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ORIGINAL RESEARCH

Risk factors for the development of venous thrombosis in patients with a central venous catheter admitted to the intensive care unit of the Roberto Gilbert Elizalde children's hospital.

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Abstract

Introduction: Advances in the management and survival of severe pediatric disease have led to an increase in thromboembolic phenomena, given the frequent need for central venous catheters (CVC). The present study describes the conditions in which venous thrombosis occurs in pediatric patients with CVC in a public referral center in Guayaquil.

Methods: This is an observational, cross-sectional study with the objective of identifying factors that are associated with the development of venous thrombosis in patients with CVC admitted to the Intensive Care Unit. Information was collected in a pre-designed chart of all patients with CVC for more than 7 days. A venous Doppler ultrasound was performed to determine the presence or absence of thrombi. Descriptive statistics were used for univariate analysis and Odds Ratio was used for the bivariate analysis.

Results: 35 patients were included in the study, 14/35 (40%) young infants, 24/35 males (69%), 19 cases (54%) with malnutrition, 10 cases (29%) with congenital heart disease, and 18 cases (51%) admitted for infections. The puncture site was femoral in 11 cases (31%), the procedure was performed by the fellow in 20 cases (57%), on a scheduled basis in 27 cases (77%), and performed in a single attempt in 28 cases (80%). The tip of the catheter was located in the superior vena cava in 23 cases (66%). The prevalence of thrombosis was 14% (95% CI 12.33-16.25). Bivariate analysis showed that none of the variables were associated with the presence of CVC thrombosis.

Conclusions: 14% of patients with CVC use for more than 7 days develop secondary venous thrombosis. The factors associated with CVC including nutritional status and related procedures could not be determined.

Key words: Hospitalization, Child/ Catheter-Related Infections; Catheters, Catheter Obstruction

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Introduction

Thromboembolic phenomena are rare in pediatrics; however, advances in the management and survival of severe pediatric disease have led to an increase in thromboembolic phenomena, given the frequent need for central venous catheters (CVC) and the presence of other factors that can alter haemostasis [1].

One of the key points in the comprehensive management of critically ill patients is the need for a safe venous line due to the complexity of the treatment [2]. Critically ill patients usually receive multiple intravenous solutions simultaneously (crystalloids, colloids, inotropics, antibiotics, blood products, parenteral nutrition, and chemotherapy) in addition to requiring hemodynamic monitoring. Hence, central venous catheters (subclavian, jugular, femoral) are inserted in all patients admitted to a PICU, which is not without risks. Infectious complications associated with CVC are the main risks; however, CVC-associated thrombosis represents an undesirable event that can complicate the treatment of patients, which is why it is important to identify the main associated risk factors in the patient population to establish prophylactic measures in a timely manner.

The evaluation of thromboembolic risk is essential in patients admitted to the hospital since based on this evaluation, the best thromboprophylactic approach will be implemented and adapted to the clinical setting and characteristics of each patient [3]. Thrombosis in children is rare compared to its prevalence in adults, but it is increasingly recognized and associated with serious consequences. Its incidence has increased in recent years due to improved medical care and the frequent need for central venous catheters that allow the survival of children with diseases such as cancer and congenital heart disease, as well as their early diagnosis and detection [4].

Central venous accesses are widely used during the treatment of patients with various diseases since 1952 when Aubaniac described the cannulation of a central vein, the subclavian. Currently, they constitute a common procedure in Pediatric Intensive Care Units (PICU) [5]. Regarding the incidence of thrombosis, it is highly variable, from 0.6% to 50% depending on whether symptomatic thromboses are detected or an active search is carried out with radiological methods. Thus, Becket al., [6] in a study carried out in a PICU, reported a rate of 18% of catheters after conducting an active search and recently, Karapinar and Cura report a 2.2% incidence of thrombosis with implanted catheters in critically ill children [5].

Our objective was to conduct a descriptive study of the variables that are associated with the development of venous thrombosis in pediatric patients with a central venous catheter admitted to the PICU of a public referral hospital in Guayas, Ecuador.

