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Research Article

Central Venous Catheter Types and Association with Bloodstream Infection in the Pediatric Intensive Care Unit: Experience of two Years

Pediatrik Yoğun Bakım Ünitesinde Santral Venöz Kateter Tipleri ve Kan Dolaşımı Enfeksiyonuyla İlişkisi: İki Yıllık Deneyimimiz

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ABSTRACT

Objective: *Central venous catheters (CVC) provides great convenience in pediatric intensive care units (PICUs). In this study, we aimed to prospectively examine patients who underwent CVC in the PICU in terms of catheter types and infections*
Methods: *We conducted our monocentric, prospective, and cohort study by including patients between January 2019 and December 2020, involving all central catheters temporarily inserted, except port-line catheters, PICCs, indwelling catheters (cuffed and uncuffed tunnel catheters), and arterial catheters. The main issue we focus on is the rate of catheter-associated bloodstream infection (CLABSI). We analyzed the relationship between infection and risk factors using binary logistic regression analysis.*
Results: *We included 26 CLABSIs with 196 CVCs. The incidence rate was 6.2/1000 catheter days. We found that the incidence of CLABSI increased in femoral catheters (OR: 0.04 p: 0.035, 95% CI: 0.49-3.49). Moreover, the incidence was increased in catheters with 3 lumens (OR: 0.06, p: 0.031, 95% CI: 0.34-1.69). The prolongation of the catheter also increases the risk of infection (OR: 0.06, p: 0.028, 95% CI: 0.56-2.36). Also, we found that the frequency of CLABSI increased in patients with underlying immunodeficiency (OR: 0.19, p: 0.007, 95% CI: 0.85-1.39) and in patients who were given total parenteral nutrition (OR: 0.02, p: 0.041, 95% CI: 0.063-2.38).*
Conclusion: *The number of studies that directly compare catheter types in pediatric patients and their relationship with CLABSI is limited. Moreover, the comparison of unrelated studies is difficult because of heterogeneity in study populations. Multicenter pediatric prospective studies focused on identifying catheter-associated infections are needed.*

Keywords: *Catheter-associated bloodstream infections, central venous catheter, pediatric intensive care unit*

ÖZ

Amaç: *Santral venöz kateterler (SVK), çocuk yoğun bakım ünitelerinde (ÇYB) büyük kolaylık sağlar. Bu çalışmada, ÇYB'de SVK uygulanan hastaları kateter tipleri ve enfeksiyon oranları açısından ileriye dönük olarak incelemeyi amaçladık.*
Yöntem: *Port-line kateterler, periferik olarak yerleştirilen santral kateterler, kalıcı kateterler (kaflı ve kafsız tünelli kateterler) ve arteryel kateterler hariç geçici olarak takılmış olan santral keteterleri içeren Ocak 2019 ile Aralık 2020 arasındaki hastaları dahil ederek monosentrik, prospektif ve kohort olarak tasarladığımız çalışmamızı yürüttük. Odaklandığımız ana konu, SVK tiplerine göre kateterle ilişkili kan dolaşımı enfeksiyonu (Kİ-KDE) oranıdır. Enfeksiyon ve risk faktörleri arasındaki ilişkiyi ikili lojistik regresyon analizi ile inceledik.*
Bulgular: *Çalışmamıza toplam 26 Kİ-KDE ile 196 SVK dahil ettik. İnsidans oranı 6.2/1000 kateter günü idi. Kateter yerleşim yerlerinden femoral kateterlerde Kİ-KDE insidansının arttığını saptadık (OR: 0.04, p: 0.035, 95% CI: 0.49-3.49). Ayrıca 3 lümenli olan kateterlerde daha az lümeni olanlara göre Kİ-KDE insidansı artmaktaydı (OR: 0.06, p: 0.031, 95%, CI: 0.34-1.69). Santral kateterin takılı kaldığı sürenin uzaması da hastalarda enfeksiyon riskinde artışa neden olmaktadır (OR: 0.06, p: 0.028, 95% CI: 0.56-2.36). Bunun yanısıra altta yatan immün yetmezliği olan hastalarda (OR: 0.19, p: 0.007, 95% CI: 0.85-1.39) ve total parenteral nutrisyon verilmiş olan hastalarda Kİ-KDE sıklığının arttığını saptadık (OR: 0.02, p: 0.041, 95% CI: 0.063-2.38).*
Sonuç: *Pediyatrik hastalarda kateter tiplerini ve bunların Kİ-KDE ile ilişkisini doğrudan karşılaştıran çalışma sayısı sınırlıdır. Dahası, çalışma popülasyonlarındaki heterojenlik nedeniyle çalışmaların karşılaştırılması zordur. Kateter ilişkili enfksiyonlara odaklanmış, çok merkezli pediatrik ileriye dönük çalışmalara ihtiyaç vardır.*

