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Comment about "Hypertonic saline solution for modifying tissue ischemia/reperfusion injury: Porcine aortic occlusion model"

Comentario sobre "Solución salina hipertónica para modificar la lesión tisular por isquemia/reperfusión: modelo porcino de occlusion de aorta"

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Escobar et al[1] published an original article evaluating the impact of a hypertonic saline solution (HSS) in an animal model of ischemia/reperfusion. The significance of this article is the experimental model that links basic research to the clinic, through an animal study stimulating a usual situation in vascular surgery, that is, aortic clamping.

Several animal models or models on ischemia/reperfusion in organs such as the liver, the gut, or the heart have been published.[2–4] The model used by Garutti et al in lung surgery may serve as an example.[5]

The purpose of this paper is to determine whether HSS reduces the ischemic/reperfusion injury in the liver, kidney, and ileum. To this end, 2 groups receiving HSS or physiological saline 15 minutes before aortic clamping were included. The authors justify the study based on endothelial damage and reperfusion-associated phenomena.[6] Different papers have shown the benefit of reestablishing volemia in ischemia/reperfusion models, for instance in the lung, during coronary surgery, or at the renal level with different solutions such as HSS or starches.[7,8]

The authors identified hemodynamic differences in the systolic index following perfusion, with rising systolic index in the SSH group as compared with the baseline, and decreasing levels among the control group. However, no differences were found in other renal or liver damage parameters, neither in the endothelin values. The creatinine values in the control group were actually higher at the end of the experiment, but these differences were not statistically significant. As mentioned during the discussion, probably no significant differences have been shown due to clamping time (15 minutes), whether because of the HSS dose administered, or because of the time at which the 3 samples were collected. Hence, in a recently published study, doses similar to HSS have shown to reduce lung damage, in combination with valproate.[9] In terms of cerebral protection, several trials show the benefits of HSS, including a recent trial in children with severe head and neck trauma.[10]

The authors do find differences in pH, which is somewhat higher with the administration of HSS; lactate values are lower in the HSS group. Differences were also found in the sodium and calcium values. The rise in calcium and sodium following HSS administration had been previously identified and is mentioned by the authors in this publication, referring to isolated cardiac muscle models where positive inotropic and lusitropic effects of HSS have also been shown, mediated by the hyperosmolality and the sodium action on the Na+ - Ca+2 exchanger, preserving the homeostasis of intracellular calcium and its release from the sarcoplasmic reticulum.[4]

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What the authors fail to discuss is the potential deleterious effect of calcium in situations of reperfusion, as has been proven for instance in cardiac surgery.[11] Deleterious effects have also been found with sodium and chlorine overload. Hyperchloremia as a result of excessive chlorine has been associated with increased mortality in the intensive care unit and in postsurgical patients, based on the amount of chlorine administered and the production of hyperchloremic acidosis.[12,13] Hypernatremia in critical care units is associated with too much salt administered and increased mortality.[14] In this case, the dose administered does not increase the mean sodium values above the normal levels, but is something to keep in mind when transferring the HSS experience to the usual clinical practice. The chlorine values are not measured and hence we do not know its impact. It will be logical to think that they rise similarly to sodium levels in the group that received HSS, but do not know to what extent and whether the rise exceeded the normal limits.

Restoring volemia with physiological saline occasionally leads to hyperchloremic acidosis; consequently, some authors recommend limiting the dose of the so-called "physiological saline," particularly following resuscitation.[12,15]

The use of colloids has not only failed to show any benefit, but may even be harmful. Starches increased mortality due to renal damage in critical patients, and particularly with SEPSIS.[16] Albumin has also been associated with increased mortality in patients with severe head trauma.[17] Volume overload is also associated with increased mortality in critical patients.[18] The need to undertake further studies comparing different solutions has encouraged different comparative essays using balanced saline solutions.[19]

As mentioned by the authors, reactive oxygen species (ROS) may play a key role in the origin of the ischemia-reperfusion phenomenon, although this could be related with low antioxidant levels. This has been seen for instance in hepatic steatosis, which is associated with mitochondrial dysfunction and excessive mitochondrial ROS production.[20]

In sum, pretreatment with HSS in this experimental ischemia/reperfusion model in animals has shown hemodynamic value and has apparently improved perfusion, with enhanced lactate and pH control levels. No differences in terms of organ damage have yet been shown; however, a relatively short clamping time could be the cause for this lack of results. The experimental model is an example of basic methodology and enables damage assessment through serum and tissue samples. Regardless of the considerations and thoughts about salt overload, the decision to transfer this experience to the clinic is difficult because of the lack of evidence, and because of the difficult choice between less volume and more salt content and a major contribution of fluids that also entail morbidity, particularly affecting the lungs and the brain.

The selected dose of HSS, 4 ml/kg at 7.5%, has been effective and is similar to that of other trials that did show organ protection[21]; furthermore, the sodium values were within the normal range. The available clinical evidence on the use of HSS is limited and inconclusive for this indication, but it has proven to be effective in hemorrhagic shock and in some head and neck trauma studies. Clinical trials in the operating room have shown, similar to this study, a hemodynamic improvement, particularly in heart surgery.[22] However, similar trials are needed in clinical practice, particularly in vascular surgery, comparing HSS to other solutions in terms of hemodynamics and tissue damage.

Basic research, whether in vitro or in animals like in this case, is a cornerstone of medical practice, and we anesthesiologists should not neglect this fact. All anesthesia departments and universities are called upon to stimulate and facilitate basic research, as few areas of specialization require so much knowledge in basic sciences, and particularly of physiology and pharmacology. In addition to the stress situations associated with surgical aggression, the metabolic response triggered shall be controlled by the anesthesiologist. Experimental models that mimic everyday clinical situations such as the one herein depicted, promote an enhanced knowledge of the effects of anesthesia with regards to different treatments. Fluid therapy is not exempt from risks and fluids shall be subject to the same consideration as any other drug. Therefore, keeping a log of the dose administered and of any associated adverse events is mandatory and essential.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

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