ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN — POLONIA
VOL. LIV, 38 SECTIO D 1999

II Klinika Anestezjologii i Intensywnej Terapii Akademii Medycznej w Lublinie
Kierownik: dr hab. Krzysztof Przesmycki

Zakład Mikrobiologii Klinicznej Szpitala w Hvidovre Uniwersytetu w Kopenhadze
Kierownik: prof. dr Hans J. Kolmos

KRZYSZTOF PRZESMYCKI, JADWIGA BIERNACKA,
ZIEMOWIT RZECKI, EWA LORENTZ, HANS-JORN KOLMOS

Prevalence of various pathogens in patients treated in intensive care unit during the 7–year period

Ocena częstości występowania różnych patogenów bakteryjnych u chorych leczonych w oddziale intensywnej terapii w okresie siedmiu lat

The risk of complications due to infections to patients in Intensive Care Units (ICU) may be as much as three times greater than to patients in other wards of the same hospital (2, 3). This risk is connected both with severe disorders of the basic life functions and the invasive diagnostic and therapeutic procedures. Traditionally, epidemiological studies concern the whole hospital or region (5). It is necessary to conduct microbiological examinations focused on individual wards, especially in ICU, as the types of pathogens and their sensitivity to antibiotics *in vitro* may vary considerably (15).

In our previous studies (8, 9), conducted in ICU during the periods 1990–1993 and 1994–1995 we observed an almost threefold decrease in the frequency of occurrence of *Escherichia coli* bacteria with a simultaneous increase in the prevalence of other Gram–negative pathogens (*Pseudomonas aeruginosa*, *Enterobacter aerogenes* and *Proteus mirabilis*), together with the tendency to increase of Gram–positive bacteria and not significant changes in the prevalence of *Staphylococcus aureus*. Therefore, we decided to expand the survey for the year 1996, to study the further changes in frequency of various pathogens and to compare the resistance of organisms in relation to consumption of antibiotics.

MATERIAL AND METHODS

The study covered all patients hospitalised in the ICU of the Department of Anaesthesiology and Intensive Therapy of Medical University School in Lublin, during the years 1990–1996. The material for microbiological examinations were samples taken routinely from blood, intravenous catheters, wounds, drains and endotracheal aspirates. Microbiological examinations were carried out at Central

Laboratory of the Teaching Hospital No. 4 in Lublin. Bacterial cultures were performed in aerobic conditions using an agar medium supplemented with blood and Chapman or Mc Conkey medium, for Gram–positive or Gram–negative bacteria, respectively. The Enteroplast EPL 21 system was used for differentiating Gram–negative bacteria. *Staphylococcus aureus* bacteria were identified as the coagulase or hemolysin positive or negative species. The bacterial cultures obtained were evaluated annually, with respect to the frequency of occurrence of individual pathogens.

After isolation and identification (genus and species) of pathogens antimicrobial susceptibility was determined on Mueller–Hinton medium, according to standard disc sensitivity criteria. Resistance was defined according to National Committee for Clinical Laboratory Standards (NCCLS tables) criteria (6). The analysis of antimicrobial susceptibility patterns of the most commonly isolated organisms was performed and compared between the periods: 1990–1991, 1992–1993, 1994–1995 and the year 1996.

Antibiotics consumption in ICU was based on the records from hospital pharmacy and number of the defined daily doses of antibiotics (DDD) ordered from hospital pharmacy. The defined daily dose is a technical unit of comparison, and not necessarily a recommended dosage. Lists of DDD are published regularly (4). To simplify calculations, consumption of antibiotics was compared between the periods 1990–1991, 1992–1993, 1994–1995 and 1996, and assessed according to frequency of antibiotics consumption (5) in the following groups: 1. – cephalosporins III generation (ceftazidime, cefoperazone, cefotaxime and ceftriaxone), 2. – aminoglycosides (amikacin, gentamicin and netilmicin), 3. – cephalosporins II generation (cefamandole and cefuroxime), 4. – penicillins III–IV generation (carbenicillin and azlocillin), 5. – other antibiotics: metronidazole, doxycycline, co–trimoxazole, penicillins I–II generation (penicillin G, amoxicillin–clavulanate and ampicillin), cephalosporin I generation (cephradine), quinolones: (ciprofloxacin and ofloxacin), glycopeptides (vancomycin and rifampin), lincomycin, clindamycin, imipenem/cilastin.

