Original Research Article

New Indian Journal of Surgery
Volume 9 Number 5, September - October 2018
DOI: https://dx.doi.org/10.21088/nijs.0976.4747.9518.17

Correlation of Soluble CD73 Levels with Serum CRP and Creatinine Levels with Assessment of Mortality and Morbidity in Patients of Acute Pancreatitis

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How to cite this article:

Faraz Ahmed, Anshuman Singh, Abhinav Arun Sonkar et al. Correlation of Soluble CD73 Levels with Serum CRP and Creatinine Levels with Assessment of Mortality and Morbidity in Patients of Acute Pancreatitis. New Indian J Surg. 2018;9(5):635-38.

Abstract

Background: Early assessment of disease severity and prediction of the course has been an important part of the initial resuscitation and management protocol in acute pancreatitis. Various markers for severity assessment ranging from multi parametric scores like Ranson, APACHE II, modified Glasgowto single laboratory markers like serum creatinine, IL -1, IL -6 are complex or lack sensitivity. The present study deals with the role of soluble CD73 (sCD73) and its correlation with serum CRP and creatinine levels in patients of acute pancreatitis. *Methodology:* SerumCD73, qCRP and creatinine was measured in patients of acute pancreatitis who presented to the surgical emergency within 120 hours of the onset of pain.The serum levels of CD73, qCRP and serum creatinine were correlated with the clinical severity of acute pancreatitis, duration of hospital say. Serum levels of CRP, creatinine and sCD73 levels were independently assessed in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) for defining cut-off levels for prediction of diseases outcome. *Results:* Serum levels of sCD73 were significantly different in mild, moderate and severe acute pancreatitis (17.75±7.38 vs 25.69±7.92 vs 35.50±7.88 $p \leq 0.0001$). Similarly the sCD73 levels had significantly high correlation with the duration of hospital stay ($r = 0.75$, $p \leq 0.0001$) but duration of stay was poorly correlated to either CRP or creatinine levels ($r = 0.236$ and 0.130 respectively $p =$ 0.069 and 0.322 respectively). Unfortunately, none of the markers had high sensitivity or specificity for predicting mortality. *Conclusion:* Soluble CD73 levels at the time of admission can be a reliable prognostic marker to assess the severity, hospital course and final outcome of acute pancreatitis however,the findings in this study demand a larger multicentre study so as to validate the results with greater significance.

Keywords: Acute Pancreatitis; Prognostic Marker; CD 73).

Introduction

Acute pancreatitis [AP] may have a wide spectrum of clinical implications [1,2] with its natural history ranging from a benign self-limiting disease to a severe form that can eventually lead to sepsis and death with up to 15-25% mortality [3,4,5,6]. Early assessment of disease severity and prediction of the course has been an important part of the initial resuscitation and management protocol. Patients suspected to develop severe acute pancreatitis may benefit from early admission to ICU care and aggressive resuscitation [7]. Organ failure has been described the most crucial factor in the development of the severe form of disease according to the Revised Atlanta Classification, 2012. Various markers for severity assessment had been developed ranging from multi parametric scores like Ranson, APACHE II, modified Glasgowetc to single laboratory markers like serum creatinine, IL -1, IL -6 etc [8]. Single laboratory markers, with the advantage of easy repeatability have gained attraction for monitoring disease response to therapy. Of the various single laboratory markers, serum CRP levels have gained popularity particularly because of being readily

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Received on 23.06.2018, **Accepted on** 10.07.2018

available, inexpensive and early rise and relatively stable levels during the course of the disease [9]. In a study performed by Maksimow et al., serum levels of CD73 in patients with acute pancreatitis at the time of admission were significantly higher than in healthy controls. Further, the activity of soluble CD73 (sCD73) varied inversely with the disease severity and was found to be more sensitive and specific in outcome prediction than the rest of the markers. Serum CRP and to some extent serum creatinine levels, being the most consistently used single laboratory marker for the disease severity, we planned to find the correlation between sCD73 levels with serum CRP and creatinine levels in patients of acute pancreatitis.

