**Perioperative Mortality**

**Intraoperative Anesthetic Management Matters**

OBVIOUSLY, we all wish for our patients to do well. We learn about our patients’ comorbidities and develop anesthetic plans that impress colleagues and oral board examiners. We make efforts to influence our patients’ outcomes by implementing protocols for perioperative β-adrenergic blockade and postoperative analgesia. But are there more important factors readily within our control that we are not addressing? Consider the following scenarios:

- Are you working alone? Are you hesitant to ask a colleague to help as you induce or awaken a patient with a potential difficult airway or a bad heart?
- Are you too experienced (or arrogant) to use a checklist when putting your anesthesia machine in working order early in the morning? Do you think checklists are only for rookies and paranoid airline pilots?
- Are you overseeing patients while working as part of an anesthetic team, but too tired to wander to the back of the operating suite to help awaken and extubate an elderly patient who should be fine? You have an experienced member of your team in that room, so why should it matter?
- Have you avoided using a neuromuscular blockade monitor because it is not very reliable and seems to have a bad battery most of the time? Why worry—today’s muscle relaxants wear off quickly and rarely need to be reversed, right?

In this issue of *Anesthesiology*, Arbous et al.¹ provide a jolting report on the positive impact that anesthesia providers can have on their patients. How? Simple anesthetic management principles seem to have a major effect on perioperative mortality. The routine use of an equipment checklist (odds ratio, 0.61), direct availability of an anesthesiologist to help lend a hand or trouble-shoot when needed (odds ratio, 0.46), the use of full-time compared with part-time anesthesia team members (odds ratio, 0.41), the presence of two members of the anesthesia team at emergence (odds ratio, 0.69), and reversal of muscle relaxants at the end of anesthesia (odds ratio, 0.10) had dramatic, positive effects that were associated with reduced perioperative mortality within 48 h after surgery and anesthesia.

This report is remarkable in several ways. First, it is one of the few that have shown anesthetic management processes to dramatically reduce perioperative mortality. Second, it reports perioperative mortality rates matching a number of recent reports. Importantly, it supports the recent insightful article by Lagasse² about perioperative mortality and his suggestion that the US anesthesia community may have overestimated its impact on improving patient safety in the past two decades. Finally, the authors have used a unique and thoughtfully planned multiinstitutional survey and case-control methodology to evaluate this low (but not low enough)—frequency outcome.

It should not be surprising that perioperative anesthetic management processes can make a difference. The US Federal Aviation Administration has long required the use of pilot checklists for evaluating the airworthiness of aircraft and starting procedures, a requirement strongly supported by outcomes of real and simulated air flight. Why would our specialty, so often required the use of pilot checklists for evaluating the airworthiness of aircraft and starting procedures, a requirement strongly supported by outcomes of real and simulated air flight. Why would our specialty, so often compared to piloting, be different? The Federal Aviation Administration also requires two pilots for most commercial aircraft operations, nicely matching the report’s finding that the presence of two anesthesia providers at emergence is associated with lower perioperative mortality. The positive impacts of immediate availability of anesthesiologist when needed and continuity of anesthesiologist providers in the care of individual patients likewise make sense but, until this study, rarely have been shown to be associated with reduced perioperative mortality.

Have we really overestimated our positive impact on patient safety? Clearly, a number of recent studies suggest that our oft-quoted estimate of 1:200,000 or more patients who have an anesthetic-related death may be flawed.³ The basis for this estimate is accurate but usually misinterpreted. Eichhorn et al.⁴ reported this low rate of anesthetic-related mortality in *healthy* patients, an important distinction occasionally neglected in anesthesiologist patient safety statements. This current study, like

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others, suggests that the anesthetic-related mortality rate is still too high. The good news is that we have room for improvement and, now, data to support anesthetic management changes that may help.

The study of rare medical events is extremely difficult; it often is extraordinarily frustrating to obtain numerators large enough or denominators that are sufficiently robust to allow calculation of frequencies of the events and subsequent analyses for potential risk factors. Arbous et al. have used a multiinstitutional study technique common to clinical research in other medical specialties, notably cardiology, but infrequently attempted in anesthesiology and the study of perioperative mortality. This process has provided the authors with (unfortunately) a sufficient number of perioperative deaths to allow case-control analyses, a good way to seek associations between rare events and potential risk factors.

In general, efforts to seek associations between rare medical events and potential risk factors follow a progression. First, case reports and small case series describe unusual outcomes. If enough of these unusual outcomes can be gathered (typically at least 20 are needed, assuming valid controls can be assessed), a case-control methodology can be used to seek possible but not proven risk factors. Subsequently, potential risk factors identified by case-control studies must be evaluated prospectively in large populations to ascertain their validity. Finally, potential interventions to decrease the frequency of these rare events can be tested in randomized, prospective trials. The current study’s elegant methodology takes advantage of the large numbers of perioperative death reports that they collected in multiple institutions by creatively and prospectively seeking data from randomly selected controls within each of those institutions. This methodology is applicable to many rare perioperative events and should be a model often copied in the future.

