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Original Research

Estimation of Serum Level of Procalcitonin as the Reliable Marker for the Assessment of the Post Operative Infection after Surgery

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ABSTRACT:

Objective: Hospital-acquired pneumonia (HAP) is a common side effect of abdominal surgery. This study looked at procalcitonin (PCT) and C-reactive protein (CRP) as potential early markers for the diagnosis of postoperative HAP after abdominal surgery. **Methodology:** This study involved 100 patients who underwent abdominal surgery. White blood cell counts, the highest body temperature ever recorded, serum levels of CRP and PCT, and every day up until postoperative day (POD) 5 were recorded. Chest radiography was performed both before surgery and every day subsequently up to POD 5. **Results:** HAP was reported to be present in 14% of the patients. Patients with HAP reported significantly greater levels of CRP and PCT compared to those without HAP in the biomarkers assessed after POD 1. (P 0.05). In POD 2, PCT outperformed CPR in terms of sensitivity and specificity (84% and 72% compared to 70% and 60%, respectively). PCT had a threshold of 1.4 ng/ml on POD 2.On POD 3, 4, and 5, the sensitivity and specificity of PCT and CRP were comparable. **Conclusion:** PCT and CRP are trustworthy indicators for predicting early postoperative HAP following abdominal surgery. Diagnoses on POD 2 were substantially more accurate with PCT than CRP. After POD 2, there was no discernible difference in the biomarkers' capacity to make a diagnosis.

Keywords: Procalcitonin, Post-operative infection, Abdominal surgery

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INTRODUCTION

The healing process and postoperative rise in proinflammatory cytokines caused by surgical trauma are part of the usual course of events after surgical interventions [1]. This illness manifests as a non-specific systemic and frequently local inflammatory response syndrome without bacterial infection. Because non-specific serum parameters used for infection diagnosis, such as C-reactive protein (CRP) or white blood cell count (WBC), are frequently elevated, it can be difficult to distinguish between the presence of an early postoperative bacterial infection and a benign unspecific inflammatory syndrome [2]. Procalcitonin (PCT) has been demonstrated to be a more accurate marker in the early postoperative infection detection following cardiac, intestinal, and major brain procedures than the traditional laboratory parameters (such as CRP and WBC).[3-6] While PCT is largely produced by the thyroid's parafollicular cells as a calcitonin precursor hormone in healthy people, patients with sepsis and inflammation have been found to have extra pathological pathways. In these conditions, inflammatory cytokines like TNF-alpha and IL-1beta as well as components of microbe cell walls or membranes like lipopolysaccharides or peptidoglycans may stimulate the creation of PCT.[7-9] A cut-off level of 0.5 micrograms/L has been reported by several researchers as suggesting a significant likelihood of systemic bacterial infection.[7-10]There aren't many research on the use of PCT in for early bacterial infection diagnosis. As PCT is known to be elevated in bacterial infections, it is a possible target for the early diagnosis of a number of disorders, notably sepsis [11,12]. Moreover, it can be utilised to identify bacterial pneumonia, especially when combined with a ventilator [13]. After surgery, severe trauma, and burns, PCT levels are known to increase even in the absence of infection [14-16].

The major goals of the current experiment were to use PCT and CRP as biomarkers for the early diagnosis of

postoperative HAP as well as perioperative risk factors for HAP following abdominal surgery.

METHODOLOGY

This prospective observational research with 100 participants was conducted between August 2015 and July 2016. Patients provided written informed permission, and the ethics committee (MFM-IRB; R/16.03.47) accepted the study procedure. During elective abdominal surgery, patients underwent upper gastrointestinal, hepato-pancreatico-biliary, or colorectal resections. Exclusion criteria for the trial included immunosuppressive medications, long-term corticosteroid therapy, extrapulmonary infections either before or after surgery, use of mechanical ventilation during preoperative assessment, pregnancy, chronic renal insufficiency, and liver dysfunction.

All patients received prophylactic doses of cefamandole (2,000 mg i.v.) and metronidazole (500 mg i.v.) 45 minutes before surgery and continued to receive them for up to 2 days afterward.

The data included the patient's age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) status, smoking history, history of chronic obstructive pulmonary disease (COPD), history of asthma, history of other co-morbidities, type and length of surgery, length of intensive care unit (ICU), and length of hospital stay.

