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Correlation of Interleukin-6 Serum Level and Surgical Site Infection in Post Major Surgery Patient

Supomo*

ABSTRACT

Background: Surgical site infections (SSI) are a common surgery complication which early diagnosis is important to initiate an adequate therapy promptly. Objective: To explore the possibility of using serum Interleukin-6 (IL-6) in patients who had major surgery as a biomarker to predict SSI.

Patients and Methods: From October to December 2011, 50 patients who underwent major surgery in Sardjito General Hospital Department of Surgery, Yogyakarta were followed up for their IL-6 serum on the third day following the surgery. The patients were also assessed whether they contracted SSI or not.

Results: SSI was present in sixteen out of 45 patients (35.6%). The serum IL-6 level was higher in the group which SSI present where 84.5% of the sample was higher than 10 pg/ml. The Chi-square test showed SSI is related to abnormal IL-6 level (OR 4.941, $p<0.05$).

Conclusion: Post-operative IL-6 higher than normal serum level was associated with SSI. The result indicates that IL-6 serum level may be a useful predictor of the occurrence of SSI in patients who underwent major surgery.

Keywords: Interleukin-6, major surgery, surgical site infection

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Thoracic and Cardiovascular Surgery Division, Department of Surgery, Dr. Sardjito General Hospital, Universitas Gadjah Mada, Indonesia

*Corresponding to: Supomo, Department of Surgery, Faculty of Medicine, Dr. Sardjito General Hospital, Universitas Gadjah Mada, Sleman, Yogyakarta 55281, Indonesia
supomo.tkv@mail.ugm.ac.id

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INTRODUCTION

Surgical site infections (SSI) are a common complication of surgery that adds significantly to the morbidity, length of hospital stay and cost of treatment.[1,2] Early diagnosis of SSI is important to initiate an adequate, prompt therapy.[1] Sardjito Education Center Hospital held 35 major operations in 2015. The occurrence of SSI was 3%. Some efforts to reduce SSI include early detection using biomarkers. Damaged tissue due to trauma, surgical intervention, and the postoperative healing process can lead to the production of pro-inflammatory cytokines and can induce a non-specific systemic inflammatory response syndrome without true infection. Unfortunately, classical markers of infection cannot differentiate an inflammation from an infection.[1]

Interleukin-6 (IL-6) is a pleiotropic cytokine which actions include modulation of proliferation, differentiation, and maturation of hematopoietic progenitors and other cell lineages; growth regulation of certain carcinoma cell lines, and control of cellular metabolic activities. Recently, some clinical studies have described the IL-6 response to trauma, burns, and elective surgery. Although IL-6 is considered as an integral mediator of the physiologic acute phase response to injury, excessive and prolonged post injury elevations of serum IL-6 levels are associated with morbidity and mortality.[2,3] Our study aimed to explore the correlation between IL-6 serum level and SSI in post major surgery patient.

MATERIALS AND METHODS

Study design

The study was designed as a prospective observational study conducted from October to December 2011 in the Department of Surgery of Dr. Sardjito General Hospital, Yogyakarta. The study was approved by ethical committee of Faculty of Medicine of Universitas Gadjah Mada in conjunction with the teaching hospital Dr. Sardjito General Hospital (#KE/KF/303/EC), and all study participants had signed informed consent.

Patients Enrollment

The sampling method was consecutive sampling where a total of 50 patients were recruited. As many as 4 patients were excluded because their medical record were lack of data about the presence or absence of surgical site surgery.

The inclusion criteria were surgical patients who underwent a major surgery at Sardjito General Hospital, which include craniotomy, laparotomy, cholecystectomy, thoracotomy, vascular surgery, rib clipping, varices striping, cardiac surgery, mastectomy, soft tissue tumors, tumor of the oral cavity, open reduction internal fixation, limb amputations,

skin graft, open prostatectomy, hydrocolectomy, orchiectomy or orchidopexy, and ureter lithotomy.

The exclusion criteria were patients who have been diagnosed with the infection before surgery; patients with chemical burns or trauma, pancreatitis; patients with HIV-AIDS or other immunological disorders; and patients with renal failure.

