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EDITORIAL

Has the Surviving Sepsis Campaign been successful in Spain?



¿Ha tenido éxito la campaña sobrevivir a la sepsis en España?

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Although overall mortality related to sepsis has been increasing due to the increased incidence of sepsis, the case-fatality rate has been decreasing over a similar period of time.¹ During the last 20 years there has not been any scientific breakthrough in the sepsis field, thus, many of the recent improvements might be due to the performance improving program “Surviving Sepsis Campaign” (SSC).² The initial aims of the SSC, which arose from the Declaration of Barcelona in October 2002, were to raise public and professional awareness of sepsis and its treatment, and the development of practice guidelines. In partnership with the Institute of Healthcare Improvement, key elements of the first edition guidelines published in 2004 were identified and organized in short treatment protocols called “bundles”. A recent update was published in 2013 with removal of the 24-hour bundle and changes in recommendations for fluids and vasopressor administration based on recent scientific evidence.

In Spain, a wide national educational program based on the SSC guidelines (Edusepsis study) was launched in 2006. It was associated with improved guideline compliance and lower hospital mortality.³ In 2011 a second education program was launched to promote the early use of antibiotics (ABISS-Edusepsis study).

In this issue of *Medicina Intensiva* Sánchez and colleagues⁴ analyze the evolution of sepsis-related mortality

in Spain by comparing two cohorts of patients with severe sepsis or septic shock treated in 41 Spanish ICUs during two time periods: the first group (630 patients with data collected between November–December 2005) was the pre-intervention group in the Edusepsis study, and the second group (718 patients with data collected between April–June 2011) was the pre-intervention group in the ABISS-Edusepsis study. In addition, they examined the association between compliance with the bundles and in-hospital mortality in both cohorts. Compliance with resuscitation bundle was significantly higher in the 2011 group (5.7% vs. 9.9%) and was associated to lower risk of mortality [OR 0.60 (0.36–0.99)]. The 2011 group had lower in-hospital mortality (44.0% vs. 32.6%). They conclude that the observed reduction in the in-hospital mortality rate “is attributable to improvements in early sepsis care including a higher compliance with resuscitation bundle”.

The major methodological weakness of this study is the lack of a control group. Even though various logistic regression models were developed using the baseline risk factors available to the investigators, comparing mortality rates before and after an intervention ignores the underlying secular trend and may lead to misleading conclusions.⁵ Furthermore, baseline patients’ characteristics were different regarding location before ICU admission and the source of infection. A time series analysis would have been helpful to determine whether the rate of change of mortality changed significantly once the campaign was introduced. A cluster randomized trial including hospitals with and without an SSC program would provide better scientific evidence.

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Several questions arise from the findings of this study: First, the reduction in mortality was seen with modest improvements in bundle compliance, which could suggest that either the interventions included are powerful elements in decreasing mortality or other factors like earlier patient identification, better coordination among departments, or other institutional cultural changes could have accounted for the mortality benefit. Nevertheless, the bundle implementation process itself could also explain in part that discrepancy. "Bundles" were described as "a group of interventions that, when executed together, result in better outcomes than when implemented individually". In one single-center quasi-experimental study with a resuscitation bundle compliance of 11%, the accomplishment of more than four out of seven interventions of the bundle was associated with a significant reduced risk of mortality.⁶ The mortality has been also found to be lower even if completion of the bundle was achieved a little beyond the specific time limits. All these findings suggest that it might not be strictly necessary to complete all the tasks to obtain benefits. Second, how long did the participant ICUs maintain the SSC program? A first observational analysis of the international SSC database showed that the longer a hospital continued the SSC program, the better its compliance with the bundles, and the lower observed in-hospital mortality.⁷ The implementation of a national sepsis program in the Netherlands during 3.5 years decreased mortality in both sepsis and non-sepsis patients but only in participating hospitals.⁸ Finally, the 2011 study group showed statistically significant improvements in compliance with the elements of the Early goal-directed therapy (EGDT). Recent trials addressed to validate the EGDT strategy in the emergency department showed no differences in comparison with less invasive hemodynamic resuscitation protocols, what raises questions about whether the original study was flawed. However, recent comprehensive analysis suggest the low mortality reported in the studies ProCESS, ARISE, and ProMISe might reflect not only patient selection but also improvements in care during the last decade.⁹

