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The effect of Absolute Neutrophil Count (ANC) on early surgical site infection in Implanted Central Venous Catheter (ICVC)

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ABSTRACT

Purpose: The aim of this study was to evaluate surgical site infection (SSI) rates related to implanted central venous catheters (ICVC) in pediatric hematology and oncology patients with respect to absolute neutrophil count (ANC) levels.

Patients and methods: From January 2004 to December 2015, pediatric patients with ICVC insertion were investigated retrospectively. Patients were divided into four groups according to preoperative ANC levels and Granulocyte-colony stimulating factor (G-CSF) usage. Immediate and early surgical site infections were evaluated 7 and 30 days following surgery.

Results: In total, 1143 patients were enrolled. Patients were placed into 4 groups: 930 patients in group 1 with an ANC≥500/μL without G-CSF, 149 in group 2 with an ANC≥500/μL after G-CSF usage, 36 in group 3 with an ANC <500/μL without G-CSF, and 28 in group 4 with an ANC<500/μL even after G-CSF administration. Rates of immediate and early SSIs were not statistically different between groups. In the two-group analysis (group 1 and 2 *vs.* 3 and 4), the number of immediate and early SSIs were not also different, respectively.

Conclusion: There was no correlation between ANC levels and immediate and early SSI occurrence after ICVC placement.

Level of Evidence: III

Implanted central venous catheters (ICVC) are necessary for the management of pediatric hematology and oncology patients undergoing chemotherapy and bone marrow transplantation. [1,2] The risk of infection related to ICVC placement may increase with a lower absolute neutrophil count (ANC).[3,4]

However, clinical data regarding the incidence of postoperative surgical site infections (SSI) after ICVC insertion in pediatric patients with severe neutropenia, defined as an ANC of less than 500/μL, has not been clearly shown in the previous studies. The purpose of this study was to evaluate immediate and early SSI rates of ICVC in pediatric hematology and oncology patients in relation to their ANC levels.

1. Patients and Methods

1.1. Inclusion of patients

Pediatric hematology and oncology patients who underwent ICVC insertion between January 2004 and December 2015 were included for this study. Medical records were retrospectively reviewed to obtain patient details including gender, age at ICVC insertion and removal, type of catheters used, ANC count before operation, diagnosis, and post-operative complications. Patients who underwent ICVC insertion due to other causes, such as short bowel syndrome or hemodialysis were excluded.

ICVCs comprised of ports (Celsite®; B.Braun, Melsungen, Germany, Healthport®; Baxter, Deerfield, IL, USA) and Hickman® catheters (2-lumen or 3-lumen, Bard Access System, Salt Lake City, UT, USA). All patients underwent chemotherapy for at least one month prior to ICVC insertion. Cut-down or sono-guided access were applied according to planned vessels of internal, external jugular, or subclavian vein under general anesthesia in the operating theater by 5 experienced surgeons. Patients with febrile conditions did not undergo ICVC insertion in accordance with the guidelines of our institution.

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Table 1
Patient demographics and operation-related data

	Total	Group 1	Group 2	Group 3	Group 4	*P* values
	N = 1143	N = 930	N = 149	N = 36	N = 28	
Age at operation (months)	94.7 ± 82.9	92.3 ± 67.5	102.7 ± 149.4	114.6 ± 65.7	102.6 ± 72.7	0.212
Male (%)	684 (59.8)	563 (60.5)	87 (58.4)	21 (58.3)	13 (46.4)	0.169
No. of hematologic malignancy (%)	511 (44.7)	391 (42.0)	70 (47.0)	26 (72.2)	24 (85.7)	<0.001
Preoperative ANC (/μL)	3896.3 ± 6988.0	3201.6 ± 3225.2	9793.7 ± 16362.4	336.5 ± 147.9	164.8 ± 175.8	<0.001
Hickman catheter (%)	729 (63.8)	564 (60.6)	109 (73.2)	30 (83.3)	26 (92.9)	<0.001
Rt. IJV (%)	1052 (92.0)	849 (91.3)	147 (98.7)	32 (88.9)	24 (85.7)	0.329
Duration of catheter (days)	173.4 ± 234.2	148.2 ± 273.4	288.0 ± 181.1	290.4 ± 241.8	246.0 ± 213.6	0.106