An evaluation of the statistical significance for the differences observed between the study periods was conducted by Chi–square test or Fisher exact test. For significant differences $p < 0.05$ has been adopted.

RESULTS

The demographic data of patients treated in the years 1990–1996 in ICU did not significantly differ during the time of the study. Patients were admitted to ICU from other hospital wards (58–69%) or from Accident/Emergency Dept. (29–38%) and other hospitals (2.5–5%); after surgery (41–50%), multiorgan trauma (17–22%) or from medical departments (7.1–12%). Number of patients treated in ICU annually did not differ significantly between the years 1990–1996. However, in the years 1994–1996 the number of bed days significantly increased to 3,180, from 1,275–1,626 bed days in 1990–1993.

Demographic and clinical data did not significantly differ during the time of the study, except for the smaller number of patients admitted to ICU after surgical procedures in 1991 or with multiorgan trauma in 1993 and significantly greater number of patients admitted with acute respiratory failure in 1992 and with sepsis in 1994–1996.

In the years 1990–1996, 659 positive microbial cultures were obtained from 307 patients with infection for the total number of 829 patients hospitalised in ICU. No statistically significant differences were observed in the frequency of positive microbiological tests performed in individual years

(32–38% of the total number of patients). Similarly, no significant differences were noted in the percentages of polymicrobial cultures (26–36%), antibiotic resistant bacteria (11–20%) and the occurrence of fungi (2–4%).

The prevalence of most frequently isolated Gram–negative pathogens (percentage of total number of positive cultures) in individual years presents Figure 1. *Escherichia coli* bacteria occurred less frequently in the years 1990–1996 (the decrease from 44.7% to 10.6%), with a simultaneous significant increase in the occurrence of *Pseudomonas aeruginosa* in the years 1990–1996 (the increase from 2.6% to 29.8%). Other Gram–negative bacteria were *Proteus mirabilis* (2.2–9.0%) and pathogens identified less frequently (1.7–6.0%): *Klebsiella pneumoniae*, other strains of *Pseudomonas*, *Acinetobacter anitratus*, *Serratia marcescens* and *Ervinia herbicola*. In general, the percentage of Gram–negative bacteria decreased from 60% of all pathogens in 1990 to 48% in 1996, with a corresponding increase in infections caused by Gram–positive bacteria.

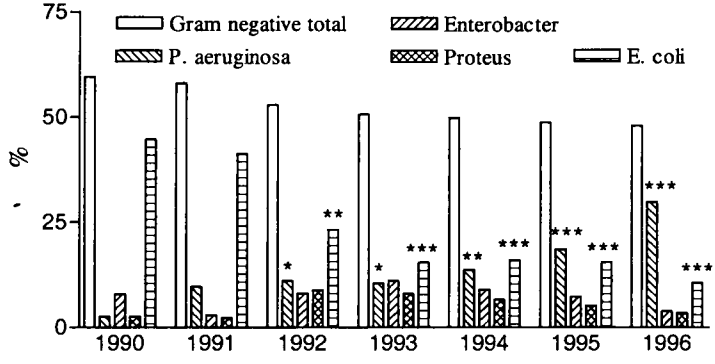

Fig. 1. Prevalence of most frequently isolated Gram–negative pathogens (percentage of total number of positive cultures) in individual years
* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, Chi square test, vs. the year 1990

Gram–positive bacteria constituted approximately 40% of all isolated bacteria at the beginning of survey. After 7 years of the study, the increase in the percentage of Gram–positive bacteria to 52% was observed. The significant increase in the occurrence of *Staphylococcus aureus* was also noticed; from 25.4% in 1990 to 48.9% in 1996 (Figure 2). Other Gram–positive bacteria were identified less frequently and did not show any constant changes during the period 1990–1996. There were identified other staphylococci: *Staphylococcus epidermidis* and *albus* 3.1–17.3%, *Bacillus subtilis* 1.5–4.9%, *Streptococcus* and *Aerococcus spp.* 3.5–8.8%.

