Procalcitonin is a good tool to guide duration of antibiotic therapy in patients with severe acute pancreatitis

A randomized prospective single-center controlled trial

Rong Qu, *MD,* ***Yan Ji,*** *MD,* ***Yun Ling,*** *MD,* ***Chu-Yang Ye,*** *MD,* ***Si-Ming Yang,*** *MD,* ***Yan-Yuan Liu,*** *MD,* ***Ri-Yan Yang,*** *MD,* ***Yu-Feng Luo,*** *MD,* ***Zhi Guo,*** *MD.*

ABSTRACT

الأهداف: التحقق من الفائدة الطبية للكالسيتونين للتحكم بمدة العلاج بالمضاد الحيوي للمرضى المصابين التهاب البنكرياس الحاد.

الطريقة: شملت هذه الدراسة 71 مريض مصاب بالتهاب البنكرياس الحاد خلال الفترة من مارس 2009م حتى سبتمبر 2011م في قسم العناية الحرجة، مستشفى هويتشو الطبي المركزي، قوانغدونغ، الصين. تم قياس الكالسيتونين يومياً بواسطة اختبار المقايسة المناعية المشابه في مجموعة الدراسة . تم تقسيم المرضى إلى مجموعتين مجموعة الدراسة (مجموعة PCT) ومجموعة العلاج بالمضاد الحيوي (مجموعة الشاهد). لم يتم استخدام العلاج بالمضاد الحيوي حتى ظهور العلامات الحيوية وأعراض الالتهاب وكانت قيمة PCT أكثر من s0.5 نانوغرام/مل. قمنا كذلك بالتوقف من استخدام العلاج بالمضاد الحيوي حين تطور أعراض الالتهاب والعلامات الحيوية أو كانت قيمةPCT أكثر من 0.5 نانوغرام/مل لمدة تزيد عن 3 أيام في مجموعة الشاهد. تم وصف المضاد الحيوي واستخدم لمدة 2 أسبوع وذلك للتأكد من اختفاء أعراض الالتهاب لمدة تزيد عن 3 أيام.

النتائج: كانت مدة العلاج بالمضاد الحيوي ومدة الإقامة في المستشفى في مجموعة الدراسة (35 مريض) أقل إحصائياً 10.89±2.85 ضد 16.06±2.48 يوم والقيمة الإحصائية $p<0.001$ و 16.66±4.02 ضد 23.81±7.56 يوم القيمة الإحصائية $p<0.001$ عن مجموعة الشاهد (36 مريض) بدون أي آثار أكلينيكية سلبية وكانت مدة الإقامة أقل إحصائياً أيضاً.

خاتمة: يعد الكالستونيون مادة آمنة وفعالة للتحكم بمدة العلاج الحيوي في المرضى المصابين بالتهاب البنكرياس الحاد.

Objectives: To investigate the clinical usefulness of procalcitonin (PCT) for guiding duration of antibiotic therapy in patients with severe acute pancreatitis (SAP).

Methods: A total of 71 patients with confirmed severe acute pancreatitis from March 2009 to September 2011 in the Department of Critical Care Medicine of Huizhou Municipal Central Hospital, Guangdong, China were enrolled in this study. Procalcitonin was measured daily by a semi-quantitative immunoassay in the study group. Patients were randomly assigned into 2 groups including a PCT-guided group (study group) and a prophylactic antibiotic therapy (control group). Antibiotic therapy in the study group was not applied until clinical signs and symptoms of infection appeared (PCT value was >0.5ng/ml). We discontinued the antibiotic therapy if clinical signs and symptoms of infection improved and PCT was <0.5ng/ml over 3 days. In the control group, antibiotic therapy was administrated for 2 weeks, or antibiotic therapy was continued because of confirmed infection until clinical signs and symptoms of infection disappeared over 3 days.

Results: In the study group (35 patients), the duration of antibiotic therapy and hospitalization was significantly shorter than the control group (36 patients) (10.89±2.85 versus 16.06±2.48 days, $p<0.001$, and 16.66±4.02 days versus 23.81±7.56 days, $p<0.001$) without negative clinical effects and the cost of hospitalization was significantly lower.

Conclusion: Procalcitonin is a helpful and safe tool for guiding duration of antibiotic treatment in patients with severe acute pancreatitis.

