Journal of Experimental and Clinical Medicine
http://dergipark.ulakbim.gov.tr/omujecm

Clinical Research

J. Exp. Clin. Med., 2016; 33(1): 7-10
doi: 10.5835/jecm.omu.33.01.003

Serum procalcitonin level in monitorization of surgical site infections in neonates

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ARTICLE INFO

Article History
Received 17 / 09 / 2015
Accepted 05 / 10 / 2015

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Keywords:
Neonate
Procalcitonin
Surgery
Surgical site infection

ABSTRACT

A retrospective study was performed to evaluate the role of white blood cell (WBC), C-reactive protein (CRP) and procalcitonin (PCT) levels in the follow-up and treatment of surgical site infections (SSI) in neonates. Neonates who underwent surgical intervention (n:34) were evaluated for gestational age, sex, diagnosis, inflammatory markers (WBC, CRP, PCT), clinical findings, results of cultures and response to antimicrobial treatment. Records of 34 neonates and 36 surgical interventions were included to the study. Twenty (58.8%) of patients had SSI. Postoperatively CRP, WBC and PCT levels were increased (77%, 77%, 77% respectively) in patients with SSI. Postoperatively CRP, and WBC levels were increased (57% and 64% respectively) in patients without SSI. In conclusion, CRP levels and WBC count were significantly increased in 77% of cases after surgery. Increased PCT levels were detected only in patients with SSI. PCT levels may be considered as the most valuable marker to monitor SSI in neonates after surgery.

1. Introduction

Deficient innate immunity and neutrophil functions cause higher incidence of surgical site infections (SSI) in neonates compared to adults and children. The incidence of SSI was reported as 14.9% in neonates (Shankar et al., 2001). Blood stream infections and wound infections account 70% of all SSI cases (Shankar et al., 2001). Therefore, close follow-up should be performed to all neonates who underwent surgical intervention and require neonatal intensive care.

In neonatal sepsis, C-reactive protein (CRP), interleukin-6, interleukin-8 and procalcitonin (PCT) levels have been used to diagnose early onset disease and to evaluate the effectiveness of treatment (Pavcnik-Arnol et al., 2010; Auriti et al., 2012). PCT is an inactive pro-peptide form of active hormone calcitonin. It increases markedly in septic conditions and considered as a good predictor of severe infection (Kocabaş et al., 2007; Davidson et al., 2013). It has been reported that PCT levels have more reliable diagnostic accuracy for neonatal infections than other markers (Kocabaş et al., 2007; Pavcnik-Arnol

et al., 2010; Davidson et al., 2013). On contrary, it has been reported that interpretation of PCT levels in neonates is difficult because of its physiologic increase after birth (Takakura et al., 2013). Although, early infection markers have been used in diagnosis of neonatal sepsis, there is very limited data about the use of these markers in SSI in neonates. Therefore, a retrospective study was performed to evaluate the role of white blood cell count (WBC), CRP and PCT levels in the follow up and treatment of SSI in neonates.

2. Methods

The study was performed under the recommendations of World Medical Association Declaration of Helsinki. The patients who were followed in Kırıkkale University Neonatal Intensive Care Unit between 2011 and 2013 were included to the study. Newborns that required surgical intervention and neonatal intensive care were enrolled in the study. Medical reports of neonates for the last year were evaluated for gestational age, sex, diagnosis, preoperative and postoperative infection parameters (CRP, PCT and WBC), clinical findings, results of cultures and response to infection treatment retrospectively. The neonates included to the study had no clinical or microbiological evidence of infection prior to surgery. Community-acquired infections were excluded from the study.

2.1. Evaluation of PCT and CRP

The patients who were followed in Kırıkkale University Neonatal Intensive Care Unit between 2011 and 2013 were included to the study. PCT assay was performed by immunfluorescence by sandwich method (MiniVIDAS, VIDAS kit, BioMeriux, France). The normal limits of PCT were 0-0.05 ng/mL. PCT levels for localized infection was 0.05-0.5 ng/mL, 0.5-2 ng/mL for sepsis, 2-10 ng/mL for severe sepsis and more than 10 ng/mL for septic shock (Davidson et al., 2013). CRP levels were evaluated with immunoturbidimetric method with spectrophotometer (Beckman Coulter, Beckman Instruments Inc. Indianapolis, USA). The normal limit for CRP was considered as 0.01-5 mg/L.

