# EARLY-TERM PORT CATHETER COMPLICATIONS IN PEDIATRIC PATIENTS RECEIVING CORTICOSTEROID THERAPY

# KORTİKOSTEROİD TEDAVİSİ ALAN ÇOCUK HASTALARDA ERKEN DÖNEM İNTRAVENÖZ PORT KATETER KOMPLİKASYONLARI

PORT CATHETER COMPLICATIONS

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**Özet**

Amaç: Kortikosteroid tedavisinin yara iyileşmesini olumsuz yönde etkilediği bilinmektedir. Çalışmamızda kortikosteroid tedavisi alan çocuk hastalarda intravenöz port kateterin (IvPK) güvenirliğini inceledik. Gereç ve Yöntem: IvPK uygulanan çocuk kanser hastaları çalışmaya dâhil edildiler. Hastalar 3 gruba ayrıldılar; grup 1: IvPK uygulananlar; grup 2: IvPK + sadece kortikosteroid tedavisi alanlar; grup 3. IvPK + kombine kortikosteroid tedavisi alanlar. Hastalarda yaş, cins, primer hastalık, kemoterapi tedavileri, erken dönem IvPK komplikasyonları değerlendirildi. Bulgular: Toplam 73 hasta değerlendirildi. Hastaların preoperatif kemoterapi alma süresi 32.6±31.7 gün (5-64); toplam IvPK komplikasyon oranı %30.1; IvPK kullanım süresi 13.2±8.3 ay (1-36) bulundu. Grup 2'de 3 (%17.6), grup 3'de 4 (%18.1) hastada erken dönemde yara iyileşmesinde bozulma ve/veya lokal enfeksiyon görüldü. Kemoterapi alan 7 hastada (%17.9) ortalama 16.5±4.6 gün (10-22); kemoterapi almayan 7 hastada (%20.5) ortalama 24.4±7.3 gün (12-34) yara iyileşmesinde bozulma ve/veya lokal enfeksiyon görüldü. Tartışma: Tek başına kortikosteroid veya kombine kortikosteroid tedavisi alan çocuk hastalarda erken dönemde IvPK komplikasyonları görülmekle birlikte kemoterapi almayan hastalara göre anlamlı fark bulunmadı. Ancak IvPK uygulaması, kemoterapinin bilinen potansiyel yan etkileri nedeniyle olabildiğince tedaviye ara verildiği dönemde veya tedaviye başlamadan önce tercih edilmelidir.

**Anahtar Kelimeler**

İntravenöz Port Kateter; Enfeksiyon; Kortikosteroid; Kemoterapi

**Abstract**

Aim: Corticosteroid therapy is known to adversely affect wound healing. We studied the safety of intravenous port catheter (IvPC) application in pediatric patients receiving corticosteroid therapy. Material and Method: Pediatric cancer patients who underwent IvPC placement were enrolled. The patients were divided into three groups. Group 1: Those who underwent IvPC placement; group 2: Those who underwent IvPC placement + corticosteroid therapy alone; and group 3: Those who underwent IvPC placement + combined corticosteroid therapy. Age, sex, primary disorder, chemotherapy regimens, and early-term complications were compared between the groups. Results: A total of 73 patients were studied. The mean duration of chemotherapy was 32.6±31.7 (range 5-64) days; the total IvPC complication rate was 30.1%; the mean duration of IvPC use was 13.2±8.3 (range 1-36) months. Impaired wound healing and/or local wound infection at an early period occurred in 3 (17.6%) patients in group 2 and 4 (18.1%) patients in group 3. Impaired wound healing and/or local wound infection occurred at a mean of 16.5±4.6 (range 10-22) days in 7 (17.9%) patients who received chemotherapy and at a mean of 24.4±7.3 (range 12-34) days in 7 patients (20.5%) who did not. Discussion: Although early-term IvPC complications are seen in pediatric patients receiving corticosteroids alone or in combination, there was no significant difference compared to patients who did not receive chemotherapy. However, as a result of the well-known potential side effects of chemotherapy, IvPC should be administered at treatment-free intervals or before treatment onset whenever possible.

