Calprotectin, a powerful biomarker for the diagnosis of bacterial infections

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INTRODUCTION

The rapidly growing problem with antibiotic resistance has resulted in demands for more specific and restricted use of antibiotics. Biomarkers which in early stage of an infection can distinguish between bacterial and viral infection could possibly reduce the use of antibiotics. Calprotectin is one of the most abundant proteins in the cytosol of neutrophil granulocytes and is released upon activation of neutrophils.

The aim of this study was to investigate the performance of calprotectin as a marker for bacterial infection and its possibility to distinguish between bacterial and viral infections.

METHODS

The study group consisted of 432 subjects including 144 healthy noninfected controls and 288 patients with confirmed etiology of their infections, 185 patients with bacterial infection, 54 with viral infection, 26 with mycoplasma infection, and 23 with a bacterial infection as a secondary infection to influenza.

Calprotectin was measured in serum samples with particle enhanced turbidimetric assay (Gentian AS, Norway). Heparin Binding Protein (HBP) and Procalcitonin were analyzed by sandwich immunoassays (Hycult Biotech, The Netherlands and Thermo Fisher Scientific, Sweden).

RESULTS

Performance of Calprotectin in diagnosis of bacterial infections as well as in distinguishing between bacterial and viral infections was compared to performance of Procalcitonin and HBP. Compared to healthy subjects, all three biomarkers were significantly elevated in all diagnosis (Table 1). Calprotectin level was significantly higher in all diagnosis caused by bacterial infections compared to levels in viral infections (zzz, P < 0.001). Concentration of PCT in bacterial pneumonia was significantly higher zzz, (P < 0.001) than the concentration in the viral group, whereas the levels in Streptococcal tonsillitis and in Mycoplasma pneumoniae were not significantly different compared to levels in patients with viral infections. HBP concentration was not significantly different in viral and bacterial infections (Fig 1, Table 1). Calprotectin was the only biomarker with ability to distinguish between infections caused by Streptococcus or Mycoplasma and viral infections (Fig 2., Table 2)
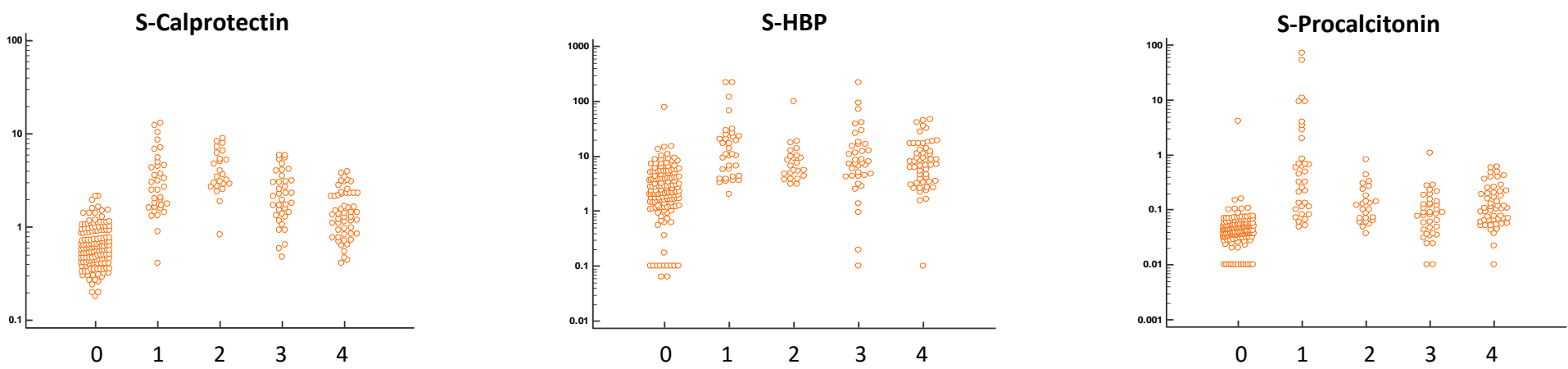
0= Healthy, 1= Bacterial pneumonia, 2= Mycoplasma pneumonia, 3= Streptococcal tonsillitis, 4= Viral infections

Fig 1. Distribution of Calprotectin, HBP and Procalcitonin concentrations in patients with respiratory tract infections, separated by verified clinical diagnosis.