Serum levels of CRP and PCT, as well as the highest recorded body temperature, were noted prior to surgery and on each day up until postoperative day (POD) 5.Chest radiography was performed daily and before operations up until POD 5. After surgery, patients were routinely evaluated for pneumonia symptoms. Patients with consistently increased PCT and/or CRP underwent examinations in order to identify and rule out extrapulmonary infective effects based on their clinical presentation. As an initial course of antibiotic therapy until the findings of a sputum culture were known, patients with pneumonia were given 1.2 g of amoxicillin and clavulanate. The drug was now modified in response to the identified bacterium (s).[17]HAP was diagnosed by looking for purulent sputum, a fever of more than 38°C, a white blood cell count of more than 11,000 or less than 3,000/mm3, or fresh pulmonary infiltrates on a chest X-ray [12]. To detect bacterial isolates, sputum samples underwent a thorough microbiological culture. The culture was declared effective if it had fewer than 106 colony forming units per millilitre. CRP and PCT levels were measured using an enzyme-linked immunosorbent assay in separate blood samples that were kept frozen at 20°C (ELISA).The main objective of the current study was to assess the role of PCT in the early prediction of HAP following major abdominal surgery and to compare its diagnostic accuracy to that of CRP using serial daily postoperative serum PCT and serum CRP analyses from POD 1 to 5. Finding the post-abdominal surgery perioperative risk factors for HAP was the secondary objective. Monoclonal antibodies that are specific for PCT are coated on a plate for use in enzyme-linked immunosorbent assays. To bind to antibodies, samples and standards are pipetted into the wells. Biotinylated anti-human PCT antibody is added after washing. The streptavidin-labeled antibody is then added after a second wash.

STATISTICAL ANALYSIS

The sample size was chosen based on how well PCT and CRP could identify and forecast postoperative HAP. According to past studies' findings [13], 97 patients would be needed to discover a 17% difference in the diagnostic accuracy of PCT and CRP at a 0.05 error rate and an 80% research power. Data were evaluated using SPSS Statistics version 16 software (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was applied in order to validate the reasonableness of the assumption of normalcy. Results are presented as the mean SD, median, and interquartile range for continuous variables, and as number (n) or percentage (%) for categorical variables.Categorical characteristics (including gender, ASA status, smoking status, and surgical incision) were compared between patients with and without HAP using the chi-square test or Fisher's exact test (co-morbidities: COPD and asthma). To compare continuous data, the Mann-Whitney U test or Student's t test was utilised (CRP and PCT kinetics). In order to assess intragroup variations in CRP and PCT kinetics, the Wilcoxon signed-rank test was performed.

RESULTS

Two hundred individuals who underwent major abdominal surgery were prospectively enrolled in the study. Postoperative HAP was identified in 28 patients (14%). A total of 3, 7, and 4 patients were found at PODs 4, 5, and 6, respectively, with a median value of POD 5 in each case. Table 1 compares patients' demographic and perioperative data between those with and without postoperative HAP. Prolonged ICU stays (7 days) and hospital stays (13 days) were significantly linked with the development of postoperative HAP ($P < 0.001$).Table 2 summarises the findings of the univariate and multivariate logistic regression analyses of the independent perioperative factors associated with the development of postoperative HAP. The study's significant risk factors included age 60, smoking 40 packs/years, upper or upper/lower abdominal incision, and surgery duration of 3 h ($P = 0.001$, 0.014, 0.011, and 0.031, respectively). The most common bacterial pathogen isolated in this study was Staphylococcus aureus (35.7%), which was followed by Pseudomonas aeruginosa (28.6%), E. coli (21.4%), and Klebsiella species (14.3%). During the first four days following surgery, there were no appreciable differences in WBC count (cells/mm3) between patients with and

without postoperative HAP. Preoperative PCT levels were not noticeably different between patients with and without postoperative HAP (P = 0.258). Patients with and without postoperative HAP experienced a significant increase in PCT on POD 1, with values of 1.04 ng/ml (0.78-1.40) and 0.8 ng/ml (0.69-1.09), respectively, and no obvious difference between the two (P = 0.153). PCT levels in patients without postoperative HAP significantly decreased from POD 2 to 0.22 ng/ml (0.18-0.30) on POD 5. In patients with postoperative HAP, it increased on POD 2 to 1.52 ng/ml (1.17-1.91) and remained elevated after that. The median PCT values were 1.5 and 1.53 ng/ml on POD 4 and POD 5, while the median CRP levels were 150 mg/L and 148.5 mg/L, respectively. These numbers matched the postoperative diagnosis of HAP.

Table 1: Characteristics of patients [17]

Variables	Hospital acquired pneumonia (N= 28)	Without infection (N=172)	p-value
Age	62 ± 10	45 ± 11	< 0.001
BMI	26 ± 8	28 ± 4	
Sex			0.53
Male	20 (71.4%)	108 (62.7%)	
Female	8 (28.5%)	64 (37.2%	
Asthma	4 (14.2%)	10 (5.8%)	1.0
COPD	2 (7.1%)	14 (8.1%)	0.6
Surgical duration	3.6 ± 0.7	2.9 ± 0.5	< 0.001
Type of surgery			0.036
Laparoscopic incision	2 (7.1%)	58 (33.7%)	
Lower abdomen surgery	2 (7.1%)	30 (17.4%)	
Upper abdomen surgery	24 (85.7%)	84 (48.8%)	
Length of Hospital stay	13 ± 1	8 ± 1	< 0.001