Anahtar kelimeler: *Kateter ilişkili kan dolaşımı enfeksiyonları, santral venöz kateter, çocuk yoğun bakım ünitesi*

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INTRODUCTION

Safe and effective venous access is essential for providing care to children in pediatric intensive care units (PICUs). Central venous catheters (CVCs) are usually applied for long-term treatments such as blood transfusion, inotropic agents, and parenteral nutrition in intensive care units [1,2]. Catheter-associated bloodstream infections (CLABSIs) are the most common healthcare-associated infection reported in a network of 1003 hospitals in the United States between 2011 and 2014 [3]. In previous studies, CLABSIs have been shown to significantly increase mortality, morbidity, length of hospital stay, and cost [4-7]. In general, studies involving risk factors of CLABSIsmostly include adult patients. The risk of CLABSI depends on many factors: choice of the device, technique of insertion, the technique of management, and prompt removal [1,2,8]. In the previous studies; risk factors such as neutropenia, prolonged mechanical ventilation, total parenteral nutrition have been identified for the development of CLABSI [8,9].

When we review the literature on this topic; no specific studies related to the type of catheter have been observed in pediatric intensive care patients. In our study; we aimed to prospectively examine the relationship between the particular subtype of the CVCs and the frequency of CLABSIs and the type of infections (frequency and microorganisms) in our clinic.

MATERIAL and METHODS

We conducted a prospective cohort study of CLABSI incidence and association with the characteristics of catheters. This study includes all CVCs, except port-line catheters, permanent catheters, and arterial catheters, inserted from a month to 18 years of age between January 2019 and December 2020 in our tertiary care hospital's PICU.

The study was conducted by the ethical standards stated in the 'Declaration of Helsinki'. The local ethics committee approved the study (protocol number: 2020/05-09).

Population

Patients between a month to 18 years of age who needed to be admitted to the PICU of our hospital and who were followed up with CVCs for at least 48 hours between January 2019 and December 2020 were included in the study. Patients with CLABSI for the second time during the study period were included in the study only once.

Catheters

All of the central catheters temporarily inserted during the study period in our tertiary care hospital's PICU in two years were included. Port-line catheters, permanent catheters (cuffed-tunneled and non-cuffed tunneled catheters), peripherally inserted central catheters (PICCs), and arterial catheters were excluded in this study. Also, those catheters which have been removed in less than 48 hours were excluded.

Protocols for insertion of the central venous catheters

During the study period, catheters were placed by pediatric intensivists or pediatric intensive care fellows. We used a solution of alcoholic 4% chlorhexidine gluconate as an antiseptic solution to clean the site before applying. Practitioners cleaned the surgical area with antiseptics after they are prepared according to full barrier protection measures (sterile gloves, mask, bone, and long-sleeved sterile box). Central venous catheters were inserted by ultrasound-guided Seldinger method to the internal jugular, femoral and subclavian veins. After the application of the catheter, a transparent semipermeable dressing is made around it. It is replaced when the dressings are loose, moist, and get dirty. Also, even if nothing happens, dressing is renewed every 48 hours period [10]. In our study, only catheters inserted using a percutaneous route were included. Catheters inserted with cut down or implanted were not included. We implement a bundle care program to reduce the CLABSI incidence in our intensive care.