Surgical Site Infections

SSI were diagnosed according to the criteria of the Center for Disease Control and Prevention.[2] It was diagnosed in the presence of pus, abscess, or cellulitis in surgical wound site found within 30 days following the surgery, or 1 year in implant case.

Interleukin-6 Concentration

The IL-6 level was measured with enzyme-linked immunosorbent assay (ELISA) from the patient's serum taken on the third day after the surgery.

Data Analysis

All statistical analysis was performed with the Statistical Package for the Social Sciences program version 17.0 (SPSS Inc. Released 2008. Version 17.0. Chicago: SPSS Inc). The patient characteristics were expressed as frequencies. All variables were compared using the Chi-square test, α=0.05.

Table 1 Patient Characteristics

Variables	Median (min-max)	n	%
Age	48 (22-27)		
Sex			
Male		21	46.70%
Female		24	53.30%
Surgical wound classification			
Clean		23	51%
Clean contaminated		15	33%
Contaminated		5	11%
Dirty		2	5%
Surgical Site Infection			
Present		16	35.60%
None		29	64.40%
Type of Infection			
Superficial		12	75%
Deep		4	25%

Table 2 Correlation between IL-6 and SSI

	Surgical site infection						
	Present		None				
	n	%	n	%	OR	95% CI	p-value
IL-6							
Abnormal	14	45.20%	17	54.80%	4.941	0.944-25.875	0.045
Normal	2	14.30%	12	85.70%			

RESULTS

Patient Characteristics

Forty-five consecutive patients were included in the study. There were 21 males and 24 females. The median age was 48 (range 22-77 years). Sixteen patients (35.6%) developed SSI within 30 postoperative days. Based on the type of surgical wound: 8 (50%) were clean surgical wound, 3 (18.75%) were clean-contaminated wound, 4 (25%) were contaminated the wound, and 1 (6.3%) was a dirty wound. Twelve patients had superficial SSI and four patients had deep SSI (Table 1). There was no significant relationship between the type of surgery wounds and SSI events (p=0.721).

In the group of patients with SSI, IL-6 was increased to higher than 10 pg/ml in 14 (87.5%), while the other two patients had a normal IL-6. In the group of patients without SSI, the serum IL-6 was increased in 17 patients, but 12 patients had a normal IL-6 (Table 2). The Chi-square test showed a significant relationship between the abnormal level of IL-6 and SSI (p =0.045).

DISCUSSION

The postoperative period may increase susceptibility to infections because of surgical trauma and anesthesia-induced transient immunosuppression.[2] SSI is a common complication of surgery which occurs if there is a surgical wound contaminated by pathogenic microorganisms and cannot be countered by the patient's immune response.[1] The most frequent pathogenic microorganism is *Staphylococcus aureus*.[3]

An inflammatory cytokine response after surgery is physiologic and associated with response to surgical trauma.[2] Interleukin-6 functions as a pro-inflammatory and anti-inflammatory molecule, a modulator of bone resorption, a promoter of hematopoiesis, and an inducer of plasma-cell development. Interleukin 6 (IL-6) is increased in patients with surgery, trauma, burns, critical illness and infections.[4,5] Postoperative serum IL-6 increase is proportional to the magnitude of surgical stress has been studied previously. Increased serum IL-6 correlated with the extent of tissue injury, surgical approach and procedural complexity.[6] The serum IL-6 level in normal individuals is approximately 1 pg/ml, and in this study, the threshold laboratory value for the IL-6 level was greater than 10 pg/ml.[7]

In this study, we found significant correlation between Interleukin level and SSI ($p<0.05$). Our result supported a study suggesting IL-6 can be used as a predictor of the incidence of sepsis in cancer patients who undergo major surgery.[2] Sander et al. also stated that an increased IL-6 after CPB is predictive of infection after cardiac surgery in patients with impaired left ventricular function.[8]

CONCLUSION

Our study showed abnormal serum IL-6 is correlated with SSI. It indicates that IL-6 serum level may be used as predictors of the occurrence of SSI in patients who underwent major surgery.

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DISCLOSURE

The author reports no conflicts of interest in this work.

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