Although conclusions from one study should not lead to wholesale changes in practice, the findings in this study support many plausible assumptions that improvements in anesthetic management processes can positively influence patient outcomes. The use of equipment checklists, immediate availability of anesthesiologists to help when needed, especially to provide extra assistance at emergence from anesthesia, and routine reversal of muscle relaxants are processes that should be seriously considered when seeking opportunities to improve the perioperative outcomes of anesthetized patients.

Mark A. Warner, M.D. Mayo Clinic College of Medicine, Rochester, Minnesota. Warner.mark@mayo.edu

References


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Complex Regional Pain Syndromes in Children and Adolescents

DIAGNOSIS and treatment of complex regional pain syndromes (CRPS) I and II (also known as reflex sympathetic dystrophy and causalgia, respectively) continue to generate controversy among clinicians and frustration and suffering for patients. The work of Dadure et al. published in this issue of Anesthesiology revisits the topic. Several case series of adults referred to specialist physicians found that prolonged pain, impairments, disability, and serious complications were common. Conversely, a more favorable clinical course was reported in a recent population-based epidemiologic study. Choice among therapies often seems to depend more on what type of clinician sees the patient, rather than on evidence derived from prospective controlled clinical trials. Treatments include various forms of physical therapy, systemic medications, regional anesthetic approaches, including sympathetic or somatic nerve block injections or neuraxial infusions, spinal cord stimulation, destruction of sympathetic ganglia, and even amputation of affected extremities. Overall, across medical specialties, there is a growing emphasis on active physical therapy and on restoration of normal limb function as a key component of recovery. The quality of the evidence for many commonly performed procedures is relatively weak. Controversy persists regarding the relative importance of peripheral, autonomic, and central mechanisms in the initiation and maintenance of pain and limb dysfunction.
ders among children and adolescents had been described only in sporadic case reports and very small case series before the 1970s; since then, there has been a rapidly growing number of case series and clinical outcome studies. For purposes of this discussion, the term pediatric CRPS refers to occurrence in both children and adolescents. Pediatric CRPS seems different from adult CRPS in several respects, as listed in table 1.

In this issue of Anesthesiology, Dadure et al. report very favorably on the combined use of intravenous regional blockade with bupivacain along with distal continuous sciatic blockade in the popliteal fossa to treat a group of pediatric patients with CRPS who had not responded to 6 months of treatment with physical therapy and cognitive-behavioral treatment. Their results seemed extremely impressive. Patients showed rapid improvement in pain scores and limb function. For patients with CRPS restricted to the foot, ankle, and lower leg, continuous distal sciatic blockade using a popliteal fossa catheter has several potential advantages compared with epidural blockade, including avoidance of contralateral sensory and motor block, urinary retention, and hypotension. Sparing of contralateral strength and sensation as well as ipsilateral upper leg motor function facilitates ambulation and participation in active physical therapy. Continuous peripheral blockade is an emerging approach for children as well as adults after many types of extremity surgery.

These results, although impressive, should be viewed with some caution in view of the short duration of follow-up. Their report would have been far stronger had they reported on the pain scores, limb function, and school attendance of these children at 6 months or longer after the procedure. In-person evaluations are ideal, although there are practical difficulties in getting children and their parents to travel again to a tertiary center after they have become pain free. Although there are some limitations to mail- or telephone-based questionnaires (e.g., absence of a physical examination), these types of follow-up would still be helpful for assessing longer-term outcomes.

A second concern with the study of Dadure et al. relates to the study design, with a single-group, open-label, combination treatment. Without separate evaluation of intravenous regional blockade and continuous popliteal fossa blockade, it is difficult to determine which components of their treatment regimen were most important to improving outcomes. Pediatric trials are made more difficult by a number of factors, including limited numbers of patients in any single center and a general reluctance to use placebos or other control groups in the setting of chronic pain in a “vulnerable” population. Nevertheless, without some type of control condition and without separate evaluation of the two interventions being applied, conclusions about efficacy must be made with considerable caution.

Other forms of neuropathic pain also show marked differences between adults and children. Postherpetic neuralgia and trigeminal neuralgia occur only rarely in children. In adults with a brachial plexus injury, neuropathic pain seems quite common, severe, and persistent. In contrast, pain behaviors are only very rarely seen after perinatal brachial plexus injury. A recent case series found that pain behaviors and self-mutilation occurred more commonly in severely affected infants after nerve grafting procedures.

Animal models of nerve injury also show age-related differences in biologic consequences, in spontaneous pain-related behaviors, and in development of mechanical allodynia and hyperalgesia to mechanical or thermal stimuli. Infant rats have been studied extensively as a model for the ontogeny of pain responses. One of the more promising models for neuropathic pain in adult rats involves ligation of the tibial and peroneal branches of the sciatic nerve, with sparing of the sural nerve. In adult rats, this produces marked allodynia and other pain behaviors. Recent work by Howard, Fitzgerald, Beggs, and their colleagues examined the effects of these same nerve lesions in infant and adolescent rats (Simon Beggs, Research Fellow, University of Toronto, personal communication, October 2004). Remarkably, rats that underwent the tibial and peroneal nerve ligations before day 33 of life did not exhibit allodynia or hyperalgesia or related spinal cord immunohistologic changes as seen in older animals. This cutoff age in rats would correspond roughly to the age of 8 yr in humans. It is tempting to speculate that further study of the biologic bases of these age-related differences in rats might shed light on the rarity of CRPS in children before the age of 8 or 9 yr.