The WBC, CRP and PCT results obtained 24 hour prior and 24 hour after the surgical intervention were considered in the evaluation. Also, results of markers obtained 24 hour after antimicrobial administration were included.

3. Results

Records of thirty-four neonates and thirty-six surgical interventions were included. Male to female the ratio was 11/6. The mean gestational age of the patients was 37.7±2.9 weeks. The list of surgical interventions and diagnosis of patients are listed in Table 1.

Twenty of the patients (58.8%) were considered as SSI and nine of them were diagnosed as wound infection (n:9, 26.5%), six of them were ventilator-associated pneumonia (n:6, 17.6%) and five of them were blood stream infection (n:5, 14.7%).

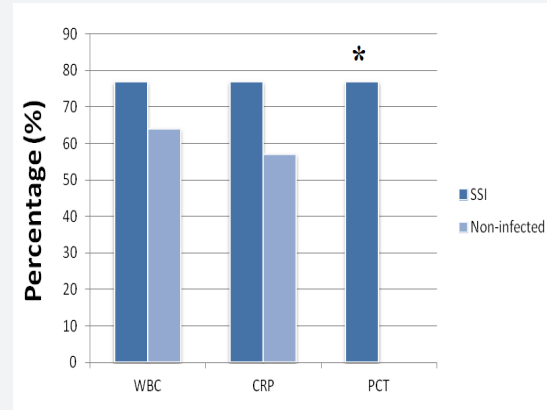

Fig. 1. The comparison of all markers in patients with and without SSI (*; p<0.05).

Patients who developed wound infection were those operated for oesophageal atresia (n:7), Hirschsprung's disease (n:1) and isolated colonic perforation (n:1). The patients who experienced ventilator-associated pneumonia were those operated for oesophageal atresia (n:3), total colonic aganglionosis (n:2) and gastrochisis (n:1). Blood stream infection was occurred in patients who were operated for total colonic aganglionosis (n:2), Hirschsprung's disease (n:1) and congenital diaphragmatic hernia (n:2).

Table 1. The list of diagnoses and surgical interventions of the patients.

Diagnosis	Number of patients	Surgical Intervention
Oesophageal atresia, trachea-oesophageal fistula	12	Primary oesophageal anastomosis and TE fistula repair.
Anorectal malformation	4	Colostomy
Total colonic aganglionosis	4	Rectal biopsy, ileostomy
Hirschsprung's disease	2	Rectal biopsy, colostomy
Gastrochisis	1	Primary repair
Malrotation and midgut volvulus	4	Ladd procedure
Congenital diaphragmatic hernia	4	Diaphragm repair
Infantile hypertrophic pyloric stenosis	1	Pyloromyotomy
Isolated colonic perforation	1	Colostomy
Umbilical cord hernia	1	Primary repair

When preoperative and postoperative CRP and WBC were evaluated in patients with SSI (n:9), 77% of patients with SSI had increased CRP levels (n:7) and 77% of them had increased WBC (n:7) in postoperative period compared to preoperative levels. PCT levels were also found increased in 77% (n:7) of cases with SSI postoperatively.

The 57% (n:8) of the patients without SSI had increased postoperative CRP levels. In patients without SSI, mean level of WBC was 11.500/mm^3 and WBC levels were increased in 64% of patients (n:9) postoperatively. The PCT levels were less than 0.05 in all patients without SSI. The comparison of all markers in patients with and without SSI was given in Fig. 1.

The postoperative levels of infection markers in different SSI are outlined in Fig. 2a, 2b, 2c. The antimicrobial treatments of all patients were changed at 2-5th postoperative day according to antimicrobialcultures. PCT levels were decreased in all cases and considered as a response to antimicrobial treatment (Fig. 2). In contrast, high WBC count and higher levels of CRP were detected during the all clinical course of antimicrobial treatment.

