616.24-002-053.31:616.12-089

Risk factors of ventilator-associated pneumonia in neonates after cardiac surgery with cardiopulmonary bypass

Khemio Arnes S.[1], Zgrzheblovska L.[2], Moshkivska L.[1], Boyko S.[1], Cheburahin V.[1], Truba Y.[1], Lazoryshynetz V.[1]

[1] National M.M. Amosov Institute of Cardiovascular Surgery from National Academy of Medical Sciences of Ukraine (Kyiv)
[2] Shupyk National Medical Academy of Postgraduate Education (Kyiv)

Objective: identify the risk factors of ventilator-associated pneumonias in newborns after cardiac surgery with cardiopulmonary bypass.

Methods: 39 patients of neonatal age with congenital heart diseases who underwent cardiac surgery and who were on mechanical ventilation for more than 24 hours in the postoperative period were included in this study.

Results: during this investigation 39 patients were examined. The strains of microorganisms that most often cause ventilator-associated pneumonia in newborns have been found: Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterococcus faecalis. Patients who are on artificial ventilation for more than 72 hours, and those who undergo surgery with a high level of complexity, are more likely to develop pneumonia.

Conclusions: Newborns after cardiac surgery with cardiopulmonary bypass with ventilator-associated pneumonia have a longer stay in the intensive care unit.

Key words: *ventilator-associated pneumonia, nosocomial infections, antibiotics, newborns, cardiac surgery, cardiopulmonary bypass, congenital heart disease.*

Ventilator-associated pneumonia (VAP) is the main cause of complications and prolongation of the postoperative period, they are especially dangerous for neonatal patients after heart surgery, as they cause a high incidence and mortality rate of this category of children. The statistical data indicate that morbidity and mortality of patients in cardiosurgical ICU is up to 16–31% higher than it is in patients of general ICU departments [1–6].

It has been established that VAP belong to nosocomial infections that may occur during the stay of patients in the intensive care unit [4, 5, 7]. Ventilator-associated pneumonia is defined as a nosocomial pneumonia that occurs within 48 hours after the beginning of mechanical ventilation. They make the 20% of all nosocomial infections that can develop in patients in the department of PICU. The contingent of cardiosurgical patients has a high incidence of VAP (2.9–21.6/1000 days of mechanical ventilation) compared to patients of the general ICU (2.9–11.6/1000 days of mechanical ventilation). The presence of VAP in patients of the department of PICU leads to an extended duration of stay in the ICU, prolonged ventilation of the lungs and is associated with an increased level of lethality [4].

The National Nosocomial Infection Surveillance (NNIS) has established the main criteria for VAP diagnosing in children at <1 year of age:

- worsening of gas exchange rates (saturation <94%),
- temperature instability for no apparent reason,
- leukopenia (<4 • 10^9/l) or leukocytosis (>15 • 10^9/l), increase of band neutrophils >10%),
- appearance of purulent sputum or change in the nature of sputum or an increase in the number of secretions from the respiratory tract,
- tachypnea or apnea, shortness of breath, chest wall involvement during breathing,
- wheezing,
- cough,
- bradycardia (<100 beats per minute) or tachycardia (>170 beats per minute),
- X-ray signs: new infiltrative foci or spread of existing infiltrative foci, cavitation, consolidation, pneumatocele [7].

The possible risk factors for VAP include: younger age at the time of surgery, presence of concomitant genetic syndromes, a high level of complexity of surgical intervention according to the Risk Adjusted Congenital Heart Surgery Score (RACHS-1), longer duration of surgery and a longer duration of extracorporeal circulation, an extended stay in the ICU and delayed sternum closure in patients [1–7].

It was established that cardiac surgery with cardiopulmonary bypass leads to the activation of the pro-inflammatory mechanisms of the immune system. The main reasons are: contact of patient's blood with the components of the extracorporeal circulation machine, trauma due to ischemia and reperfusion, surgical trauma. These factors damage the function of the immune system, since they lead to a decrease in the number of lymphocytes, and decrease the function of neutrophils. The compromised immune system directly correlates with the frequency of onset and development of such postoperative complications as the systemic inflammatory response syndrome, sepsis and multiple organ failure [3, 7, 8].

Objective. Identify the risk factors for ventilator-associated pneumonia in newborns after cardiac surgery with cardiopulmonary bypass, and isolate strains of microorganisms that cause ventilator-associated pneumonias in newborns.

Materials and methods. From January 2015 to January 2017 in the Amosov National Institute of Cardiovascular Surgery 540 patients with congenital heart defects were operated with cardiopulmonary bypass, 39 of them were neonates staying on mechanical ventilation for more than 24 hours during the postoperative period, these patients were included in a retrospective case-control study.

