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ORIGINAL ARTICLE

Central venous catheter placement in children with thrombocytopenia

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ABSTRACT

BACKGROUND: The use of central venous catheter (CVC) is essential in the management of chronically ill children. Thrombocytopenia is a common hematological finding in these patients, with an increased risk of bleeding during the insertion of CVC. No clear guidelines are reported regarding the CVC positioning in patients with disorders of hemostasis, and prophylactic platelet (PLT) transfusions are still controversial. Aim of this study was to report the bleeding risk in pediatric patients with thrombocytopenia who underwent positioning of CVC.

METHODS: A retrospective single-center study of all CVCs surgically inserted over a 2-year period (April 2011 – April 2013) at our institution was performed. Age, gender, diagnosis, type of CVC, hematological values (hemoglobin and PLT count, prothrombin international normalized ratio, active partial thromboplastin time) and post-operative bleeding complications were compared between patients with PLT count below (group A) and above 50×10^9/L (group B).

RESULTS: Seventy-two CVC procedures were performed in 67 patients, with a median age of 45 months. Of these, 25 (35%) catheters were positioned in 25 patients included in group A and the remaining 47 (65%) in 42 patients in group B. All twenty-five cases in group A received a prophylactic PLT transfusion prior to the procedure. Bleeding complications were reported in only two cases in group A (8%).

CONCLUSIONS: CVC placement in pediatric patients with thrombocytopenia can be safely performed. We believe a randomized multicenter study could be necessary to determine the benefit of PLT transfusions in children with a PLT count below the recommended level of 50×10^9/L.

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Central venous catheters (CVCs) play an important role in the management of children with chronic disease by providing a venous access for frequent blood withdrawals, administration of chemotherapy, total parenteral nutrition, blood products and drugs. Some patients requiring the positioning of a central venous access are thrombocytopenic and the risk of bleeding is correlated with the platelet (PLT) count. Bleeding complications may present as insertion site bleeding, subcutaneous hematoma, mediastinal hematoma, or hemothorax.

Current recommendations state that a PLT count of 50×10^9/L is sufficient to perform this procedure and a prophylactic PLT transfusion is considered necessary to reduce the risk of bleeding prior the insertion of CVC.[1]

Previous studies have reported a low rate of complications in adults with disorders of hemostasis and suggested that the placement of CVCs without a pre-procedural transfusion can

be safe; however, no clear guidelines are delineated for children with thrombocytopenia.[2-4]

The purpose of this study was to report our single-institution experience in the positioning of CVCs in children with severe thrombocytopenia over a 2-year period.

Materials and methods

We retrospectively evaluated the medical records of all CVCs inserted in pediatric patients at the Division of Pediatric General and Thoracic Surgery, Bambino Gesù Children's Hospital of Rome, Italy, between April 2011 and April 2013.

In our unit, according to internal guidelines, surgical CVC placements are only performed in case of an urgent CVC procedure in patients between the ages of 1 month and 18 years or elective CVC placement only in patients with a weight lower than 8000 g, a disorder of hemostasis, or a PLT count less than 50×10^9/L.

Patients were eligible for this study only if they required a surgical CVC insertion and were in accordance with the previous criteria.

We excluded from this study patients in which CVCs were inserted percutaneously following the Seldinger technique, which is performed by interventional radiologist and carried out only for elective CVC placements in patients with PLT count more than 50×10^9/L, or peripherally inserted central catheters (PICC), normally positioned by our anesthetic team.

Patients of age less than 1 month were not included in this study because CVC placements in newborns are performed by neonatologist surgeons.

An experienced team in the operating room placed all catheters surgically. All procedures were performed under general anesthesia. The preferred site of insertion for CVC was the internal jugular vein. The choice of catheter type was based upon the clinical indications. Post-procedure chest radiographs were performed to assess the correct position of the catheter and to evaluate the possibility of complications related to the procedure.

From the patient's medical records the following data were extracted: age, gender, diagnosis, type of catheter, PLT count prior and after the catheter placement, hemoglobin (Hb) level, prothrombin international normalized ratio (INR), active partial thromboplastin time (aPTT), transfusion of platelets, and bleeding complications.

For each patient INR, aPTT and PLT count were measured prior to CVC insertion. The range for normal values for INR and aPTT in our laboratory is 0.86 to 1.12 and 25 to 34 s, respectively. Normal PLT value ranges from 150 to 450×10^9/L.

Disorders of hemostasis were defined as an INR level >1.5 and PLT count of $\leq50\times10^9$/L.

