

## Intravenous Infusion-Related Nosocomial Infections in Children

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**ABSTRACT** A prospective study was conducted to obtain the basic data of intravenous infusion-related nosocomial infections at the Pediatric Department Child Health, Cipto Mangunkusumo Hospital in Jakarta during the period of March - May 1998. Subjects were patients with a single intravenous infusion without any other invasive measures. All patients were admitted at the intermediate and ordinary ward that was classify to the First and Second Class, Third Class according to room rate and number of beds. From 62 patients with intravenous infusion, 21 were infected (33.9% with 95%CI; 0.226; 0.471). Complications of intravenous infusions were skin infiltrations (17/62), phlebitis (8/62), bacteremia (4/62), and septicemia (1/62). The most frequently found microorganism were *Staphylococcus epidermidis*, *Enterobacter aerogenes*, *Acinobacter calcoaceticus*, *Serratia marcescens*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. The results of the sensitivity tests of those microorganisms proved that all bacteriae, Gram positive as well as Gram negative were sensitive to the following antibiotics (in decreasing order): cyprofloxacin, amikacin, gentamicin, cefphyrome and ceftriaxon. Gram positive bacteriae were also sensitive to vancomycin and cephalotin. [Paediatr Indones 1999; 139:145-153]

### Introduction

Nosocomial infection is one that develops during hospitalization and is not present or incubating at the time of admission to the hospital. A nosocomial infection may give rise to clinical symptoms during hospital stay, or after being sent home. Nosocomial infection is an important nursing health problem in hospitals all over the world and

presents great consequences for the hospitals and the society.<sup>1,2</sup> Peripheral intravenous infusions are very important in medical treatment for delivering fluids and electrolytes, blood transfusions, parenteral medication, total parenteral nutrition, as well as for chemotherapy.<sup>3</sup> In 1974, two years after the introduction of plastic catheters for intravenous infusion therapy, it was found out that intravenous infusion may lead to complication such as phlebitis, and bacteremia/septicemia.<sup>4,6</sup>

The results of many studies indicate that the risk of infection caused by intravenous infusions varies between 3.5 to 57%.<sup>7-9</sup> Risk factors for complications include age of the patient, kind of disease, catheter material, duration of the infusion, care of the catheter, and skill of the medical personnel.<sup>4,10</sup> The microorganisms causing infusion-related infection are usually of the flora found in the patient.<sup>4,10</sup> The most important factor is the entrance of the skin flora as a consequence of contamination of the tip of the intravenous catheter, during insertion.<sup>11</sup> The incidence of rate of infusion related nosocomial infection in neonate of is 55.5% with a mortality rate of 24.7%.<sup>9</sup> This incidence rate was quite different from surveillance a year latter, i.e. 2.8%.<sup>2</sup> The purpose of this study was to obtain data about intravenous infusion-related nosocomial infections in children at the Pediatric Department of the Cipto Mangunkusumo Hospital Jakarta.

## Methods

This prospective study was done at the Pediatric Department of the Cipto Mangunkusumo Hospital during the period March 1998 - May 1998. The population in this study consisted of new patients admitted at the Intermediate Ward, First/Second Class, and Third Class of ordinary ward, who were given a single intravenous infusion. The criteria of exclusion were neonate, the infusion duration less than 48 hours, infusion done by venesection, patients referred by another hospital, and patients who received other invasive measures besides intravenous infusion.

Before intravenous insertion the first blood culture was taken and put into BHI medium (Brain Heart Infusion). Afterward the patient was observed daily to determine if there were local symptoms (infiltration/phlebitis) or systemic symptoms/sepsis. At the time of discontinuation of the infusion, venous blood was again taken and a second blood culture was performed. Also the tip of the catheter was cut with a sterile scissors and cultured it in a thioglycolate medium (THIO). The catheter tip culture was examined qualitatively and a bacteriologic sensitivity test was done by Disc diffusion on the Kirby Bauer variety. The method used in this study is to make a record of all the necessary data of the patient on a particular form. The data were processed by Epi Info 6.04 and the results were presented descriptively.

