laparotomia – inne</i>	1	1.0
Gastroschisis operation <i>Operacja wytrzewienia</i>	1	1.0
Total <i>Ogółem</i>	99	100.0
No data <i>Brak danych</i>	12	
2 or more operations <i>2 operacje lub więcej</i>	12	

In our investigation the dominant effect of infections were sepsis and pneumonia, which are not directly connected with the surgical site. This is in concordance with many other authors' observations (7, 8, 9). Some authors do describe surgical site infections, but these are isolated reports with no confirmation in multi-centre studies (10, 6). As it was stressed before, in our own studies the dominant problems in the studied group are sepsis and pneumonia. The observation is interesting, because a statistically significant connection between surgical procedure and the incidence of pneumonia has been observed. The studied group is highly differentiated by various coexisting illnesses complicated by significant organ immaturity at birth. Patients required various surgical procedures, hence it is difficult to draw common conclusions. So far some of the types of surgical procedures have not been indicated as

risk factors for infections, while in the studied group such a connection was shown; it refers to e.g. photocoagulation of retinal vessels (12). Many researchers studying the epidemiology of nosocomial infections exclude the group of VLB newborns from the analysis in the group of newborns undergoing operations, claiming that the diversity of this specific population would interfere with the process of drawing common conclusions. There is, however, one common characteristic in this diverse group of VLBW newborns – they require re-intubation before the procedure, or prolonged mechanical ventilation is a procedure evidently increasing the risk of pneumonia.

In the experience of American authors, the risk factors for infections are late PDA closure procedures (6 or more days after diagnosis) and the very low birth weight of newborn (11).

Table III. Infections diagnosed after surgery in the study population.

Tabela III. Zakażenia rozpoznane po zabiegu operacyjnym u noworodków w badanej populacji.

Description of operation <i>Opis zabiegu</i>	Performed surgical procedures <i>Wykonane zabiegi</i> [liczba / %]		Infection <i>Zakażenie</i>					Incidence [%] <i>Zachorowalność</i>
			BSI	PNEU	NEC	Total <i>Ogółem</i>	Number of <i>% liczba</i>	
Introduction of Holter valve <i>Wprowadzenie zastawki Holtera</i>	5	4.5	1	1	0	2	4.5	90.0
Introduction of drain to pleural cavity through intercostal space <i>Wprowadzenie drenu do jamy opłucnowej przez międzyżebrze</i>	5	4.5	1	5	0	6	6.8	136.0
Temporary ileostomy <i>Czasowa ileostomia</i>	9	8.1	1	1	1	3	6.8	75.6
Laser photocoagulation of choroid/retina <i>Laserowa fotokoagulacja zmiany naczyniówki/siatkówki</i>	20	18	0	1	1	2	9.1	45.5
PDA closure <i>Zamknięcie przetrwałego przewodu tętniczego</i>	49	44.1	14	33	1	48	72.7	148.4
Others <i>Pozostałe</i>	23	20.7	5	3	0	8	6.8	29.6
Total <i>Ogółem</i>	118	100	22	44	3	69	100	90.1
Incidence (%) <i>Zachorowalność (%)</i>			18.5	37.0	2.5	58.0	18.5	

BSI – bloodstream infection/*zakażenie krwi*PNEU – pneumonia/*zapalenie płuc*;NEC – necrotizing enterocolitis/*martwicze zapalenie jelit*

No effective methods of prophylaxis have been described so far. Previous experience connected with perioperative antibiotic prophylaxis refers mostly to adult patients and infants (13,14). It is connected with the difficulty of qualifying the microbiological purity of the surgical site (15), which is usually assessed with the criteria and classification of clean wounds, clean-contaminated wounds, contaminated wounds, dirty wounds by the National Academy and Sciences and National Research Council (16), but based on experience in adult surgery. Moreover, VLBW newborns are patients exceptionally often treated with antibiotics, especially in the perinatal period. Hence neither in Poland nor around the world does there exist a recommendation of scientific societies regarding perioperative antibiotic prophylaxis (14). No positive results of using corticosteroids in cardiac procedures have been shown (17). However, the use of central catheters introduced peripherally and the use of EMCO have been indicated as factors significantly lowering the risk of infections in procedures in the abdominal cavity (e.g. Surgery for diaphragmatic hernia [(8)).

CONCLUSIONS

Taking into consideration the fact that surgical procedure in VLBW – newborns significantly increases the risk of pneumonia and to a minor degree the risk of NEC and BSI, further detailed investigation in the field of perisurgical epidemiology is needed in order to elaborate a more deeply oriented and more effective strategy of infection prevention in the group of VLBW – newborns.

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