Despite the observed decrease in mortality there is still a room for improvement. The main challenge remains early recognition and rapid response to patients with sepsis. Screening for sepsis in the emergency department and hospital wards is essential. Integration of clinical assessment, laboratory and microbiological results using clinical informatics will provide rapid diagnostic and prognostic information. Biomarkers such as procalcitonin and advanced PCR/electrospray ionization mass spectrometry are helpful for early invasive bacterial infection detection and prompt pathogens identification respectively. In addition, strategies to reduce ICU delayed transfer such as the setting-up of Rapid Response Systems (RRS) supported by automated alert systems should be considered. According to recent research the National New Early Warning Score which is widely used by RRSs is more accurate than the qSOFA score for predicting death and ICU transfer in non-ICU patients with suspected infection.¹⁰

The results of this study should encourage efforts to implement the SSC revised protocols as a means to improve

outcomes, even if the mechanisms of how change occurred are still unclear. It makes sense to continue with the quality improvement strategy based on multifaceted intervention, powerful educational program, recruitment of multidisciplinary leaders, and a database allowing for audit and feedback.

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Conflict of interests

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References

1. Bouza C, López-Cuadrado T, Saz-Parkinson Z, Amate-Blanco JM. Epidemiology and recent trends of severe sepsis in Spain: a nationwide population-based analysis (2006–2011). *BMC Infect Dis.* 2014;14:3863.
2. Damiani E, Donati A, Serafini G, Rinaldi L, Adrario E, Pelaia P, et al. Effect of performance improvement programs on compliance with sepsis bundles and mortality: a systematic review and meta-analysis of observational studies. *PLOS ONE.* 2015;10:e0125827, <http://dx.doi.org/10.1371/journal.pone.0125827>
3. Ferrer R, Artigas A, Levy MM, Blanco J, González-Díaz G, Garnacho-Montero J, et al., for the Edusepsis Study Group. Improvement in process of care and outcome after a multicenter severe sepsis educational program in Spain. *JAMA.* 2008;299:2294–303.
4. Sánchez B, Ferrer R, Suárez D, Romay E, Piacentini E, Gomà G, et al. Declining mortality for severe sepsis and septic shock in Spanish ICUs: a two cohorts study in 2005 and 2011. *Med Intensiva.* 2016.
5. Thompson MP, Reeves MJ, Bogan BL, DiGiovine B, Posa PJ, Watson SR. Protocol-based resuscitation bundle to improve outcomes in septic shock patients: evaluation of the Michigan Health and Hospital Association Keystone Sepsis Collaborative. *Crit Care Med.* 2016 [Epub ahead of print].
6. Castellanos-Ortega A, Suberviola B, García-Astudillo LA, Holanda MS, Ortiz F, Llorca J, et al. Impact of the Surviving Sepsis Campaign protocols on hospital length of stay and mortality in septic shock patients: results of a three-year follow-up quasi-experimental study. *Crit Care Med.* 2010;38:1036–43.
7. Levy MM, Dellinger RP, Townsend SR, Linde-Zwirble WT, Marshall JC, Bion J, et al. The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. *Intensive Care Med.* 2010;36:222–31.
8. Van Zanten AR, Brinkman S, Arbous MS, Abu-Hanna A, Levy MM, de Keizer NF, Netherlands Patient Safety Agency Sepsis Expert Group. Guideline bundles adherence and mortality in severe sepsis and septic shock. *Crit Care Med.* 2014;42:1890–8.
9. De Backer D, Vincent JL. Early goal-directed therapy: do we have a definitive answer? *Intensive Care Med.* 2016;42:1048–50.
10. Churpek MM, Snyder A, Han X, Sokol S, Pettit N, Howell MD, et al. qSOFA, SIRS, and early warning scores for detecting clinical deterioration in infected patients outside the ICU. *Am J Respir Crit Care Med.* 2016 [Epub ahead of print].