The role of female endocrine development in susceptibility to CRPS in childhood deserves further study. Some sex differences in pain responses in rats and humans are estrogen dependent. The marked lower extremity predominance in pediatric CRPS is not adequately explained. Children and adolescents commonly sustain both upper and lower extremity injuries in sports and other forms of play, but a Colles fracture at the wrist or a supracondylar fracture at the elbow only very rarely produces neuropathic pain in general, or CRPS in particular, in children and adolescents. In adults, workplace injuries and overuse syndromes are relatively common in the upper extremities, and these may be important contributing factors to the occurrence of upper extremity CRPS in these age groups.

Perhaps the most remarkable feature of most pediatric CRPS case series is that most subjects had near-complete resolution of limb dysfunction and disability, and a marked reduction in their pain scores. In many of these case series, improvement was accomplished for most patients with a regimen of active physical therapy, with or without an intensive cognitive-behavioral regimen, but without use of nerve blocking procedures or other...
more medically based interventions.25,27 Sherry et al.27 have reported relatively large case series of children with CRPS (their preferred term is reflex neurovascular dystrophy), showing high rates of resolution of pain and recovery of limb function using a regimen with active exercises, and some psychoeducational interventions. This group makes essentially no use of medications or nerve blocks. Sherry et al.39,40 emphasize the importance of individual and family psychological issues in the perpetuation of this condition. In the view of Sherry et al., nerve blocks are unnecessary and may be counterproductive because they reinforce the patient taking a passive, rather than active, role in his or her recovery. The role of psychological factors in CRPS in both adults and children is controversial.31–44

Many of the early pediatric case series that reported good recovery using physical therapy, with or without cognitive-behavioral treatment, involved admission of the patients to an inpatient rehabilitation unit that permitted many hours daily (e.g., 5–6 h) of physical therapy.25,26 In the current healthcare environment, at least in the United States, pediatric inpatient rehabilitation beds are relatively scarce, and there is great difficulty getting third-party payer approval for treating patients with CRPS in this type of milieu. Our group previously conducted a randomized prospective controlled trial of outpatient physical therapy and cognitive-behavioral treatment, with two groups differing in the frequency of physical therapy sessions.9 Both groups showed good improvement in pain scores and excellent improvement in limb function scores over the 6-week intervention period and at long-term follow-up over 2–5 yr. However, in our cohort, recurrent episodes were common (25% of patients), and nearly half of the patients at some point after the 6-week controlled trial received epidural infusions, lumbar sympathetic blocks, or both to treat persistent pain.

Some of the discrepancies in outcomes between groups may relate to differences in patient populations and referral patterns among centers. For example, among the patients in case series by pediatric rheumatologists, only a minority of patients had an identifiable injury, surgery, or trauma.25,27 Conversely, nearly 90% of our patients have had a discrete traumatic event that seemed to trigger their CRPS.9,26 These differences may reflect in part the specialties involved: A high percentage of referrals to our program come from orthopedic surgeons and neurologists. Recent work by Sethna et al.45 in our group examined quantitative sensory testing in a cohort of 55 pediatric patients with CRPS. Eighteen of these patients (33%) met criteria for CRPS II by showing sensory abnormalities in the distribution of a peripheral nerve on careful sensory and psychophysical evaluation.

Complex regional pain syndrome has remained a puzzle for more than 140 yr.46 The report of Dadure et al. adds another potential treatment for children and adolescents with CRPS. Further mechanistic study and clinical trials may help to clarify which patients should receive which treatments, and in which sequence.3

Charles B. Berde, M.D., Ph.D.,* Alyssa Lebel, M.D.* * Department of Anesthesiology, Perioperative and Pain Medicine, Children’s Hospital, and Harvard Medical School, Boston, Massachusetts. charles.berde@childrens.harvard.edu

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**Table 1. Differences between Adult and Pediatric CRPS**

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<th>Clinical Feature</th>
<th>Adults</th>
<th>Children and Adolescents</th>
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<tr>
<td>Extremities affected</td>
<td>Upper &gt; lower</td>
<td>Lower &gt;&gt; upper (6:1)</td>
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<tr>
<td>Sex ratio</td>
<td>Moderate female predominance (2–4:1)</td>
<td>Marked female predominance (7:1)</td>
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<tr>
<td>Prognosis</td>
<td>Excellent recovery in most cases</td>
<td>Excellent recovery in most cases</td>
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CRPS — complex regional pain syndrome.
45. Sethna NF, Meier P, Zurakowski D, Berde C: Cutaneous sensory abnormalities in children with CRPS types I and II. Abstracts, Combined American and Canadian Pain Societies, May 2004; Vancouver, BC, Canada