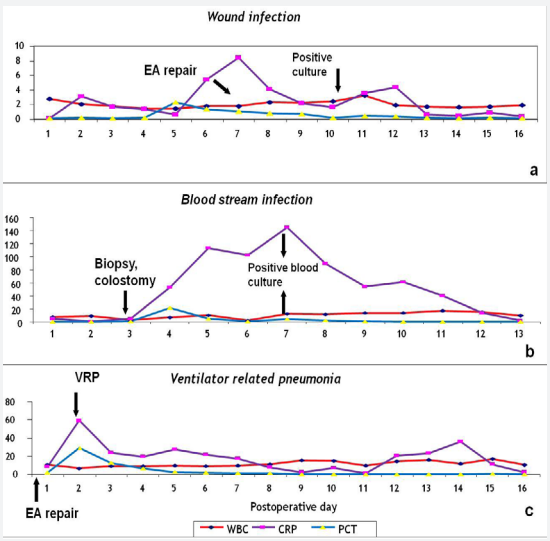

Fig. 2. a, b, c. Case samples for postoperative levels of WBC, CRP and PCT after different SSI. (a) Wound infection in patient with EA: CRP level is increased on the day of oesophageal repair. Positive culture was detected on the 3th postoperative day and all markers were found increased. (b) Blood stream infection in patient with TCA: CRP and PCT are increased in the next day after colostomy and biopsy and considered as early sign of infection. (c)Ventilator associated infection in patients with EA: Increased levels of CRP and PCT were detected on the second postoperative day. (**EA:** Oesophageal atresia; **TCA:** Total colonic aganglionosis; **VRP:** Ventilator associated pneumonia)

4. Discussion

Hospital-acquired infections especially SSI cause high morbidity and mortality. The impaired immunity, prolonged hospitalization, surgical intervention and newborn period increase this risk (Önen et al., 2002; Boybeyi et al., 2013). Therefore, neonates who underwent surgical intervention should be closely followed-up in neonatal intensive care units in order to prevent SSI. Also, infection monitoring is essential to manage the antimicrobial treatment.

Early detection of bacterial sepsis in surgical neonates is difficult for various reasons. Early warning signs and symptoms are often non-specific and difficult in hospitalized patient. Also, it is not easy to distinguish signs of neonatal sepsis from other surgery related conditions. Since microbiological culture results cannot be obtained until at least 48-72 hours, laboratory tests are required for accurate and rapid identification of SSI. Although, PCT, IL-6, IL-8 and TNF-α levels are commonly used to detect early and late onset neonatal sepsis, the role of inflammatory markers in detection of neonatal SSI has not been evaluated commonly previously (Auriti et al., 2012). Therefore, in the present study we evaluated the role of WBC count, PCT and CRP in the follow up and treatment of SSI in neonates.

Surgically ill neonates have higher risk of SSI because of deficient neutrophil activation and lack of tool-like receptors (Bhattacharyya and Kloske, 1990). Since abdominal wounds are very close to umbilicus, wound infection is the most common SSI in neonates (Bhattacharyya and Kloske, 1990). We encountered both wound infection and ventilator-associated infections in our patients.

In the present study, we found that CRP levels and WBC count are significantly increased in 77% of cases after surgery. Although, these markers increased in all cases, increased PCT levels were detected only in patients with SSI. It has been reported that PCT levels rise 4 hours after bacterial exposure, peak at 6 to 8 hours and remain elevated at 24 hours (Dandona et al., 1994; Pavcnik-Arnol et al., 2010; Davidson et al., 2013). Although, it has been shown that PCT, IL-6 and TNF-α were useful markers to determine the prognosis of neonatal sepsis, CRP and WBC has no similar efficacy (Dandona et al., 1994). It was reported by Pavcnik-Arnol et al. (2010) that interleukin-6 and interleukin-8 are more valuable markers in detection of neonatal SSI than PCT and CRP. They claimed that interpretation of PCT is difficult since it can be physiologically increased after birth (Pavcnik-Arnol et al., 2010).

In the present study, we found that PCT levels were decreased as a response to antimicrobial treatment also.

However, CRP levels and WBC count did not respond to antimicrobial treatment in the early period. Therefore, we suggest that PCT can be used not only to detect SSI but also to evaluate the response to antimicrobial treatment. Although, there is no study evaluating the cost effectiveness of SSI screening, we claim that the cost of WBC, CRP and PCT screening might be more cost effective than prolonged antimicrobial treatment and prolonged stay in neonatal intensive care unit.

Since we have limited number of patients, it is difficult to have a firm conclusion about the specificity and/or sensitivity of these markers in the diagnosis and follow-up of SSI in neonates. Therefore, randomized controlled studies are needed to define the most useful marker to detect neonatal SSI. However, when we consider the role of these markers in other neonatal infections, our study confirms that increased level of PCT is more specific to SSI in neonates.

In conclusion, neonates who underwent surgical intervention should require closed monitoring for SSI. Among several inflammatory markers, CRP, WBC count and PCT can be used for infection monitoring in the early postoperative period. Since CRP levels were affected by surgical inflammation, PCT levels may be considered as the most reliable marker for SSI in neonates.

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