**Keywords**

Vascular Access Devices; Infection; Steroids; Drug Therapy

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## Introduction

In pediatric hematology and oncology patients, intravenous access lines are very frequently placed as a result of a variety of requirements including chemotherapy administration, fluid-electrolyte treatment, total parenteral nutrition, and for venous blood sampling [1]. Therefore, intravenous port catheters (IvPC) are widely used to meet prolonged intravenous access needs of pediatric patients [2]. IvPCs are easy and safe to place and do not limit patients' daily activities [3]. Unlike other central venous catheters, IvPCs contain a reservoir with a silicone membrane through which injections are done. This reservoir and catheter are placed entirely into the subcutaneous area with a brief surgical procedure. The reservoir of IvPCs, together with its special port needle, is used to administer medications and to take blood samples [4].

Patients with IvPCs are administered corticosteroid therapy, alone or in combination, against malignant conditions. However, preoperative corticosteroid therapy is known to adversely affect wound healing [5]. Corticosteroids suppress inflammatory response, collagen synthesis, epithelization, and immunological resistance [6,7]. Furthermore, some chemotherapy agents suppress fibroblast proliferation and collagen synthesis, thereby affecting wound healing adversely [8]. In this context, these medications are hypothetically expected to affect wound healing adversely and increase wound infections in patients who continued to receive chemotherapy at the time of IvPC application for compelling reasons. Therefore, we studied early-term IvPC complications in patients receiving corticosteroid and/or combined corticosteroid therapy against malignancy.

## Material and Method

Pediatric patients in whom an IvPC was placed between 2007 and 2016 at Mersin University School of Medicine, Department of Pediatric Surgery were retrospectively studied. Pediatric cancer patients with IvPC placement were enrolled, without consideration of chemotherapy protocol, dose, or duration. A control group (group 1, n=34) and two study groups were formed: patients receiving alone corticosteroid therapy (group 2, n=17) and patients receiving combined corticosteroid therapy (group 3, n=22). Patients in the control group did not receive any chemotherapy during the time when the IvPC was inserted. Patients receiving either corticosteroid or combined corticosteroid therapy were defined as chemotherapy groups (group 2 + group 3). The ALL BFM 2000, AML BFM 2004, and LL BFM 95 treatment protocols were applied for all patients where patients who were administered corticosteroid alone in the first 8 days and then combined steroids [9-11]. Age, sex, primary disorder, chemotherapy regimens, and early-term complications were compared between the groups. Early-term catheter-associated complications included poor wound healing and local/systemic infections in the first month. Mechanical or metabolic complications were not taken into consideration. This study was approved by the Clinical Research Ethics Committee, and the relatives of all participating patients gave written informed consent before study entry.

IvPC placement was performed under general anesthesia in the operating room. Second-generation cephalosporins, in two doses, were administered for surgical antibioprophylaxis. Port catheters were placed through the internal jugular vein or subclavian vein under ultrasonographic guidance using the Seldinger technique. C-arm fluoroscopy was used throughout the procedure. The reservoir part of the IvPC was placed at the midclavicular line, above the pectoral muscle, and under the skin. It was then irrigated with 1/100,000 heparin solution. A plain posteroanterior chest film was taken to rule out pneumothorax and to verify the position of the catheter after the surgery. Use of the IvPCs began at least four days after placement. The statistical analysis of the study data was done using the chi-squared test (Fisher's exact test). The values were expressed as mean and standard deviation.

