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Bakteryjne zapalenie płuc w następstwie mechanicznej wentylacji u osób leczonych w oddziałach intensywnej opieki – znaczenie epidemiologiczne

Bacterial pneumonia as a result of mechanical ventilation in patients treated in intensive care units – epidemiological importance

Streszczenie

Wstęp. Odrespiratorowe zapalenie płuc (VAP) należą do najczęściej występujących zakażeń szpitalnych w Oddziale Intensywnej Terapii (OIT). Najpoważniejszymi czynnikami ryzyka wystąpienia VAP jest intubacja dotchawicza oraz mechaniczna wentylacja.

Cel. Celem pracy była ocena częstości występowania odrespiratorowego zapalenia płuc oraz określenie rodzajów czynników mikrobiologicznych z pobranych materiałów z drzewa oskrzelowego.

Materiał i metody. Badaniem objęto 42 osoby (mężczyźni – 59,5%; kobiety 40,5%) hospitalizowane w OIT, u których zastosowano mechaniczną wentylację płuc. Wydzielinę z dróg oddechowych aplikowano na stałe podłoża agarowe: Columbia agar z 5% krwią baranią, agar czekoladowy, podłoże McConkeya oraz Sabourauda. Identyfikację wyhodowanych szczepów bakteryjnych oparto na określeniu ich właściwości biochemicznych, z wykorzystaniem testów komercyjnych (bio-Merieux): ID 32E i ID 32GN oraz testów ID 32 STAPH i API 20 STREP.

Wyniki. Z grupy 42 pacjentów poddanych mechanicznej wentylacji (59,5% ogółu hospitalizowanych) VAP stwierdzono u 17 (40,5%) osób. W pobranym materiale wyhodowano 30 (34,9%) szczepów pałeczek Gram-ujemnych oraz 19 (22%) szczepów ziarenkowców Gram-dodatnich, 13 (15,1%) grzybów. Największą liczbę izolowanych szczepów stwierdzono u osób, u których była prowadzona wentylacja zastępcza do 20 doby hospitalizacji.

Wnioski. Najczęściej izolowanymi drobnoustrojami z górnych dróg oddechowych były pałeczki Gram-ujemne; pacjenci przyjęci do OIT z innych oddziałów byli skolonizowani florą bakteryjną oddziału macierzystego; czas utrzymania oddechu zastępczego zwiększa ryzyko występowania odrespiratorowego płuc.

Słowa kluczowe: odrespiratorowe zapalenie płuc, wentylacja mechaniczna, oddział intensywnej terapii, izolowane bakterie.

Abstract

Introduction. Ventilator-associated pneumonia (VAP) is among the most common hospital infections in an Intensive Care Unit (ICU). The most important risk factors of VAP are endotracheal catheterization and mechanical ventilation.

Aim. The objective of the study was evaluation of the prevalence of ventilator-associated pneumonia, and determination of the type of microbiological agents in specimens collected from the bronchial tree.

Material and methods. The study covered 42 patients: 59.5% of males and 40.5% of females, hospitalized in the Intensive Care Unit (ICU), in whom mechanical ventilation was applied. Airway secretion was grown on a solid agar medium: Columbia agar with 5% sheep blood, chocolate agar, McConkey and Sabouraud media. Identification of the bacterial strains grown was based on the determination of their biochemical properties, with the use of commercial assays (bio-Merieux): ID 32E and ID 32GN and tests ID 32 STAPH and API 20 STREP.

Results. In the group of 42 patients who received mechanical ventilation (59.5% of the total number of hospitalized patients) VAP developed in 17 patients (40.5%). From the specimens 30 (34.9%) strains of Gram-negative rods, 19 (22%) strains of Gram-positive cocci, and 13 (15.1%) fungi were grown. The largest number of strains was isolated in patients who received artificial ventilation until day 20 of hospitalization.

