Commentary

Thoracic epidural anesthesia in sepsis - is it harmful or protective?

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See related research by Freise *et al*., http://ccforum.com/content/13/4/R116, and Lauer *et al*., http://ccforum.com/content/13/4/R109

Abstract

Research interest in epidural anesthesia during sepsis has grown over the past years and studies have tried to determine its mechanisms, which should, theoretically, protect organs and reduce morbidity and mortality. However, different experimental approaches in different animal models have provided conflicting results over whether epidural anesthesia has protective or harmful effects and whether these alter depending on the phase of sepsis, the spread of epidural anesthesia or additional supportive therapies. In the future, more standardized research is necessary to integrate the results of all studies, which have been published.

The hypothesis that a systemic or a regional reduction of sympathetic activity - for example, induced by thoracic epidural anesthesia - might have positive effects on the perfusion and oxygenation (that is, increase them) of splanchnic organs like the liver and gut and that reduction of pain improves pulmonary function sounds profound. Although interest in this field of research has been increasing over the past years, detailed knowledge about the effects of increased or reduced sympathetic activity on organ perfusion and oxygenation and the mechanisms involved, as well as how these change or sympathetic activity changes immunomodulation during pathophysiological conditions, is still lacking. In recent issues of *Critical Care*, Freise and colleagues [1] and Lauer and colleagues [2] presented studies that provide interesting information concerning this subject.

Freise and colleagues used an established animal model - Sprague-Dawley rats that were fitted with thoracic epidural catheters and treated with cecal ligation and puncture. Intravital microscopy was used to investigate sinusoidal diameters, loss of sinusoidal perfusion, sinusoidal blood flow, and permanent leukocyte adhesion to sinusoidal and venolar endothelium. In their experiments, cardiac output - measured in an additional group of animals, which were not investigated with intravital microscopy - remained constant in animals with induced sepsis with and without epidural anesthesia. From their intravital microscopy results they concluded that sinusoidal blood flow increased in the sepsis group and was normalized in the group with sepsis and thoracic epidural anesthesia. However, sinusoidal vasoconstriction was not ameliorated by thoracic epidural anesthesia and nor was liver tissue injury affected.

Lauer and colleagues concentrated on a second important organ function: pulmonary function. While there is broad agreement that thoracic epidural anesthesia improves postoperative pulmonary function, the underlying mechanisms - for example, via reduction of abdominal pain after general abdominal surgery - still remain unclear [3]. Lauer and colleagues revealed that - at least in their animal model - thoracic epidural anesthesia modulated the nitric oxide (NO) pathway and exerted positive - that is, lower levels of exhaled NO - effects on pulmonary endothelial integrity in hyperdynamic septic rats, but not in hypodynamic septic rats. In the latter, thoracic epidural anesthesia led to increased pulmonary edema despite reduced amounts of exhaled NO. This study shows the importance of distinguishing between different phases of disease, especially during early (hyperdynamic) and late (hypodynamic) sepsis. One has to keep in mind that the authors did not describe any differences in volume management within their experimental groups and, thus, intravascular normovolemia could not be proven in either.

In general, both studies add interesting results to the necessary discussion about the usefulness of epidural anesthesia during sepsis. However, up till now there is still a lack of really comparable studies. Why is this so?

NO = nitric oxide.

Increased sympathetic activity plays an important role in the development of different pathophysiological conditions - for example, during endotoxemia [4-7], hemorrhagic shock [8] and even during and after routine abdominal surgical procedures [9]. Thus, epidural anesthesia might decrease mortality during sepsis, especially as splanchnic hypoperfusion and hypoxia are said to be key factors in the development of systemic inflammatory response syndrome, sepsis and multiple organ failure [10].

Diverse studies, however, have presented contradictory results concerning this, with some reporting decreased mortality in older animal studies [11] and newer meta-analyses [12,13] and others reporting increased mortality in an animal model [14]. The main problem with all the published studies is that hardly any are comparable with each other. Humans and different animals (for example, pigs, rats, mice, rabbits) have been used, either systemic or regional reduction of sympathetic activity has been investigated (effects of clonidine, spinal anesthesia, epidural anesthesia), and the method of epidural anesthesia has differed, from lumbar epidural anesthesia in older studies to thoracic epidural anesthesia in recent studies, including or not the nervi accelerantes. However, to prove an effective reduction in sympathetic activity, and especially that the spread of epidural anesthesia is working, is very difficult, especially in clinical situations [15]. Few of the studies deliver definitive proof of this.

Hence, the most important considerations for future studies on the effect of epidural anesthesia on sepsis or endotoxemia are normovolaemia at any point of the experiment, a clear definition and timeline of hypodynamic and hyperdynamic circulation in sepsis, the proven spread of the epidural anesthesia, which includes or excludes the nervi accelerantes (thereby reducing or maintaining cardiac output, respectively), and the continuous, proven reduction of sympathetic activity - including or excluding the adrenal glands - during the different phases of the developing pathophysiological conditions. Surrogate parameters like sinusoidal width or the number of perfused sinusoids should be used with care to judge sinusoidal perfusion, as laboratory findings should be treated cautiously if not accompanied by definitive - and relevant - physiological changes.

Although studies like those from Freise and colleagues and Lauer and colleagues have increased our understanding of how reduction of regional sympathetic activity can influence different organ functions during sepsis, we still largely lack understanding of the underlying mechanisms, and this will persist as long as there are no standardized, or at least fairly definitive, studies on reduced sympathetic activity during sepsis. Only with these studies we will know, whether thoracic epidural anesthesia is harmful or protective in sepsis.

Competing interests

The authors declare that they have no competing interests.

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