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ORIGINAL

Venous-to-arterial carbon dioxide difference in the resuscitation of patients with severe sepsis and septic shock: A systematic review☆

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KEYWORDS
Septic shock;
Severe sepsis;
Venous-to-arterial difference of carbon dioxide;
Lactate;
Tissue perfusion

Abstract
Introduction: The way to assess tissue perfusion during the resuscitation of patients with severe sepsis and septic shock is a current subject of research and debate. Venous oxygen saturation and lactate concentration have been the most frequently used criteria, though they involve known limitations. The venous-to-arterial difference of carbon dioxide (pCO_2 delta) is a parameter than can be used to indicate tissue perfusion, and its determination therefore may be useful in these patients.
Methods: A qualitative systematic review of the literature was made, comprising studies that assessed pCO_2 delta in adult patients with severe sepsis or septic shock, and published between January 1966 and November 2016 in the Medline-PubMed, Embase-Elsevier, Cochrane Library, and LILACS databases. There was no language restriction. The PRISMA statement was followed, and methodological quality was evaluated.
Results: Twelve articles were included, all of an observational nature, and including 10 prospective studies (9 published since 2010). Five documented greater mortality among patients with high pCO_2 delta values, in 3 cases even when achieving venous oxygen saturation targets. In 4 studies, a high pCO_2 delta was related to lower venous oxygen saturation and higher lactate levels, and another 3 documented lesser percentage lactate reductions.

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Conclusion: The parameter pCO_2 delta has been more frequently assessed in the management of patients with severe sepsis during the last few years. The studies demonstrate its correlation to mortality and other clinical outcomes, defining pCO_2 delta as a useful tool in the management of these patients.

PALABRAS CLAVE
Shock séptico;
Sepsis grave;
Diferencia venoarterial de dióxido de carbono;
Lactato;
Perfusión tisular

La diferencia venoarterial de dióxido de carbono en la reanimación de pacientes con sepsis grave y shock séptico: una revisión sistemática

Resumen
Introducción: La forma de evaluar la perfusión tisular durante la reanimación de pacientes con sepsis grave y shock séptico es tema de estudio y debate en la actualidad. La saturación venosa de oxígeno y el lactato han sido los criterios más utilizados; sin embargo, presentan limitaciones reconocidas. La diferencia venoarterial de dióxido de carbono (delta de pCO_2) es una variable que puede indicar el estado de perfusión tisular, por lo que su evaluación puede ser útil en estos pacientes.
Métodos: Revisión sistemática cualitativa de la literatura que incluyó estudios que evaluaron el delta de pCO_2 en pacientes adultos con sepsis grave o shock séptico, publicados entre enero de 1966 y noviembre de 2016 en las bases de datos Medline-PubMed, Embase-Elsevier, Cochrane Library y LILACS. No tuvo restricción de idiomas. Se siguió la declaración PRISMA y se evaluó la calidad metodológica.
Resultados: Doce estudios fueron incluidos, todos observacionales, 10 prospectivos, 9 publicados a partir del 2010. Cinco documentaron una mayor mortalidad entre pacientes con delta de pCO_2 alto, en 3 incluso cuando conseguían metas de saturación venosa de oxígeno. En 4 estudios, un delta de pCO_2 alto se relacionó con una menor saturación venosa de oxígeno y niveles mayores de lactato, y otros 3 documentaron un menor porcentaje de disminución de lactato.
Conclusión: El delta de pCO_2 ha sido evaluado en el manejo de los pacientes con sepsis grave y shock séptico con mayor frecuencia en los últimos años. Los estudios demuestran su relación con la mortalidad y otros desenlaces clínicos, de tal forma que puede ser una herramienta útil en el manejo de estos pacientes.

Introduction

Sepsis is one of the main causes of admission to Intensive Care Units (ICUs). This heterogeneous and complex syndrome can result in a 20–50% mortality rate, depending on the severity of the clinical condition,[1,2] which in turn is conditioned to the presence of organ dysfunction mediated by different mechanisms of cell damage. The way in which the different individual mechanisms interact is not fully understood, though sepsis is known to involve microvascular anomalies, and a decrease in oxygen supply and/or deficient utilization of the available oxygen constitute a central element of such organ dysfunction.[3] The early identification of tissue damage is therefore crucial in the management of these patients.

The measurement of certain physiological variables of use in assessing tissue perfusion status has been proposed in the initial care of such patients. In its early versions, the Surviving Sepsis Campaign recommended the measurement of venous oxygen saturation (SvO_2), evaluated as mixed venous saturation or central venous oxygen saturation ($SvcO_2$), and lactate concentration in this respect, with the definition of a series of target values intended to secure adequate patient resuscitation.[4] This proposal was essentially based on the early intervention protocol published by Rivers et al., advocating the ''normalization'' of $SvcO_2$, central venous pressure (CVP) and mean arterial pressure, with the purpose of improving tissue perfusion.[5] Other investigators, fundamentally Jones et al., reinforced the idea that lactate can also be used in protocols of this kind.[6,7]

Although the usefulness of the protocol was evaluated in the context of randomized clinical trials, each of the mentioned variables has known limitations, and the use of a single variable does not seem to be the best way to assess tissue perfusion.[8,9] More recently, multicenter clinical trials have been unable to confirm the usefulness of the protocol developed by Rivers et al., and the measurement of $SvcO_2$ as a guide in patient resuscitation has been questioned.[10–12] As a result of the above, the latest version of the Surviving Sepsis Campaign does not recommend the use of this variable as an initial resuscitation goal or target in the management of such patients.[13]

Other parameters for the assessment of tissue perfusion are therefore needed to guide therapy. One such parameter