Elevated β-defensin levels in patients with an infection and their association with IL-6 production

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Abstract

The inflammatory process is characterized by the production of a variety of molecules such us IL-6, C-reactive protein (CRP) and the antimicrobial peptides defensins. Interleukin-6 (IL-6) is a central mediator of the acute-phase response and a primary determinant of hepatic production of CRP. Defensins are endogenous antibiotics with microbicidal activity against Gram-negative and Gram-positive bacteria, fungi, enveloped viruses and protozoa. They are secreted by epithelial tissue in response to inflammation. In this study, we sought to evaluate the levels of IL-6, β-defensin 1 (BD-1), β-defensin 2 (BD-2) and CRP levels in serum of patients (336 patients for IL-6, BD-1, BD-2 and 302 patients for CRP), with inflammation of infectious, non-infectious etiology (including cancer and arthritis) and 30 healthy individuals. Our aim was to examine the potential of β-defensins to serve as novel markers of inflammation. Statistical analysis demonstrated that there is a very strong positive correlation between the levels of IL-6 and the levels of BD-2 ($p < 0,001$ and $r = 0,565$). In addition, there is a significant correlation between the levels of IL-6 and the levels of BD-1 ($p < 0,001$ and $r = 0,2568$), the levels of BD-1 and the levels of BD-2 ($p < 0,001$ and $r = 0,4415$) and the levels of BD-1 and the levels of CRP ($p = 0,0041$ and $r = 0,1646$).

Background – Aim of the Study

The innate immunity system includes recognition, phagocytosis and destruction of pathogens, induction of inflammation and antimicrobial agents. Human defensins, which are small cationic peptides produced by neutrophils and epithelial cells, are antimicrobial peptides that function in the host innate defense. In humans, β defensins are constitutively expressed in various mucosa and epithelial cells where they can be up-regulated in response to infectious and inflammatory stimuli. HBD-2 was first isolated from psoriatic scales and it is expressed in the skin as well as in urinary, gastrointestinal and respiratory epithelia. Researches support that gene regulation of defensins occurs via signal transduction pathways common to other innate immune responses, utilizing transcription factors, such as nuclear factor NF-kB and NF-IL6. It has been suggested that NF-kappa B is an important mediator for activation of the IL-6 gene. Interleukin-6 (IL-6) is a multifunctional a pro-inflammatory cytokine that plays a central role in host defense and acute phase response.

The aim of our study was to examine if circulating levels of β-defensin 1 (BD-1) and β-defensin 2 (BD-2) are increased during inflammation and to examine their correlation to levels of IL-6 and CRP in serum of patients with inflammation of infectious, non-infectious origin.

Materials and Methods

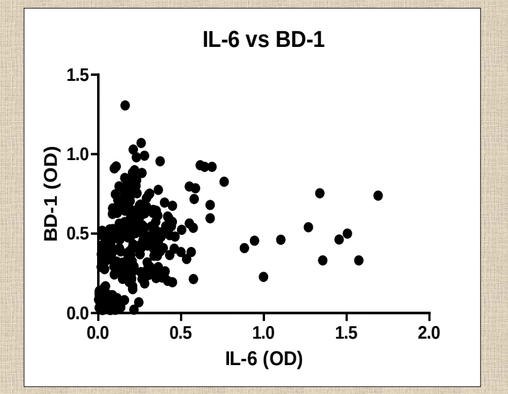
Sera: Sera obtained from 336 patients for IL-6, BD-1, BD-2 and 302 patients for CRP, with inflammation of infectious, non-infectious etiology (including cancer and arthritis) and 30 healthy individuals.

IL-6, BD-1, BD-2 quantification: was performed using Elisa kits for the quantitative measurement of natural BD-1 and IL -6 in a sandwich Elisa format (Peprotech).

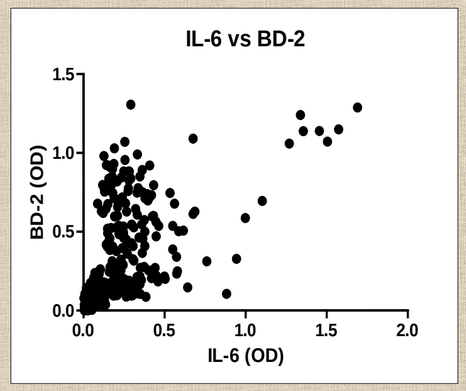
Results

Pearson's analysis showed that there is a significant association between the levels of IL-6 and the levels of BD-2. Furthermore, there is a correlation between the levels of IL-6 and BD-1, the levels of BD-1 and BD-2, the levels of BD-1 and CRP.

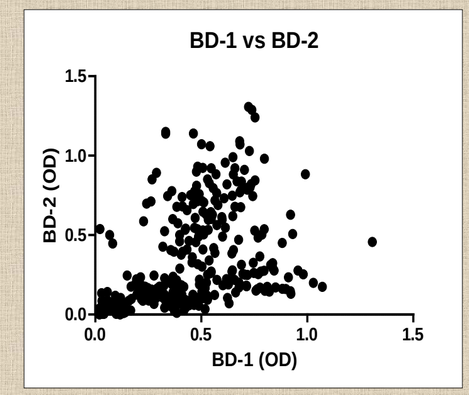
➢**IL-6 is correlated with the levels of BD-1. Pearson r=0.2568, p<0.0001.**



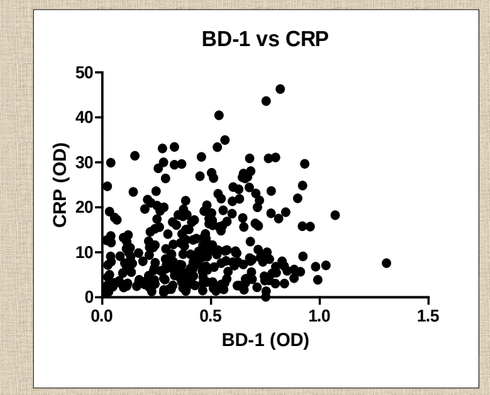
➢**IL-6 is correlated with the levels of BD-2. Pearson r=0.565, p<0.0001.**



➢**BD-1 is correlated with the levels of BD-2. Pearson r=0.4415, p<0.0001.**



➢**BD-1 is correlated with the levels of CRP. Pearson r=0.,1646, p=0.0041.**



Conclusions

Our results demonstrate that there is a remarkable correlation between the levels of IL-6 and the levels of BD-2 and therefore BD-2 can be used as markers of inflammation.