

Evaluation of Device-associated Nosocomial Infections in a Paediatric Intensive Care Unit

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ABSTRACT

Objectives: The aim of this study was to evaluate the rate of device-associated healthcare-associated infections (DA-HAI) in a paediatric intensive care unit (PICU). In addition, the identities of the responsible micro-organisms and of their antibiotic sensitivities were determined.

Subjects and Methods: Patients who had been treated and followed-up in a PICU for more than 48 hours between January 2008 and December 2013 were included in the study. Device-associated nosocomial infections were defined by the Centers for Disease Control (CDC) criteria.

Results: Nosocomial infections were detected in 244 of the 7376 patients over the six-year period. A diagnosis of DA-HAI was made in 75 (30.7%) of these infections. The rates of device utilization were 26% for mechanical ventilators, 6% for central venous catheters and 0.9% for urethral catheters. The rate of device-associated infections was 30.7%, and their frequency was 1.9/1000 patient-days. The device-associated nosocomial infection rates for mechanic ventilators, central and urethral catheters were 5.6, 1.62 and 3.77 per 1000 patient-days, respectively. Of these infections, *Pseudomonas aeruginosa* was the most frequent pathogen. Patients who developed hospital infections had longer durations of ICU hospitalizations and more often had to use mechanical ventilators and central and urinary catheters.

Conclusions: The duration of hospitalization and the use of mechanical ventilators and central and urinary catheters were related to the increases in nosocomial infections. Therefore, target-oriented active surveillance should be regularly performed, and the superfluous employment of invasive devices should be avoided.

Keywords: Intensive care unit, invasive device utilization, surveillance

Evaluación de infecciones nosocomiales asociadas con dispositivos en una unidad de cuidados intensivos pediátricos

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RESUMEN

Objetivos: El objetivo de este estudio fue evaluar la tasa de infecciones asociadas con la atención a la salud e infecciones asociadas con dispositivos (IAAS-IAD) en las unidades de cuidados intensivos pediátricos (UCIP). Además, se determinó la identidad de los microorganismos responsables y su sensibilidad antibiótica.

Sujetos y métodos: En el estudio se incluyeron pacientes que habían sido tratados y recibido seguimiento en una UCIP durante más de 48 horas entre enero de 2008 y diciembre de 2013. Las infecciones nosocomiales asociadas con dispositivos fueron definidas por los criterios de los Centros de Control de Enfermedades (CCE).

Resultados: Las infecciones nosocomiales fueron detectadas en 244 de los 7376 pacientes durante un período de seis años. Se realizó un diagnóstico de IAAS-IAD en 75 (30.7%) de estas infecciones. Las tasas de utilización de dispositivos fueron 26% para los ventiladores mecánicos, 6% para los catéteres venosos centrales, y 0.9% para los catéteres uretrales.

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La tasa de las infecciones asociadas a dispositivos fue de 30.7%, y su frecuencia fue 1.9/1000 pacientes-días. Las tasas de infección nosocomial asociada con dispositivos fueron 5.6, 1.62 y 3.77 por 1000 pacientes-días para los ventiladores mecánicos, los catéteres centrales y los uretrales, respectivamente. De estas infecciones, Pseudomonas aeruginosa fue el patógeno más frecuente. Los pacientes que desarrollaron infecciones hospitalarias tuvieron hospitalizaciones de ICU de más larga duración, y tuvieron que utilizar ventiladores mecánicos y catéteres centrales y urinarios más a menudo.

Conclusiones: *La duración de la hospitalización y el uso de ventiladores mecánicos y catéteres centrales y urinarios, estuvieron relacionados con los aumentos en las infecciones nosocomiales. Por lo tanto, debe realizarse regularmente una vigilancia activa orientada a estos objetivos, y debe evitarse el empleo superfluo de dispositivos invasivos.*

Palabras claves: unidad de cuidados intensivos, utilización de dispositivos invasivos, vigilancia

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INTRODUCTION

Device-associated healthcare-associated infections (DA-HAI) constitute a considerable amount of healthcare associated infections (HAI). These infections pose a great risk, especially for patients hospitalized in the intensive care unit (ICU), which is responsible for approximately 10 to 15 per cent of nosocomial infections. Nosocomial infections may be due to the poor clinical conditions of the patients and the prevalent use of invasive procedures, such as mechanical ventilators, central venous- and arterial catheters and urethral catheters.