Population and methods

Study design

The design is an observational, descriptive, cross-sectional study.

Setting

The study was carried out in the Intensive Care Unit of the Roberto Gilbert Elizalde Children's Hospital of the Board of Charity of Guayaquil, Guayas, Ecuador. The study period was from September 1, 2018 to February 28, 2019. The field period was considered the exposure time. Data collection was completed on March 30, 2019.

Participants

The sample or reference population was patients hospitalized at the institution. The sample consisted of the total number of patients admitted to the PICU in whom a central venous catheter was used for a period greater than or equal to 7 days. Patients with hemodynamic instability (use of amines) and patients with high-frequency mechanical ventilation were excluded.

Variables

The descriptive demographic variables were age, weight, and sex. The clinical variables were comorbidities, and cause of hospitalization. The descriptive variables were related to the use of the central intravenous device including the anatomical puncture site, number of catheter lumens, type of catheterization, personnel who placed it, number of attempts, CVC permanence time, complications, and reason for CVC removal.

Data sources/ measurement

A survey was conducted with direct observation and consultation of the clinical record as the primary data source. The data were compiled in an electronic sheet.

Bias

Medical records with incomplete data were excluded, so the imputation of lost or excluded data was avoided.

Study size

The sample was non-probabilistic, in which all potentially eligible cases from the Pediatric Hospital were included.

Management of quantitative variables

The quantitative variables are presented in scale with means and standard deviation. Nominal quantitative variables are presented as frequency and percentages.

Statistical Methods

Descriptive statistics were used. The confidence interval for proportions was used to describe prevalence. The statistical package was SPSS® (IBM Corp, Released 2013. Windows, Version 22.0. Armonk, NY, USA). A univariate analysis was performed with measures of central tendency. The bivariate analysis was used with the dependent variable as the presence or absence of CVC thrombosis and the independent variables of the procedure and nutritional. The Odds Ratio and its confidence interval are reported with the *P* value.

Results

Participants

The number of patients potentially participating in the study was 50 cases, of which only 35 were eligible by meeting the established inclusion criteria.

Participant characteristics

14/35 (40%) of the cases were infants under 1-year, 9/35 cases (26%) were preschool from 1 year to 4 years old, 6/35 cases (17%) were schoolchildren from 5 to 11 years, and 6/35 cases (17%) were adolescents 12 years and over. There were 24/35 males (69%) and 11/35 females (31%). Males were the most prevalent with 24 cases (69%). 54% of the patients presented malnutrition (see Table 1).

Of the total of the investigated patients, children who had the central venous catheter for the longest period of time were those with congenital heart disease (29%), followed in frequency by children without any comorbidity. There was a lower percentage of patients with a history of previous surgeries, congenital malformations, or other comorbidities (9% each). There was also a lower percentage of patients with epilepsy and autoimmune disease (6%).

The main cause of hospitalization of the children in the sample was due to an infectious disease (51% of the cases), followed by a cardiological cause in 20%, frequently followed by other causes of hospitalization not included in Table 1, such as neurological diseases, and hematological disorders (11%). A lower percentage were patients admitted for surgery (9%), trauma, neoplasms, or metabolic diseases (3% each).

Table 1 General descriptions of the research group

	Frequency n=35	%
Age		
Infant (less than 1 year)	14	40%
Preschool (1-4 years)	9	26%
School (5 - 11 years)	6	17%
Adolescent (over 12 years old)	6	17%
Sexo		
Male	24	69%
Female	11	31%
Nutritional condition		
With malnutrition	19	54%
Normal	16	46%
Comorbidities		
None	9	26%
Previous surgery	5	14%
Congenital heart disease	10	29%
Congenital malformation	3	9%
Epilepsy	2	6%
Autoimmune disease	2	6%
Hypercoagulability (inherited thrombophilias)	1	3%
Other	3	9%
Main cause of hospitalization		
Infection	18	51%
Heart disease	7	20%
Surgery	3	9%
Neoplasia	1	3%
Trauma	1	3%
Metabolic disease	1	3%
Other	4	11%

