The Surviving Sepsis Campaign

Campanha de Sobrevivência à Sepse

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SUMMARY

BACKGROUND AND OBJECTIVES: *The mortality of severe sepsis and septic shock remains unacceptably high unacceptably high. Similar to an acute myocardial ischemic attack and an acute brain attack, the speed and appropriateness of therapy administered in the initial hours after the syndrome develops likely influence outcome. The Surviving Sepsis Campaign hopes to increase clinician and public awareness of the incidence of sepsis, severe sepsis, and septic shock, to develop guidelines for the management of severe sepsis, and to foster a change in the standard of care in sepsis management that will result in a 25% reduction in mortality in the next 5 years.*

CONTENTS: *The first phase was the introduction of the campaign at several major international critical care medicine conferences. Phase 2 of the campaign consisted of an international consensus committee with the purpose of creating evidence-based guidelines for the management of severe sepsis and septic shock. Phase 3 of the campaign aims to operationalize the executive summary recommendations into a set of practical yet valid performance measures. Changing clinicians' behaviors in response to published data has long been a glaring failure in medicine. These recommendations are intended to provide guidance for the clinician caring for a patient with severe sepsis or septic shock.*

CONCLUSIONS: *The campaign aims to establish a model to facilitate qualified research translation into good medical practice trough educational programs in a simple and practical manner.*

Key Words: *sepsis, septic shock, sepsis surviving campaign, severe sepsis*

The mortality of severe sepsis (infection induced organ dysfunction or hypoperfusion abnormalities) and septic shock (hypotension not reversed with fluid resuscitation and associated with organ dysfunction or hypoperfusion abnormalities) in most hospitals remains unacceptably high[1,2]. Similar to an acute myocardial ischemic attack and an acute brain attack, the speed and appropriateness of therapy administered in the initial hours after the syndrome develops likely influence outcome. When patients with myocardial infarction receive evidence-based interventions mortality is reduced. Up to now there has been no attempt to reproduce such an approach in severe sepsis. The Surviving Sepsis Campaign hopes to change that. The campaign, initiated in 2002, is comprised of three phases.

The first phase was the introduction of the campaign at several major international critical care medicine conferences, beginning with the ESICM meeting in Barcelona in 2002, and followed by the Society of Critical Care Medicine meeting in 2003. The overall goal of the campaign is to increase clinician and public awareness of the incidence of sepsis, severe sepsis, and septic shock, to develop guidelines for the management of severe sepsis, and to foster a change in the standard of care in sepsis management that will result in a reduction in mortality. The hope is to reduce mortality by 25%.

Phase 2 of the campaign consisted of an international consensus committee with the purpose of creating evidence-based guidelines for the management of severe sepsis and septic shock. To begin this process, a group of international critical care and infectious disease experts in the diagnosis and management of infection and sepsis, representing 11 organizations, gathered in 2003 to develop guidelines that the bedside clinician could use to improve outcome in severe sepsis and septic shock. Lead authors on recent positive clinical trials were excluded from the process to limit potential bias. The meeting was partially funded by unrestricted industry grants. There were no industry members of the committee. There was no industry input into guidelines development and no industry presence at any of the meetings. Industry awareness or comment on the recommendations was not allowed. The sponsors of the educational grants did not see the recommendations until the manuscript was peer reviewed and accepted for publication in final form.

The recommendations from the consensus conference were graded based on a modified Delphi methodology with categorization as previously described[3]. The methods for this document build upon a 2001 publication sponsored by the International Sepsis Forum, and use the same method of grading recommendations[4]. All articles were initially reviewed based on subgroup assignments and typically by two to three participants. Survival (28-30 day) was the standard outcome measure used to assess outcome benefit and when an alternative was used this is stated in the rationale. Where strong trial evidence existed for outcome benefit in critically ill populations known to contain a larger number of sepsis patients, these trials were considered in determination of recommendation grading. Each participant completed a conflict of interest form and individuals were not assigned to a subgroup topic if they had a potential conflict of interest. The executive summary of the

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guidelines process with key recommendations was finalized and approved by the consensus committee and by sponsoring organizations in December 2003. That document was subsequently published in both *Critical Care Medicine* and *Intensive Care Medicine*[5,6], and represented an historic step for critical care, worldwide. The guidelines represent an international consensus on the best available standard for management of sepsis.