Table 1. Concentrations of studied biomarkers and possibility to differentiate between healthy population and patients with infections (*) as well as between bacterial and viral infections (z)

Group	Calprotectin [mg/L] Median (IQ range)	HBP [µg/L] Median (IQ range)	PCT [µg/L] Median (IQ range)
Healthy	0.61 (0.43-0.92) n=144	2.24 (1.40-4.28) n=145	0.042 (0.034-0.057) n=144
Viral infection	1.38 (0.84-2.30) n=53***	8.05 (3.50-14.5) n=53***	0.105 (0.064-0.210) n=52***
Bacterial pneumonia	2.58 (1.64-4.6) n=34***, zzz	11.0 (4.38-23.1) n=34***, z	0.383 (0.113-1.96) n=34***, zzz
Mycoplasma pneumonia	3.52 (2.84-5.81) n=24***, zzz	6.59 (4.47-10.1) n=23***	0.112 (0.067-0.207) n=24***
Streptococcal tonsillitis	2.14 (1.37-3.22) n=37***, zzz	7.59 (4.37-16.6) n=37***	0.085 (0.041-0.131) n=37***

***=p<0.001, ** p<0.01, * p<0.05, zzz p<0.001, zz p<0.01, z p<0.05;   *= Infected vs healthy; z= Bacteria vs virus

Table 2. The AUROC results for the three biomarkers for distinction between different diagnosis of bacterial and viral infections.

Diagnosis	AUROC (95% CI)		
	Calprotectin	HBP	PCT
Bacterial pneumonia	0.774 (0.669-0.858)	0.614 (0.501-0.719)	0.728 (0.619-0.820)
Mycoplasma pneumonia	0.903 (0.811-0.960)	0.519 (0.399-0.637)	0.529 (0.409-0.647)
Streptococcal tonsillitis	0.684 (0.576-0.779)	0.531 (0.422-0.639)	0.604 (0.494-0.707)

CONCLUSION

Calprotectin is a promising biomarker for diagnosis of bacterial infections. Our results indicate that Calprotectin is superior to HBP in differentiation between viral and bacterial infections. Calprotectin is also superior to Procalcitonin in differentiation between viral infections, and Streptococcal tonsillitis or Mycoplasma infections.

Rapid determination of serum/plasma calprotectin should be an improvement in the management of infections and allow more selective use of antibiotics.
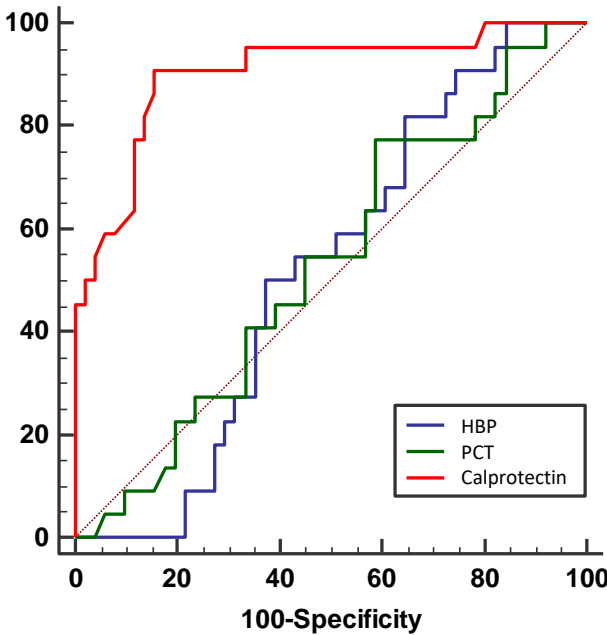

Fig 2. ROC curves for Mycoplasma pneumoniae vs viral infections