Characteristics of the procedures

The main location of the CVC was the subclavian vein in 43% followed by the femoral vein in 31% and the jugular vein in 26%. This corresponds to a location of the

tip of the catheter at the level of the superior vena cava in 66% of cases and at the level of the inferior vena cava in 34%. 86% of the investigated patients had a bilumen central venous catheter. 57% of the central venous catheters were placed by the PICU postgraduate doctor, the surgery resident (34%), or the inten-sivist physician (9%). 80% of patients who had a central venous catheter were punctured once at the time of placement, 17% were punctured twice, and to a lesser extent, 3% received more than three punctures. The main cause of the removal of the central venous catheter was due to termination of treatment in 54% of cases, 26% withdrew due to suspected infection, 14% due to the presence of thrombi, and 3% due to discharge (see Table 2).

Main results

The prevalence of CVC-associated thrombosis was 14.29% (5 cases) (95% CI 12.33-16.25): 4 preschool and 1 infant; 3 males and 2 females; 3 children with adequate nutritional status. Two of the children had a history of congenital heart disease, 1 had hypercoagubility disorder and 2 had no associated comorbidity. In 2 cases, the main cause of hospitalization was due to infection and 2 cases due to decompensation of heart disease, 1 debuted with supraventricular tachycardia.

The thrombus localization sites were the femoral and subclavian level in 2 cases, respectively, and 1 located at the jugular level. All venous catheters were bilumen, placed by the intensivist fellow in 3 cases, 1 by surgery, and 1 by an intensivist physician. 3 central venous catheters were scheduled, 2 were placed urgently, all with a single puncture at the time of the procedure. All 5 catheters were removed after identification of the thrombus.

Bivariate analysis

None of the variables were statistically associated with a risk for the presence of thrombosis (See Table 3).

Discussion

The total number of children in whom central venous catheter-associated thrombosis was diagnosed was 14%, a result that differs from those reported at the regional level, which range from 22% to 34.1% [6, 7]. In Europe, the frequency is 1.18% [5]. Thrombosis occurred more frequently in preschool children, which differs from previous publications that re-port a higher risk in children under 1 year and over 12 years [1]. The predominant sex was male (n = 3) but this was not statistically significant, which is in agreement with studies that established that sex was not related to the presence of CVC thrombosis [8].

Adequate nutritional status or malnutrition was not associated with a higher prevalence of thrombosis; however, in a study published in Spain, thrombosis occurred more frequently in children of lower weight [9]. In relation to comorbidi-ties, children with CVC-associated thrombosis had underlying congenital heart disease (n = 2), hypercoagubility disor-der (n = 1), or no present comorbidities (n = 2). None of these factors were associated with a higher prevalence of CVC thrombosis, although some reports have identified congenital heart disease and hypercoagubility states as risk factors [1].

Table 2 Características del procedimiento

	Frequency n=35	%
Anatomical location of the CVC		
Femoral	11	31
Subclavian	15	43
Jugular	9	26
Number of CVC lumens		
Bilumen	30	86
Monolumen	5	14
Personnel performing the procedure		
Intensive Fellow	20	57
Surgeon	12	34
Intensivist	3	9
Catheterization type		
Scheduled	27	77
Urgent	7	20
Rechanneling	1	3
Number of attemps		
One	28	80
Two	6	17
Three o más	1	3
Catheter tip location		
Superior Vena Cava	23	66
Inferior Vena Cava	12	34
Reason for CVC withdrawal		
End of treatment	19	54
Thrombosis	5	14
Suspectec Infection	9	26
Discharge	1	3
Others	1	3