## Results

A total of 73 pediatric patients were studied. Table 1 shows the primary disorders, chemotherapy regimens, and catheter-related complications. The mean age of the patients was 5.6±4.2 (range 1-17) years; 56 were male and 17 were female. The duration of preoperative chemotherapy was 32.6±31.7 (range 5-64) days. A total of 22 (30.1%) patients suffered IvPC-associated complications. The duration of IvPC use was 13.2±8.3 (range 1-36) months. Impaired wound healing and/or local wound infection occurred at an early period in 3 (17.6%) patients in group 2 and in 4 (18.1%) patients in group 3 (p=0.073). Impaired wound healing and/or local wound infection occurred at a mean of 16.5±4.6 (range 10-22) days in 7 (17.9%) patients who received chemotherapy and at a mean of 24.4±7.3 (range 12-34) days in 7 patients (20.5%) who did not, at the time interval of IvPC insertion (p=0.78). Signs of local infection such as hyperemia, local temperature increase, and purulent discharge were observed within the first month in 14 patients, two of whom subsequently developed sepsis. Four patients had wound site culture proliferation. The proliferated microorganisms included Candida albicans in two patients and coagulase negative Staphylococcus aureus in two other patients. Cath-

Table 1. Primary disorder, chemotherapy, and catheter complications in patients who underwent intravenous port catheter placement

| Primary diagnosis | N | Early-term (0-1 month) | Later-term (>1month) |
|---|---|---|---|
| | Corticosteroid (group 2) | | |
| ALL | 14 | 1 | 2 |
| Lymphoma | 3 | 2 | - |
| | Mixed therapy (group 3) | | |
| ALL | 15 | 4 | 1 |
| AML | 3 | - | 1 |
| Lymphoma | 2 | - | - |
| Histiocytosis | 2 | - | - |
| Subtotal | 39 | 7 | 4 |
| | No therapy (group 1) | | |
| ALL | 21 | 4 | 3 |
| Wilms' tumor | 3 | 1 | 1 |
| Neuroblastoma | 5 | 1 | - |
| Hepatoblastoma | 2 | 1 | - |
| Osteosarcoma | 2 | - | - |
| Retinoblastom | 1 | - | - |
| Subtotal | 34 | 7 | 4 |
| Total | 73 | 14 | 8 |

eters could be spared in only 3 patients in whom wound care and systemic antibiotherapy caused a regression in signs and symptoms of infection. However, 11 catheters were removed.

## Discussion

In this study, among pediatric patients who underwent IvPC placement at the time of chemotherapy, 7 of 39 (17.9%) patients developed wound dehiscence and/or local infection. However, 7 of 34 (20.5%) pediatric patients who did not receive chemotherapy also developed local infection.