Prevalence of antimicrobial susceptibility of the most commonly isolated organisms (*E. coli*, *P. aeruginosa*, *S. aureus*) did not differ statistically between the periods of the study 1990–1991, 1992–1993, 1994–1995 and 1996, except for an increased resistance to cephradine by *E. coli* species. Amikacin from the aminoglycosides, and amoxicillin–clavulanate from penicillins showed the best antimicrobial properties against Gram–negative, and Gram–positive organisms; respectively. Antimicrobial susceptibility of main pathogens to cephalosporins of III generation did not differ significantly during the study period.

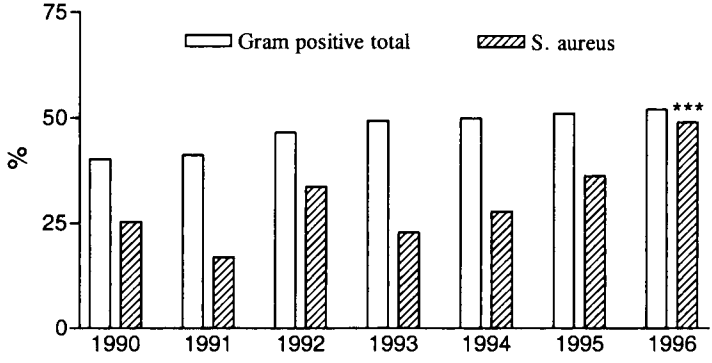

Fig. 2. Prevalence of Gram–positive pathogens and *S. aureus* (percentage of total number of positive cultures) isolated in individual years
*** $p < 0.001$, Chi square test, vs. the year 1990

Consumption of all antibiotics and cephalosporins of III generation (45% of all antibiotics) did not differ statistically between the years 1990–1991 and 1992–1993. Consumption of aminoglycosides, cephalosporins of II generation and penicillins of III–IV generation showed a significant decrease in the years 1992–1993 and a significant increase in the years 1994–1996. In the years 1994–1996, consumption of all antibiotics significantly increased except the decreased consumption of cephalosporins of III generation.

DISCUSSION

In the years 1950–60 serious infections were primarily caused by Gram–positive bacteria. In the following years, 1970–1980 a significant increase (30–fold) was observed in the number of Gram–-negative rods in hospital infections (10). This growth was associated with the fact that these bacteria are extremely undemanding with respect to their environment. Bacteriological examinations carried out in Poland in the 1980's confirmed a very high percentage of Gram–negative bacteria in hospital infections, especially in ICU, where they comprised 90.8% of pathogens (10) and 71.5% (1).

Bacteriological examinations in patients with bacteremia and sepsis also showed a significant percentage of Gram–negative bacteria in 57% of positive microbial blood cultures (11). However, the following retrospective epidemiological studies, conducted in Italy in the years 1987–1990, which covered patients with bacteremia treated in ICU, showed a significant increase in the percentage of Gram–positive bacteria – up to 70% in positive microbial blood cultures (11, 12). The increasing importance of Gram–positive bacteria in infections at ICU was also confirmed by the extensive international microbiological studies conducted in Europe EPIC in 1992 (13). According to these studies, bacteria of the *Enterobacteriaceae* group occurred most frequently (34%); however, the next most frequently occurring pathogen was *Staphylococcus aureus* (30.1%) and other Gram–positive bacteria e.g. *S. epidermidis* and others (19.1%) and *Streptococci* (7.1%). The results of those comprehensive studies, which covered 10,038 patients, showed that almost 50% of bacteria noted at ICU were

Gram–positive. This may suggest a further change in the profile of bacteria types with serious clinical consequences.