Saudi Med J 2012; Vol. 33 (4): 382-387

From the Department of Critical Care Medicine (Qu, Ji, Ling, Ye, Yang, Liu, Yang, Luo), Guangdong Huizhou Municipal Central Hospital, Guangdong, and the Department of Hematology (Guo), General Hospital of Beijing Military Area, Beijing, China.

Received 28th December 2011. Accepted 12th March 2012.

Address correspondence and reprint request to: Dr. Rong Qu, Department of Critical Care Medicine, Guangdong Huizhou Municipal Central Hospital, 41 E'ling North Road, Huizhou of Guangdong 516001, China. Tel. +86 (752) 2288517. Fax. +86 (752) 2288517. E-mail: gzdd2004@yahoo.com.cn

Most of acute pancreatitis takes a mild, self-limiting course. However, approximately 20% of patients experienced a severe attack. Infections were observed in 30-40% of patients who had over 30% necrosis of pancreas. Those patients were also associated with a substantial increase of mortality.[1] Timely and accurate diagnosis of pancreatic infections are needed which will be helpful for further therapeutic decision-making. Severe acute pancreatitis (SAP) can lead to systemic inflammatory response syndrome (SIRS) and sepsis. Immediate antibiotic therapy is essential for improving survival in patients with sepsis.[2] Despite apparently clear sepsis definitions,[3] it is difficult for us to distinguish SIRS or sepsis in clinical practice at earlier stage of disease. But, the administration of antibiotics is not essential for patients with SIRS. Besides, profound clinical experience, a valid tool for the diagnosis of pancreatic infections and sepsis was definitely needed. Currently, fine-needle aspiration (FNA) is still a diagnostic gold standard for the diagnosis of pancreatic infections.[4] Unfortunately, it demands high standard technical equipment and personal experience, and because of the potential risk of complications, we cannot render guided FNA an easily accessible and cost-effective approach. On the other hand, a multitude of inflammatory variables has been proven to be of little value in discriminating pancreatic infections and associated sepsis from systemic SIRS4.[5] Facing this clinic dilemma, procalcitonin (PCT) has emerged as a laboratory variable that meets this demand.[6] Procalcitonin is the inactive pro-peptide with 116 amino acids, which can generate biologically active hormone calcitonin. In 1993, Assicot et al[7] first described that plasma concentrations of procalcitonin were significantly increased in patients with bacterial and fungal infections and sepsis. Since then, it has been largely confirmed that procalcitonin is the only one among a large array of biochemical parameter, which closely correlates with the inflammatory host response to microbial infections.[8] Moreover, several recent studies show that procalcitonin is a valuable tool to guide antibiotic treatment in patients with pulmonary diseases.[6,9,10] Procalcitonin concentrations remarkably increased upon inflammation in the context of severe bacterial infections and showed a log-normal decrease upon recovery. Therefore, procalcitonin may serve as a surrogate biomarker, which can help physicians to estimate the likelihood for relevant bacterial infections, and decide upon the need for antibiotic therapy in individual patients. In acute pancreatitis, procalcitonin has been shown to predict the development of infected necrosis accurately.[11,12] To date, there is no report about the issue of usefulness of procalcitonin determinations for guiding duration of antibiotic treatment in patients with severe acute pancreatitis. Therefore, we aimed to find the role of daily procalcitonin serum determinations for guiding antibiotic treatment in patients with severe acute pancreatitis in the present randomized trial.

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

Methods. This trial was approved by the Ethics Committee of Guangdong Huizhou Municipal Central Hospital for Human Research. The written informed consent was obtained from individuals or their legal guardian. The study was conducted according to principles of the Helsinki Declaration.

Eligible patients including 71 patients according to the Atlanta criteria for diagnosis of SAP[13] were enrolled from March 2009 to September 2011. General criteria for inclusion were: 1) onset of severe acute pancreatitis was less than 24 hours and 2) age was over 18 years. The exclusion criteria included any of the following: 1) the time interval between diagnosis and study inclusion >24 hours, 2) age of less than 18 years, 2) thyroid disease (such as thyroid adenoma), 3) shock (such as hypovolemic shock), 4) need of surgical interventions (such as surgery of cleaning necrosis of pancreas).