The main factor in the selection of patients was long-term ventilation (>24 hours) in the postoperative period. For all patients, only the first episode of pneumonia was analyzed. The diagnosis of ventilator-associated pneumonia was made according to NNIS criteria. The mean age of the patients was 7.0 [6 to 8] days. The average weight of patients was 3.2 [3.2–3.3] kg. Exclusion criteria included patients with positive bacteriological examination of blood and swabs from the nasopharynx, or primarily infected with non-sterile cultures at the time of hospitalization, premature neonates, patients who had pneumonia in the preoperative period. General characteristics of patients are presented in table 1.

During this study, the patients were divided into two groups: a control group (21 patients) without ventilator-associated pneumonia in the postoperative period and a study group (18 patients) with ventilator-associated pneumonia.

Clinical examination of patients was carried out by means of objective and instrumental diagnostic methods using *Drager Infinity Delta* monitor, as well as laboratory examination methods: general and biochemical blood

Table 1

Characteristics of patients

Characteristics	Value
Age (days, Me [Q_{25}; Q_{75}])	7,0 [6–8]
Weight (kg., Me [Q_{25}; Q_{75}])	3,2 [3,2–3,35]
Sex: boys (n, %) girls (n, %)	24 (61,5%) 15 (38,5%)
PRISM Score (M±SD)	5,6±2,5
RACHS-1 Score (M±SD)	4,15 ±0,9
Bypass time (min., M±SD)	216,6±46,5
Cross-clamp time (min., M±SD)	97,0±29,1
Delayed sternal closure (n, %)	12 (31%)
Reoperation (n, %)	15 (38%)
Mechanical ventilation duration (days, Me [Q_{25}; Q_{75}])	2 [1,7–6,0]
Duration of stay in the ICU (days, M±SD)	24,2±13,3
Mortality (n, %)	2 (5%)

*Statistical abbreviations: n – number of patients, M – mean value; SD – standard deviation; p – significance value; Me – median, [Q_{25}; Q_{75}] – interquartile range

analysis. A specialized examination included X-ray employing a portable X-ray device *Ziehm Vision RFD* and fibrobronchoscopy by bronchoscope *FB-8V Pentax*.

The material for cultures was taken from: the upper respiratory tract, the flushing after bronchoscopic examination. The material was analyzed in the Institute's microbiological laboratory.

Statistical analysis of data was carried out using the computer program SPSS v. 17 (*Statistical Package for the Social Sciences*, USA). The distribution of data according to the normal law was verified using the Kolmogorov-Smirnov test. When comparing two linked samples, the Student's t-test for connected samples (Paired Samples T-test) was used, and the Correlate Bivariate Pearson correlation was applied when two independent samples were compared. Differences were considered significant at $p<0.05$. The level of risk was established with a confidence interval (CI) of 95%.

Results and discussion. During the study, the correlation between the occurrence of ventilator-associated pneumonia and the following factors was analyzed: age of patients, weight, sex, Pediatric Risk Mortality Score (PRISM) during the first 24 hours after hospitalization, the complexity of surgical intervention according to the RACHS-1 scale, the duration of extracorporeal circulation, the duration of the cross-clamp time during the perfusion period, the delay in the sternum closure, reoperation, the duration of mechanical ventilation in the postoperative period, the length of stay in the ICU, administration of empirical antibiotic therapy in the preoperative period since hospitalization, lethality.

Table 2

Results of bacteriological culture of sputum from the trachea in patients of the study group with VAP

Microorganism	% patients
Pseudomonas aeruginosa	25,0%
Klebsiella pneumoniae	16,7%
Enterococcus faecalis	16,7%
Klebsiella oxytoca	8,3%
Acinetobacter baumannii	8,3%
Acinetobacter iwofii	8,3%
Staphylococcus aureus	8,3%
Staphylococcus epidermidis	8,3%
Negative cultures	0%

Material for bacteriological cultures were taken from all patients, the results of microbiological analysis of cultures from the upper respiratory tract in newborns with VAP are presented in table 2.

As it can be seen from table 2, the most common pathogens of VAP in newborns are ***Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterococcus faecalis***.