The most characteristic observation in the present study was a further decrease in the percentage of *Escherichia coli* (to 10.6%) and a further increase in the percentage of *Pseudomonas aeruginosa* (to 29.8%) when compared with earlier observations (8, 9). American retrospective studies (14), comparing the profile of secondary infections in patients treated in one hospital in the years 1975–1978 and 1979–1982, showed a similar significant decrease in the percentage of *Escherichia coli* bacteria. On the other hand, later studies, also conducted in one centre (during the years 1987–1991), comparing the change in bacteria types found at ICU, showed that *Pseudomonas aeruginosa* – more resistant to aminoglycosides and beta–lactams, occurred significantly more often (15). Similarly, European EPIC studies (13) confirmed that at present *Pseudomonas* is the most frequent Gram–negative bacteria isolated in 28.7% of patients hospitalised in ICU, which is second only to *Staphylococcus aureus* – 30.1%.

The results of our studies confirmed a significant share of Gram–positive bacteria 52%, with the dominant participation of *Staphylococcus aureus* – 48.9% of the total number of pathogens found in ICU. These infections are commonly assumed to be caused by invasive diagnostic and therapeutic procedures, especially catheterization of large vessels. Another reason is the growing resistance of *Staphylococci* to antibiotics (14).

Based on the comparison of demographic and clinical data during the period of the study it is difficult to find other reasons for the differences observed in the bacterial cultures within the population. Demographic data did not significantly differ during the time of the study and clinical data showed no constant changes during the period 1990–1996 that might cause the typical decrease in the number of *E. coli* bacteria and the increase in the number of *Pseudomonas* during this time. Consumption of all antibiotics and cephalosporins of III generation (the main antibiotics used in ICU) did not change during 1990–1993 (9). The same consumption and profile of main antibiotics do not exclude the possibility that the changes observed among Gram–negative micro–organisms in 1990–1993 could be explained by the profile of antibiotics used earlier in ICU i.e. before the introduction of cephalosporins.

The significant increase of consumption of all antibiotics in the years 1994–1996 could be explained by the increased number of bed days and patients admitted to ICU with sepsis (8). The consumption of cephalosporins of III generation even decreased significantly in the last period of the study. One reason for the continuous high consumption of cephalosporins of III generation was probably their wide spectrum of antimicrobial activity. The significant decrease of consumption of aminoglycosides, cephalosporins of II generation and penicillins of III–IV generation observed in the years 1992–1993, and its significant increase in the years 1994–1996, could be related to the changes observed in antimicrobial resistance among *Enterobacteriaceae* over time (7).

CONCLUSIONS

1. The study confirmed the continuous change in the profile of pathogen types found in ICU, toward Gram–positive bacteria with the dominant participation of *Staphylococcus aureus*.

2. At the same time, a significant decrease in the frequency of occurrence of *Escherichia coli* bacteria, with an increase in the prevalence of *Pseudomonas aeruginosa* was observed.

3. Demographic and clinical data, and the consumption of main antibiotics and antimicrobial susceptibility did not change in a way which would explain the increase in prevalence of Gram–positive bacteria.