ANC: absolute neutrophil count, IJV: internal jugular vein

Table 2
Comparison of surgical site infections according to groups

	Total	Group 1	Group 2	Group 3	Group 4	*P* values		
	N = 1143	N = 930	N = 149	N = 36	N = 28	1 *vs* 2 *vs* 3 *vs* 4	1 *vs* 3	2 *vs* 4
7-day SSI (%)	19 (1.66)	15 (1.61)	2 (1.34)	0	2 (7.14)	0.120	0.443	0.059
30-day SSI (%)	32 (2.80)	27 (2.90)	4 (2.68)	0	1 (3.57)	0.761	0.300	0.817

SSI: surgical site infection

1.2. Medical chart review and division of patients

ANC levels were checked one day prior to or on the day of the operation following which a decision to administer granulocyte colony-stimulating factor (G-CSF) was made. Subcutaneous G-CSF injections at a dose of 50 μg/m^2 of body surface area were administered to patients with an ANC less than 500/μL, unless contraindicated.

All patients were divided into four groups according to their ANC level and their requirement for G-CSF; group 1: an ANC ≥ 500/μL without G-CSF, group 2: an ANC ≥ 500/μL after G-CSF administration, group 3: an ANC < 500/μL without G-CSF, and group 4: an ANC < 500/μL even after G-CSF administration. For group 4 patients, repeated G-CSF injections were not performed.

Immediate and early SSIs were evaluated on post-operative days 7 and 30. SSI was defined as at least one of the following; (1) purulent drainage with or without laboratory confirmation, (2) positive culture from the operative incision or the catheter, (3) presence of pain or tenderness, localized swelling, redness, or heat at the operation site.

1.3. Data analysis

Continuous data were represented as the mean with standard deviation, and categorical data were represented as proportions and percentages. Dichotomous variables were analyzed with the chi-square test. Continuous variables were assessed using the independent *t* test when they were normally distributed while the Mann-Whitney U test was used if the variables exhibited non-normal distribution. All statistical analyses were performed with the SPSS version 21.0, software (SPSS Inc., Chicago, USA). A *p* value of <0.05 was statistically significant.

This study was conducted with the approval of the institutional review board of our center (IRB No.: 1504-042-663). The authors have no conflicts of interest to declare.

2. Results

A total of 1143 patients underwent ICVC placement and 684 (59.8%) were male with a mean age of 94.7 months at the time of operation. Five hundred and eleven patients (44.7%) had hematologic malignancies and 632 patients had solid tumors. Hickman catheters were placed in 729 patients (63.8%), most commonly in the Rt. internal jugular vein. Duration of catheter maintenance was not different between the groups. Group 1 to 4 consisted of 930, 149, 36, and 28 patients, respectively (Table 1).

In total, 19 (1.66%) and 32 patients (2.80%) presented with immediate and early surgical site infections, respectively. In the 4-group analysis, the number of patients in each group with immediate and early SSIs were 15 (1.61%), 2 (1.34%), 0, and 2 (7.14%) and 27 (2.90%), 4 (2.68%), 0, and 1 (3.57%), respectively. Each group did not show any differences in the immediate and early SSI ($p = 0.120$, 0.761) (Table 2). Number of catheter removals due to 7-day and 30-day SSI were 2 (0.17%) and 11 (0.96%) respectively and 13 in total. Port removal due to SSI was observed in only 1 patient.

Immediate SSIs occurred in 17 (1.58%) and 2 patients (3.13%) when comparing the combined groups of 1 and 2 with groups 3 and 4, respectively, with no statistical differences ($p = 0.346$). The rate of early SSIs was also not different between ANC ≥ 500/μL and <500/μL patients ($p = 0.537$) (Table 3). Comparison of groups 1 and 3, patients who did not receive G-CSF injections, was performed for immediate and early SSIs. The rate of immediate and early SSIs were 1.61% vs. 0 ($p = 0.443$) and 2.90% vs. 0 ($p = 0.300$), respectively, with no statistical significance (Table 2). Groups 2 and 4, patients who had G-CSF administered, were compared for immediate and early SSI rates. Complication rates were 1.34% vs. 7.14% and 2.68% vs. 3.57%, respectively and *p* values were not statistically significant ($p = 0.059$ and 0.817) (Table 2).

The frequencies of 7 and 30-day SSIs according to the G-CSF administration (group 1 + 3 *vs.* 2 + 4) were compared. Each value was 1.55% *vs.* 2.26% ($p = 0.499$), and 2.80% *vs.* 2.82% ($p = 0.982$), without any statistical significance found (Table 4).