Hospital infections are important causes of increasing morbidity and mortality (1–4). These infections may be better controlled with sufficient follow-up of surveillance results in each hospital, by comparing these results with those of other hospitals, and by taking effective precautions against these infections. The National Nosocomial Infection Study (NNIS)-based scoring of invasive device-associated infections provides protocols for the proper measurement and standardizations of these procedures.

The present study was a surveillance study performed in an ICU of a paediatric hospital, which is the largest study in that area conducted in Turkey. We aimed to determine the DA-HAI rates, their responsible pathogens and the antibiotic sensitivities of these pathogens. We also aimed to monitor the changes in these parameters over a six-year period, and in doing so, we propose more efficient preventive measures and to contribute to the planning of empirical antibiotherapy.

SUBJECTS AND METHODS

In this study, data were prospectively collected from patients who had been hospitalized due to infectious or non-infectious reasons at the paediatric ICU of Diyarbakir Paediatric Diseases Hospital between January 1, 2008 and December 31, 2013, with a diagnosis of HAI on follow-up. This hospital is a state-run hospital under the regulation of the Ministry of Health and provides inpatient and outpatient treatment services for the southeastern Anatolia region and has 567 beds. This hospital's paediatric ICU includes 20 beds (with two reserved for

patient isolation), seven mechanical ventilators, two resident pediatricians, six nurses and two personnel staffing each shift. At this hospital, 4189 patients were followed-up between 2008 and 2011.

During the duration of the study, an active prospective surveillance was performed in the paediatric ICU five days/week by a resident internist who specialized in infectious diseases and by two nurses employed for infection control. In this study, the overall HAI rates, the invasive device-utilization rates and the DA-HAI rates were monitored.

From each patient who was thought to have developed HAI, culture samples were obtained from the blood, urine, sputum, cerebrospinal fluid, wound site, catheters and from the endotracheal aspirates, if the patient received mechanical ventilation.

BACTEC Peds Plus™/F (BD, Sparks, MD) culture bottles were used for collecting blood samples. The Phoenix automated culture system was used to identify the organisms and their antibiotic sensitivities. The reports, which were written according to the standards of the Clinical and Laboratory Standards Institute, USA, were assessed. The clinical and laboratory results were investigated at the time of diagnosis. Laboratory results included positive cultures, which were obtained from presumably sterile sites (blood, central nervous system fluid, pleural and peritoneal fluids), peripheral leukocyte and platelet counts, C-reactive protein (CRP) levels and new infiltrations on radiological images. Clinical results included fever, pulmonary auscultation findings and hypotension. The clinical, radiological, laboratory and culture results of patients with an HAI diagnosis were recorded on the standard forms of the NNIS-system and the data were recorded daily into computers. The diagnosis of HAI was made according to the criteria of the Centers for Disease Control and Prevention.

For data scoring, the following formulae were used: hospital infection rate (%) = (number of infections/hospitalized patients) × 100; density of incidence = (number of infections/days of hospitalization) × 100; rate of device utilization = (number of days with invasive interventions/days of hospitalization) and DA-HAI rate = (number of infections associated

with invasive device utilization/number of days with invasive interventions) × 1000. The statistical data analysis was performed using SPSS 15.0 statistical package software.

RESULTS

During the six-year study period, there were 244 HAI episodes in 218 of 7376 patients. Seventy-five (30.7%) of these infections were classified as DA-HAI. Of the 72 patients who developed DA-HAI, 30 (42%) were female and 42 (58%) were male. Of these 72 patients, 60 (88.3%) had a previously diagnosed primary or chronic underlying disease. The rate of hospital infection was 6.1% in the paediatric ICU. Blood stream infections were the most frequent HAI, with the rate of 2.04/1000 patient days. Distributions, percentages and the incidence rates of HAI, which were classified according to the infection sites, are presented in Table 1. In the present study, 57 of the DA-HAIs were related to ventilator associated pneumonia (VAP) and 14 were related to urinary catheter-related infections (UC-RI).

