Special Article

Pitfalls in the Management of Sepsis in Thailand

Chaiwut Sawawiboon MD*1

*1 Department of Emergency Medicine, Faculty of Medicine, Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand

Septicemia is a major cause of death for patients in the intensive care unit. Patient care is not only a function of doctors or nurses but also requires teamwork from all healthcare professionals. Starting from the screening of the patient in the emergency room, management of these patients includes; early antimicrobial therapy, controlling the source of the infection, initiating hemodynamic therapy, admitting the patient to the intensive care unit, monitoring and surveillance for complications of mechanical ventilation and multiple organ failure. Managing all of these require the expertise of multidisciplinary physicians. Lack of understanding and knowledge in the management of clinical practices can predispose the patient to errors in the treatment of patients here, in Thailand. This present guideline is acceptable as an international standard and is the current practice of the Faculty of Medicine, Vajira Hospital, Navamindradhiraj University. This is an example of the multidisciplinary management of septicemia patients in a university hospital in Thailand as set by international standards.

Keywords: Pitfalls, Septicemia, Intensive care unit, Practices, Thailand

J Med Assoc Thai 2014; 97 (Suppl. 1): S137-S141 Full text. e-Journal: http://www.jmatonline.com

At present, there is various updated information in the treatment of septicemia^(1,2) in regard to: the pathogenesis, new developments in the technology of medical devices, hemodynamic monitoring processes, new antimicrobial agents with a broad spectrum of activity for treating pathogens, and new knowledge resulting from good clinical research in the management of the complications of sepsis (i.e. deep vein thrombosis prophylaxis, appropriate glycemic control for critically ill patients, mechanical ventilation, stress ulcer prophylaxis etc). It is realized, however, that secondary mortality rate for sepsis remains high and sepsis is a significant cause of death in critically ill patients as a whole⁽³⁻⁵⁾. The access and understanding of the problems from errors in the treatment of sepsis in Thailand require initial data to help correlate the limited resources of doctors, healthcare professionals and other stakeholders in the treatment of sepsis for every institution. Patient characteristics, whether in terms of: race, residence, age, underlying diseases, the rights to medical treatment, and economic status impact the treatment protocols for every patient. The authors cannot deny that these factors relate to the treatment

Correspondence to:

Sawawiboon C, Department of Emergency Medicine, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok 10300, Thailand. Phone: 087-785-2777, 089-037-2277 E-mail: hlexxxx@gmail.com and overall health status of the patient. This may lead to the likelihood of a positive treatment response and subsequently, the patients' survival. To transcend the trap or pitfalls in medicine and in the treatment of patients with sepsis, nursing and healthcare professionals must have the knowledge and skills to care for patients at each of these steps:

Screening and diagnosis of septicemia period

Especially in patients with septicemia, the symptoms are complicated in terms of the hosts' response against various infections. Severe sepsis is defined as the presence of physiological changes with the worsening of systemic manifestations. These manifestations are predominantly seen in tissue hypoperfusion that leads to septic shock, organ dysfunction and death. The current definition of sepsis⁽⁶⁾ remains a clinical diagnosis that is based, primarily, on the expertise of physicians. A condition of systemic inflammatory response syndrome (SIRS) is one diagnostic criterion for sepsis. SIRS is considered to be present when patients have more than one of the following clinical signs: (1) a body temperature greater than 38° C or less than 36° C; (2) a heart rate greater than 90 beats per minute; (3) tachypnea, manifested by a respiratory rate greater than 20 breaths per minute or hyperventilation, as indicated by a PaCO₂ of less than 32 mmHg; (4) an alteration in the white blood cell count. This is as a white blood cell count greater than 12,000/ cu mm or a count less than 4,000/cu mm and the presence of more than 10 percent of immature neutrophils ("bands"). The problem of diagnosing sepsis is that if the patient takes aspirin, the temperature may not be increased. In addition, if the patient is on maintenance antihypertensive drugs, beta blockers, etc., the heart rate may not be increased. Further complicating matters, patients who have respiratory compromise, have stopped breathing or have sedation that drops the respiratory rate below 20 breaths per minute will not exhibit tachypnea. These will complicate in determining the diagnosis of SIRS. Based on criteria for the diagnosis of SIRS, if the physician is not proficient, mistakes are possible and there could be a resulting misdiagnosis. Diagnosis of SIRS is ambiguous and does not indicate the severity of the underlying disease. Although the team may be able to confirm the diagnosis of SIRS, physicians will still have to investigate other clinical signs caused by the infection to confirm the diagnosis of sepsis. Physicians may have several different opinions, even with regard to the same patient. Here is one of the common pitfalls in the management of sepsis, which has proven to be very important. If physicians are unable to distinguish the sepsis patients, they are likely to become more serious and the physician will not be able to manage correctly these patients. Moreover, many physicians have misinterpreted medical conditions of patients with severe sepsis and may have missed the signs of organ dysfunction and failed to recognize higher lactate levels, greater than 4 mmol/ $L^{(7)}$. This misinterpretation is a significant error because the lactate level is the only parameter that can accurately predict the risk of death in the sepsis patient. A lactate level above the upper, normal limit is indicative of organ dysfunction and severe sepsis. These patients must be treated in an urgent manner. Lactate level is just a diagnostic tool to be checked at the point of care to achieve a fast diagnosis that can be used within 1-2 minutes to ascertain whether the patient is at a high risk of death and needs to be followed-up quickly with the appropriate treatment. In actual practice, it is necessary to understand the correct definition of severe sepsis as well as making an expeditious diagnosis. The survival of these patients is dependent on the level of organ dysfunction, which can occur in any system without the presence of abnormally high lactate levels. A lactate level above the upper, normal limit is sufficient to render a diagnosis of severe sepsis.