Table 3

Statistical characteristics of patients with VAP and patients without VAP

Characteristics	Patients with VAP (n=18)	Patients without VAP (n=21)	p
Age (days, Me [Q_{25}; Q_{75}])	7,0 [5,5–10,1]	7,0 [6,0–8,0]	0,8
Weight (kg., Me [Q_{25}; Q_{75}])	3,2 [3,1–3,3]	3,4 [3,2–3,4]	0,6
Sex: boys (n, %) girls (n, %)	12 (67%) 6 (33%)	12 (57%) 9 (43%)	0,8
PRISM Score (M±SD)	6,7±2,7	4,7±2,0	0,2
PRISM Score >10 (n, %)	3 (16%)	0 (0%)	0,05
RACHS-1 Score (M±SD)	4,2±1,0	4,1±0,9	1,0
RACHS-1 Score = 6 (n, %)	3 (16%)	0 (0%)	0,05
Bypass time (min., M±SD)	228,2±60,2	205,0±28,4	0,4
Cross-clamp time (min., M±SD)	92,2±23,7	101,0±34,6	0,3
Delayed sternum closure (n, %)	6 (33%)	6 (28%)	0,9
Reoperation (n, %)	9 (50%)	6 (28%)	0,09
Mechanical ventilation duration (days, Me [Q_{25}; Q_{75}])	4 [2,3–5,8]	2 [1,4–2,9]	<0,05
Mechanical ventilation duration >72 hrs. (n, %)	12 (67%)	6 (28%)	<0,05
Duration of stay in the ICU (days, M±SD)	32,2±14,8	17,4±7,3	<0,05
Empirical antibiotic therapy during preoperative period (n, %)	8 (44%)	0 (0%)	<0,01
Mortality (n, %)	1 (5,5%)	1 (4,8%)	1,0

*Statistical abbreviations: n – number of patients, M – mean value; SD – standard deviation; p – significance value; Me – median, [Q_{25}; Q_{75}] – interquartile range

As it can be seen from table 3, the distribution of patients by age, weight, sex is homogeneous, the difference is not statistically significant between the two groups ($p>0.5$), since these factors are not risk factors for VAP occurrence. In both groups neonates have a statistically insignificant difference in the PRISM pediatric risk score ($p<0.05$), but in the VAP group, there are patients with a high pediatric risk of mortality at the time of hospitalization (>10 PRISM score), which indicates a statistically significant difference in the distribution of patients according to this factor ($p=0.05$). The difference in the duration of the extracorporeal circulation and the cross-clamp time during the perfusion period is also not statistically significant between the two groups ($p>0.05$). Delayed sternum closure and reoperation are not risk factors for VAP, as the difference between the two groups according to these parameters is not statistically significant ($p>0.05$). Mortality in the study group and in the control group is not statistically different ($p=1.0$). Assessment for the presence of genetic syndrome was not established due to the absence of patients with genetic pathology.

The difference in the complexity of surgery for both groups of patients was insignificant ($p>0.05$). However, in the VAP group, there were patients with a high score (6 points) of surgical intervention according to RACHS-1, which indicates a statistically significant difference in the distribution of patients according to this factor ($p=0.05$).

Patients whom empirical antibacterial therapy was administrated in the preoperative period since hospitalization have less propensity to develop VAP in the postoperative period, considering that the distribution of patients by this factor is statistically significant ($p<0.01$).

Patients of the study group with VAP have longer duration of mechanical ventilation and prolonged stay in the ICU, as the difference between the two groups according to this factors is statistically significant ($p<0.05$). It was established that the duration of mechanical ventilation more than 72 hours after the surgery was associated with the onset of VAP, as the difference between both groups was statistically significant ($p<0.05$), which indicates that the longer the patient is on mechanical ventilation in the postoperative period, the more likely the occurrence of VAP.

Conclusions

1. Ventilator-associated pneumonia in newborns after cardiac surgery with cardiopulmonary bypass leads to a prolonged stay of patients in the ICU.
2. Patients with 10 or more points according the scale of pediatric risk of mortality during the first 24 hours after hospitalization are more likely to develop ventilator-associated pneumonia in the postoperative period.
3. Patients that are on mechanical ventilation more than 72 hours after surgery have higher propensity to develop ventilation-associated pneumonia in the postoperative period.
4. Patients who undergone a surgical intervention with high complexity are more likely to develop ventilator-associated pneumonia in the postoperative period.
5. Patients whom empirical antibacterial therapy was administrated in the preoperative period since hospitalization have a lower risk of developing ventilator-associated pneumonia after surgery.

