Severe Sepsis and Septic Shock in Pregnancy

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Question 1:
The use of standard clinical criteria for systemic inflammatory response syndrome (SIRS) may be misleading in an intrapartum patient, given the common finding of elevated heart rate (if volume depleted), elevated white blood cell count, and decreased PaCO₂ from frequently encountered maternal hyperventilation during the second stage. You also mentioned in your article that SIRS and the Modified Early Warning Score cannot reliably predict sepsis, intensive care unit (ICU) transfer, or death in gravid patients. What modification do you propose, if any, to define SIRS in intrapartum patients?

Response from Drs. Barton and Sibai:
As we noted in our article, the presenting signs and symptoms of sepsis during pregnancy can be variable and differ from the nonpregnant state as a consequence of the unique physiology of pregnancy. Clearly the current sepsis criteria may not be stringent enough for use in pregnancy, and we proposed more conservative values for the diagnosis of SIRS, including a heart rate greater than 110 beats per minute (bpm), respiratory rate of 24 breaths per minute, and a white blood count of greater than 15,000/mm³. These guidelines, however, have not yet been validated in pregnant or postpartum women.

Question 2:
If bowel (for example, complicated small bowel obstruction or anastomosis disruption with previous gastrointestinal surgery) is considered the primary source of sepsis in a pregnant patient, is there a role for antifungal coverage?

Response from Drs. Barton and Sibai:
Risk factors for the development of fungal infections include immunosuppressive medications, multiple lumen catheters, peritonitis, and large or small bowel surgery. Although these factors are clearly associated with an increased risk for sepsis, they are less common in the obstetric population, and therefore were not included in our algorithm; nor would antifungal therapy be indicated as initial treatment of sepsis unless a high likelihood of fungal infection was present. If present or suspected, treatment of fungal infections to reduce the high morbidity and mortality rate with these infections is indicated. Antifungal therapy can include micafungin or caspofungin, both of which are U.S. Food and Drug Administration (FDA) pregnancy category C medications. Dosing for micafungin is 100–150 mg intravenously each...
day; for caspofungin, a single 70-mg intravenous loading dose should be administered on Day 1, followed by 50 mg intravenously daily thereafter.

**Question 3:**
Clinical endpoints for volume resuscitation can be suboptimal in septic and trauma patients. Some studies report up to 85% of patients will still show signs of inadequate tissue perfusion with abnormal serum lactate and/or base deficit levels despite normalized vital signs and adequate urine output.²⁻⁴ Can you elaborate on appropriate goals for volume resuscitation?

**Response from Drs. Barton and Sibai:**
*Determining adequacy of tissue and organ perfusion in the setting of sepsis can be difficult. Clinical indices that have been used to assess this perfusion have included mean arterial pressure (MAP), urine output, mentation, capillary refill, blood lactate, and mixed venous oxygen saturation.⁵ Invasive and more elaborate methods to assess volume status include central venous pressure obtained with a central venous catheter, systolic and pulse pressure variation using arterial waveforms, left ventricular end-diastolic area using echocardiography, and inferior vena cava diameter assessed by ultrasonography. With further study, it is hoped that these technologies can complement the clinical indices for determination of adequacy of tissue and organ perfusion. Until these new technologies are validated, it appears that bundle therapies with the goals of reversing oliguria, improving capillary refill, and abating hyperlactinemia with improvement in hemodynamic variables such as MAP remain the mainstay of assessing the success of volume resuscitation.*

**Question 4:**
Although not mainstream, there is some evidence to support immunoglobulin use in the management of sepsis. What are your thoughts on the use of intravenous immunoglobulins in sepsis management?

**Response from Drs. Barton and Sibai:**
The administration of polyclonal intravenous immunoglobulins has been associated with either a reduced morbidity or an improved survival rate in different populations of patients with sepsis, severe sepsis, and septic shock.⁶ A recent Cochrane review⁷ noted 17 trials in adults treated with polyclonal immunoglobulins. Using high-quality trials only, no reduction in deaths of adults was seen with polyclonal immunoglobulin use. In the monoclonal immunoglobulin trials, anti-endotoxin antibodies showed no benefit, while the anti-cytokines showed a very small reduction in deaths among adults with sepsis. Given this review of immunoglobulin use in sepsis and the lack of studies involving pregnancy-related sepsis, we would not advocate its administration in the initial management of severe sepsis or septic shock.

**Question 5:**
Different organs require different MAPs for adequate perfusion. Some protocols on gravid patients receiving cardiopulmonary bypass suggest MAPs of greater than 70 mm Hg to maintain adequate uterine artery perfusion. In sepsis management, however, the recommendation is to achieve MAPs greater than 65 mm Hg. Does a MAP greater than 65 mm Hg provide optimal uterine artery perfusion for resuscitation in septic pregnant patients?

**Response from Drs. Barton and Sibai:**
The goals for resuscitation in shock are to restore effective tissue perfusion and normalize cellular metabolism. This is best achieved by objective evidence of increased perfusion including improvement in urine output, capillary refill,
mental status. In those patients with a viable intrauterine pregnancy, objective evidence can also include improvement or stabilization of the fetus status. Assessing the perfusion of any end organ, including the uterus, kidney, liver, or brain is difficult, and the regulation of perfusion of each organ may differ. The guidelines for adequate resuscitation in nonpregnant individuals have been to maintain the MAP greater than 65 mm Hg, but a higher MAP may indeed be required to provide desired uterine perfusion in pregnancy, particularly in the setting of underlying poor placental function such as pre-existing hypertension or diabetes.

Question 6:

Pregnant patients start out with chronic respiratory alkalosis with metabolic response. The serum bicarbonate and CO₂ levels are therefore, at baseline, significantly lower in pregnant patients. Should there be a correction factor for this in pregnant patients to better interpret and make use of arterial blood gasses for help with sepsis management?

Response from Drs. Barton and Sibai:

Indeed there are several physiologic respiratory adaptations in pregnancy, including increased O₂ consumption, a higher arterial pH, a lower arterial pCO₂, and a lower serum bicarbonate level. Further, the pO₂ is often decreased in the third trimester in patients in the supine position, particularly if there is excessive uterine distention from multiple gestation or hydramnios. A precise bicarbonate level would have little effect on management, as bicarbonate replacement in lactic acidosis has been shown to be ineffective. Further, the treatment target is not the lactic acidosis but the underlying conditions causing the acidosis. A target of a lower pCO₂ value is reasonable as this is consistent with the respiratory physiologic adaptations of pregnancy.

References: