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ORIGINAL STUDY

The predictive ability of interleukin-6 for infection after major surgery

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Abstract

Objective: The aim was to evaluate the role of interleukin (IL)-6 in prediction of infection after major surgeries.

Background: An early sensitive and specific marker for postoperative infection would be of interest. The cytokines such as IL-6 and IL-10 have been shown to relate to the severity of postoperative sepsis and patient outcome.

Patients and methods: The study was conducted prospectively at Shebin Elkom Teaching hospital in the period from January 2015 to October 2016 on 50 consecutive patients undergoing elective major surgical procedures. Septic complications were recorded for 4 days postoperatively. For evaluation, patients were allocated into two groups on the basis of signs of sepsis: group A with signs of infection and group B without infection. Cytokine levels were measured after the clinical data were recorded. All data were then analyzed.

Results: IL-6 specificity and sensitivity were 90 and 100%, respectively. The difference in IL-6 concentrations in patients with infection on day 2 and day 4 was significant (P = 0.015). The correlation between IL-6 levels and infection was significant (r's = 0.55). IL-6 levels on days 2 and 4 were significantly higher in patients with infection than in those without infection (P < 0.001).

Conclusion: IL-6 may be an excellent diagnostic test for early detection of infection, particularly insidious infections that may not have been clinically evident.

Keywords: Cytokine in infection, Interleukin-6, Postoperative infection

1. Introduction

Recent therapeutic advances, both medical and surgical, have improved early postoperative outcome. Despite this progress, certain patients remain at high risk of infection and the attendant morbidity and mortality. Routine conventional laboratory tests, such as C-reactive protein (CRP) and white blood cell count, cannot distinguish patients with early infection from those who had inflammatory response only but without infection [1].

Major surgical trauma may induce a nonseptic systemic inflammatory response syndrome (SIRS) that can be difficult to distinguish from early postoperative sepsis. Considering the difficulties in diagnosis of infection in critically ill patients, an early sensitive and specific marker for SIRS would be of interest [2].

The cytokines such as interleukin-6 (IL-6) and IL-10 have been shown to relate to the severity of sepsis and patient outcome. IL-6 is a pleiotropic cytokine that functions as a proinflammatory and anti-inflammatory molecule. It is produced by stimulated macrophages and monocytes when the tissue is injured. The normal serum IL-6 level is 1 pg/ml. It is one of the earliest mediators of the physiological short-term phase reactants to injury. IL-6 levels increase rapidly within 12 h after trauma and remain so for 24 h, and then decrease over the next 24 h [3].

Recently, IL-6 was proved to be a good independent early marker of postoperative sepsis, severe sepsis, or septic shock after major oncological
surgery. Persistently elevated IL-6 levels 24–72 h after surgery are indicative of infections. The rapid normalization of IL-6 levels can be used to refute the suspicion of infection. Early diagnosis could allow early goal-directed therapy, which has been shown to decrease mortality in severe sepsis [4].

The aim of this study was to evaluate IL-6, on the first postoperative day, as an early marker of subsequent postoperative sepsis after major surgery.

2. Patients and methods

The study was conducted prospectively at Shebin Elkom Teaching Hospital in the period from January 2015 to October 2016 on 50 consecutive patients undergoing elective major surgical procedures.

Patients who were admitted for major gastrointestinal or gynecological surgeries with surgery expected to last more than 3 h were included, whereas patients who had preoperative treatment with anti-inflammatory drugs, corticosteroids, or morphine or patients who had immunosuppressive illness other than neoplasm were excluded from the study. All clinical, radiological, and laboratory data were collected prospectively for all patient.

Each day, the attending physician evaluated all the patients for signs of SIRS, sepsis, severe sepsis, or septic shock. Standard supportive care, surgical procedures (drainage of abscesses, etc.), and broad-spectrum antibiotics were provided to all septic patients.

Pneumonia was diagnosed if infiltrates were present on the chest radiograph and, if possible, a positive culture from sputum or bronchial fluid. Abscesses and peritonitis were diagnosed by ultrasonography or computed tomography scan, together with growth of pathogenic bacteria from aspirated pus. Urinary tract infections were diagnosed by the evidence of leukocyturia and growth of pathogen in the urine culture. Septic complications were recorded for 5 days postoperatively. For evaluation, patients were allocated into two groups on the basis of signs of sepsis.

Blood samples were collected in glass tubes before surgery (day 0) and then postoperatively on the morning of day 2 and the morning of the day 4. Blood was processed within 2 h. It was centrifuged at 400 rpm for 15 min and then at 10,000 rpm for 15 min. Sera were stored at −80 °C. Cytokine levels were measured after the clinical data were recorded.