Procalcitonin was measured daily by a semi-quantitative immunoassay and the parameter was monitored over a maximum of 28 consecutive days in the study group. Patients were randomly assigned to either a procalcitonin-guided (study group) or a antibiotic (control group) therapy. Antibiotic therapy in the PCT-guided group was not applied until clinical signs and symptoms of infection appeared and the procalcitonin value was >0.5ng/ml.[14,15] Antibiotic therapy in the PCT-guided group was discontinued if clinical signs and symptoms of infection improved and procalcitonin decreased to <0.5 ng/ml over 3 days. In the control group, antibiotic therapy was administrated for 14 days, or antibiotic therapy was continued because of confirmed infection until clinical signs and symptoms of infection disappeared over 3 days. In both groups, the type of antibiotic substance chosen was either according to the expected microbiologic spectrum and/or adjusted to the isolated organisms whenever possible, and the other basic therapy had no difference, such as gastrointestinal decompression, intravenous injection of Stilamin (somatostatin) for 2 weeks and so on.

Age, gender, sequential organ failure assessment (SOFA)[16] score, and the Acute Physiology And Chronic Health Evaluation-II (APACHE-II)[17] score for stratification of disease severity and clinical parameters were documented in all patients. The duration of intensive care unit stay, antibiotic treatment, all length of hospitalization, cost of hospitalization, and the outcome including multi-organ dysfunction syndrome (MODS)[18] or no and survival/death were recorded.

Continuous variables are presented as mean±standard deviation and 95% confidence interval (95%CI) for descriptive statistics. Differences between the 2 groups were assessed by Student's t-test for continuous variables. For comparison of proportions (gender, multi-organ dysfunction syndrome, antibiotic substance classes, mortality) we used chi-squared test using Statistical Package for Social Sciences Version 13.0. A *p*-value less than 0.05 was considered statistically significant.

Results. Of 71 patients, 35 (25 mens and 10 womens) were randomly assigned to the PCT-guided group and 36 (26 mens and 10 females) were assigned to control group. In both treatment groups, there were no significant differences in age, gender distribution, disease severity as reflected by SOFA score of the first day and APACHE-II score on the first day and the distribution of antibiotic substance classes used (**Table 1**).

The outcome and effect of patients. In the present prospective randomized study, the length of antibiotic treatment in the PCT-guided group was 10.89±2.85 days; it was significantly shorter than that in the control group with 16.06±2.48 days ($p<0.001$) without any negative effects on treatment (**Table 2, Figure 1**). The duration of intensive care treatment in the PCT-guided group with 11.11±2.94 days was significantly shorter than that in the control group with 14.83±2.49 days ($p=0.000$, **Table 2**). And the duration of hospitalization in the PCT-guided group was 16.66±4.02 days, it was significantly shorter than that in the control group ($p<0.001$) with 23.81±7.56 days. At the same time, the cost of hospitalization in PCT-guided group with 24401.00±2631.41 US dollars were significantly lower than that in the control group with 27813.00±2529.37 US dollars ($p<0.001$, **Table 2**).

Discussion. Pancreatic infections and sepsis are major complications in severe acute pancreatitis with significant impact on management and outcome. Regardless of the achievements in the critical care, in patients with severe acute pancreatitis still lead to hospital death from 6-47% of cases. In Multi-organ Dysfunction Syndrome (MODS) patients with at least

Table 1 - Patients characteristics in 71 patients with confirmed severe acute pancreatitis in Huizhou Municipal Central Hospital, Guangdong, China.

Patient's characteristics	PCT-guided (n=35)	Control group (n=36)	*P*-value
Gender			0.998
Male	25	26	
Female	10	10	
Age (years)			0.968
Mean±SD	43.21±11.12	43.72±10.98	
95% CI	39.40-47.02	40.01-47.43	
AAPACHE-II score			0.739
Mean±SD	11.29±1.62	11.42±1.58	
95% CI	10.73-11.85	10.89-11.95	
SOFA score	2.49±0.53	2.38±0.49	0.798
Mean±SD	(2.31-2.67)	(2.21-2.55)	
95% CI			
Antibiotic substance classes (%)			0.476
Carbapenem	31.1	31.3	
Levofloxacin	20.7	20.5	
Metronidazole	15.5	15.1	
Cefoperazone + sulbactam	10.4	10.7	
Piperacillin + tazobactam sodium	10.3	10.4	
Fluconazol	10.2	9.9	
Others	1.8	1.9	

PCT - procalcitonin, SOFA - sequential organ failure assessment, APACHE-II - acute physiology and chronic health evaluation-II, SAP - severe acute pancreatitis

Table 2 - The outcome and effect of patients in 71 patients with confirmed severe acute pancreatitis in Huizhou Municipal Central Hospital, Guangdong, China.