References

1. Bedside prediction rule for infections after pediatric cardiac surgery / Algra S., Driessen M., Schadenberg A. et al. // Intensive Care Med. – 2012. – Vol. 38. – P. 474–81.
2. The relationship between inflammatory activation and clinical outcome after infant cardiopulmonary bypass / Allan C., Newburger J., McGrath E. et al. // Anesthesia & Analgesia. – 2012. – Vol. 111. – P. 1244–51.
3. Infecciones asociadas a la atenciyn en salud en pacientes pediбtricos post-operados de cardiopatнas congйnitas / Barriga J., Cerda J., Abarca K. et al. // Revista Chilena de Infectologна. – 2014. – Vol. 31 (1). – P. 16–20.
4. Actualizaciyn del Consenso "Neumonна asociada a ventilaciyn mecбnica" Primera parte Aspectos diagnysticos / Fica A., Cifuentes M., Hervй B. // Revista Chilena de Infectologна. – 2012. – Vol. 28 (2). – P. 130–51.
5. Nosocomial infections in pediatric cardiovascular surgery patients: a 4-year survey / Grisaru-Soen G., Paret G., Yahav D. et al. // Pediatric Critical Care Medicine. – 2012. – Vol. 10. – P. 202–6.
6. Infecciyn nosocomial en postoperados de cirugна cardнaca / Guardia M., Jordan I., Urrea M. // iAnestesiologна Pediatrca. – 2012. – P. 69 (1). – 34–8.
7. Ventilator-associated pneumonia in children after cardiac surgery in The Netherlands / Roeleveld P. P., Guijt D., Kuijper E. J. et al. // Intensive Care Med. – 2012. – Vol. 37. – P. 1656–63.
8. Роль цитокінів у прогнозуванні післяопераційних ускладнень у дітей / Мошківська Л. В., Хеміо Арнес С. Г. та ін. // Вісник серцево-судинної хірургії. – 2016. – № 2. – С. 79–82.

Фактори ризику вентилятор-асоційованих пневмоній у новонароджених після кардіохірургічних операцій зі штучним кровообігом

Хеміо Арнес С. Г.[1], Згржебловська Л. В.[2], Мошківська Л. В.[1], Бойко С. М.[1], Перепека І. А.[1], Лазоришинець В.В.[1]

[1] ДУ «Національний інститут серцево-судинної хірургії імені М. М. Амосова НАМН» (Київ)
[2] Національна медична академія післядипломної освіти імені П. Л. Шупика (Київ)

Мета дослідження – визначити фактори ризику виникнення вентилятор-асоційованих пневмоній у новонароджених після кардіохірургічних операцій зі штучним кровообігом.

Методи. В дослідження включено 39 пацієнтів неонатального віку з вродженими вадами серця, яким проведено кардіохірургічну операцію і які перебували на штучній вентиляції легень більше 24 год. в післяопераційному періоді.

Результати. Обстежено 39 пацієнтів. Були виявлені штами мікроорганізмів, що найчастіше спричинюють вентилятор-асоційовані пневмонії у новонароджених: *Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterococcus faecalis*. Пацієнти, які перебувають на штучній вентиляції легень більше 72 год., і ті, яким проведено оперативне втручання з високим рівнем складності, мають більшу вірогідність виникнення пневмоній.

Висновки. Новонароджені після кардіохірургічних операцій зі штучним кровообігом, у яких виникла вентилятор-асоційована пневмонія, довше перебувають у відділенні реанімації та інтенсивної терапії.

Ключові слова: *вентилятор-асоційовані пневмонії, нозокоміальні інфекції, антибіотики, новонароджені, кардіохірургічні операції, штучний кровообіг, вроджені вади серця*.

Факторы риска вентилятор-ассоциированных пневмоний у новорожденных после кардиохирургических операций с искусственным кровообращением

Хемио Арнес С. Г.[1], Згржебловская Л. В.[2], Мошковская Л. В.[1], Бойко С. Н.[1], Перепека И. А.[1], Труба Я. П.[1], Лазоришинец В. В.[1]

[1] ГУ «Национальный институт сердечно-сосудистой хирургии имени Н. М. Амосова НАМН» (Киев)
[2] Национальная медицинская академия последипломного образования имени П. Л. Шупика (Киев)

Цель исследования – определить факторы риска возникновения вентилятор-ассоциированных пневмоний у новорожденных после кардиохирургических операций с искусственным кровообращением.

Методы. В исследование включено 39 пациентов неонатального возраста с врожденными пороками сердца, которым выполнена кардиохирургическая операция и которые находились на искусственной вентиляции легких более 24 часов в послеоперационном периоде.

Результаты. Обследовано 39 пациентов. Были обнаружены штаммы микроорганизмов, чаще всего вызывающие вентилятор-ассоциированные пневмонии у новорожденных: *Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterococcus faecalis*. Пациенты, находящиеся на искусственной вентиляции легких более 72 ч., и те, которым проведено оперативное вмешательство с высоким уровнем сложности, имеют большую вероятность возникновения пневмоний.

Выводы. Новорожденные после кардиохирургических операций с искусственным кровообращением, у которых возникла вентилятор-ассоциированная пневмония, находятся более продолжительное время в отделении реанимации и интенсивной терапии.

Ключевые слова: *вентилятор-ассоциированные пневмонии, нозокомиальные инфекции, антибиотики, новорожденные, кардиохирургические операции, искусственное кровообращение, врожденные пороки сердца*.