The rates of DA-HAI per 1000 device days and the device

utilization rates over the study’s six-year period are presented in Table 2. Patients with a VAP diagnosis were hospitalized for a mean duration of 144 ± 163.7 days (median: 63 days) and they were diagnosed with VAP at 61.4 ± 91.5 days (median 23 days) of hospitalization. The demographic characteristics of the paediatric ICU patients diagnosed with VAP are presented in Table 3. The responsible micro-organisms were determined in 24 of the 75 DA-HAI cases. The most frequently isolated micro-organism was *Pseudomonas* spp (62.5%). Colistin was the most effective antimicrobial agent against *Pseudomonas aeruginosa*, as revealed by in vitro susceptibility tests. Distribution of isolated micro-organisms from DA-HAIs are presented in Table 4.

Table 1: Distribution of healthcare-associated infections (HAI) according to the infection sites

| | Number of infections | Per cent of total infections | Incidence rates |
|-------------------------------------------|----------------------|------------------------------|-----------------|
| Bloodstream infection | 81 | 33.19 | 2.04 |
| Ventilator-associated-pneumonia | 57 | 23.36 | 1.43 |
| Pneumonia | 51 | 20.90 | 1.28 |
| Urinary tract infection | 18 | 7.37 | 0.45 |
| Urinary catheter related infection | 14 | 5.73 | 0.35 |
| Gastrointestinal infection | 9 | 3.68 | 0.22 |
| Skin and soft tissue infection | 8 | 3.27 | 0.20 |
| Catheter-associated bloodstream infection | 4 | 1.63 | 0.10 |
| Surgery site infection | 1 | 0.40 | 0.02 |
| Others* | 1 | 0.40 | 0.02 |
| Total | 244 | 100 | 6.1 |

*Conjunctivitis

Table 2: Rates of device-associated hospital-associated infections (DA-HAI) per 1000 device days and device utilization ratios for six years

| Year | Patients (n) | Patient (day) | Ventilation (day) | Ventilatory utilization ratio | VAP (n) | Rate of VAP | | | | | | | | |
|--------------|--------------|---------------|-------------------|-------------------------------|-----------|-------------|-------------|-------------|----------|------------|-------------|-------------|-----------|-------------|
| 2008 | 660 | 2808 | 355 | 0.13 | 1 | 2.82 | 6 | 0.00 | 0 | 0.00 | 1 | 0.00 | 0 | 0.00 |
| 2009 | 1128 | 4677 | 823 | 0.18 | 5 | 6.08 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 |
| 2010 | 979 | 5556 | 1493 | 0.27 | 8 | 5.36 | 226 | 0.04 | 0 | 0.00 | 665 | 0.12 | 0 | 0.00 |
| 2011 | 1422 | 6992 | 1332 | 0.19 | 7 | 5.26 | 516 | 0.07 | 0 | 0.00 | 1068 | 0.12 | 1 | 0.00 |
| 2012 | 1674 | 8917 | 2269 | 0.25 | 19 | 8.37 | 827 | 0.09 | 3 | 3.63 | 976 | 0.11 | 5 | 5.12 |
| 2013 | 1513 | 10732 | 3892 | 0.36 | 17 | 4.37 | 847 | 0.08 | 1 | 1.18 | 1006 | 0.09 | 8 | 7.95 |
| Total | 7376 | 39682 | 10164 | 0.26 | 57 | 5.6 | 2422 | 0.06 | 4 | 1.6 | 3716 | 0.09 | 14 | 3.77 |

VAP: ventilator associated pneumonia; CC-BSI: central catheter-associated bloodstream infection; UC-RI : urinary catheter-related infection

Table 3: Demographic characteristics of patients diagnosed with ventilator-associated pneumonia (VAP) in the paediatric intensive care unit

| | n = 57 (%) | or average ± SS (the variation range) |
|------------------------------------|---------------|---------------------------------------|
| Gender | | |
| Female | 34 (59.6) | |
| Male | 23 (40.4) | |
| Age (month) | 34.4 ± 52.2 | (1–184) |
| Hospitalization time (days) | 144 ± 163.7 | (11–638) |
| Detection of the first day of VAP | 61.4 ± 91.5 | (4–350) |
| Day of hospitalization after VAP | 82.6 ± 122.3 | (1–630) |
| Day of death (based on admissions) | 109.2 ± 107.3 | (11–388) |
| Mortality | 31 (54.3) | |