The next crucial step, in addition to patient screening and confirming the diagnosis of severe

sepsis, is the administration of antimicrobial agents, which have established activity against all likely pathogens possible and need to be given as soon as possible. If the physician is unable to find the source of infection or the cause of the infection is unknown, antimicrobial therapy is dependent on several factors. These factors include the patients' age, underlying diseases, and the severity of infection as is manifested in organ dysfunction. Physicians must be cautious to observe and monitor these patients diligently. Blood cultures should be obtained as appropriate before the administration of antimicrobial agents(8-11). To optimize the identification of the causative organisms, it is necessary to obtain at least two sets of blood cultures (both aerobic and anaerobic) prior to initiating antimicrobial therapy. At least one set of cultures should be obtained percutaneously and one set should be drawn through each vascular access device. This is unnecessary if the device was recently inserted (less than 48 hours). Most physicians often focus on the blood culture as the primary diagnostic tool but forget that cultures of other sites and sources (preferably quantitative where appropriate) such as urine, cerebrospinal fluid, wounds, respiratory secretions, or other bodily fluids may be the source of infection. Any fluid in question should also be obtained before antimicrobial therapy if doing so does not cause a significant delay in the administration of antibiotics^(12,13). In addition, there are a lot more details that can set traps or pitfalls, which create errors in the diagnosis, and treatment of severe septicemia. Physicians need to have the relevant knowledge and expertise, especially during the initial resuscitation period as is in accordance to the guidelines of early goal-directed therapy⁽¹⁴⁾.

Initial resuscitation period

In the first 6 hrs of resuscitation, the goals of initial resuscitation of sepsis-induced hypoperfusion should include all of the following as a part of the treatment protocol:

A) CVP equal to 8-12 mmHg.

B) MAP equal to or greater than 65 mmHg.

C) Urine output equals to or greater than 0.5 mL/kg/hr.

D) Superior vena cava oxygenation saturation $(ScvO_2)$ or mixed venous oxygen saturation (SvO_2) 70% or 65%, respectively.

An obvious problem is the ability of the physician to insert central line catheters for CVP measurement. Due to this limitation, continuous treatment is, at times, compromised. Each hospital or institution should be encouraged to provide training opportunities for physicians to obtain the ability and confidence to become adept at this procedure. The central line catheter is not only useful for measuring CVP but also helps physicians with initial fluid resuscitation in patients in septic shock. A patent, reliable central line catheter allows the administration of parenteral nutrition and drugs in high concentrations, and can be used for advanced procedures such as inserting a temporally pacemaker and hemodialysis as needed. Some physicians avoid inserting central line catheters by a venous cutdown and this is another critical error. Because this procedure is not currently recommended or in use, physicians do not routinely use arterial or venous cutdown procedures as a method for inserting catheters⁽¹⁵⁾. Use of CVP to assess fluid responsiveness is another key error because the CVP is not used or correlated with fluid responsiveness^(16,17).