Circulating IL-6 was measured by enzyme immunoassay. The assays were performed in duplicate using kits provided by Immunotech (Marseille, France). The minimum concentration detected was 3 pg/ml. The intra-assay and inter-assay coefficients of variation of enzyme immunoassay kits ranged from 5 to 10%.

Data were analyzed by Statistical Package for the Social Sciences (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp) program version 26. Continuous quantitative variables were expressed as mean, SD, and range, whereas categorical qualitative variables were expressed as number and percentage. The results of comparing the correlation between two continuous variables were indicated by the correlation coefficient (r) using correlation analysis. P value was considered significant if it was less than 0.05.

3. Results

Postoperatively, patients were classified into two groups according to the occurrence of infection: group A, which consisted of 19 patients with postoperative infection, and group B, which consisted of 31 patients with no signs of infection.

In group A, 14 patients (73.68%) were male, whereas five patients (26.32%) were female. Age was 39.42 ± 14.17 years. In group B, 24 patients (77.42%) were male, whereas seven patients (22.58%) were female. Age was 33.71 ± 11.9 years. No significant difference was found between both groups regarding demographic data (Table 1).

For IL-6 concentration, the normal reference range was 12–92 pg/ml. Preoperatively, the mean IL-6 level in group A (166.9 ± 92.4 pg/ml, range: 42–365) was lower than group B (633 ± 1426 pg/ml, range: 28–5100) but without significant difference. On day 2, the mean level in group A (332.1 ± 175.7 pg/ml, range: 109–670) was significantly higher than group B (110 ± 143.6 pg/ml, range: 12–820) (P < 0.001). On day 4, the mean level in group A (154.3 ± 86.8 pg/ml, range: 51–338) was also significantly higher than group B (42.58 ± 25.61 pg/ml, range: 12–92) (P < 0.001) (Table 2).

In group A, the mean IL-6 was significantly higher on day 2 (P = 0.05) and day 4 (P = 0.028) than preoperatively. Moreover, it was significantly higher on day 2 than day 4 (P = 0.015). In group B, the mean IL-6 was significantly higher preoperatively than...
day 2 ($P = 0.001$), whereas there was no significant difference between day 2 level and day 4 level. Descriptively, 19 of 22 patients in group A had higher levels of IL-6 than preoperative levels, whereas all patients in group B had normal or lower levels on day 2. Thus, its specificity and sensitivity were 90 and 100%, respectively. The correlation between IL-6 levels and infection was significant ($r = 0.55$).

4. Discussion

IL-6 is a pleiotropic cytokine that functions as a proinflammatory and anti-inflammatory molecule. It is produced by stimulated macrophages and monocytes when the tissue is injured. Serum IL-6 level can be a marker of inflammation associated with trauma and sepsis and increases after major gastrointestinal or gynecological surgeries [5].

IL-6 concentration may be a superior indicator of postoperative infection, as it increases more rapidly and returns to normal more quickly than other markers like CRP or the erythrocyte sedimentation rate. IL-6 levels peak in the first 6–12 h after surgery and fall back to baseline by 48–72 h after surgery. Elevated IL-6 levels at 24–72 h after surgery are indicative of postoperative infection [6].

Our findings were comparable to other studies in which 48-h postoperative infected patients had higher plasma IL-6 concentrations than those who were not infected ($P < 0.05$). In our study, bacterial growth on culture of the discharge and clinical features of wound infection are the gold standards for diagnosis of a postoperative infection. All 19 infected patients showed local induration, warmth, and gaping after primary wound closure. When the wound was left open, a bacteriologically confirmed discharge from the wound was present on day 6 [7].

In patients with infection, the IL-6 levels peaked on day 2 before a clinical evidence of an infection was apparent. Persistent elevation of IL-6 on day 4 correlated with clinically detected infection.

IL-6 may be an earlier and more accurate marker for the detection of infection than other marker like CRP that peaked on day 4 [1].

4.1. Conclusion

IL-6 is an excellent diagnostic test for early detection of infection, particularly insidious infections that may not have been clinically evident. Careful administration of these tests with clinical correlation may help to ensure that each patient with infection after major surgeries is managed with the most appropriate therapeutic regimen.

Ethical approval statement

The institutional committee’s ethical criteria were followed during all proceedings. The Ethics Committee approved the study.

Conflicts of interest

There are no conflicts of interest.

References