CVC: central venous catheter

According to a study conducted in Bogotá, the most frequent comorbidity of patients with CVC was congenital heart disease (24.4%) followed by patients who did not present comorbidities (19.5%) [8]. The main

cause of hospitalization was due to infection (n = 2) and decompensation of underlying heart disease (n = 2), similar to a 2015 Vargas-Ureña study in Bogotá in which the main cause of hospital admission was infection (42.1%) [8]. The identified thrombi were at the femoral and subclavian levels. These results coincide with those published in a 2015 study in Bogotá by Vargas-Ureña which reported that the most frequent location was the femoral vein (41.5%) followed by the subclavian vein (27.1 %) [8]. Although the femoral route has been identified as a risk factor for thrombosis, occurring in 90% [5], this finding was not corroborated in the present study. All central venous catheters were bilumen, similar to those found in a reference study in which the number of lumens was a risk factor for thrombosis, in contrast to other studies [5]. In previous studies, complications associated with CVC were higher when it was placed by less experienced specialists [10]; however, this association could not be verified in this study. Central venous catheter placement was scheduled (n = 3) with only one attempt (n = 5). As reported, no higher risk of thrombosis was associated with the number of attempts [55].

All central venous catheters were removed after the diagnosis of thrombosis and anticoagulant treatment with sodium heparin infusion was started. As reported by Duarte-Batista in 2010 in Sao Paulo, CVC removal is part of the treatment. However, some studies recommend not removing the catheter if some of the following conditions are met: the distal tip of the catheter is in the correct position (at the junction between the superior vena cava and the right atrium); the catheter is functional (good blood flow); if its permanence is mandatory or vital for the patient; or there is no fever or any information that suggests the presence of infection (thrombophlebitis). Conversely, others recommend removing the catheter and establishing anticoagulant or fibrinolytic therapy as a therapeutic option [8].

Table 3 Bivariate analysis

	Thrombosis N=5	No thrombosis N=30	OR	CI 95%	*P*
Malnutrition	2 (40%)	17 (56.6%)	0.51	0.074-3.51	0.49
Superior cava tip	3 (60%)	20 (66.6%)	0.75	0.107-5.238	0.77
Felow as controller	3 (60%)	19 (63.3%)	0.87	0.125-6.030	0.8 8
>1 attempt	1 (20%)	5 (16.7%)	1.25	0.114-13.676	0.86
Urgent procedure	2 (40%)	5 (16.7%)	3.33	0.438-25.400	0.25
Comorbidities	3 (60%)	22 (73.3)	4.18	0.798-21.908	0.094

OR: odds ratio, CI 95%: CI: 95% confidence interval.

Conclusions

14% of patients with central venous catheter use for more than 7 days develop secondary venous thrombosis. The thrombi were located in the superior vena cava and inferior vena cava at the level of the catheter location, which could be confirmed by Doppler ultrasound. Factors associated with CVC involving nutritional status and related procedures could not be determined.

Abbreviations

CVC: Central venous catheter. PICU: Pediatric Intensive Care Unit.

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Authors' contributions

The author performed the conceptualization, data curation, formal analysis, acquisition of funds, research, resources, software, writing - original draft, validation, visualization, methodology, project management, writing: review and editing.

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Availability of data and materials

The data sets generated and / or analyzed during the current study are not publicly available due to the confidentiality of the participants, but are available through the corresponding author upon reasonable academic request.

Ethical statements

The protocol for this investigation was approved by the Bioethics Commission of the Faculty of Medical Sciences of the Catholic University of Santiago de Guayaquil and the Teaching and Research Commission of the Roberto Gilbert Elizalde Children's Hospital of the Guayaquil Charity Board.

Protection of people

The author declares that the procedures followed were in accordance with the ethical standards of the responsible human experimentation committee and in accordance with the World Medical Association and the Singapore Declaration.

Data confidentiality

The author declares that she has followed the protocols of her workplace regarding the publication of patient data without identification.

Publication consent

The author has obtained the informed consent of the guardians of the patients and the respective assent. This document is in the possession of the corresponding author. The authorization for the publication of this article has been signed in case by the tutors or parents.

Conflicts of interest

The author declares that she has no conflicts of interest..

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