The selection of the type of intravenous (IV) fluid used for initial resuscitation is another common error. Most physicians are often not aware of the ingredients contained in each type of IV fluid, the quantity necessary, and the method of fluid resuscitation for the treatment of septic shock. If they are not up to date in current research, they will often be biased towards the use of albumin for fluid resuscitation. The updated information is that albumin therapy is associated with a reduction in mortality and is no safer for the occurrence of acute kidney injury than has been seen with other colloids⁽¹⁸⁾. Furthermore, not being aware of the potential risks from the use of hydroxyethyl starches (HES) for fluid resuscitation in cases of severe sepsis and septic shock can further compromise the patients involved⁽¹⁹⁻²¹⁾. Most physicians still use dopamine as the first choice of a vasopressor to raise blood pressure but currently the recommendation is for the use of norepinephrine as the first choice in septic shock due to better outcomes⁽²²⁾. The resuscitation target is another factor that has created physicians mistakes. They do not have a clear understanding of the ScvO₂ and how it is affected by a number of factors such as blood transfusions, the use of dobutamine, and alternatives to the targets of treatment such as the lactate clearance, etc^(23,24). The most important factor in early resuscitation is the achievement of the target as soon as possible. This should be accomplished within the first 6 hours after which the patient should be referred to another area that is ready to care for critically ill patients. Mistakes in this area can lead to the lack of continuous therapy and will immediately and directly affect the survival of patients.

Supportive therapy of severe sepsis period

Additional errors, common in the patients' care in this period, are that physicians evaluate their treatment goals for patients achieved by the monitoring of ScvO_2 or conditions of hemodynamic stability therefore enabling the prevention of complications caused by sepsis. DVT prophylaxis, positioning the patients' head to 30-45 degree elevation to prevent ventilator associated pneumonias, stress ulcer prophylaxis, appropriate glycemic control in critically ill patients, appropriate settings for mechanical ventilation, the avoidance of inappropriate of blood transfusions, guidelines for corticosteroids, and weaning by hospital protocols. There are so many errors caused by the lack of physicians' knowledge and the management of the patients in whole system.

Conclusion

Treatment of patients with septicemia requires several bodies of knowledge. General physicians who are not specialists are likely to fall into the pitfalls found in medicine resulting in medical errors. It is necessary, therefore, that each hospital needs to construct guidelines for the complicated treatment of sepsis by preparing a sepsis bundle in accordance to individual potential and resources available to enable continuous patient care. The patients' care starts with screening, diagnosis, treatment, and the prevention of complications. The data clearly prove that the sepsis bundle protocol is useful in reducing mortality rates of sepsis patients⁽²⁵⁾ Fig. 1 exhibits, the sepsis bundle protocol of the Faculty of Medicine, Vajira Hospital, Navamindradhiraj University.

Potential conflicts of interest

None.

References

- Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med 2008; 36: 296-327.
- Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 2013; 41: 580-637.
- 3. Levy MM, Dellinger RP, Townsend SR, Linde-



Survival Sepsis Campaign Guideline

Fig. 1 The sepsis bundle protocol of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University.

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.

- 4. van der Poll T, Opal SM. Host-pathogen interactions in sepsis. Lancet Infect Dis 2008; 8: 32-43.
- Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001; 29: 1303-10.
- Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med 2003; 31: 1250-6.
- 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. Crit Care Med 2010; 38: 367-74.
- 8. Levy MM, Pronovost PJ, Dellinger RP, Townsend

S, Resar RK, Clemmer TP, et al. Sepsis change bundles: converting guidelines into meaningful change in behavior and clinical outcome. Crit Care Med 2004; 32 (11 Suppl): S595-7.

- 9. Weinstein MP, Reller LB, Murphy JR, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. Rev Infect Dis 1983; 5: 35-53.
- Blot F, Schmidt E, Nitenberg G, Tancrede C, Leclercq B, Laplanche A, et al. Earlier positivity of centralvenous- versus peripheral-blood cultures is highly predictive of catheter-related sepsis. J Clin Microbiol 1998; 36: 105-9.
- 11. Mermel LA, Maki DG. Detection of bacteremia in adults: consequences of culturing an inadequate volume of blood. Ann Intern Med 1993; 119: 270-2.
- American Thoracic Society; Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilatorassociated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005; 171: 388-416.