Variables	PCT-guided (n=35)	Control group (n=36)	*P*-value
The case fatality (%)	20.0	22.2	0.988
Multi-organ dysfunction syndrome (%)	68.6	69.4	0.873
The time of intensive care treatment (days)			0.000
Mean±SD	11.11 ± 2.94	14.83 ± 2.49	
95% CI	10.11 - 12.11	13.99 - 15.67	
The duration of hospitalization (days)			0.000
Mean±SD	16.66 ± 4.02	23.81 ± 7.56	
95% CI	15.28 - 18.04	21.25 - 26.37	
The length of antibiotic treatment			0.000
Mean±SD	10.89 ± 2.85	16.06 ± 2.48	
95% CI	9.91 - 11.87	15.22 - 16.90	
The cost of hospitalization			0.000
Mean±SD	24401.00 ± 2631.41	27813.00 ± 2529.37	
95% CI	23498.68 - 25303.32	26957.23 - 28668.77	

PCT - procalcitonin. MODS - Multi-organ Dysfunction Syndrome, SAP - severe acute pancreatitis

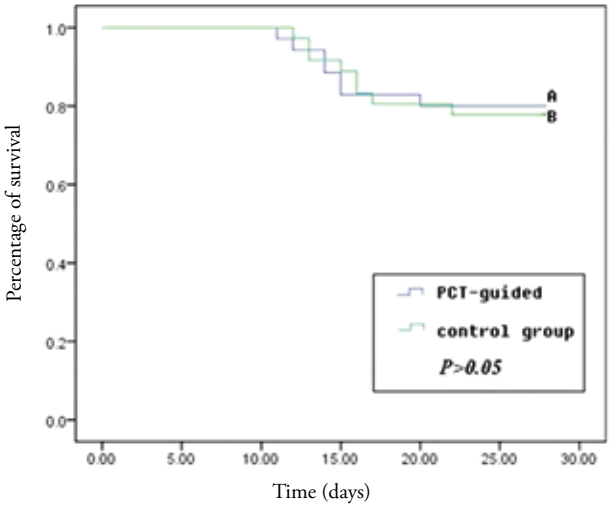

Figure 1 - Kaplan-Meier curves showing the survival rate according to the study group (A; n=35) and control group (B; n=36) in 28 days (p=0.988).

2 failing organs, the hospital mortalityrates may be as high as 50-91%.[19] Infections are observed in 40-70%[18] of patients with severe acute pancreatitis and they are also associated with a substantial increase of mortality. Timely and accurate diagnosis of pancreatic infections is needed. Currently, what we can do for the patients may be prophylactic antibiotic therapy, although it is controversial to the role of antibiotic prophylaxis in severe acute pancreatitis (ACG guidelines and British guidelines).[20,21] However, the development of drug resistance by bacterial species is a compelling issue to reconsider indications and administration of antibiotic treatment. Adequate indications and duration of therapy are particularly important for highly potent antibiotic treatment in severe acute pancreatitis. Thus, valid inflammatory biomarkers for diagnosis of pancreatic infections and sepsis are essentially needed.

Several recent studies showed that procalcitonin could be a better one among a large series of inflammatory variables that offers this possibility.[22-28] Müller et al[26] thought that initial procalcitonin level accurately predicted blood culture positivity in patients with community acquired pneumonia, procalcitonin measurement had the potential to reduce the number of drawn blood cultures in the emergency department and to implement a more targeted allocation of limited health-care resources. Nobre et al[22] found that a protocol based on serial procalcitonin measurement allowed reducing antibiotic treatment duration and exposure in patients with severe sepsis and septic shock without apparent harm. Rau et al[18] found that monitoring of procalcitonin allowed early and reliable assessment of clinically relevant pancreatic infections and overall prognosis in SAP. Nevertheless, Schuetz et al[15] reported that patients with lower respiratory tract infections, a strategy of procalcitonin guidance compared with standard guidelines resulted in similar rates of adverse outcomes, as well as lower rates of antibiotic exposure and antibiotic-associated adverse effects. Therefore, the usefulness of procalcitonin in patients with severe acute pancreatitis remains controversial.