Definition of central catheter-associated bloodstream infection

Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America is adopted for the definition of CLABSI, in our clinic [11]. If bacteremia or fungemia is detected in a patient who has been using a central venous catheter for more than 48 hours and has multiple positive blood cultures from a peripheral vein and clinical signs of infection (such as fever, chills, and/or hypotension), and a bloodstream infection is excluded, except for a visible central catheter. defined as CLABSI in the absence of an other resource.

To diagnose CLABSI, one of the specified criteria must be present: a positive result of a semi-quantitative (>15 CFU per catheter segment) or quantitative (>10^2 CFU per catheter segment) catheter culture in which the same organism is isolated from a blood culture from a catheter and from a peripheral blood sample; simultaneous quantitative blood cultures (catheter versus peripheral blood) with >3:1 CFU/mL blood ratio; different time to positivity (growth in a blood culture obtained through a catheter hub should be detected at least 2 hours before an equal volume of a peripheral blood sample taken simultaneously).

Study process and data collection

A case report form was prepared. The form started to be filled as soon as the catheter was inserted. Participants were followed from catheter insertion to removal only until one course of CLABSI. Data were prospectively collected by clinicians. About the catheter; an indication of insertion, type, diameter, number of lumens, vein to which it is inserted (jugular, femoral, subclavian), whether it is inserted urgently or electively, whether it is the first catheter, the length of stay (in days), and the presence of a microbial agent in the blood and catheter culture, the microorganism type were prospectively recorded. About the patient; age, gender, weight, the primary diagnosis at admission if any the condition and duration of stay in the invasive mechanical ventilation for longer than 48 h, whether or not total parenteral nutrition was given from the catheter and its duration, duration of the hospitalization in days, were recorded prospectively. If several catheters were inserted in the same patient, a catheter form was completed for each one.

Statistical analysis

Statistical analyses were performed using SPSS 20 software (IBM, Armonk, NY, USA). First of all, numerical and categorical data were evaluated by descriptive statistical methods. Distributions of numerical variables were examined by visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov). The mean and standard deviation were used as the distribution was homogenous. Non-homogeneous data were shown with median and interquartile ranges.

The incidence rate was defined as the number of new CLABSIs relative to the total number of catheter days in our study. The definition of the number of catheter days was specified as the number of days between insertion and removal of CVCs. The confidence interval for each incidence was 95%.

We examined binary logistic regression analysis to determine independent predictors of CLABSI. Hosmer-Lemeshow goodness of fit statistics was used to assess model fit. A 5% type-I error level was used to infer statistical significance. The results were interpreted and reported by the researchers. Statistically, a p-value of less than 0.05 was considered significant.

Sample size

The sample size of our study was determined based on the total number of CVCs in the intensive care. Because the aim of us was to obtain an overview of CVCs of PICU patients. All of them were therefore included in our study.

RESULTS

Characteristics of the patients

We included a total of 196 patients. The patients' median age at placement days was 13 (IR-interquartile

range-: 7-26) months; median weight was 8 (IR: 7-15) kg; median height was 72 (IR: 62-103) cm. The median length of hospitalization was 61 (IR: 15-132) days and the median duration of CVCwas 22 (IR:11-33) days. No relationship was found between the height and weight of the patients and the frequency of CLABSI.Underlying diseases at admission was respiratory deficiency (76; 39%), sepsis (59; 30%), cardiovascular deficiency (37; 19%) and neurologic diseases (24; 12%). On the other hand, some of the foremost underlying chronic diseases of patients' were neurologic and genetic diseases (74; 42%), hematologic diseases (34; 17%), metabolic diseases (12; 6%), and immunodeficiency rate at admission (23; 13%) is specified in Table 1. Also, a total of 62 (32%) of the patients had defined immunodeficiency. Immunodeficiencies that have been identified were; neutropenia (39; 62%), Severe combined immunodeficiency (2; 3%), Common variable immunodeficiency (3; 5%), T cell deficiency(6; 10%), Hypogammaglobulinemia (10; 16%), Griscelli syndrome (1; 2%), and DiGeorge syndrome (1; 2%). Immune deficiency accompanied all of our patients with underlying hematological and oncological diseases. Neurological diseases were spinal muscular atrophy, congenital muscular dystrophy, and neurodegenerative diseases. There is no defined immunodeficiency in these patients. The patients with neurological, genetics, and metabolic diseases and by identified immunodeficiency are included in the immunodeficiency group. Immunodeficiency was identified in all of our patients who received TPN and they were included in both groups for statistical analysis.

