CRITICAL CARE

LETTER

Matrix metalloproteinases and their inhibitors as biomarkers of severity in sepsis

Leonardo Lorente*[1], María M Martín[2], Jordi Solé-Violán[3], José Blanquer[4] and José Antonio Páramo[5]

See related commentary by Hoffmann *et al.*, http://ccforum.com/content/13/6/1006

We read with interest the commentary by Hoffmann and colleagues [1] on our manuscript recently published in *Critical Care* showing that matrix metalloproteinase (MMP)-9, MMP-10 and tissue inhibitor of matrix metalloproteinases (TIMP)-1 could be new biomarkers of severity and mortality in sepsis [2]. As they stated, the lack of serial measurements of MMPs and TIMPs over clinical evolution was as a limitation of our study. Despite this limitation, our results suggest that MMPs and TIMPs may be of pathophysiological significance in sepsis.

Some clinical studies have found higher circulating levels of MMP-9 [2-4] and TIMP-1 [2,3] in septic patients than in healthy controls, and higher levels of TIMP-1 [2,3] or MMP-9 [4] in nonsurviving than in surviving septic patients. Our study also reports, for the first time, that MMP-10 circulating levels are also elevated in septic patients [2]. According to the results of some *in vitro* studies, MMP-10 could play a role in infection, since increased MMP-10 gene transcription was observed after infective stimulation of human and mice cells.

On the other hand, we think the correlation between MMP-9, TIMP-1 and markers of coagulopathy, and the lower MMP-9/TIMP-1 ratio in nonsurviving than in surviving septic patients found in our study, may be associated with a higher prothrombotic/antifibrinolytic state, responsible for the capillary thrombosis, multiple organ dysfunction, and death.

Finally, from a therapeutic perspective, the development of modulators of MMP/TIMP activity could be used as a new class of drugs for the treatment of severe sepsis [5].

Abbreviations

MMP = matrix metalloproteinase; TIMP = tissue inhibitor of matrix metalloproteinases.

*Correspondence: lorentemartin@msn.com
[1]Intensive Care Unit, Hospital Universitario de Canarias, Ofra s/n. La Cuesta, La Laguna 38320, Santa Cruz de Tenerife, Spain
Full list of author information is available at the end of the article

Acknowledgements

The present study was supported, in part, by a grant from the Canary Islands Foundation for Health and Research (FUNCIS number PI 42/07) (Tenerife, Spain), by a grant from the Working Group on Infectious Diseases of the Spanish Society of Intensive Medicine, Critical Care, and Coronary Units (GTEI-SEMICYUC-2009), by funding from the Rafael Clavijo Foundation for Biomedical Research (Tenerife, Spain) and by the UTE project CIMA (University of Navarra, Spain).

Author details

[1]Intensive Care Unit, Hospital Universitario de Canarias, Ofra s/n. La Cuesta, La Laguna 38320, Santa Cruz de Tenerife, Spain
[2]Intensive Care Unit. Hospital Universitario Nuestra Señora de Candelaria. Crta del Rosario s/n. Santa Cruz de Tenerife - 38010. Spain
[3]Intensive Care Unit. Hospital Universitario Dr. Negrín. Barranco de la Ballena s/n. Las Palmas de Gran Canaria - 35010. Spain
[4]Intensive Care Unit. Hospital Clínico Universitario de Valencia. Avda. Blasco Ibáñez nº17-19. Valencia - 46004. Spain
[5]Atherosclerosis Research Laboratory. CIMA-University of Navarra. Avda Pío XII nº55. Pamplona - 31008. Spain

Competing interests

The authors declare that they have no competing interests.

Published: 19 January 2010

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doi:10.1186/cc8211
Cite this article as: Lorente L, *et al.*: Matrix metalloproteinases and their inhibitors as biomarkers of severity in sepsis. *Critical Care* 2010, **14:**402.