Materials and Methods

A prospective cross-sectional comparative study was carried out in the Department of General Surgery of King George's Medical University, Lucknow, India from November 2014 to May 2016. Sixty patients of acute pancreatitis were enrolled in the study as the target population who presented to the Surgical Emergency within 120 hours of the onset of pain. The patients of AP who presented to the surgical emergency after 120 hours of pain onset or with recurrent attack of AP or with co-existing surgical illness were excluded from the target population. (Diagnosis and classification of acute pancreatitis were made according to the Revised Atlanta Classification, 2012).

Venous blood samples of the patients diagnosed with acute pancreatitis were taken at the time of admission. Serum was separated after centrifugation and stored in cryofreeze (-20 degree Celsius). The patients were followed closely in their hospital course and categorized on the basis of presence of organ failure (defined by Modified Marshall score of ≥ 2) into mild, moderate or severe acute pancreatitis categories as per the revised Atlanta classification. Serum creatinine levels and quantitative CRP levels were measured from the hospital laboratory with the routinely used reference values. Serum levels of sCD73 were measured by BOSTER Human CD73/NT5E PicoKine™ ELISA Kit. The assay principle used a monoclonal antibody from mouse specific for CD73 which was precoated onto the wells.

The values of serum levels of CD73, qCRP and serum creatinine were matched with the clinical severity of acute pancreatitis during the subsequent hospital course as determined by the presence or absence of organ failure (Organ failure determined according to Modified Marshall scoring used in revised Atlanta classification, 2012). Length of hospital stay was considered to be a surrogate marker for patient morbidity and compared with the disease severity and the levels of all the markers into consideration. Levels of CRP, creatinine and sCD73 levels were independently assessed in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) for defining cutoff levels for prediction of mortality in patients of acute pancreatitis. The levels of these biomarkers were also correlated with the length of hospital stay in all the three subgroups.

Statistical analysis. Results were presented as Mean +/- SD and percentages. Unpaired t-test was used to compare the continuous variables between the two groups. One way analysis of variance (ANOVA) with Bonferroni post-hoc pairwise comparison tests was used to compare more than two means. Receiving operating curve was drawn to find the cutoff value of CD73, CRP and creatinine for prediction of mortality in the patients of acute pancreatitis. The Pearson correlation coefficient was calculated to find the correlation between two continuous variables (levels of biomarkers and length of hospital stay in our case). All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

Results

Serum levels of CD73 at the time of admission were higher in the patients of acute pancreatitis than in healthy reference subjects. Total mortality in the study group was 16.7%. All the cases who expired were in the SAP category contributing to 43.47% mortality in the patients with SAP.

Table 1: Correlation coefficient among the study parameters

		Correlations			
		CD73	**S. Creatinine**	**S. CRP**	**Hospital stay (in days)**
sCD73(0)	Pearson Correlation	1			
	p-value				
S.Creatinine	Pearson Correlation	0.130	1		
	Sig. (2-tailed)	0.322			
S.CRP(0)	Pearson Correlation	0.236	0.396**	1	
	Sig. (2-tailed)	0.069	0.002		
HOSPITAL STAY(in days)	Pearson Correlation	0.754**	0.292*	0.222	1
	Sig. (2-tailed)	0.0001	0.024	0.088	

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).

Duration of hospital stay and sCD73 levels were significantly different in all the three subgroups of severity. However, there was no significant difference in the serum CRP levels at admission between moderate and severe acute pancreatitis. None of the markers had high sensitivity or specificity for predicting mortality (Table 1).

The serum levels of sCD73 had significantly high correlation (r = 0.75, p = 0.0001) with the length of hospital stay but was poorly correlated to either CRP or creatinine levels (r = 0.236 and 0.130 respectively p = 0.069 and 0.322 respectively). Levels of CRP and creatinine had poor correlation with the length of hospital stay.