Conclusions. The microorganisms most often isolated from the upper airways were Gram-negative rods; patients admitted to ICU from other wards were colonized with bacterial flora conveyed with them from the original ward; the duration of artificial ventilation increases the risk of occurrence of ventilator-associated pneumonia.

Keywords: ventilator-associated pneumonia, mechanical ventilation, Intensive Care Unit, isolated bacteria.

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INTRODUCTION

Epidemiological, clinical and microbiological studies show that patients treated in Intensive Care Units (ICUs) are much more frequently exposed to the risk of development of hospital infections, compared to other wards. One of the most frequently diagnosed hospital infections is hospital acquired pneumonia – HAP, which develops 48 hours after admission of a patient to hospital. A type of hospital acquired pneumonia is ventilator-associated pneumonia (VAP), which develops 48-72 after the onset of artificial ventilation or catheterization of a patient [1]. The most important risk factors of VAP are endotracheal catheterization and mechanical ventilation, which increase the risk of infection by 3-21 times [2,3]. In the 1950s, the majority of hospital acquired infections were caused by Gram-positive bacteria, mainly *Staphylococcus aureus*; however, in the 1970s – by Gram-negative bacteria, such as *Escherichia coli,* and *Pseudomonas aeruginosa.* In the subsequent decade, Gram-positive bacteria resistant to antibiotics became important: *Staphylococcus aureus,* coagulase-negative staphylococci, and *Enterococcus* sp. In the 1990s, an increase was observed again in the number of infections caused by Gram-negative bacteria (34% of infections). At present, an increased importance of Gram-positive bacteria is noted with respect to hospital-acquired infections [4].

Among many factors which cause ventilator-associated pneumonia, the following are of the greatest importance: changes in bacterial flora as a result of the primary disease, stress, antibiotic therapy applied, exposure to pathogenic bacteria in the course of treatment of the primary disease, interventions during treatment (e.g. airway suctioning), and duration of mechanical ventilation [5]. Infection with a hospital microorganism resistant to antibiotics, which occurs in patients hospitalized for longer than 7 days, is also a factor related with unfavourable prognosis. In patients in whom VAP is caused by multiresistant microorganisms, 70-80% of cases end in death. In the ICU, more than 50% of used antibiotics are designed for the treatment of patients with VAP [6]. Among patients treated at ICUs, the frequency of infections is especially high – 45-60% of the total number of patients, including 20-50% of hospital acquired infections [7].

AIM

The objective of the study was evaluation of the prevalence of ventilator-associated pneumonia, and determination of the types of microbiological agents, in order to diagnose VAP in specimens collected from the bronchial trees of patients treated in the ICU of the Provincial Hospital in Radzyń Podlaski.

MATERIAL AND METHODS

The study covered 42 patients hospitalized in the ICU of the Provincial Hospital in Radzyń Podlaski, selected from among 62 patients, i.e. all the patients treated in this unit during the 12-month period of 2010, based on the criterion of application of mechanical ventilation. The study group constituted 67.7% of the total number of patients who received treatment in the ICU, and covered 25 males (59.5%) and 17 females (40.5%).

The study was of a retrospective character; the data and information collected from the records of the Microbiological Laboratory and medical records of 62 patients treated at the ICU were used for analyses

Based on the microbiological tests performed on the bronchial tree secretions, pneumonia was diagnosed in 17 (40.5%) patients. Due to the persistence of pathological symptoms – in 11 hospitalized patients a microbiological test was repeated several times. During the period of the study, a total number of 92 airway secretion specimens were analyzed. Of these, in 6 cases a negative result was obtained.