Table 4: Micro-organisms isolated from patients with positive endotracheal aspirate culture and urinary cultures

| Micro-organism types | VAP | UC-RI | Total n (%) |
|-------------------------------------|-----------|----------|-----------------|
| <i>Acinetobacter baumannii</i> | 3 | - | 3 (12.5) |
| <i>Pseudomonas aeruginosa</i> | 12 | 3 | 15 (62.5) |
| <i>Staphylococcus aureus</i> | 1 | - | 1 (4.17) |
| <i>Escherichia coli</i> | - | 2 | 2 (8.33) |
| <i>Serratia marcescens</i> | - | 1 | 1 (4.17) |
| <i>Stenotrophomonas maltophilia</i> | 2 | - | 2 (8.33) |
| Total | 18 | 6 | 24 (100) |

VAP: ventilator-associated pneumonia; UC-RI : urinary catheter-related infection

DISCUSSION

Paediatric ICUs have the advantages of providing healthy surveillance, qualified personnel, improved resuscitation capabilities and follow-up with specialized clinicians. However, due to the common use of broad-spectrum antibiotics, cross-infections due to frequent patient–personnel contact and various invasive interventions, these units also have the unavoidable risks of infection and colonization with resistant pathogens. The frequent contact between health personnel and patients and the invasive interventions constitute the primary risks of infection development. The physical conditions of ICUs, patient density, patient/nurse ratios and wide and improper use of antibiotics are also important risk factors. The rates of HAI are generally higher in children than in adults. Roughly, these rates are between six and seven per 100 hospitalized children, whereas it is around for adults (6).

The circumstances that increase the incidence of HAI more profoundly in children than in adults vary. These include a higher frequency of complicated cases, especially in paediatric and newborn ICUs, intravenous line problems (thin veins, intravenous line dysfunction due to uncontrolled movements in paediatric patients), the necessity for administration of drugs more frequently due to a shorter half-life of drugs in children and lastly, the higher requirement for nursing care and manipulations for stabilization of paediatric catheters (7).

In recent years, observational studies in the USA reported HAI rates to be between 6% and 13.7% in the paediatric ICU (8). In a multicentre study in the USA, the HAI incidence in the paediatric ICU was 12.9%, and the HAI incidence per 1000 patient days varied between 1.1% and 36.6% (9). An incidence of 11.9% was reported in a nationwide prevalence study in the USA (10).

Infections developing in the paediatric ICU are important causes of morbidity and mortality, and they significantly prolong the hospitalization period. Among the HAIs observed in paediatric ICUs, pneumonia causes the highest mortality rates and the most significant prolongation of hospitalization, and it is mostly connected with the use of mechanical ventilators (11, 12). One study revealed that VAPs constituted 95% of nosocomial pneumonia cases in the paediatric ICU (13). Factors related to VAP include premature birth, weaker immune responses, increased permeability of the mucous membranes, prolonged intubation, prolonged mechanical ventilation, empirical antibiotic use, use of H₂ blockers and antacids, prior bloodstream infections, low birthweight, opiate treatment and re-intubation (1, 2).

When comparing our results with the NNIS data, we found that the utilization of mechanical ventilators was at the 25th percentile and the rates of VAP were above the 90th percentile. According to these results, our rates of ventilator use were below average, while our VAP rates were higher. This may be because intubations are applied more frequently during emergency conditions, there is poor compliance to infection prevention measures during the cleaning of mechanical ventilator components, prolongations in ventilator treatment periods,

more severe underlying diseases, insufficient qualification of the supportive personnel and possibly, most importantly, poor hand hygiene.