Key recommendations of the executive summary publication, listed by category and not by hierarchy, include early goal-directed resuscitation of the septic patient during the first 6 hours after recognition; appropriate diagnostic studies to ascertain causative organisms before starting antibiotics; early administration of broad-spectrum antibiotic therapy; reassessment of antibiotic therapy with microbiology and clinical data in order to narrow coverage, when appropriate; a usual 7 to 10 days of antibiotic therapy guided by clinical response; source control with attention to the method that balances risks and benefits; equivalence of crystalloid and colloid resuscitation; aggressive fluid challenge to restore mean circulating filling pressure; vasopressor preference for norepinephrine and dopamine; cautious use of vasopressin pending further studies; avoiding low-dose dopamine administration for renal protection; consideration of dobutamine inotropic therapy in some clinical situations; avoidance of supranormal oxygen delivery as a goal of therapy; stress-dose steroid therapy for septic shock; use of recombinant activated protein C in patients with severe sepsis and high risk for death; with resolution of tissue hypoperfusion and in the absence of coronary artery disease or acute hemorrhage, targeting a hemoglobin of 7-9 g/dl; appropriate use of fresh frozen plasma and platelets; a low tidal volume and limitation of inspiratory plateau pressure strategy for acute lung injury (ALI) and acute respiratory distress syndrome (ARDS); application of a minimal amount of positive end-expiratory pressure in ALI/ARDS; a semi-recumbent bed position unless contraindicated; protocols for weaning and sedation/analgesia, using either intermittent bolus sedation or continuous infusion sedation with daily interruptions/lightening; avoidance of neuromuscular blockers, if at all possible; maintenance of blood glucose < 150 mg/dl after initial stabilization; equivalence of continuous veno-veno hemofiltration and intermittent hemodialysis; lack of utility of bicarbonate use for pH ≥ 7.15; use of deep vein thrombosis/stress ulcer prophylaxis; and consideration of limitation of support where appropriate. Pediatric considerations included a more likely need for intubation due to low functional residual capacity; more difficult intravenous access; fluid resuscitation based on weight with 40-60 ml kg or higher needed; decreased cardiac output and increased systemic vascular resistance as the most common hemodynamic profile; greater use of physical examination therapeutic endpoints; unsettled issue of high-dose steroids for therapy of septic shock; and greater risk of hypoglycemia with aggressive glucose control[6].

These recommendations are intended to provide guidance for the clinician caring for a patient with severe sepsis or septic shock, but they are not applicable for all patients. Recommendations from these guidelines cannot replace the clinician's decision-making capability when he or she is provided with a patient's unique set of clinical variables. Although these recommendations are written primarily for the patient in the ICU setting, many recommendations are appropriate targets for the pre-ICU setting. It should be noted that valid circumstances may sometimes prevent physicians from accomplishing all recommendations in a specific patient, especially in the pre-ICU setting.

It takes on average 17 years from discovery of effective therapies to their routine use. The transfer of research from the bench to the bedside is a long, tortuous process – one that is not driven by anything very clear and seems to be based more on fad and coincidence than on a keen, evidence-based evaluation of the literature. What motivates clinicians to change? There are several obvious factors, including quality of the evidence, magnitude of the treatment effect, precision of the treatment effect, risk/benefit ratio, and cost/benefit analysis. In addition, there are intangible factors that drive the rate at which clinicians adapt research into new standards of care. These include physiological rationale for a new intervention, peer pressure, and how easy it is to use or apply a new intervention. Changing clinicians' behaviors in response to published data has long been a glaring failure in medicine. We would like to believe that, with the dawn of the information age, this lag time between the publication of rigorous data and incorporation into routine practice at the bedside would finally be reduced. In general, for guidelines to be used, caregivers must be aware of them, agree with their recommendations, and have the ability to use them[7]. The SSC is working in all three of these areas. One of the primary goals of the Surviving Sepsis Campaign is to establish a model that will facilitate translation of high quality research to bedside clinical practice. This is the cornerstone of phase 3 of the campaign.

