Response

To the Editor:

We appreciate the comments from Dr Davis about our recent consensus statement in CHEST and his concerns regarding our association of tetracaine with methemoglobinemia. Methemoglobinemia is a serious adverse event that has been reported to occur with multiple topical anesthetics including benzocaine, prilocaine, lidocaine, and tetracaine. Benzocaine is by far the most commonly reported agent with respect to association with methemoglobinemia, which could occur in a dose-independent fashion, even after a single benzocaine spray. The US Food and Drug Administration has issued multiple Public Health Advisory warnings about methemoglobinemia with the use of benzocaine sprays during medical procedures.

Although the literature suggests a lower association of methemoglobinemia with tetracaine, the risk still exists and its nature is further confounded by the popularity of a particular pharmaceutical preparation, Cetacaine, containing benzocaine 14%, butyl aminobenzoate 2%, and tetracaine 2%, making it difficult to separate the action of the two drugs. Numerous reports have reported on the association of Cetacaine and methemoglobinemia and have discouraged its use in medical procedures.

We agree with Dr Davis that all the topical anesthetic agents used during flexible bronchoscopy have the potential for toxicity. Our goal was to alert the chest physician to the risk of methemoglobinemia but we could have better delineated the attributed risk to different topical anesthetic agents. However, the data surrounding this differential risk with various agents are scant, and our panel felt the need to increase the general alertness to a potentially very serious condition.

A consensus statement is not designed to provide evidence-based practice guidelines, but rather, suggestions for good clinical practice and a forum for debate. This is exactly what this letter to the editor and response are embodying.

References


Early Mobilization Testing in Patients With Acute Stroke

To the Editor:

For the past 11 years, we have been studying very early mobilization (EM) (out of bed) in people with acute stroke. The elegant review by Schwickert and Kress in a recent issue of CHEST (December 2011) of the emerging research on EM of patients treated in the ICU brought home the parallels that exist between EM research, regardless of the population studied.

Inactivity, at least in the first days to weeks, appears to be the norm after having a stroke or being managed in the ICU.
Inactivity may simply be a consequence of the intensive monitoring, investigation, and treatment protocols, combined with high dependence on others to move. Or bed rest may be consciously prescribed by the treating team. There is no doubt, however, that the potential harms of bed rest, and the benefits of activity, both outlined by Schweickert and Kress,1 should provide incentive for us to minimize bed rest as much, and as soon, as possible. In the stroke population and perhaps more broadly, further incentive for promoting early physical activity comes from experimental studies demonstrating the experience-dependent nature of neuroplasticity3 and the role physical activity plays in helping drive recovery of the damaged brain. In short, it is biologically plausible that EM may be helpful for acute patients, if it is not harmful.

The question of harm cannot be ignored. Cardiovascular and respiratory stability drive many decisions about out-of-bed activity in clinical practice. Of course “stability” is not always easy to define. In stroke, there is also concern that activity may diminish blood flow in an already injured brain. Not surprisingly, therefore, early EM research has addressed whether it is safe and feasible. In ICU studies to date (which exclude stroke), EM appears to be safe. Our phase 2 trial (AVERT [A Very Early Rehabilitation Trial]) found very early and frequent mobilization (<24 h after stroke) to be safe, feasible, and cost effective; it also promoted early return of unassisted walking. Patients with hemorrhagic or ischemic stroke (any age or stroke severity) admitted to a stroke unit were eligible. Physiologic entry criteria applied, and patients needed to be rousable, but not fully conscious. AVERT phase 3 is now under way. Almost 1,200 patients (final N = 2,104) from five countries have participated to date, and we expect trial recruitment to end in early 2015.

EM represents a significant paradigm shift. The clinical trials currently under way across a range of populations will help inform the development of evidence-based protocols.

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REFERENCE


Response

To the Editor:

We thank Dr Bernhardt and the AVERT (A Very Early Rehabilitation Trial) Trialist Collaboration for their response to our recent review1 and applaud their scientific efforts to test very early mobilization in stroke. Clinicians’ concern for end-organ dysfunction resulting from therapy-related increases in oxygen consumption continues to be a major impediment to activity in the earliest days of critical illness. Efforts are underway to standardize criteria for defining stability to drive ICU physiotherapy consultation. As the burden of ICU survivorship is further clarified,2 the opportunity for mobilization and rehabilitation programs to provide enduring improvements in both physical and neurocognitive function must be tested. Preliminary data suggest that ICU-based interventions may confer protection against hospital readmission or death.4 As Dr Bernhardt and colleagues highlight, the possibility that early activity enhances neuroplasticity and might reduce chronic brain dysfunction after critical illness is appealing.5 We look forward to the outcomes of AVERT phase 3 and other upcoming trials of early mobilization after an acute illness.

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