In the present study, our results showed that the length of antibiotic treatment in the procalcitonin-guided group was significantly shorter than that in

the control group without any negative effects on treatment. Because procalcitonin rapidly decreased to reference values in successfully treated patients, whereas the patients in the absence of infection revealed procalcitonin values less than 0.5ng/ml throughout the clinical course, and the length of antibiotic treatment in the procalcitonin-guided group was shorter than that in the control group. Otherwise, the duration of intensive care treatment and hospitalization in the study group was shorter than that in the control group. Because the procalcitonin help us to detect the absence of infection, the duration of intensive care treatment and hospitalization in the study group was shorter. In the procalcitonin-guided group the cost of hospitalization was significantly lower than that in the control group. Monitoring of procalcitonin is helpful for guiding antibiotic treatment in patients with severe acute pancreatitis. This may help develop an optimized antibiotic regimen with beneficial effects on microbial resistance and costs in hospital.

There are several limitations to this study. First, the sample size is small in our study. Another limitation is the lack of procalcitonin exact value because of semi-quantitative parameter. Further study should include a larger number of samples, and procalcitonin is measured by a quantitative immunoassay, so that the results should be made more available.

In conclusion, procalcitonin is a helpful and safe parameter for guiding duration of antibiotic treatment in patients with severe acute pancreatitis. It may be beneficial on effects of microbial resistance and costs in hospital.

Acknowledgment. *We would like to thank Drs. Xiao Tang and Hangyong He from Beijing Institute of Respiratory Medicine, Beijing Chao-Yang Hospital, Capital Medical University, Beijing, China for their help with the work.*

References

1. Dambrauskas Z, Gulbinas A, Pundzius J, Barauskas G. Meta-analysis of prophylactic parenteral antibiotic use in acute necrotizing pancreatitis. ***Medicina (Kaunas)*** 2007; 43: 291-300.
2. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S,et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. ***Crit Care Med*** 2006; 34: 1589-1596.
3. Dellinger RP, Levy MM, Carlet JM, Bion J,Parker MM, Jaeschke R, et al. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. ***Crit Care Med*** 2008; 36: 296-327.
4. Nathens AB, Curtis JR, Beale RJ, Cook DJ,Moreno RP, Romand JA, et al. Management of the critically ill patients with severe acute pancreatitis. ***Crit Care Med*** 2004; 32: 2524-2536.
5. Marshall JC, Vincent JL, Fink MP, Cook DJ Rubenfeld G Foster D, et al. Measures, markers, and mediators toward a staging system for clinical sepsis: A report of the fifth Toronto Sepsis Round table, Toronto, Ontario, Canada, October 25-26, 2000. ***Crit Care Med*** 2003; 31: 1560-1567.
6. Christ-Crain M, Müller B. Procalcitonin in bacterial infections–hype, hope, more or less? ***Swiss Medical Weekly*** 2005; 135: 451-460.
7. Assicot M, Gendrel D, Carsin H, Raymond J, Guilbaud J, Bohuon C. High serum procalcitonin concentrations in patients with sepsis and infection. ***Lancet*** 1993; 341: 515-518.
8. Simon L, Gauvin F, Amre DK, Saint-Louis P, Lacroix J. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. ***Clin Infect Dis*** 2004; 39: 206-217.
9. Tasabehji WR, Al-Quobaili FA, Al-Daher NA. Usefulness of procalcitonin and some inflammatory parameters in septic patients. ***Saudi Med J*** 2008; 29: 520-525.
10. Nobre V, Harbarth S, Graf JD, Rohner P, Pugin J. Use of procalcitonin to shorten antibiotic treatment duration in septic patients. A randomized trial. ***Am J Respir Crit Care Med*** 2008; 177: 498-505.
11. Riche FC, Cholley BP, Laisne MJ, Vicaut E, Panis YH, Lajeunie EJ, et al. Inflammatory cytokines, C reactive protein, and procalcitonin as early predictors of necrosis infection in acute necrotizing pancreatitis. ***Surgery*** 2003; 133: 257-262.
12. Olah A, Belagyi T, Issekutz A, Makay R, Zaborszky A. Value of procalcitonin quick test in the differentiation between sterile and infected forms of acute pancreatitis. ***Hepatogastroenterology*** 2005; 52: 243-245.
13. Bradley EL 3rd. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, Ga, September 11 through 13, 1992. ***Arch Surg*** 1993; 128: 586-590.
14. Schuetz P, Christ-Crain M, Albrich W, Zimmerli W, Mueller B. Guidance of antibiotic therapy with procalcitonin in lower respiratory tract infections:Insights into the ProHOSP study. ***Virulence*** 2010; 1: 88-92.
15. Schuetz P, Christ-Crain M, Wolbers M, Schild U, Thomann R, Falconnier C, et al. Effect of Procalcitonin-based Guidelines Compared to Standard Guidelines on Antibiotic Use in Lower Respiratory Tract Infections: The ProHOSP Randomized Controlled Trial. ***JAMA*** 2009; 302: 1059-1066.
16. Ho KM,Lee KY,Williams T, Finn J, Knuiman M, Webb SAR. Physiology and Chronic Health Evaluation (APACHE) II score with organ failure scores to predict hospital mortality. ***Anaesthesia*** 2007; 62: 466-473.
17. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. ***Critical Care Medicine*** 1985; 13: 818-829.
18. Rau BM, Kemppainen EA, Gumbs AA, Büchler MW, Wegscheider K, Bassi C, et al. Early assessment of pancreatic infections and overall prognosis in severe acute pancreatitis by procalcitonin (PCT): a prospective international multicenter study. ***Ann Surg*** 2007; 245: 745-754.