Table 2: Studying the Risk Factors for Hospital-Acquired Pneumonia After Major Abdominal Surgery Using Univariate and Multivariate Logistic Regression Analysis[17]

Variables	Adjusted (multivariate analysis)		Unadjusted (Univariate analysis)	
	Odd ratios	p-value	Odd ratios	p-value
Age	3.12 (2.35 –4.85)	0.001	3.61 (1.92–5.21)	0.0001
BMI	-	-	1.31 (0.62–1.58)	0.35
Sex	-	-	1.24 (0.74–1.65)	0.23
Asthma	-	-	1.83 (0.74–2.34)	0.28
COPD	-	-	2.60 (0.42–4.75)	0.41
Surgical duration (<3 hours)	2.41 (1.74–4.64)	0.03	2.62 (1.95–5.30)	0.001
Laparoscopic surgery	-	-	1.32 (0.63–2.10)	0.29
Lower abdomen surgery	-	-	2.14 (0.75–4.72)	0.32
Upper abdomen surgery	3.82 (2.63–5.21)	-	4.21 (2.45–6.75)	0.0001

DISCUSSION

In our study, postoperative HAP was reported by 14% of participants. According to estimates, 9 to 40% of patients who have abdominal surgery will develop postoperative pneumonia.[18,19,20] A protein called acute-phase CRP is secreted by the liver in response to stimulation. After stimulation, secretion begins to increase and reaches its peak 48–48 hours later [21]. Within 4 hours of the right stimulation, PCT can be detected in the circulation, peaking after 8 hours [22]. The results of our analysis showed that PCT had a significantly higher diagnostic accuracy than CRP on POD 2. On POD 3, 4, and 5, the diagnostic effectiveness of PCT and CRP did not differ significantly.

In order to identify a possible predictor of postoperative HAP development, we examined the analyses of CRP and PCT on POD 2 and 3. For patients with and without postoperative HAP, there were no discernible variations in WBC count or body temperature on POD 2 and 3. The results of our investigation showed that PCT increased on POD 1 in people with and without postoperative HAP. After POD 1, patients without postoperative HAP had their PCT steadily fall, but those with postoperative HAP saw their PCT rise. The AUC of PCT was 0.844 on POD 2 with a sensitivity of 84% and specificity of

72% using cut-off values of 1.4 ng/ml on both days, while it was 0.895 on POD 3 with a sensitivity of 88% and specificity of 72%.PCT production is elevated, particularly following gastrointestinal surgery. These elevated levels during abdominal surgery may be related to translocation of germs from the GI tract temporarily due to inadequate gut perfusion.[16{ Oberhofer et al[23]. evaluated and compared the roles of perioperative CRP and PCT for the early detection of infectious complications following colorectal surgery. The optimal cut-off values for infectious complications were discovered to be 1.34 g/L for PCT and 99.0 mg/L for CRP. Also, they discovered that the PCT level on POD 2 and the CRP level on POD 3 both had comparable predictive values for the emergence of infectious problems. POD 7 served as the median day for the clinical diagnosis of postoperative infections, and postoperative CRP. Mokart et al. [24] examined the relevance of changes in interleukin-6, PCT, and CRP levels in the serum as a predictor of septic problems following major cancer surgery on 50 patients. They came to the conclusion that PCT and IL-6 are important early indicators of postoperative sepsis in cancer patients after major surgery. In their investigation, the cut-off value for PCT on POD 1 was 1.1 ng/ml, with sensitivity being 81% and specificity being 72%. According to earlier research [11,12,13,23], PCT is a valid indicator for the early detection of ventilator-associated pneumonia and postoperative infection complications.[25] However, numerous studies found no additional utility for PCT in predicting postoperative infection [26]. A number of studies have compared PCT with CRP for the detection of postoperative infectious complications [23,27], and earlier studies have demonstrated that PCT is more sensitive than CRP for the early detection of postoperative septic issues following major surgery [24,28]. Some studies [29] showed that CRP is more sensitive than PCT, nevertheless. The risk factors for pneumonia in surgical patients may be examined in order to lessen the likelihood of this complication. Age > 60 years, 40 pack-years of smoking, an upper abdominal incision, and a 3-hour surgery were all found to be significant risk factors in the current study for the development of postoperative HAP. Postoperative pulmonary problems have been associated with age >55 [30,31], upper or upper/lower abdominal incision [30], a history of smoking [32], and surgery lasting more than 2.5 hours [31].

CONCLUSION

In conclusion, PCT and CRP are trustworthy markers for predicting early postoperative HAP after abdominal surgery. PCT's ability to make diagnoses on POD 2 was significantly better than CRP's. Following POD 2, there was no appreciable difference in the diagnostic ability of the two biomarkers. Postoperative infection issues may be indicated by consistently increased PCT levels after abdominal surgery of more than 1.4 ng/ml on POD 2 and 3 and CRP values of more than 145 mg/L on POD 3. However, to validate our findings, more study is required.

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