The collected specimens were analyzed with the use of qualitative and quantitative diagnostic methods. Airway secretion was applied directly on solid agar medium: Columbia agar with 5% sheep blood, chocolate agar, McConkey and Sabouraud media. The media were incubated at the temperature of 35^{o}C, maintaining adequate oxygen conditions. The identification of the grown bacterial strains was based on the determination of their biochemical properties, with the use of commercial assays (bio-Merieux): ID 32E and ID 32GN. Also the following tests were applied ID 32 STAPH and API 20 STREP: ID 32E and ID 32GN, respectively for identification of *Enterobacteriaceae* rods and glucose non fermenting bacilli, while the tests ID 32 STAPH and API 20 STREP were used for the identification of cocci [8]. Considering the small number of the examined patients (preliminary study), statistical calculations were limited to basic analyses (real numbers), with consideration of mean values.

RESULTS

In the study group, males dominated (59.5%), and especially patients aged over 50 (76.2%); patients aged 50-69 constituted 42.9%, and those aged 70-89 – 33.3%. Table 1 presents the complete structure of the patients in the study according to gender and age.

Among 42 patients treated in the ICU in Radzyń Podlaski, the largest number – more than a half of the patients (22) previously treated in other wards, were those hospitalized first in the Hospital Emergency Department, followed by the Internal Diseases Ward – 8 patients, Surgical Ward – 7, Neurology Ward – 2, Pulmonology Ward and Orthopaedic Ward – 1 patient each. One patient was admitted from another hospital. The largest number of patients hospitalized in the ICU received treatment for 1-20 days (51.6% of the total number of patients in the study). Few patients represented the remaining categories distinguished for duration of hospitalization in the ICU. These data are presented in Table 2, as well as information concerning the mean number of days of hospitalization.

During hospitalization, 22 patients from among the total number of those in the study died (14 males and 8 females), i.e. more than a half of the patients examined (52.4%) with VAP – 81.8% of them were aged 50 or older. The mean age of the females who died was 57.8, while males – 50.5. It should be emphasized that a half of the deceased, both males and females, were aged 50-69 (Table 3).

TABLE 1. Structure of respondents broken to gender and age.

Age categories	Gender		Total
	Females	Males	
10-29	0	3	3
30-49	1	6	7
50-69	10	8	18
70-89	6	8	14
Total	17	25	42

TABLE 2. Number of days of hospitalization among patients in ICU – broken to gender.

No.	Day of hospitalization	Gender		Total	Mean number of days of hospitalization		Total
		Females	Males		Females	Males	
1	1-20	10	22	32	12.9	8.4	9.4
2	21-40	1	2	3	28	27.5	27.75
3	41-60	3	0	3	49	0	49
4	61-80	2	1	3	72	72	72
5	81-100	1	0	1	86	0	86
	Total	17	25	42	49.58	22.18	48.63

In the material collected from the patients for microbiological analyses, a total number of 86 bacterial species were identified. Thirty strains of Gram-negative rods (34.9%) were isolated from cultures, including 28 (32.5%) strains belonging to the family *Enterobacteriaceae,* 24 (27.9%) strains of glucose non-fermenting bacilli, and 19 (22%) Gram-positive cocci, while 13 (15.1%) of the samples were fungi. The largest number of strains from the family *Enterobacteriaceae* belonged to the *Klebsiella* species – 18 (20.9%), including *Klebsiella pneumoniae* 8 (9.3%); 5 of these species showed β-lactamase activity of an extended spectrum (ESBL), and also *Klebsiella oxytoca* – 2 (2.3%) showed the ability to hydrolyze oxyimino-β-lactams. Among glucose non-fermenting bacilli cultured from specimens there dominated the bacteria *Pseudomonas aeruginosa* – 15 (17.4%) and *Acinetobacter baumanii* – 9 (10.4%), whereas among Gram-positive cocci – *Staphylococcus aureus* – 15 (17.4%), including 5 (5.8%) *Staphylococcus aureus MSSA* (Table 4).

TABLE 3. Deaths among patients with VAP treated in ICU – broken to gender and age.

Age categories	Gender				Total	
	Females		Males		N	Mean age
	N	Mean age	N	Mean age		
10–29	0	0	1	27	1	27
30–49	1	38	4	42	5	41.2
50–69	5	62.8	6	63.8	11	63.36
70–89	2	82.5	3	77.6	5	79.6
Total	8	57.8	14	50.5	22	52.79

TABLE 4. Species of microorganisms cultured from biological material collected from patients in ICU.