IvPCs increase the quality of life of cancer patients because they provide a long-lasting intravenous access. Today, IvPCs are placed under ultrasonographic guidance [12]. As skin integrity is re-established after placing IvPCs subcutaneously, the tasks limiting daily activities and quality of life, such as daily wound care and washing, are eliminated. However, it is well known that chemotherapy impairs wound healing and creates a tendency for infections [13,14]. Almeida et al. reported that corticosteroids adversely affected wound healing and delayed wound closure [14]. Talas et al. reported that dexamethasone impaired tracheal anatomosis in a dose-dependent manner [5]. Naycı et al. showed that 5-fluorouracil delayed colonic anastomosis healing [8]. In our study, IvPC infection was detected in 22 (30.1%) of 73 patients, in other words 0.75/1000 per catheter-day. The total duration of IvPC use was 13.2±8.3 (range 1-36) months. IvPCs were removed due to the elimination of the indication in 54 (3/4) patients and due to local infection in 19 (1/4) patients. An analysis of the potential early-term (<1 month) adverse effects of chemotherapy in IvPC placed patients revealed that 7 (17.9%) of 39 patients experienced delayed wound healing and/or local infection. Four patients had bacterial proliferation in wound cultures. However, we could not make a clear distinction between delayed wound healing and local infection. First, the examination findings of both conditions are very similar. Second, delayed wound healing does not occur necessarily with infection, and wound cultures may prove negative in some local infections. The adverse effects of chemotherapy can be assessed by measuring tissue's tensile strength and/or tissue hydroxyproline level, but we did not, and cannot, perform these tests due to ethical concerns [5,8]. A factor in favour of the view that local infection occurred as an IvPC complication in our patients is that a delay in wound healing in corticosteroid therapy starts soon after the surgical procedure, i.e. within 3-4 days [5,8]. In our own series, delayed wound healing and/or local infection occurred at a mean of 16.5±4.6 (range 10-22) days in patients who were on chemotherapy and 24.2±7.3 (range 12-34) days in those who were not. An early-term (<1 month) evaluation of patients who underwent IvPC placement and who did not receive chemotherapy showed that 7 (20.5%) of 34 patients also developed local infection. This suggests that, contrary to our expectation, chemotherapy does not cause IvPC complications at the early term. The literature studies on this subject have produced contradicting results. This may be explained by heterogeneity of study samples and the lack of controlled randomization. Kilic et al. reported that IvPC complications occurred at a rate of 22%; they added that non-infectious catheter-related complications occurred at a greater rate in those who received corticosteroid therapy [15]. Yazici et al. reported that IvPC-related infections occurred at an incidence of 1.96/1000 catheter-days; local infections at a ratio of 1/3; and catheter removal as a result of catheter infection at a ratio of 1/7 [16]. Miliaraki et al. reported an infection rate of 2.62 day for central catheters placed in pediatric cancer cases [17]. Chang et al. reported an IvPC-associated infection rate of 5.6%; they also added that frequent catheter use did not increase the rate of catheter infection but using them for the purpose of administering total parenteral nutrition increased it [18]. The main characteristics of our study that made it unique among others are that pediatric patients who were hematology/oncology patients formed the whole study group, placement of all IvPCs were by the same surgical team using standard surgical technique, and there was a high level of training and knowledge of ancillary health staff in caring for and using these catheters. In our study IvPC infections occurred at an early period (<1 month) in 14 (19.1%) patients and at a late period (>1 month) in 8 (10.9%) patients. Early-term catheter-associated complications can occur secondary to technical reasons, early catheter use, and catheter care. It has been reported that the ancillary health staff's level of knowledge about antisepsis measures and catheter use are also important factors in the occurrence of catheter infections [19]. Although we considered that these factors were the case for our patients, we could not explain why early-term (<1 month) complications were more common than late-term (>1 month) complications. Keum et al. reported that early-term complications following IvPC occurred in 4.5% of patients, while late-term complications had a rate of 4.9% [12]. Catheter removal is not recommended for local infections, but wound site care and antibiotic therapy are recommended as first-step treatments. However, catheter removal is recommended in treatment-unresponsive cases whose overall clinical condition deteriorates or for cases of persistent fever and blood culture proliferations [20]. In the present study IvPC catheters were removed in 11 (4/5) of 14 patients who had early-term catheter complications unresponsive to antibiotherapy and wound care. To conclude, both of our overall IvPC complication and early-term IvPC infection rates were higher than those reported in the literature. These results should be reviewed in detail with the aim of lowering these figures.

The main limitation of our study was that we did not made any classification based on chemotherapy dose and duration. Rather, whether patients received corticosteroids alone or in combination at the time of IvPC placement was the only factor that was taken into account. This was because the total number of study subjects was low, and we did not form an adequate number of groups to make more robust comparisons. Even so, the study groups were found to have comparable complication rates. Another limitation of this study is that the patient group not receiving chemotherapy at the time of IvPC placement cannot serve as the control group of the patient groups that received corticosteroids, alone or in combination. This group was employed to give us an idea. Hence, these limitations should be taken into consideration when interpreting the results of this study. There is a need for prospective randomized clinical trials with a larger population size to further clarify this subject.

In conclusion, we did not find differing rates of catheter complications in pediatric patients who underwent IvPC placement

while receiving chemotherapy (either alone or in combination) than for those who did not receive chemotherapy during the same period. However, as a result of the well-known potential side effects of chemotherapy, IvPCs should be placed at treatment-free intervals or before treatment is begun whenever possible. Nevertheless, IvPCs that were placed at the time of chemotherapy due to compelling reasons were found to be safe.

### *Competing interests*

The authors declare that they have no competing interests.

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