Patients with a preoperative PLT count less than the recommended threshold of 50×10^9/L received platelet transfusion within one hour prior to CVC placement. The dose of PLT given per transfusion was 1 unit random-donor PLT per 10 kg of body weight.

Bleeding complications were categorized as either major or minor. Major bleeding complications were defined as those that required surgical intervention or caused significant morbidity or mortality. Minor bleeding complications required either minimal or no intervention.

A second set of samples was collected within 24 hours after the insertion of the catheter for assessment of Hb level and PLT count.

To evaluate hematological differences prior and after the surgical procedure, we divided the patients into two groups: group A included patients with a low preoperative PLT count ($\leq50\times10^9$/L), group B with a normal preoperative PLT count ($\geq50\times10^9$/L).

Statistical analysis

The variable aPTT, INR and PLT count were analyzed as factor predictive of bleeding complications. Univariate statistical analysis was done using the Fisher test and analysis of variance (ANOVA). P values less or equal to 0.05 were considered significant.

Results

During the 2-year study period, a total of 72 CVC insertions were performed in 67 pediatric

patients: 43 males (64%) and 24 female (36%). The median age at surgery was 45 months (range, 1 month – 17 years).

The principal characteristics of the population are shown in Table I.

The most frequent indication for CVC insertion was hematological malignancies (45 cases, 67%) followed by solid tumors (12 cases, 18%). The remaining patients were treated for renal diseases (6 cases, 9%), whereas 4 patients were included in the category "other diseases" which included the following: Farber's lipogranulomatosis (1 case), malnutrition (1 case), osteopetrosis (1 case) and Wiskott-Aldrich syndrome (1 case).

Of the 72 catheters positioned, the venous access site was the right internal jugular vein in 62 cases (86%) and the left internal jugular vein for 10 cases (14%). Lines inserted were all tunneled cuffed catheters (25 Leonard, 22 Hickman, 19 Broviac, 5 Quinton, 1 Groshong), of which 15 (21%) had a single lumen and double lumen in the remaining 57 (79%).

The median PLT count at time of CVC insertion of the study population was 250×10^9/L (range, 7-834×10^9/L). Twenty-five of 67 patients with a pre-operative PLT count less than 50×10^9/L were found and included in group A. Of these 25 patients, 24 (96%) cases were treated for hematological malignancies (9 acute lymphoblastic leukemia, 4 acute myeloid leukemia, 9 myelodysplastic syndrome, 1 Hodgkin lymphoma and 1 non-Hodgkin lymphoma) and 1 patient for hemolytic-uremic syndrome.

The remaining 42 cases showed a pre-operative PLT level above 50×10^9/L and were included in the group B. Of these 42 patients, the majority of patients required positioning of CVC for hematological diseases in 21 (50%) patients, followed by solid tumors in 12 (29%) cases. In group B, 4 cases required a CVC repositioning due to a malfunction of the central line and a total of 47 CVC insertion procedures were performed in this series.

Platelets were transfused prior to catheter insertion in all patients (100%) included in group A (37% of the cohort), which showed a median PLT count of 24 x 10^9/L (range 7-48×10^9/L). Of these, 11 (44%) children in this series exhibited preoperative PLT count ranging from 20×10^9/L to 50×10^9/L, whereas 14 (56%) patients showed PLT count less than 20×10^9/L.

Median pre-operative PLT count in the group B was 317 x 10^9/L (range 53×10^9/L – 834×10^9/L) and no patient included in this group received a preprocedural PLT transfusion. No patients received plasma transfusion prior to CVC insertion.

Hematological values of the patients undergoing the central line placement are shown in Table II.

Mean aPTT and INR values were within normal limits in both groups and did not differ significantly.

TABLE I.—*Baseline characteristics of the study population.*

Characteristics	Group A PLT<50×10^9/L	Group B PLT>50×10^9/L	Total (%)
N. patients	25	42	67
Median age (range), months	52 (1-204)	26 (1-215)	45 (1-215)
M/F ratio	13/12	30/12	43/24
CVC placements	25 (35%)	47 (65%)	72
Right IJV	21 (84%)	41 (87%)	62 (86%)
Left IJV	4 (16%)	6 (13%)	10 (14%)
Diagnosis			
Hematologic malignancies	24 (96%)	21 (50%)	45 (67%)
Other malignancies	0	12 (29%)	12 (18%)
Renal failure	1 (4%)	5 (12%)	6 (9%)
Other diseases	0	4 (9%)	4 (6%)
Preoperative PLT transfusion	25 (100%)	0	25 (37%)
Bleeding complications	2 (8%)	0	2 (3%)

PLT: platelets; IJV: internal jugular vein.