- Muscedere J, Dodek P, Keenan S, Fowler R, Cook D, Heyland D. Comprehensive evidence-based clinical practice guidelines for ventilator-associated pneumonia: diagnosis and treatment. J Crit Care 2008; 23: 138-47.
- 14. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001; 345: 1368-77.
- O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Bethesda, MD: National Institutes of Health, 2011.
- Hughes RE, Magovern GJ. The relationship between right atrial pressure and blood volume. AMAArch Surg 1959; 79: 238-43.
- 17. Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. Chest 2008; 134: 172-8.
- Delaney AP, Dan A, McCaffrey J, Finfer S. The role of albumin as a resuscitation fluid for patients with sepsis: a systematic review and meta-analysis. Crit Care Med 2011; 39: 386-91.
- Guidet B, Martinet O, Boulain T, Philippart F, Poussel JF, Maizel J, et al. Assessment of hemodynamic efficacy and safety of 6% hydroxyethylstarch 130/0.4 vs. 0.9% NaCl fluid replacement in patients with severe sepsis: The

CRYSTMAS study. Crit Care 2012; 16: R94.

- 20. Perner A, Haase N, Guttormsen AB, Tenhunen J, Klemenzson G, Aneman A, et al. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. N Engl J Med 2012; 367: 124-34.
- 21. Myburgh JA, Finfer S, Bellomo R, Billot L, Cass A, Gattas D, et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. N Engl J Med 2012; 367: 1901-11.
- 22. De Backer D, Aldecoa C, Njimi H, Vincent JL. Dopamine versus norepinephrine in the treatment of septic shock: a meta-analysis*. Crit Care Med 2012; 40: 725-30.
- Jones AE, Shapiro NI, Trzeciak S, Arnold RC, Claremont HA, Kline JA. Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: a randomized clinical trial. JAMA 2010; 303: 739-46.
- 24. Jansen TC, van Bommel J, Schoonderbeek FJ, Sleeswijk Visser SJ, van der Klooster JM, Lima AP, et al. Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. Am J Respir Crit Care Med 2010; 182: 752-61.
- 25. Nguyen HB, Corbett SW, Steele R, Banta J, Clark RT, Hayes SR, et al. Implementation of a bundle of quality indicators for the early management of severe sepsis and septic shock is associated with decreased mortality. Crit Care Med 2007; 35: 1105-12.

ข้อผิดพลาดในการรักษาภาวะติดเชื้อในกระแสโลหิตในประเทศไทย

ชายวุฒิ สววิบูลย์

การติดเชื้อในกระแสโลหิตเป็นสาเหตุสำคัญของการเสียชีวิตของผู้ป่วยในหออภิบาลในประเทศไทย การดูแลรักษาไม่ได้เป็นหน้าที่ของใคร คนใดคนหนึ่งไม่ว่าจะเป็นแพทย์หรือพยาบาล หากแต่ต้องอาศัยการทำงานเป็นทีมร่วมกันดูแลผู้ป่วย ดั้งแต่การค้นหาผู้ป่วยที่ห้องฉุกเฉิน การให้ยาปฏิชีวนะคว้ยความรวดเร็ว การควบคุมแหล่งติดเชื้อ การรักษาเพื่อฟื้นฟู ระบบไหลเวียนโลหิตเบื้องต้น การส่งต่อผู้ป่วยเข้าสู่หออภิบาล การติดตาม และเฝ้าระวังภาวะแทรกซอน ทั้งจากการใส่เครื่องช่วยหายใจและภาวะล้มเหลวของอวัยวะต่าง ๆ ซึ่งต้องใช้ความเชี่ยวชาญของแพทย์แบบสหสาขาวิชาชีพ การขาดความเข้าใจและองค์ความรู้ ในแนวทางปฏิบัติที่ถูกต้องทำให้เกิดข้อผิดพลาดในการรักษาผู้ป่วยในประเทศไทยเป็นอย่างมาก ได้นำเสนอ แนวทางในปัจจุบันที่เป็นที่ยอมรับในต่างประเทศ และแนวทางการปฏิบัติของคณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช ซึ่งถือเป็นตัวอย่างของการดูแลผู้ป่วยติดเชื้อในกระแสโลหิตแบบสหสาขาในโรงพยาบาลระดับมหาวิทยาลัย ตามมาตรฐานสากลของประเทศไทย