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ORIGINAL

Effects of antibiotic administration delay and inadequacy upon the survival of septic shock patients[☆]

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Abstract

Objective: To assess how antibiotic administration delay and inadequacy influence survival in septic shock patients.

Design: A prospective, observational cohort study was carried out between September 2005 and September 2010.

Scope: Patients admitted to the ICU of a third level hospital.

Patients: A total of 342 septic shock patients.

Interventions: None.

Variables of interest: The time to antibiotic administration (difference between septic shock presentation and first administered dose of antibiotic) and its adequacy (in vitro susceptibility testing of isolated pathogens) were determined.

Results: ICU and hospital mortality were 26.4% and 33.5%, respectively. The median delay to administration of the first antibiotic dose was 1.7 h. Deceased patients received antibiotics significantly later than survivors (1.3 ± 14.5 h vs. 5.8 ± 18.02 h; $p = 0.001$). Percentage drug inadequacy was 12%. Those patients who received inadequate antibiotics had significantly higher mortality rates (33.8% vs. 51.2%; $p = 0.03$). The coexistence of treatment delay and inadequacy was associated to lower survival rates.

Conclusions: Both antibiotic administration delay and inadequacy exert deleterious effects upon the survival of septic shock patients, independently of their characteristics or severity.

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PALABRAS CLAVE
Shock séptico;
Antibióticos;
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Retraso;
Inadecuación

Efectos del retraso y la inadecuación del tratamiento antibiótico en la supervivencia de los pacientes en shock séptico

Resumen
Objetivo: Evaluar cómo influye el retraso en la administración de la primera dosis de antibiótico y la inadecuación de la pauta seleccionada en la supervivencia de los pacientes en shock séptico.
Diseño: Estudio prospectivo de cohortes observacional realizado entre septiembre de 2005 y septiembre de 2010.
Ámbito: Pacientes hospitalizados en la UCI de un hospital de tercer nivel.
Pacientes: Trescientos cuarenta y dos pacientes con cuadro de shock séptico.
Intervenciones: Ninguna.
Variables de interés principales: Se determinó el tiempo hasta la administración del antibiótico (diferencia entre la presentación del shock séptico y la primera dosis de antibiótico) y la adecuación del mismo (susceptibilidad in vitro de los microorganismos aislados).
Resultados: La mortalidad en UCI fue del 26,4% y a nivel hospitalario del 33,5%. La mediana de retraso en la administración de la primera dosis de tratamiento antibiótico fue de 1,7 h. Los pacientes fallecidos recibieron el antibiótico significativamente más tarde ($1,3 \pm 14,5$ h frente a $5,8 \pm 18,02$; $p = 0,001$) que los supervivientes. El porcentaje de inadecuación del tratamiento antibiótico fue del 12%. Los pacientes tratados inadecuadamente presentaron cifras de mortalidad hospitalaria significativamente más altas (33,8% frente a 51,2%; $p = 0,03$) respecto a los que recibieron una pauta antibiótica adecuada. La coexistencia de retraso e inadecuación en el tratamiento antibiótico se asoció a una menor supervivencia de los pacientes.
Conclusiones: Tanto el retraso como la inadecuación del tratamiento antibiótico tienen efectos negativos sobre la supervivencia de los pacientes en shock séptico independientemente de las características de estos o de su estado de gravedad.

Introduction

Although the mortality rate associated to sepsis remains high, its prognosis has improved in recent years.[1] The development and subsequent adoption in clinical practice of the Surviving Sepsis Campaign (SSC) are largely responsible for this change. A number of initiatives have demonstrated at both multicenter level and on an isolated basis that adoption of the SSC is not only feasible but is associated to important improvements in patient survival and sociosanitary cost savings.[2–5]

The basic instrument of the mentioned Campaign is a series of ''bundles'', consisting of groups of interventions and treatments which when applied jointly and within a given (and usually short) time period are expected to exert a synergic effect and thus afford better outcomes than when such measures are applied individually. However, the level of evidence supporting each measure varies and is subject to change as further experience is gradually gained. An example of this is hemodynamic resuscitation, fundamented upon a randomized study[6] which nevertheless has not been corroborated by a recently published study.[7] For obvious reasons, the administration of antibiotics is not regulated by the same criteria, and the indication of such drugs is exclusively based on observational studies. Such studies have evidenced the deleterious effects of delays in antibiotic administration and inadequate antibiotic treatment choice upon septic patient survival.[8–11] Nonetheless, it must be mentioned that the studies are often heterogeneous–some focusing on specific disorders such as community-acquired pneumonia, ventilator associated pneumonia or bacteremia–and do not necessarily address the development of severe sepsis or septic shock associated to such disorders.

The present study evaluates the influence of delays in administering the first dose of antibiotic and inadequacy of the selected antibiotic treatment regimen upon the survival of patients with septic shock.

Patients and methods

Study population

A prospective, observational cohort study was made, involving all the patients over 18 years of age admitted to the Intensive Care Unit (ICU) with septic shock according to the definitions proposed by the SCCM/ESICM/ACCP/ATS/SIS12 Consensus Conference during the period between September 2005 and September 2010 (both months included).

Infection was suspected from the presence of an infectious focus documented by radiological or laboratory test data consistent with infection or a clinical syndrome associated to a high probability of infection or shock not explainable by other causes.

The severity of the patients was assessed using the Acute Physiology and Chronic Health Evaluation (APACHE II) score and the Sepsis-related Organ Failure Assessment (SOFA) score. The APACHE II was applied following the first 24 h of