Discussion

Serum levels of sCD73 at the time of admission were significantly correlated (r = 0.754, p = 0.0001) to the length of hospital stay while CRP and creatinine levels had no significant correlation. There was no significant correlation between sCD73 levels with that of CRP or creatinine. sCD73 levels at the time of admission were also found to be significantly different in all the three severity subgroups of AP. Total mortality in the study group was 16.7% (10 patients expired out of 60). All the cases who expired were in the SAP category contributing to 43.47% mortality in the patients with SAP (10 out of 23 patients with severe AP). Serum CD73 (36.28±9.17 vs 24.75±10.11; p=0.001), creatinine (2.46±1.29 vs 0.77±0.64; p=0.0001) and CRP levels (95.79±21.55 vs 68.09±31.49; p=0.003) were all significantly greater in the patients who expired during the hospital course than the patients who were alive and discharged. However, all the three markers had poor sensitivity and specificity at the predefined cutoff values for predicting mortality at the time of admission (Table 1). The mean duration of hospital stay was longer in case of severe AP as compared to mild AP (17.43±3.28 vs 7.10±1.64; p<0.01). However, no significant difference was found between duration of hospital stay in severe and moderate acute pancreatitis.

The increase in the levels of sCD73 in direct proportion to the disease severity can be explained by the fact that CD73 being a molecule expressed on the surface of vascular endothelial cells and circulating lymphocytes is shed into circulating blood during the chemo-attraction that occurs during acute inflammation. It expresses ecto-5′-nucleotidase activity and converts the proinflammatory ATP to anti-inflammatory molecule adenosine and therefore is an important molecule in the anti-inflammatory arm of the pathogenesis of acute pancreatitis [10-14]. A study on 161 patients byMaksimow et al. 2015 gave an insight into probable role of sCD73 in early prognosis prediction and possible therapeutic benefits when upregulation of sCD73 was targeted.

The high positive correlation between sCD73 levels and the length of hospital stay which may be taken as a surrogate marker for patient morbidity may prove to be an early predictor for initiation of early aggressive resuscitation in patients of acute pancreatitis so as to prevent the development of severe form of the disease.

Conclusion

Serum CD73 levels at the time of admission had no significant correlation with CRP or creatinine levels but had significant positive correlation with the length of hospital stay which was considered a surrogate marker for patient morbidity. The findings in this study demand a larger multicentre study so as to validate the findings with greater significance.

References

1. Whitcomb DC. Clinical practice. Acute pancreatitis. N Engl J Med. 2006;354:2142–2150.
2. Nagar AB, Gorelick FS.Acute pancreatitis. CurrOpin Gastroenterol. 2004;20:439–443.
3. Beger HG, Rau BM. Severe acute pancreatitis: Clinical course and management. World J Gastroenterol. 2007; 13:5043–5051
4. Kong L, Santiago N, Han TQ. Clinical characteristics and prog- nostic factors of severe acute pancreatitis. World J Gastroenterol. 2004;10:3336–38.
5. Halonen KI, Leppaniemi AK, Puolakkainen PA. Severe acute pan- creatitis: Prognostic factors in 270 consecutive patients. Pancreas. 2000;21:266–271.
6. Banks PA, Freeman ML. Practice Parameters Committee of the American College of Gastroenterology, Practice guidelines in acute pancreatitis. Am J Gastroenterol. 2006; 101:2379.
7. Warshaw AL. Pancreatic necrosis: to debride or not to debride- that is the question. Ann Surg. 2000;232:627.
8. Bradley EL. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, Georgia, September 11 through 13, 1992. Arch Surg. 1993;128:586–90.
9. Fagenholz PJ, Castillo CF, Harris NS. Increasing United States hospital admissions for acute pancreatitis, 1988-2003. Ann Epidemiol. 2007;17:491.
10. Junger WG. Immune cell regulation by autocrine purinergic signalling. Nat Rev Immunol. 2011;11:201–212.
11. Linden J, Cekic C . Regulation of lymphocyte function by adenosine. ArteriosclerThrombVasc Biol. 2012;32: 2097–2103.
12. Haskó G, Csóka B, NémethZH. A(2B) adenosine receptors in immunity and in ammation. Trends Immunol. 2009;30:263–270.
13. Deaglio S, Dwyer KM, Gao W. Adenosine generation cata- lyzed by CD39 and CD73 expressed on regulatory

T cells mediates immune suppression. J Exp Med. 2007; 204:1257–65.

14. Eltzschig HK, Sitkovsky MV, Robson SC. Purinergic signaling during in ammation. N Engl J Med. 2012; 367:2322–33.