Isolated microorganism	N
Escherichia coli	8
Klebsiella pneumoniae	3
Klebsiella pneumoniae ESBL(+)	5
Klebsiella oxytoca ESBL(+)	1
Klebsiella oxytoca	1
Enterobacter cloace	3
Citrobacter frendii ESBL(+)	1
Citrobacter frendii	3
Proteus mirabilis	1
Proteus vulgaris	1
Enterobacter aerogenes	1
Haemophilus influense	2
Pseudomonas aeruginosa	15
Acinetobacter baumanii	9
Staphylococcus aureus	10
Staphylococcus aureus MSSA	5
Streptococcus pneumoniae	4
Candida tropicalis	2
Candida albicans	11

TABLE 5. Bacteria isolated from material collected from the bronchial tree in patients with the diagnosis of VAP – broken to duration of artificial ventilation.

Original ward of patient's hospitalization	Day of artificial ventilation			
	5	10	15	20
Hospital Emergency Department 9 patients	• *Staphylococcus aureus* MSSA • *Streptococcus pneumoniae* • *Escherichia coli* • *Candida albicans*	• *Pseudomonas aeruginosa* • *Acinetobacter baumanii*	• *Acinetobacter baumanii* • *Hemophilus influense*	• *Pseudomonas aeruginosa* • *Escherichia coli* • *Klebsiella oxytoca* • *Staphylococcus aureus*
Surgical Ward 1 patient	Negative	• *Acinetobacter baumanii* • *Candida albicans*	*	*
Orthopaedic Ward 1 patient	• *Streptococcus pneumonia*	*	• *Acinetobacter baumanii*	*
Internal Medicine Ward 4 patients	• *Candida albicans* • *Proteus mirabilis* • *Klebsiella oxytoca* • *Staphylococcus aureus*	• *Acinetobacter baumanii* • Staph*ylococcus aureus* • *Candida albican*	• *Acinetobacter baumanii* • *Pseudomonas aeruginosa* • *Streptococcus pneumonia* • *Proteus vulgaris*	*
Pulmonology Ward 1 patient	*	• *Acinetobacter baumanii*	*	*
From other hospitals 1 patient	• *Klebsiella pneumonia* ESBL(+) • *Pseudomonas aeruginosa*	• *Klebsiella pneumonia* ESBL(+)	*	*

*Empty boxes in the table mean that the material for microbiological analysis was not collected due to discharge of a patient from the ward, or for various other reasons.

In the group of 17 patients with the diagnosis of ventilator-associated pneumonia, microbiological material collected from the airways was analyzed to investigate the microbial colonization according to the duration of artificial ventilation. The largest numbers of isolated strains (mixed microbial flora) were observed in patients who received artificial ventilation until day 20 of hospitalization. These were patients hospitalized in the Hospital Emergency Department (HED), colonized by the strains *Pseudomonas aeruginosa, Escherichia coli, Klebsiella oxytoca,* and *Staphylococcus aureus*. During the first 15-day period of ventilation of patients hospitalized in the HED, there were grown *Acinetobacter baumanii, Hemophilus influense*, in the Orthopaedic Ward – *Acinetobacter baumanii*, and in the Internal Medicine Ward – *Acinetobacter baumanii, Pseudomonas aeruginosa, Streptococcus pneumonia,* and *Proteus vulgaris* (Table 5).

The data in Table 6 show that the duration of artificial ventilation exerts an effect on the frequency of occurrence of ventilator-associated pneumonia - the longer the duration of ventilation the higher the risk of pneumonia occurrence. In the examined group of patients, ventilator-associated pneumonia was diagnosed before day 5 in 3, before day 10 - in 7, and also in 7 patients hospitalized in ICU for at least 15 days.