Compliance with infection control precautions has profound importance in reducing the development of VAP. A study by Muszynski *et al* revealed that the implementation of an evidence-based care bundle to prevent ventilator associated tracheobronchitis by a multidisciplinary team with real-time feedback was associated with a decreased rate of ventilator associated tracheobronchitis in the paediatric ICU (16). This study suggests that the bundle application is necessary to prevent DA-HAI in paediatric ICUs. It is important to avoid the unnecessary use of invasive devices in ICU patients, and they should be removed at the earliest appropriate time, which will substantially reduce the development of DA-HAIs.

When comparing our results with the NNIS data, we found that the utilization of central and urinary catheters was at the 10th percentile between 2008 and 2010, and at the 25th percentile in 2011. Central catheter-associated bloodstream infection (CC-BSI) and UC-RI were at the 10th percentile, which reveal lower than average infection rates. Catheter utilization rates were at the 10th percentile in 2012 and 2013, while the infection rates were above the 90th percentile.

The high infection rates may be due to the shortage of supportive personnel, personnel not meeting the demands of the increasing patient days, imperfections of the catheter applications, unsterile conditions, daily wound dressings with sterile gauzes, or poor compliance of the health personnel with hand hygiene.

Isolated infectious micro-organisms and their antibiotic sensitivities may be different between hospitals or even between different clinics in the same hospital. Gram-negative bacteria constitute the more frequent infectious causes in paediatric ICUs, although Gram-positive bacteria can also be detected. In our study, the most frequent Gram-negative infectious agent was *Pseudomonas* spp.

In VAP, risk factors for *P. aeruginosa* include chronic obstructive lung disease, prolonged duration of mechanical ventilator utilization and the previous use of antibiotics (14, 15). In our study, the most prominent features of the isolated *Pseudomonas* spp were their resistance to antiseptic agents [it is known that they display inherent resistance to many antibiotics] (16). Therefore, the hospitalization period and mortality could increase in DA-HAI cases caused by *Pseudomonas* spp. In our study, methicillin resistant *Staphylococcus aureus* (MRSA) constituted a very low percentage of the causative agents. A study performed by Erdem *et al* revealed that the incidence of *S. aureus* infections was declining rapidly in Turkish ICUs, with potential impacts on empirical treatment strategies (17).

The inappropriate use of antibiotics is a widespread global problem. It has been reported that an average of 30% of hospitalized patients receive antibiotics, and between 25% and 65% of these treatments are improper. A study performed in Akdeniz University in Turkey revealed that 43% of in-hos-

pital antibiotic use was not proper (18). Due to the frequent and inappropriate use of antibiotics in the paediatric ICU, infections caused by multidrug-resistant micro-organisms develop and difficulties are encountered in their management. In particular, employment of third-generation cephalosporins, fluoroquinolones and carbapenem derivatives plays important roles in the development of infections by resistant micro-organisms (19).

In general, antibiotic resistance rates at ICUs in Turkey are higher than those in NNIS hospitals in the USA. In comparison to the NNIS reports, ceftriaxone-resistant *Enterobacter* spp was encountered at a rate of 48.1% versus 48.2% and fluoroquinolone-resistant *P aeruginosa* was encountered at a rate of 51.1% versus 29.1%. High rates of resistance were observed in all broad-spectrum antibiotics frequently used in ICUs (20). In a study conducted among four International Nosocomial Infection Control Consortium (INICC)-member hospitals in Peru, it was observed that the DA-HAI associated micro-organisms were MRSA (73.5%), ceftazidime-resistant *Pseudomonas aeruginosa* (62%), imipenem-resistant *Pseudomonas* spp (36.1%) and ceftazidime-resistant *Enterobacter* spp [40.8%] (21).

In conclusion, it is essential to protect patients against infections, and likewise, the rates of DA-HAI, such as VAP, CC-BSI and UC-RI should be reduced. The improper use of invasive devices in ICU patients should be avoided, and they should be removed at the earliest possible time to reduce the development of DA-HAI.

The efforts of the hospital infection control committee to reduce nosocomial infections with continuous education programmes are likely more important than antibiotherapy. Our main goal should be to protect ICU patients from infections. Therefore, it is essential to augment the compliance to advised directives, to provide complete participation in education programmes and to control and monitor compliance very strictly. Meanwhile, rational antibiotherapy policies should also be developed.

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