Table 1. Demographic and clinical characteristics of the children with cental venous catheters.

Gender (F; %) (M; %)	(88; 45%) (108; 55%)
Age (months)- median (IR)	13 (7-26)
Weight (kg)- median (IR)	8 (7-15)
Height (cm)- median (IR)	72 (62-103)
Length of hospitalization (days) median (IR)	61 (15-132)
Duration of CVC (days) median (IR)	22 (11-33)
Underlying diseasesat admission (N/%)	
- Respiratory deficiency	76 (39)
- Sepsis	59 (30)
- Cardiovascular deficiency	37 (19)
- Neurologic diseases	24 (12)
Immunodeficiency rate at admission	23 (13)
One of the foremost underlying chronic diseases	
- Neurologic and genetic diseases	74 (42)
- Hematologic diseases	34 (17)
- Metabolic diseases	12 (6)
- Immune deficiency	23 (13)

CVC: Central venous catheter, IR: Interquartile range, N: Number.

Characteristics of the catheters

Indication of CVC were no vascular access (120; 61%), required inotropic treatment (35; 18%), extracorporeal treatment (41; 21%) (Table 2). Characteristics of catheter types are given detailed in Table 2.

Table 2. Description of the catheters.

CVC type (N; %)	
- Simple CVC	(154; 79%)
- Hemodialysis catheter	(42; 21%)
CVC placement (N; %)	
- Jugular	(150; 77%)
- Subclavian	(24; 12%)
- Femoral	(22; 11%)
Indication of CVC (N; %)	
- No vascular access	(120; 61%)
- Required inotropic treatment	(35; 18%)
- Extracorporeal treatment	(41; 21%)
Number of lumens (N; %)	
- 1	(16; 8%)
- 2	(100; 51%)
- 3	(80; 41%)
CVC diameter (F-French)-median (IR)	5 (4-5)
CVC length (cm)-median (IR)	8 (8-12)

CVC: Central venous catheter, IR: Interquartile range, N: Number.

The incidence rate

We included a total of 196 CVCs and 26 CLABSIs. The total time of catheter use was 4180 days. The incidence rate(Number of CLABSIs/Total catheter days x1000)was 6.2/1000 catheter-days (95% CI: 0.92-7.91). The confidence interval was determined 95%.

Characteristics of the CLABSI

Microbial agentsin catheter infections was determined as gram-negative (18; 69%), fungus (5; 19%), gram-positive (3; 12%). Identified microorganisms were; *Klebsiella pneumonia* (7;

28%), *Pseudomonas aeruginosa* (5; 20%), *Klebsiella oxytoca* (2; 7%), *Escherichia coli* (2; 7%), *Serratia marcescens* (1; 3%), *Burcholderia cepacia* (1; 3%), *Proteus mirabilis* (1; 3%), *Candida albicans* (2; 7%), *Candida parapsilosis* (2; 7%), *Candida glabrata* (1; 3%) and Coagulase negative staphylococcus (*Staphylococcus epidermidis*, *Staphylococcus hemolyticus*, ...) (3; 12%).