REFERENCES

1. Badylak–Kępińska K. et al.: Najczęstsze zakażenia bakteryjne występujące w okresie pooperacyjnym u chorych leczonych w oddziale intensywnej opieki medycznej. Anestezjologia Intensywna Terapia, 17, 60, 1985.
2. Daschner F.D. et al.: Nosocomical infections in intensive care wards: a multicenter prospective study. Intensive Care Med., 8, 5, 1982.
3. Donowitz L.G., Wenzel R.P., Hoyt J.W.: High risk of hospital–acquired infections in the ICU patient. Crit. Care Med., 10, 355, 1982.
4. Fris H.: Antibiotikaforbrug i definerede daglige doser (DDD) – fordele og ulemper. Ugeskr. Laeger, 146, 2565, 1987.
5. Koontz F.P.: A review of traditional resistance surveillance methodologies and infection control. Diagn. Microbiol. Infect. Dis., 15, 43S, 1982.
6. National Committee for Clinical Laboratory Standards. Performance Standards for Antimicrobial Susceptibility Testing; Fourth Informational Supplement. NCCLS Document M 100–S4. NC–CLS, Villanova, PA, 1992.
7. Neu H.C., Duma R.J., Jones R.N.: Antibiotic resistance: epidemiology and therapeutics. Diagn. Microbiol. Infect. Dis., 15, 53S, 1992.
8. Przesmycki K. et al.: Prevalence of various pathogens in patients treated in an Intensive Care Unit during a 6–year period. Med. Sci. Monit., 3, 708, 1997.
9. Przesmycki K. et al.: Retrospektywna ocena częstości występowania różnych patogenów bakteryjnych u chorych leczonych w oddziale intensywnej terapii w okresie 4 lat. Anestezjologia Intensywna Terapia, 28, 73, 1996.
10. Rybicki Z. et al.: Ocena populacji bakterii wyhodowanych z dróg oddechowych i ich odporności na antybiotyki w materiale intensywnej terapii. Anestezjologia. Intensywna Terapia, 20, 93, 1988.
11. Silvestri L. et al.: Bacteraemia in Intensive Care Unit: a four–year survey. Recent Advances in Anaesthesia, Pain, Intensive Care and Emergency, APICE, Trieste, 6, 185, 1991.
12. Silvestri L. et al.: Gram–Positive Bacteraemia in Intensive Care Unit. Recent Advances in Anaesthesia, Pain, Intensive Care and Emergency, APICE, Trieste, 7, 561, 1992.
13. Spencer R.C.: Nosocomical infection in the intensive care unit: a question of surveillance. Intensive Care World, 10, 173, 1994.
14. Stillmann R.I., et al.: Emergence of coagulase negative staphylococci as major nosocomical bloodstream pathogens. Infect. Control, 8, 108, 1987.
15. Stratton C.W. et al.: Focused microbiologic surveillance by specific hospital unit as a sensitive means of defining antimicrobial resistance problems. Diagn. Microbial. Infect. Dis., 15, 11S, 1992.
16. The Veterans Administration Systemic Sepsis Cooperative Study Group. Effect of high dose glucocorticoid therapy on mortality in patients with clinical signs of systemic sepsis. N. Engl. J. Med., 317, 659, 1987.

Otrz.: 1999.11.10

STRESZCZENIE

Oceniano częstość występowania różnych patogenów bakteryjnych u chorych leczonych w oddziale intensywnej terapii (OIT) w latach 1990–1996. Zmiany w częstości występowania patogenów porównano z występującą opornością bakterii na antybiotyki i rocznym zużyciem antybiotyków. Siedmioletnia analiza epidemiologiczna wykazała stałą tendencję w zmianie częstości występowania patogenów w OIT w kierunku zwiększenia częstości występowania bakterii Gram dodatnich (od 40% do 52% wszystkich izolowanych szczepów), z przewagą *Staphylococcus aureus* (do 48,9%). Obserwowano także czterokrotne zmniejszenie częstości występowania bakterii *Escherichia coli* (od 44,7% do 10,6% wszystkich izolowanych szczepów), z jednoczesnym zwiększeniem częstości występowania bakterii *Pseudomonas aeruginosa* do 29,8%. Dane demograficzne i kliniczne oraz roczne zużycie antybiotyków i antybiotykooporność nie ulegały zmianie w sposób umożliwiający wytłumaczenie zwiększenia częstości występowania bakterii Gram dodatnich. Nie można wykluczyć wpływu zmiany antybiotyków stosowanych wcześniej na wprowadzone do leczenia cefalosporyny.