TABLE II.—*Hematologic profile of patients undergoing 72 CVC placements.*

	PLT<50×10⁹/L (N.=25)	PLT>50×10⁹/L (N.=47)	Total (N.=72)	P value
Preoperative profile				
aPTT, mean (range)	30.8 (20.1-38.3)	30.4 (22.6-38.9)	30.5	NS
INR, mean (range)	1.15 (1.00-1.71)	1.10 (0.96-1.76)	1.12	NS
Hb, mean (range)	9.3 (7.7-13.6)	10.3 (7.5-14.1)	10.0	0.013
PLT, mean (range), ×10⁹/L	24.3 (7-48)	371.4 (53-834)	250.8	<0.001
Postoperative profile				
Hb, mean (range)	9.0 (6.7-12.2)	10.0 (6.1-14.5)	9.7	0.021
PLT, mean (range), ×10⁹/L	55.9 (7-138)	353.8 (66-849)	250.4	<0.001

aPTT: activated partial thromboplastin time; INR: international normalized ratio; Hb: hemoglobin; PLT: platelets; NS: not significant.

Comparing patients in group A and group B, we noted statistically significant differences regarding the mean Hb levels before the CVC insertion (9.3 g/L *vs*. 10.3 g/L, P=0.013) and after the procedure (9.0 g/L *vs*. 10.0 g/L, P=0.021), with a mean drop of 0.3 g/dL in both groups.

In addition, we found a significant difference of PLT count before the CVC placement (P<0.001) and after the procedure (P<0.001), with a significant increase in PLT level after the preoperative transfusion, although 10 patients in the transfused group still showed a PLT value below the safety threshold of 50×10⁹/L, with a median of 31 x 10⁹/L (range 7×10⁹/L – 42×10⁹/L). However, in these 10 cases we found a pre-transfusion PLT count less than 20×10⁹/L, with a median of 13×10⁹/L (range 7×10⁹/L – 19×10⁹/L).

No major bleeding complications were reported. Minor bleeding was seen in 2 (3%) cases: 1 hematoma and 1 bleeding at the catheter insertion site that resolved with direct pressure. These complications were observed in group A and pre-operative PLT counts in these two patients were 9×10⁹/L and 19×10⁹/L, respectively. The central line was positioned in the right internal jugular vein in the first patient and in the left internal jugular vein in the other.

No minor bleedings were seen in Group B.

There were no reported complications related to platelet transfusions.

Discussion

Thrombocytopenia is a common clinical problem in patients with malignant diseases and it is associated with an increased risk of bleeding complications during any invasive procedures.

Currently, practice guidelines recommend a count of 50×10⁹/L as the minimum PLT level for lumbar puncture, epidural anesthesia, gastrointestinal endoscopy, bronchoscopy, liver biopsy, central line placement and laparotomy.[1, 5]

The need for CVC in the management of patients with malignant disease is mandatory and most of these patients are thrombocytopenic due to the disease or treatment-related hemostatic disorders.

To prevent bleeding complications secondary to thrombocytopenia, patients are often transfused prophylactically when the PLT count is below the recognized safety threshold of 50×10⁹/L.

Currently, no specific evidence-based guidelines exist regarding the benefits of this practice to minimize the bleeding complications, with a consequent great variability in the use of PLT transfusion.

Some studies have analyzed CVC insertions in patients with disorder of hemostasis and an incidence of bleeding from 4.5% to 6.5% is reported in patients with thrombocytopenia.[2-4, 6] Furthermore, Zeidler *et al.*[2] have suggested reducing the threshold for prophylactic PLT transfusion to 20×10⁹/L due to the significant increased risk of bleeding only in patients with PLT count below to 20×10⁹/L. As a matter of fact, the use of this lower transfusion trigger has also been validated by the American Association of Blood Banks.[7]

However, these studies have been performed in adult patients and CVCs were placed percutaneously using the Seldinger technique. It is

well know that there are substantial differences between children and adult patients; actually a subset analysis of the PLADO trial data found that the incidence of bleeding was significantly increased in pediatric patients, especially in patients who underwent to autologous stem-cell transplantation.[8] Probably, this higher rate of bleeding should be justified by the different intensity of chemotherapeutic regimens in children and may be responsible for structural alterations to the endothelial cells.