The infection rate of femoral catheters was higher than the other placements (OR: 0.04 p: 0.035, 95% CI: 0.49-3.49). The rate of CLABSI was increasing in patients with three catheter lumens (OR: 0.06, p: 0.031, 95% CI: 0.34-1.69) and in whom catheters were placed for longer than 10 days period (OR: 0.06, p: 0.028, 95% CI: 0.56-2.36). Also, the rate of CLABSI was higher in patients with immunodeficiency (OR: 0.19, p: 0.007, 95% CI: 0.85-1.39). In addition, neutropenia (one of the immunodeficiency subgroups) increased the rate of catheter infection (OR: 0.08, p: 0.022, 95% CI: 0.77-2.72). No effect of other immunodeficiency subgroups on the frequency of CLABSI was detected. In addition, we determined that the underlying chronic diseases have increased the catheter infections rate (OR: 0.15, P: 0.009, 95% CI: 0.91-2.11). For instance, the incidence of CLABSI was higher in patients with underlying neurological and genetic diseases(OR: 0.09, P: 0.028, 95% CI: 0.82-1.79). The hematological disease of the underlying chronic diseases was found to increase the CLABSI incidence (OR: 0.02, P: 0.045, 95% CI: 0.59-2.58). However, the underlying metabolic diseases did not show any statistical effect on CLABSI incidence. The fact that total parenteral nutrition was given through the catheter increases the risk of CLABSI (OR: 0.02, p: 0.041, 95% CI: 0.63-2.38). Furthermore; receiving mechanical ventilation support, being the first catheter, urgent insertion of the catheter did not have any statistical effect on the CLABSI rate (Table 3).

Table 3. Logistic regression analysis of risk factors associated with catheter-related infections.

	OR (95% CI)	p
CVC type		1.0
CVC placement (Femoral)	*0.04 (0.49-3.49)	0.035
CVC duration (Longer than 10 days)	**0.06 (0.56-2.36)	0.028
Count of lumens (3)	***0.06 (0.34-1.69)	0.031
CVC diameter (F-French)		0.109
CVC length (cm)		0.591
TPN infusion through the CVC	****0.02 (0.63-2.38)	0.041
Administration of invasive MV		0.658
Immune deficiency	*****0.19 (0.85-1.39)	0.007
Neutropenia	0.08 (0.77-2.72)	0.022
SCID		0.678
CVID		0.701
T cell deficiency		0.059
Hypogammaglobulinemia		0.067
Griscelli syndrome		0.564
DiGeorge syndrome		0.094
Underlying chronic diseases	******0.15 (0.91-2.11)	0.009
Neurologic and genetic diseases	0.09 (0.82-1.79)	0.028
Hematologic diseases	0.02 (0.59-2.58)	0.045
Metabolic diseases		0.866
First catheter		0.707
Urgent catheter		0.999

CI: Confidence interval, CVC: Central venous catheter, CVID: Common variable immunodeficiency, MV: Mechanical ventilation, SCID:Severe combined immunodeficiency, TPN: Total parenteral nutrition
**Logistic Regression; Cox&Snell R Square: 0,376, Nagelkerke R Square: 0,717.*
***Logistic Regression; Cox&Snell R Square: 0,429, Nagelkerke R Square: 0,855.*
****Logistic Regression; Cox&Snell R Square: 0,415, Nagelkerke R Square: 0,781.*
*****Logistic Regression; Cox&Snell R Square: 0,233, Nagelkerke R Square: 0,507.*
******Logistic Regression; Cox&Snell R Square: 0,641, Nagelkerke R Square: 0,978.*
*******Logistic Regression; Cox&Snell R Square: 0,634, Nagelkerke R Square: 0,932*

DISCUSSION

In our study, the CLABSI incidence was calculated as 6.2/1000 catheter days. We only examined the effect of non-permanent catheters. The infection rate of femoral catheters, three catheter lumens, and in whom catheters were placed for longer than 10 days period was higher than the others. The CLABSI rate was higher in patients with immunodeficiency (neutropenia), underlying chronic diseases, and receiving total parenteral nutrition. On the other hand; receiving mechanical ventilation support, being the first catheter, urgent insertion of the catheter did not show any statistical effect on the CLABSI rate.

The incidence of CLABSI in our clinic was higher than in other studies on this topic [12,13]. When the studies conducted were examined and when the

CLABSI incidence was looked into, it was seen that Carter et al. [13] were found 3.87 per 1,000 in-hospital line days. This incidence rate includes neonatal patients and catheters placed in general pediatrics and surgical services, as well as in pediatric intensive care. Also, in this study, the inclusion of totally implantable catheters, PICCs, and tunneled catheters, as well as temporary CVCs may cause the incidence rate to be lower. In the study of Broudic et al. [14], CLABSI incidence was determined 4.6/1000 catheter days for general hospitals and it was 2.4/1000 catheter days specifically for the pediatric intensive care. Unlike our study, in this study PICCs and tunneled catheters inclusion with temporary catheters may be the reason for the lower incidence of infection.

