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Are there Compelling Data that Sepsis Bundles can Improve Patient Outcomes



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Sepsis bundles are a prescriptive approach to patient management that include a number of superfluous elements, and yet omit important interventions that can improve patient outcome. The benefits and limitations of this approach are examined.

Introduction

In 2008, the standard of care for patients with sepsis is to implement a "sepsis bundle", as defined by the Surviving Sepsis Campaign (SSC), and endorsed by the US-based Institute for Healthcare Improvement (IHI). While my goal is not to argue against standards and protocols for care, I am unconvinced that the current sepsis bundles are valuable when used as recommended. Rather, there are some elements of the bundle that are useful (early goal directed therapy, EGDT), while others may be less valuable and implementation of these latter components may distract attention from essential interventions, some of which are not included in the bundles (such as how to select appropriate antibiotics and initiation of care by a rapid response team). In addition, bundles are very prescriptive and there is little opportunity to modify them for special patient populations such as the elderly, those in renal failure and those with heart failure. In fact, the SSC website states that all of the elements in the bundle must be used, and that addition of other strategies not found in the bundles is not recommended (SSC website, December 2007). Finally, several nihilists have questioned whether one of the recommendations in the bundle, the need to evaluate all patients for the use of activated protein C, is a consequence of undue industry influence (Eihacker et al. 2006).

What is Included in the Sepsis Bundle?

The currently endorsed and widely implemented sepsis bundle includes a resuscitation bundle to be achieved within 6 hours and a sepsis management bundle to be completed within 24 hours. The resuscitation bundle includes:

- Measurement of serum lactate,
- Collection of blood cultures prior to antibiotics,
- Administration of broad spectrum antibiotics within 3 hours,
- Providing aggressive fluids or pressors for those with hypotension, and
- Monitoring of central venous pressure and mixed venous oxygen tension in the setting of persistent hypotension.

The management bundle requires:

- A standard policy for use of low dose steroids,
- Evaluation of the need for activated protein C by a standard policy,
- Adequate blood glucose control, and
- Maintenance of inspiratory plateau pressures
- < 30 cm water for ventilated patients.

Do Sepsis Bundles have Benefits?

The data on the benefit of sepsis bundles are conflicting, but it is clear that when implemented, most, if not all, of the benefit comes from the use of early goal-directed therapy. In addition, the implementation of a hospital-wide rapid response team, not a specific recommendation of the bundle approach, is also invaluable to improve the outcome of sepsis patients. There are several studies describing a benefit from implementing a sepsis bundle. Gao et al. reported a significantly reduced mortality when sepsis bundles were used, but compliance was only 30% with the 24-hour elements, and 52% with the 6-hour elements, and timely antibiotic administration was given to only 74% of patients (Gao et al. 2005). These findings left it uncertain whether any of the individual bundle elements, beyond timely administration of antibiotics, were responsible for the differences in mortality. Shapiro et al. found a trend of reduced mortality in emergency department patients when managed with a sepsis protocol, compared to historical controls, but the major impact of using the protocol was to give antibiotics sooner, and to give more appropriate antibiotics. There was no difference in the use of corticosteroids or drotrecogin alpha in the protocol period, compared to the control period (Shapiro et al. 2006).

Nguyen and colleagues conducted a 2-year study of 330 emergency department patients with septic shock, and evaluated processes of care and outcomes over time, compared to a baseline period. Bundle compliance increased from 0 to 51.2%, and bundle completion led to lower mortality (21% vs. 40%), but in a multivariate analysis, only the completion of early goal directed therapy, and not the other bundle elements (CVP monitoring, broad spectrum antibiotics within 4 hours, monitoring of lactate clearance, and corticosteroid therapy for suspected adrenal insufficiency), led to decreased mortality (Nguyen et al. 2007). One reason that timely antibiotic administration had no impact was that the rate of achieving this goal stayed at approximately 90% during the study, but this did not differ from baseline rates.

Early goal directed therapy (EGDT) is an essential element in sepsis bundles, and requires administration of 5-8 liters in the first 6 hours (Rivers et al. 2001), and in the original study of EGDT, this approach by itself led to a reduction of sepsis mortality from 46% to 30%. This type of fluid resuscitation is important for the success of sepsis bundles, and as discussed above, may be the major factor leading to reduced mortality, but the freedom to modify the amount of fluid in special populations seems at odds with the SSC recommendations. El Solh et al. used a sepsis protocol in 87 elderly patients, and administered 4-6 liters of fluid in the first 6 hours (El Solh et al. 2008). In addition to the elderly, the safety of large volume resuscitation for those with pre-existing heart failure or renal failure remains unknown.

What Should be Added to Sepsis Management that is not in Bundles and What is Superfluous?

Another problem with the sepsis bundle approach is that it does not include some key interventions that can reduce mortality, while it recommends other evaluations of questionable value. For example, development of a rapid response team as a mechanism to care for septic patients has been shown to reduce mortality from all forms of shock. The benefit comes from bringing critical care interventions to patients, even before they reach the ICU. When implemented, a rapid response team reduces mortality by shortening the time required to administer fluid resuscitation and by reducing the time to antibiotic administration (Sebat et al. 2007). While sepsis bundles do not suggest that this approach is wrong, they also do not include the need to establish this type of care plan. On the other hand, sepsis bundles do include the need for a standard policy for the administration of low dose steroids and activated protein C. In addition, glucose control is included in the 24-hour bundle. All three of these recommendations seem relatively limited in value, given new data. In addition, the latest sepsis guidelines have effectively withdrawn strong support for these interventions (Dellinger et al. 2008). Hospitals that made extra interventions to be compliant with these components of the bundles may now feel that the efforts were wasted.

One important area where there is not adequate guidance in either the sepsis bundles or the sepsis guidelines is how to actually achieve the administration of adequate empiric antibiotic therapy. The bundles assume that giving antibiotics rapidly is the only goal, with no focus on how to give the correct antibiotic for each patient situation. For example, a series of specific recommendations on therapy, depending on the suspected site of infection, could be valuable. In addition, comments on specific antibiotic issues are lacking. These issues include:

- The need to use third generation cephalosporin monotherapy very cautiously in the ICU,
- Limits of using quinolones because of current resistance issues,
- Risks and benefits of combination therapy for sepsis,
- Method to combine antibiotics (avoiding dual beta-lactam therapy),
- Mode of dosing antibiotics (continuous vs. intermittent infusion),
- Impact of recent antibiotic therapy on antimicrobial selection, and
- The need to adapt therapy to local microbiology.

The new sepsis guidelines tackle some of these issues, but the bundle itself simply recommends giving "broad spectrum" antibiotics quickly, implying that any therapy is acceptable, if it is given rapidly.

Finally, the use of a sepsis bundle requires some consensus about what should be included. Although the SSC bundle is most widely used, Fong and colleagues looked at 3 different sepsis bundles (IHI's, the Joint Commission's, and the VHA system's) and found that compliance rates in a given hospital were widely variable, depending on which sepsis bundle was used as the standard for measurement (Fong et al. 2007). With this being the case, which approach is optimal, and which one should be used?

Conclusions

For all of the reasons discussed, sepsis bundles are an ineffective attempt to standardise care for critically ill patients. They include many superfluous elements, while omitting essential interventions that are likely to improve outcome. My suggestion is that hospitals focus on the most important elements of patient care in sepsis, rather than the bundle approach. These elements include rapid delivery of care (rapid response teams), EGDT (adapted to specific patient populations' needs) and the timely and accurate administration of antibiotic therapy.

For references please write to: editorial@icu-management.org

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