Phase 3 of the campaign aims to operationalize the executive summary recommendations into a set of practical yet valid performance measures. In collaboration with the Institute of Healthcare Improvement (IHI) and the Voluntary Hospitals of America (VHA), a set of user-friendly tools have been created to allow clinicians to incorporate these new recommendations into bedside care. These tools include educational programs, designed to increase awareness and agreement with the recommendations, checklists or bundles to help ensure patients receive the intervention, and performance measures, designed to provide feedback regarding how often patients receive the evidence. In addition, a set of quality indicators has been developed to precisely evaluate a hospital's performance with respect to sepsis care. Together these measures will allow hospitals to have an objective assessment of the quality of sepsis care being rendered at their institution and teach interested hospitals and teams how to improve to meet the standard of care outlined in the guidelines.

A set of core changes extracted from the SSC guidelines have been incorporated into a package of key elements or goals that, when introduced into clinical practice, have a high likelihood of reducing mortality due to severe sepsis. The package is referred to as the "sepsis change bundle" or "sepsis bundle." The aim of the sepsis bundle is twofold:

First, to eliminate the piecemeal application of guidelines that characterizes the majority of clinical environments today, and second to make it easier for clinicians to bring the guidelines into practice.

A bundle is a selected set of interventions or processes of care distilled from evidence-based practice guidelines that, when implemented as a group, provide a more robust picture of the quality of care provided. Individual hospitals can and should codify the bundle elements into customized clinical protocols that function best in their institutions. However, in order to provide standard of care therapies to patients, no one bundle element can be ignored. The criteria used for choosing the specific Guideline recommendations to be included in the sepsis bundle were: (1) the evidence suggests that the use of the intervention is associated with decreased mortality, and (2) the recommendation could be converted into data elements that can be precisely defined, with clearly identified failure modes, and which could be measured by retrospective chart audit (or potentially in real time using a checklist). In addition, the number of goals included was judged to be feasible with proper motivation and organization. The implementation of the bundles is aimed at tracking change in practice and reporting how often these evidence-based interventions are used. Engendering evidence-based change through motivational strategies while monitoring and sharing impact with healthcare practitioners is the key to improving outcome in severe sepsis.

The SSC's concerted strategy to help hospitals improve their care of septic patients is hosted a separate the web site www.IHI.org. This site provides a hospital or unit (ICU or ED) all the information and tools necessary to transform the management of sepsis at their institution so as to conform with the guidelines. Easy access to this site is afforded by going to www.survivingsepsis.org. This dynamic resource (1) allows hospitals, intensive care units or emergency departments to learn how to change clinical processes in their hospitals; (2) allows implementation of a core set of changes encompassed in the sepsis bundles; and (3) allows the measurement of the results of those changes on their way to improvement. Monitoring and sharing the results of these efforts to improve with fellow healthcare practitioners and institutions is the key to improving the care of septic patients and reducing mortality due to severe sepsis.

There is debate regarding what is more appropriate to measure processes, i.e., what we do versus outcomes, i.e., the results we get. Process measures are typically less resource intensive, require shorter follow up, and are more meaningful to caregivers[8,9]. Outcome measures, on the other hand, though more burdensome to collect, are more meaningful to patients. The measurement of outcomes poses challenges. Variation in outcome measures is a function of variation in methods of data collections and data definitions, true variation in quality, variation in case-mix, and chance [9]. Often the variation in methods of data collection and variation in case mix are larger than variation in quality. Casemix does not generally influence process measures given that they are rigorously specified.