TABLE 6. Occurrence of ventilator-associated pneumonia and duration of artificial ventilation.

Specification	Day of artificial ventilation		
	5	10	≥ 15
Number of patients with VAP	3	7	7
Mean duration of hospitalization	13.7	28.9	45.7

DISCUSSION

Since 1996 in Poland, an infection control programme has been functioning, coordinated by the Polish Association for Hospital-Acquired Infections, developed in cooperation with the Center for Disease Control and Prevention in Atlanta, USA. The investigations carried out by the Polish Association for Hospital-Acquired Infections, which consisted in a passive detection and registration of infections, showed that in hospital wards morbidity due to pneumonia remains on the level of 0.5% of hospitalized patients, while in Intensive Care Units it is as high as 4.2% [9]. These reports have been considered as an indication for controlling ventilator-associated pneumonia in the Intensive Care Unit at the Provincial Hospital in Radzyń Podlaski. Further data obtained by the Association, which came from the programme of active registration, indicated that the level of discussed infections was higher – 5.6% of cases [10]. In 1999, within the framework of the above-mentioned studies, an analysis was performed of hospital-acquired infections registration charts in ICUs, in 120 hospitals in the whole of Poland. It was found that in ICU hospital-acquired pneumonia concerned mainly patients who received respirotherapy. Per 334 patients with the diagnosis of hospital-acquired pneumonia, the ventilator was used in 264 cases. Also, in the hospital in Radzyń, a high percentage (40.5%) of cases of ventilator-associated pneumonia was found in patients in the ICU who received artificial ventilation. A slightly higher morbidity was observed among patients who in 2005 were covered by the study carried out by the research team of Heczko. The data from various scientific reports concerning the epidemiology of VAP show that this nosologic unit is diagnosed in 9.7-22.8% of those who received mechanical ventilation, and resulted in the prolongation of hospitalization by 6.5 days, on average, high mortality – up to 50%, and a considerable increase in the costs of treatment [2,11]. In turn, the studies by Zeliaś et al. show that among patients hospitalized in an ICU, ventilator-associated pneumonia was diagnosed twice as frequently as among those who had received treatment for less than 5 days [12]. These results are consistent with the results of the presented study. Epidemiological investigations show that the development of pneumonia during the period before day 4 is related with a more favourable prognosis, whereas the development of the disease after day 5 brings about the risk of infection with drug resistant microorganisms [13].

The studies by Karpiel show that among the analyzed etiologic factors of hospital-acquired pneumonia in an ICU dominated: *Pseudomonas aeruginosa (*26.5%), and *Serratia* sp. (9.2%) [14]. Other studies indicate that the cases of early hospital-acquired pneumonia usually have the same etiology as ambulatory infections, while late infections in patients receiving artificial ventilation are most often caused by Gram-negative cocci of the family *Enterobacteriaceae,* or non-fermenting bacilli of the species *Acinetobacter* and *Pseudomonas.* These are bacteria, which colonize a patient earlier and are characterized by a high resistance to antibiotics [15]. The presented results of bacteriological analysis of the clinical specimens collected in 2010 from patients hospitalized in the Provincial Hospital in Radzyń Podlaski confirmed the above-presented results, and show that among 86 isolated microorganisms the most abundant group, 54 strains, were Gram-negative rods, including 28 strains of the family *Entreobacteriaceae.* Among 23 non-fermenting bacilli, 15 were *Pseudomonas aeruginosa* and 8 – *Acinetobacter baumanii.*

CONCLUSIONS

1. The majority of patients treated in the ICU were aged 50-69, and in this age group, cases of death were at least twice as frequently noted as among patients in other age categories.
2. Patients who received treatment in the ICU, with the necessity for mechanical ventilation, were especially exposed to infection with Gram-negative rods.
3. Patients admitted to the ICU from other wards were colonized with microbial flora from their original ward.
4. The duration of artificial ventilation is a risk factor of occurrence of ventilator-associated pneumonia (VAP).

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