## Results

### 1. Characteristics of the patients

During the periods of investigation, there were 62 cases eligible for analysis, consisting of 34 males and 28 females, with an age range from 1 month to 16 years. Of the 62 patients with intravenous infusion, 21 cases became infected (33.9% with a 95%CI 22.6%; 47.1%). Table 1 indicate that the highest age proportion of infection was found in the range between 1 year and 5 years (7/16).

Table 1. Distribution of patients with nosocomial infection by to age groups

Age groups	Intravenous infusion related infection		Total
	Yes	No	
1 month - < 1 year	4	11	15
1 - < 5 year	7	9	16
5 - < 10 year	6	11	17
> 10 year	4	10	14
Total	21	41	62

The diagnosis of the patients involved in this study are shown in Table 2. The most frequent cases found were DHF (27 cases) with 8 infected cases (8/27). Four patients had malignant disease (e.g. acute leukemia, rhabdomyosarcoma, neuroblastoma) of which 2 cases were infected. Of the other diseases, only 1 case of each was infected.

Table 2. Distribution of patients by clinical diagnosis

Clinical diagnosis*	Intravenous infusion related infection		Total
	Yes	No	
DHF	8	19	27
U'ndernutrition	6	7	15
Bronchopneumonia	2	7	9
Bronchiolitis	1	3	4
Malignant disease	2	2	4
Thallasemia	1	1	2
Others	8	10	18
Total	28	49	77

\* Each patient may have more than one clinical diagnosis

## 2. Application of intravenous infusion

Fluid therapy was the reason for applying intravenous infusion in most of the cases (32/62). Table 3 shows that the proportion of infection in patients with intravenous infusion for parenteral therapy was higher than the proportion of infection in patients with fluid therapy (10/32) or blood transfusion (1/4); however, statistically the difference was not significant.

Table 3. Association between indication for infusion and nosocomial infection

Indication for infusion	Intravenous infusion related infection		Total
	Yes	No	
Parenteran therapy	10	16	26
Fluid therapy	10	22	32
Blood transfusion	1	3	4
Total	21	41	62

$$\chi^2 = 0.03; df = 1; RR = 0.79; 95\%CI : 0.42; 1.71; p = 0.8557$$

Table 4 shows that the proportion of infection in patients with a duration of infusion longer than 72 hours (9/25) was slightly higher compared with patients with a duration of infusion between 48 and 72 hours (12/37), the difference was not statistically significant.

Table 4. Association between nosocomial infection and the duration of infusion

Duration of infusion	Intravenous infusion related infection		Total
	Yes	No	
48 - 72 hours	12	25	37
> 72 hours	9	16	25
Total	21	41	62

$$\chi^2 = 0.00; df = 1; RR = 1.11; 95\%CI : 0.55; 2.23; p = 0.9859$$

Of eight cases of phlebitis five cases were infected (5/8). Table 5 shows in detail the complications caused by intravenous infusion with infection. Table 6 shows that the majority of microorganism which causes infection in this study was *Staphylococcus epidermidis* (7/21). Bacteremia was found in four cases (4/21).

Table 5. Patient distribution of infected cases caused by infusion according to sort of complication

Complication	Intravenous infusion related infection		Total
	Yes	No	
Clinical symptom (-)	10	26	36
Infiltration	5	12	17
Phlebitis	5	3	8
Sepsis/septicaemia	1	-	1
Total	21	41	62

Table 6. Type of microorganism causing of infection by intravenous infusion and bacteremia

Type of microorganism	Infection (n)	Bacteremia (n)
<i>Staphylococcus epidermidis</i>	7	1
<i>Enterobacter aerogenes</i>	4	1
<i>Acinetobacter calcoaceticus</i>	4	0
<i>Serratia marcescens</i>	3	1
<i>Pseudomonas sp.</i>	2	0
<i>Staphylococcus aureus</i>	1	1
Total	21	4

Table 7 shows that all the microorganisms which causes infection, Gram positive (*S. epidermidis* and *S. aureus*) as well as Gram negative (*A. calcoaceticus*, *E. aerogenes*, *P. aeruginosa*, *S. marcescens*), were very sensitive to ciprofloxacin, and successively amikacin, gentamicin, cephpyron and cefphyrom. The Gram positive microorganisms involved were also sensitive to vancomycin and cephalotin. All bacteriae detected in this study were usually resistant to the antibiotics which were often used clinically (such as ampicillin, chloramphenicol, erythromycin and cefotaxime).