The SSC, IHI and VHA will create valid and feasible processes measures of quality of care for severe sepsis, develop standard data collection tools and create web-based means to enter data and monitor performance. Measurements are taken by sampling an appropriate number of charts that have been coded to contain sepsis as a diagnosis and applying a provided data collection tool to gather information about the care of those patients as regards the bundle items. Each unit or hospital can easily load their data into the website and produce graphs that reveal the amount of improvement over time for specific goals and the effects of their interventions. There is a need to measure not only the intended outcome – a reduction in mortality due to severe sepsis – but also the success of the implementation of the individual evidence-based changes along the path to improvement, so-called process measures. Both process and outcomes measures are essential because it is important to assess the result of changes to know that they actually represent improvements.

The quality indicators that have been devised in coordination with VHA and based upon the exhaustive review of the sepsis literature are both valid and feasible measures. The necessary data collection is also accomplished using the pre-configured data collection tool and can be recovered simultaneously from the same sample of charts as above. The quality indicators will also serve to provide insight into the improvement process itself and allow for refinement of goals as the SSC moves forward. The establishment of robust indicators of quality with respect to sepsis care will ground the effort to create a global standard of care for sepsis management.

It is important to measure the result of changes to know that they actually represent improvements. There is a need to measure not only the outcome – a reduction in mortality due to severe sepsis – but also the success of implementation of the individual changes along the path to improvement, so-called process measures. The SSC, IHI and VHA are in the process of finalizing precise and validated process measures.

The Surviving Sepsis Campaign, in partnership with the IHI and VHA, represents an important step for international critical care societies. Recognizing the long history of delay in incorporating research into bedside care, these organizations are committed to working together to facilitate bench-to-bedside transfer of recent research. Thus, the campaign represents an ongoing commitment to excellence in patient care. The Surviving Sepsis Campaign has established a target of a 25% reduction in mortality worldwide from sepsis over the next five years. If the Surviving Sepsis Campaign is able to bring the guidelines into routine use, it is possible to achieve this goal. In order for the campaign to be successful, it will require more than good will from the international critical care community. It will require a further commitment from bedside clinicians to critically appraise new research and rapidly adopt interventions proven to be effective. The evidence for best sepsis management is a dynamic process and as additional studies are done and the results published, there will be a need for update of the guidelines and the sepsis bundles. The next guidelines revision is planned for late 2005 or early 2006.

This process will be greatly facilitated by use of sepsis bundles (Figure 1)[10].

Figure 1. A clinician, armed with a sepsis change bundle, attacks the three heads of sepsis (hypotension, hypoperfusion, and organ dysfunction). Inspired by Hercules Kills Cerberus, Renato Pettinato, 2001, in Zuccaro Palace, Agira, Sicily, Italy. Printed with the permission of the artist and the Rubolotta family.



RESUMO

JUSTIFICATIVA E OBJETIVOS: A mortalidade na sepse grave e no choque séptico permanecem em níveis inaceitavelmente elevados. Assim como, no infarto agudo do miocárdio e na doença isquêmica encefálica, para que melhores resultados possam ser alcançados no tratamento da sepse, é necessário que se proceda de forma precoce e agressiva na instituição da terapêutica adequada. A campanha de sobrevivência à sepse visa esclarecer e estimular a implementação de medidas terapêuticas baseadas em evidências científicas de qualidade, com a finalidade de tentar diminuir a mortalidade dessa entidade clínica em 25% nos próximos 5 anos.

CONTEÚDO: Inicialmente, houve divulgação da campanha em Congressos Médicos lançando um alerta à comunidade médica dos níveis alarmantes de sua incidência e mortalidade. Em seguida, desenvolveu-se e publicou-se diretrizes de tratamento baseadas na melhor evidência científica disponível para o manuseio de pacientes com sepse grave e choque séptico. A falta de mudança no comportamento da prática médica de beira de leito em resposta à literatura de boa qualidade representa uma falha imperdoável.

CONCLUSÕES: A campanha visa estabelecer um modelo que facilitará a tradução de pesquisa qualificada em boa prática médica na beira de leito, através de programas educacionais divulgando essas recomendações de forma simples e prática.

Unitermos: campanha de sobrevivência da sepse, choque séptico, sepse, sepse grave

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