3. Discussion

ICVC is essential for the treatment of children with solid or hematologic malignancies. ICVC infections are associated with significant morbidity, and, occasionally, mortality. [3,4]

Many studies have reported that neutropenia at the time of ICVC placement is significantly associated with early catheter removal. [3–12] A single-center study investigating the risks of early ICVC loss in

Table 3
Surgical site infections according to level of absolute neutrophil count

	Total	Group 1 + 2	Group 3 + 4	*P* values
	N = 1143	N = 1079	N = 64	
7-day SSI (%)	19 (1.66)	17 (1.58)	2 (3.13)	0.346
30-day SSI (%)	32 (2.80)	31 (2.87)	1 (1.56)	0.537

SSI: surgical site infection

Table 4
Surgical site infections according G-SCF administration

	Total	G-CSF (-) (Group 1 + 3)	G-CSF (+) (Group 2 + 4)	*P* values
	N = 1143	N = 966	N = 177	
7-day SSI (%)	19 (1.66)	15 (1.55)	4 (2.26)	0.499
30-day SSI (%)	32 (2.80)	27 (2.80)	5 (2.82)	0.982

G-CSF: granulocyte colony-stimulating factor, SSI: surgical site infection

195 children with leukemia and aplastic anemia recommended that clinicians avoid ICVC implantation in severely neutropenic patients. [3] In another study investigating ICVC removal within 100 days of placement in pediatric patients with acute lymphoblastic leukemia and aplastic anemia, exclusion of severely neutropenic patients resulted in less ICVC removal rate. [4] Furthermore, a study found that when children with malignancies, short-bowel syndrome and other chronic illnesses had ICVCs, neutropenia was one of the risk factors for early ICVC infection. [12]

Due to these reasons, in our institution, G-CSF has routinely been administered to increase the ANC levels to over 500/μL before catheter placement. Use of G-CSF significantly decreased the incidence of febrile neutropenia, duration of neutropenia, and length of hospitalization in pediatric cancer patients. [13,14] According to the 2006 American Society of Clinical Oncology (ASCO) guidelines, the use of G-CSF is reasonable for the prophylaxis of pediatric patients with a likelihood of febrile neutropenia. [15]

However, Cesca et al. reported that ICVC implantation in severely neutropenic pediatric patients with hematologic malignancies does not increase early (less than 30 days from the operation) catheter removal rate. [16] In another study investigating the safety of ICVCs in acute lymphoblastic leukemia children, an ANC less than 500/μL at the time of insertion did not increase the infection rate in the first 30 days after placement. [17]

In the present study, patients who had severe neutropenia at the time of ICVC placement had similar SSI rates in the first 7 and 30 days compared with patients who did not have severe neutropenia (groups 1 + 2 *vs.* 3 + 4). Furthermore, G-CSF injections in neutropenic patients did not result in differences in the rate at which surgical site infections occurred (group 2 *vs.* 4). Even when comparing total patients who received G-CSF with those who did not (group 1 + 3 *vs.* 2 + 4), there was no difference in the frequency of surgical site infection, indicating that administration of G-CSF does not prevent surgical site infection. This is similar to other previous study in which G-CSF was administered to adult cancer patients before and after surgery, and G-CSF was not advantageous in preventing severe infections. [18] This is because the patients' degree of American Society of Anesthesiologists (ASA) physical status classification or underlying medical conditions would have a greater impact on their infection risks than G-CSF administration or the number of neutrophils. [19]

The overall complication rate was less than 3% in the population with ANC > 500/μL and the incidence was not different in the low ANC group. This result correlates with recent previous studies reporting that port placement in pediatric patients with severe neutropenia can be performed without an increased incidence of port removal for infection compared with patients without severe neutropenia. [20,21]

This study has a few limitations. First, as per the guidelines of our institution the minimum level of preoperative ANC for ICVC insertion had been set at 500/μL until recently. Therefore we were able to include only a small number of patients (65; 5.6%) with an ANC of less than 500/μL. Second, due to the retrospective nature of the study, applying uniform management protocols to all patients was not possible. For future investigations, a randomized prospective control study needs to be performed.

In conclusion, an ANC level of less than 500/μL does not increase immediate and early SSI rates during the placement of ICVC in pediatric hemato-oncology patients. G-CSF could be administered if the patient is neutropenic at the time of ICVC insertion, but this does not result in a difference in the rate of SSI occurrence.

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