## Discussion

### 1. Characteristics of patients

Of 62 patients examined, there were 34 males and 28 females, whereas 21 cases (34% with CI 95%; 22% ; 47%) showed infusion related infection. The incidence rate of nosocomial infection caused by intravenous infusion in this study was similar to the

Table 7. Sensitivity test of the microorganisms which cause nosocomial infection after intravenous infusion

Antibiotic	<i>A.calcoaceticus</i> (n = 4)	<i>E.aerogenes</i> (n = 4)	<i>Pseudo-monas sp.</i> (n = 2)	<i>S.marcescens</i> (n = 3)	<i>S.aureus</i> (n = 1)	<i>S.epidermidis</i> (n = 7)
Amoxicillin/clavul.	0	1/4	(-)*	0/3	(-)*	3/7
Ampicillin sulbact	1/4	1/4	(-)*	(-)*	1/1	5/7
Oxacillin	1/4	(-)*	(-)*	(-)*	1/1	0/7
Ampicillin	0/4	0/4	0/2	0/3	0/1	1/7
Erythromycine	(-)*	(-)*	(-)*	(-)*	1/1	2/7
Chloramphenicol	2/4	1/4	1/2	3/3	0/1	1/7
Co-trikomoxazole	2/4	2/4	0/4	3/3	1/1	2/7
Gentamicin	1/4	2/4	1/2	3/3	1/1	5/7
Peniciline-G	0/4	0/4	0/2	0/3	0/	1/7
Tetracycline	1/4	1/4	1/2	0/3	1/1	4/7
Kanamycine	1/4	1/4	1/2	3/3	1/1	3/7
Amikacin	2/4	2/4	1/2	3/3	1/1	6/7
Aztreonam	0/4	1/4	1/2	3/3	0/1	1/7
Sulbenicilin	0/4	0/4	0/2	1/3	0/1	2/7
Clindamycine	(-)*	0/4	(-)*	(-)*	1/1	4/7
Céphalotine	0/4	0/4	0/2	0/3	1/1	6/7
Cefuroxime	0/4	0/4	0/2	0/3	1/1	3/7
Cefotaxime	0/4	0/4	1/2	1/3	1/1	3/7
Ceftriaxone	0/4	1/4	1/2	3/3	1/1	5/7
Clprofloksasin	3/4	4/4	1/2	3/3	1/1	7/7
Cefotian	(-)*	(-)*	1/2	(-)*	0/1	(-)*
Ceftazidime	1/4	1/4	1/2	2/3	1/1	(-)*
Cefoperazone	0/4	1/4	0/2	2/3	0/1	(-)*
Cefiksime	0/4	1/4	0/2	3/3	0/1	1/7
Vancomisin	0/4	1/4	0/2	0/3	1/1	6/7
Cefpirome	1/4	2/4	1/2	3/3	1/1	7/7

Note : 99(-)\* : was not examined. This sensitivity test was done during the periode of March 1998 - May 1998, at Microbiology Sub Division of Clinical Pathology Department of Cipto Mangunkusumo Hospital

results of the studies done by Flowers et al<sup>7</sup> Cercenando et al<sup>8</sup> (34.5% and 38.1% of cases respectively).<sup>7,8</sup> The highest proportion of infection was found in the age group of 0-8%.<sup>13,17</sup> The complication of the infusion related bacteremia found in this study 1 - 5 years (7/16). This result was not compatible with previous studies who stated that the risk of infection was greater in the age group of below 1 year.<sup>10</sup>