Besides, in the study which is designed in a tertiary care children's university hospital by Venturini et al. [12]; port catheters, PICC line catheters, and indwelling catheters in all departments of the hospital are included. A total of 388 children between October 2014 and April 2015 with all catheters under the age of 18 were included. Catheter-associated bloodstream infections rate was determined 3.73/1000 (95% CI: 2.54–5.28) central line-days. The results of the International Nosocomial Infection Control Consortium surveillance study from January 2007 to December 2012 in PICUs showed a CLABSI rate of 6.1/1000 (95% CI: 5.7-6.5) central line-days [15].

To obtain reliable data on this topic, a continuous prospective study should be conducted. A prospective study performed in 29 NICU in the United States and found that the risk of CLABSI is very low during the first week of catheterization and especially with lines inserted in the jugular vein [12,16]. In the study conducted by Ergul et al. [17], it was determined that CLABSI incidence increased with the catheter duration. Similarly in our study, there was a relation between CLABSI and catheter duration days, femoral catheters, and three-lumen catheters.

Moreover, studies are difficult to compare because of the diversity in study populations and study methods [18-20]. Larger prospective pediatric studies are needed to identify CVC types and their association with infection rates. Point prevalence studies are easier to perform than long prospective studies but may underestimate the real risk. Pediatric studies which focusing on catheter infection in such patients should be conducted to deepen our understanding of the associated risk factors.

In a prospective pediatric cohort study which was conducted by Carter et al. [13], a total of 5648 patients, 385 who developed CLABSI between 1995 and 2013 were examined. Over time, the incidence of catheter-associated infection has decreased, but in the process, the hand hygiene campaign to the risk of CLABSI has been launched. The time in this study is very long, and in this process, there is inevitably expansion and change in the infection prevention packages. This suggests that other mixing factors cannot be standardized while evaluating the effect of the type of catheter on CLABSI in the process. In this study, it was also found that the risk of catheter infection increased with increasing the number of lumens [13]. In our study, the rate of CLABSI increased in 3-lumen catheters compared to those with fewer lumens. This result shows us that choosing catheters with fewer lumens can reduce the CLABSI rate. Carter et al. [13] reported that patients' comorbidities and underlying chronic diseases increased the incidence of CLABSI. Underlying chronic comorbidities were present in most of our patients who needed catheter insertion. In our study, we determined that the underlying chronic diseases have increased catheter infections. As; genetic and neurological diseases have increased the incidence of CLABSI. This may also be associated with the need to be a longer hospitalization period. In addition, the underlying hematological diseases have also increased the incidence of CLABSI. This may be associated with the accompanying immunodeficiency of those with hematological disease. On the other hand, we determined the underlying metabolic diseases did not affect the CLABSI incidence. Also, the rate of catheter infection was higher in immunocompromised patients in our study. Similar to the results in other studies [8,9], the rate of catheter infection was increasing in patients with neutropenia. Since the intensive care follow-up of critical

hematology and oncology patients is also performed in our clinic, we think that our immunodeficiency especially the neutropenia rate is high and this may lead to an increase in susceptibility to infection and a high rate of CLABSI.

Our study has some limitations. The most important of these is the single-centered design of the study and therefore the inability to generalize the results. Also, more cases can be included by keeping the cohort research longer and the duration can be extended. Since there was a problem with the intake process of PICCs in our hospital, a limited number of cases could be inserted and CVCs were inserted to patients who could not have vascular access. For this reason, the number of catheter insertions was high with the indication of no vascular availability. Moreover, the change of CLABSI incidence over the years and factors can be specifically studied.

The incidence of CLABSIs in children hospitalized in our PICU is higher than reported in the literature. The results of our study show that choosing a catheter location other than femoral, preferring fewer lumen catheters instead of 3-lumen catheters, and removing the catheters as soon as possible can reduce the incidence of CLABSI.

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Ethics Committee Approval: The study was conducted by the ethical standards stated in the 'Declaration of Helsinki'. The local ethics committee approved the study (protocol number: 2020/05-09).

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