To the best of our knowledge, only two studies of bleeding complications in pediatric patients with thrombocytopenia undergoing placement of CVCs have been reported in the literature.[9, 10] One study evaluated the postoperative complications of Port-a-Cath in children with acute leukemia;[9] the other assessed the incidence of surgical bleeding among children with hemolytic uremic syndrome undergoing peritoneal dialysis and peripherally inserted venous catheters (PICC) positioned in subclavian or femoral vein.[10]

Our retrospective single-center study is the first report to assess bleeding complications among pediatric patients undergoing insertion of tunneled CVCs in internal jugular vein.

In our study, 35% of the procedures took place in patients with a PLT count level below the threshold of 50×10^9/L secondary to malignant diseases. In accordance to the internal hospital guidelines, PLT were transfused in these patients within one hour prior to CVC placement to reduce the risk of bleeding, providing safe insertion conditions. In the transfusion group, 58% of patients were found to have a preoperative PLT count less than 20×10^9/L.

No severe bleedings occurred in our study, confirming that severe bleeding is a rare event and not correlated with clinical and laboratory bleeding factors.

Non-severe bleedings were observed in only 8% of the patients with a preoperative PLT count less than 50×10^9/L. These patients were affected by a severe bone marrow aplasia. After the surgical procedure, a PLT level of 7×10^9/L was found in one patient and a 31×10^9/L in the other, but no PLT count check was performed one hour after the transfusion. However, these bleedings were encountered after the insertion of central lines and managed without invasive interventions or hemocomponents transfusion. The previous studies classified bleedings according to Common Terminology Criteria for Adverse Events (Version 4.0),[11] where Grade 1 are bleedings characterized by mild symptoms, such as slight oozing from the insertion site and not requiring any interventions; whereas Grade 2 are bleeding with mild symptoms that require invasive interventions or prolonged compression. In Grade 3 bleeding, transfusion, radiologic, endoscopic, or elective operative interventions are indicated, and in Grade 4 bleeding, life-threatening consequences require urgent intervention. However, Grade 1 bleedings are considered of little clinical significance and are not always taken into account. For this reason, the incidence of bleeding in our study should be about 1%.

The median PLT count among children receiving preoperative PLT transfusions (24×10^9/L) was significantly less than those not receiving transfusions (315×10^9/L); from our analysis we observed a reduction of postoperative PLT count among patients not transfused, with a mean of about 20×10^9/L; whereas, in the thrombocytopenic children an increased mean level of about 30×10^9/L was found. Although, 10% of patients in the transfused group still showed a PLT value below the safety threshold of 50×10^9/L, our findings support the use of prophylaxis PLT transfusion in these patients because it avoids a significant reduction of PLT count during the positioning of CVC with a reduction of bleeding rates, without resorting to the therapeutic transfusions in the post-operative course.

The small reduction of Hb levels documented in both groups, with a drop mean of 0.3 mg/dL, confirm the absence of major bleeding in patients with thrombocytopenia who underwent CVC placement, probably correlated with the prophylactic PLT transfusion.

However, the low incidence of bleeding complications documented in this study confirms the need of experienced clinicians to perform these high-risk procedures.

Certainly, our study is limited by its retrospective design and the small number of patients.

Transfusion guidelines recommend checking PLT count within an hour and 24 hours after the end of transfusion to determine its effectiveness.[12] However, no post-transfusion PLT count was taken prior the insertion of CVC and the procedure was performed within an hour after the transfusion, considering that bleeding is really the more clinical relevant measure than the PLT count increment. Actually, in our study no thrombocytopenic patients showed severe bleeding complications during the central line positioning and only one patient with a PLT count below 10×10^9/L after the surgical procedure was found. We believe this low value can be correlated to an excessive PLT consumption due to severe bone marrow aplasia, and PLT refractoriness can be excluded.

Conclusions

Our experience suggests that the positioning of CVC can be performed safely in patients with severe thrombocytopenia, and a preoperative PLT transfusion is required to minimize the risk of bleeding. We confirm, as reported in literature, the necessity to perform a prophylactic PLT transfusion one hour before the central line placement to increase the PLT count in thrombocytopenic patients.[13]

Furthermore, we believe a large randomized controlled study is needed in pediatric patients with thrombocytopenia to define the optimal use of PLT transfusion, establishing the category of patients most at risk of bleeding with a subsequent improvement in patient safety and a reduction in cost.

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Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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