The most prevalent cases admitted in this study were DHF (27/62) and infection was detected in 8 cases (8/27). This phenomenon is not surprising because this study was conducted, coincidentally with the outbreak period of DHF in Jakarta at that time. Two out of four patient with malignant diseases were suffered from infection due to infusion procedures in this study. The possible explanation for this finding was that the patient with malignant diseases may arise granulocytopenia, humoral immunity deficiency, and dysfunction of cellular immunity, which facilitates the development of nosocomial infections.<sup>12</sup>

## 2. Factors related to nosomial infection

The reason of applying infusion in most cases is fluid therapy (26/62). Nevertheless the proportion of infusion related infection was greater in the group of patients with parenteral medication (10/26). It might be caused by bacterial contamination due to multiple puncture of infusion set/three way stopcock when administered parenteral medication three to four times daily. Beside that, several kinds of antibiotics (vancomycin, amphotericin B, beta-lactam antibiotics), chemotherapy and electrolytes solutions can irritate the vascular endothel layer which may easily cause phlebitis/inflammation.<sup>1,13,14</sup>

The infusion catheter which was inserted for more than 48 hours will more often cause complication (phlebitis and bacteremia/septicemia). The risk of septicemia is about 2-5% if the infusion has been placed more than 48 hours. According to Kaplan-Meier the risk of getting phlebitis on the 3rd day of applying of the infusion is about 30% and after the 3rd day becomes 39-49%.<sup>15</sup> In this study the incidence of infection of the patient after applying infusion for more than 72 hours were 9 out of 25 cases, a little bit higher in compare with those cases receiving infusion for 48-72 hours period (12 out of 37 cases).

The results of studies during the last two decades showed that more than 30% of patients who were given infusion therapy obtained phlebitis which required the extraction of the infusion. In this study the complication of phlebitis was found in 8 out of 62 cases, but only 5 cases of them were proven infection based on the result of laboratory findings. This result indicated that not all the signs of phlebitis have always to be related to the process of infection. The majority of researchers came to the conclusion that phlebitis is mainly caused by physicochemical processes.<sup>10,13,16</sup> Only about 10% was related to the process of infection.<sup>4</sup>

Only one case of septicemia was found in this study (1/21). This finding is in accord with the literature which stated that septicemia caused by infusion is about 0-8%.<sup>13,17</sup> The complication of the infusion related bacteremia found in this study (4/21) may also be caused by routine invasive measures, such as venous puncture done for blood sampling.

Coagulase negative staphylococcus is the microorganism which most often cause infection, but it seldom causes bacteremia/septicemia, such as *Staphylococcus aureus*.<sup>4,13,17</sup> Of the coagulase negative staphylococcus, *Staphylococcus epidermidis* was the pathogenic microorganism most often isolated (7/21). Other microorganisms which were isolated were similar to study found by other researchers previously, such as *Staphylococcus aureus*, *Enterobacter aerogenes*, *Acinobacter calcoaceticus*, *Serratia marcescens* and *Pseudomonas sp.*<sup>4,16,17</sup>

The pattern of the sensitivity tests in this study indicates that all the Gram positive and Gram negative bacteriae which caused infection, were very sensitive to cyprofloxacin. Besides cyprofloxacin, other antibiotic which could be used against Gram positive and Gram negative bacteriae were successively amikacin, gentamicin, cephiro and cephpyrome. Gram positive bacteriae were also sensitive to vancomycin and cephalotin. The antibiotics which were often used (for example ampicillin, chloramphenicol, cotrimoksazole, erythromycin and cefotaxime) were not effective anymore for the microorganisms which caused infusion related infection. Based on the results of surveys on nosocomial infections at the Cipto Mangunkusumo Hospital in 1996, the microorganisms causing nosocomial infections were still sensitive to amikacin, gentamicin, nalidixic acid and cyprofloxacin, while the bacteriae causing nosocomial infections were already resistant against the antibiotics often used.<sup>2</sup>

We concluded that intravenous infusion is associated with high incidence of the development of nosocomial infection. The spectrum of microorganisms varies widely. Gram positive and Gram negative bacteriae causing intravenous infusion related infections in this study were very sensitive to cyprofloxacin; however, the Committee of Infectious Diseases of American Academy of Pediatrics does not recommend the use of this drug in children because of its side effect.<sup>18</sup>

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