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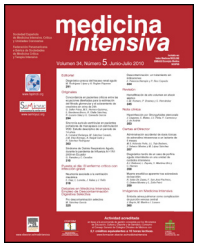

ORIGINAL

Oxidative stress in immunocompetent patients with severe community-acquired pneumonia. A pilot study☆

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KEYWORDS
Oxidative stress;
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Abstract
Objective: A comparison was made of the oxidative stress (OS) levels of patients with either viral or bacterial severe community-acquired pneumonia (sCAP) and of patients without infection (healthy volunteers (HV) and patients with acute myocardial infarction (AMI)).
Design: A prospective observational study was made.
Patients: Critically ill patients with sCAP.
Variables: The TBARS level was measured as an index of oxidative injury. SOD, CAT and redox glutathione system (GSH, GSSG, GR, GPx) activities were measured as reflecting antioxidant capacity. Severity of illness was assessed by the APACHE II, SOFA and SIRS scores.
Results: Thirty-seven subjects were included: 15 patients with CAP (12 of bacterial origin [BCAP] and 3 due to 2009 A/H1N1 virus [VCAP]), 10 HV and 12 AMI patients. Intensive care CAP mortality was 26.7% ($n = 4$). Plasmatic TBARS levels were higher in CAP patients than in HV, but similar to those recorded in AMI patients. In contrast, VCAP was associated with lower TBARS levels, and some components of the glutathione redox system were higher in BCAP patients and HV. The OS levels did not differ between survivors and non-survivors.
Conclusion: Our results suggest the occurrence of higher OS in sCAP patients compared with HV. In contrast, lower TBARS levels were observed in VCAP patients, suggesting an increase of antioxidant activity related to the redox glutathione system. However, further research involving a larger cohort is needed in order to confirm these findings.

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PALABRAS CLAVE
Estrés oxidativo;
Gripe A 2009/H1N1;
Neumonía bacteriana;
Neumonía comunitaria

Estrés oxidativo en pacientes inmunocompetentes con neumonía comunitaria grave. Un estudio piloto

Resumen
Objetivos: Comparar el estrés oxidativo (EO) en pacientes con neumonía comunitaria grave (NCG) según su etiología y respecto de voluntarios sanos (VS) y pacientes con infarto agudo de miocardio (IAM).
Diseño: Estudio prospectivo, observacional.
Pacientes: Pacientes con NCG ingresados en unidades de cuidados intensivos.
Variables: Los niveles de lipoperoxidación (TBARS) fueron considerados como índice de oxidación, mientras que SOD, CAT y la actividad del sistema redox- glutation (GSH, GSSG, GR, GPx) fueron considerados capacidad antioxidante. La gravedad de los pacientes fue valorada mediante las escalas APACHE II, SOFA y SIRS.
Resultados: Treinta y siete sujetos fueron incluidos, 15 pacientes con NCG (12 con etiología bacteriana [NB] y 3 viral 2009 A/H1N1 [NV]), 10 VS y 12 con IAM. La mortalidad global fue del 26,7% (n = 4). Los TBARS plasmáticos fueron superiores en NCG respecto de VS, pero similares al IAM. En contraste, la NV se asoció con menores niveles de TBARS e incremento de componentes del sistema redox-glutation respecto de NB y voluntarios sanos. No se observó asociación entre mortalidad y EO.
Conclusión: Nuestros resultados evidencian la presencia de EO en pacientes con NCG respecto de los controles. En contraste, la evidencia de un menor nivel de TBARS en la NV respecto de los VS sugiere un incremento de la actividad antioxidante relacionada con el sistema redox-glutation. Sin embargo, son necesarias nuevas investigaciones para confirmar estos hallazgos.

Introduction

Community-acquired pneumonia (CAP) continues, even nowadays, to be one of the most common causes of admission in Intensive Care Units (ICU) with a significant morbidity. It is, therefore, not surprising that much research has been done in improving outcomes associated with this disease.

Reactive oxygen species (ROS) are constantly produced under physiological conditions and balanced between pro- and antioxidant activity.[1] Nevertheless, in CAP, such activity might drastically be enhanced in response to primary host defence mechanism through phagocytes activation. Immune cell functions, activation of inflammatory cascades and expression of adhesion molecules are specially linked to ROS generation.[2] Due to the respiratory burst generated by the massive flux of phagocytes, an important generation and release of ROS is produced.

The ''respiratory burst'' in a phagocyte is triggered when a bacteria is phagocytised. Therefore an important generation and release of ROS might perpetuate or increase the inflammatory response. Lipids, proteins and DNA damage oxidation leads to a tissue injury.[3–5] In this context, the organism is overwhelmed by an imbalance between oxidant generation and antioxidant defenses; this situation is defined as oxidative stress (OS)[6] and contributes to cellular derangement, cell injury and death.

Lipid peroxidation mediated by free radicals is considered to be the major mechanism of cell membrane destruction and cell damage.[7] Some of the antioxidant systems that remove or inactivate ROS are superoxide dismutase (SOD; E.C. 1.15.1.1), catalase (CAT, E.C.1.11.1.6), glutathione redox system: reduced glutathione (GSH), glutathione disulfide (GSSG), glutathione reductase (GR), glutathione peroxidase (GPx, E.C. 1.11.1.9). Several studies[8–10] have demonstrated that OS occurs in different settings affecting critically ill patients, such as in ARDS or organ dysfunction.

Only a few studies have focussed on analyzing the role of OS in the pathophysiology of bacterial pneumonia in humans.[11–14] Moreover, most of them are based on experimental models. In addition, little is known regarding the pathogenesis of 2009 H1N1 viral pulmonary infection[15,16] and ROS production.[17,18] In fact, viral and bacterial pulmonary infection may play a different role in the pro- and antioxidant balance in host cells.[19,20] Thus, our aim was to compare the oxidative stress in severely ill patients with community-acquired pneumonia according to aetiology and with respect to a group of healthy volunteers and patients who suffered an acute myocardial infarction.

Materials and methods

Population samples

This study has been conducted according to the principles expressed in the Declaration of Helsinki and after obtaining local Ethics Committee approval. Signed informed consent was obtained from all patients or relatives and healthy volunteers. Oxidative stress data were not used in patients' management and did not interfere with patient care.

Consecutive patients at ICU admission were included in a prospective and observational study with diagnosis of bacterial community-acquired pneumonia (BCAP) according to ATS/IDSA Guidelines[21] or confirmed 2009 pandemic Influenza A/H1N1 pneumonia (VCAP) as reported elsewhere.[22] In brief,