19. Halonen KI, Pettilä V, Leppäniemi AK, Kemppainen EA, Puolakkainen PA, Haapiainen RK. Multiple organ dysfunction associated with severe acute pancreatitis. ***Crit Care Med*** 2002; 30: 1274-1279.
20. UK Working Party on Acute Pancreatitis. UK guidelines for the management of acute pancreatitis. ***Gut*** 2005; 54 (Suppl III): iii1-siii9.
21. American Gastroenterological Association (AGA) Institute on "Management of Acute Pancreatits" Clinical Practice and Economics Committee; AGA Institute Governing Board. AGA Institute medical position statement on acute pancreatitis. ***Gastroenterology*** 2007; 132: 2019-2021.
22. Nobre V, Harbarth S, Graf JD, Rohner P, Pugin J. Use of Procalcitonin to Shorten Antibiotic Treatment Duration in Septic Patients:A Randomized Trial. ***Am J Respir Crit Care Med*** 2008; 177: 498-505.
23. Hochreiter M, Köhler T, Schweiger AM, Keck FS, Bein B, von Spiegel T, et al. Procalcitonin to guide duration of antibiotic therapy in intensive care patients: a randomized prospective controlled trial. ***Critical Care*** 2009; 13: R83.
24. Daniels JM, Schoorl M, Snijders D, Knol DL, Lutter R, Jansen HM, et al. Procalcitonin vs C-reactive protein as predictive markers of response to antibiotic therapy in acute exacerbations of COPD. ***Chest*** 2010; 138: 1108-1115.
25. BalcI C, Sungurtekin H, Gürses E, Sungurtekin U, Kaptanoglu B. Usefulness of procalcitonin for diagnosis of sepsis in the intensive care unit. ***Critical Care*** 2003; 7: 85-90.
26. Müller F, Christ-Crain M, Bregenzer T, Krause M, Zimmerli W, Mueller B, et al. Procalcitonin Levels Predict Bacteremia in Patients With Community-Acquired Pneumonia A Prospective Cohort Trial. ***Chest*** 2010; 138: 121-129.
27. Yamis S, Gedik A, Sahin H, Batun S, Nergiz Y, Bircan K. Is procalcitonin valuable in the differential diagnosis of testicular torsion and epididymo-orchitis. ***Saudi Med J*** 2010; 31: 170-174.
28. Lacoma A, Prat C, Andreo F, Lores L, Ruiz-Manzano J, Ausina V, et al. Value of procalcitonin,C-reactive protein, and neopterin in exacerbations of chronic obstructive pulmonary disease. ***Int J Chron Obstruct Pulmon Dis*** 2011; 6: 157-169.

Related Articles

Kaya S, Yilmaz G, Arslan M, Oztuna F, Ozlu T, Koksal I. Predictive factors for fatality in pandemic influenza A (H1N1) virus infected patients. ***Saudi Med J*** 2012; 33: 146-151.

Yamis S, Gedik A, Sahin H, Batun S, Nergiz Y, Bircan K. Is procalcitonin valuable in the differential diagnosis of testicular torsion and epididymo-orchitis. ***Saudi Med J*** 2010; 31: 170-174.

Senturk T, Sarandol E, Gullulu S, Erdinc S, Ozdabakoglu O, Ozdemir B, Baran I, et al. Serum arylesterase activity is negatively correlated with inflammatory markers in patients with acute coronary syndromes. ***Saudi Med J*** 2009; 30: 334-339.