Epidural Clonidine Treatment for Refractory Reflex Sympathetic Dystrophy

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REFLEX sympathetic dystrophy (RSD) is a syndrome that can pose problems in its management because it can be of extended duration and may be relatively refractory to treatment with opioids. Preclinical work has shown that spinal $\alpha_2$ adrenoceptors can regulate nociceptive processing by an action on small primary afferents. Preclinical data in several species have shown the safety of spinal clonidine, and clinical studies have shown its efficacy in postoperative and cancer pain. Rauck et al., in this issue of the journal (page 1163), examined the effects of the $\alpha_2$-adrenoceptor agonist clonidine given epidurally to patients suffering from a pain state associated with RSD. In these studies, two doses of clonidine (300 and 700 $\mu$g) and placebo were delivered in a blinded randomized fashion through cervical or lumbar epidural catheters, respectively, for patients suffering from RSD of the upper or lower extremities. These studies revealed a reduction in the visual analog scale rating score for patients with either an upper or a lower extremity syndrome, with no difference in pain score between the two clonidine doses (although there were fewer side effects with the lower dose.) After the study, 19 patients continued receiving clonidine for periods ranging from 7 to 225 days with continued improvement in the pain report. These well controlled studies thus provide a clear indication that spinal $\alpha_2$ receptors can regulate the nociceptive processing that is engaged by the pathologic processes evoked by the original injury leading to the hyperpathia common to this syndrome.

Several points are of interest. First, although the mechanisms of this effect are not clear, the dissociation between the short-lasting hypotension and the longer lasting pain relief suggests that the changes in pain did not arise simply from a block of sympathetic function. Second, there was no difference between the analgesic efficacy of the two doses used. This suggests that there may be a plateau effect in the efficacy of the agent. Whether this plateau is due to the fact that clonidine is a partial agonist or that the pain state in these patients has several components, one of which is $\alpha_2$-insensitive, cannot be determined. Conversely, the ability to produce prominent pain relief with either of the two doses suggests that yet further reductions in dose may be possible (resulting in even fewer side effects). Given that previous studies in cancer patients and postoperative pain patients have used larger doses to obtain pain relief, one might argue that the $\alpha_2$-responsive component of the present pain state is, in fact, extraordinarily sensitive to this spinal modulation. These data suggest that further investigations are in order. Several questions that arise relate first to the consideration of the long-term efficacy of spinal clonidine. Second, it would be insightful to have crossover studies using epidural morphine and clonidine to determine whether there are definable differences in the efficacy of $\mu$-opioid versus $\alpha_2$ receptors in regulating the RSD pain state. Such information would shed light on mechanism. Finally, ample preclinical data have shown that there is a significant $\mu/\alpha_2$ interaction that may lead to further reduction in dose and enhancement of efficacy. In short, this is a provocative report.

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Use of the Electrospinegram for Predicting Harmful Spinal Cord Ischemia during Repair of Thoracic or Thoracoabdominal Aortic Aneurysms

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MANAGEMENT of patients with thoracoabdominal aneurysms remains one of the great challenges in cardiovascular surgery and anesthesia, and severe spinal cord injury is one of the common complications of such procedures. Many methods have been tried in an effort to prevent paraplegia, including systemic and in-
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trathecal “protective” drugs, spinal cord cooling, cerebrospinal fluid drainage, systemic hemodynamic manipulations, and distal shunts. Unfortunately, no method(s) has proved to be effective (although few have been tested systematically), and none is widely employed.

One approach would be to devise a better method for detecting the onset of spinal cord ischemia, so that potentially useful therapies might be applied promptly to those patients who would benefit most. This requires some means of monitoring spinal cord function monitoring. Somatosensory evoked potentials (SSEPs) recorded from the scalp after peripheral nerve stimulation have been widely employed, but this method has serious limitations. It is insensitive to selective motor tract ischemia (i.e., there is a documented potential for false negative recordings), and SSEP can be abolished by peripheral nerve (as distinct from spinal cord) ischemia, leading to false positives (i.e., a loss of waveform when there is no actual spinal cord ischemia). Motor evoked potentials (MEPs; using either magnetic or electrical stimuli delivered at the scalp) would seem to offer some advantages, but their extraordinary sensitivity to anesthetics and temperature, for instance, has prevented their widespread use.

In the current issue of Anesthesiology, Stühmeier et al. (page 1170) present their clinical experience with a method that has obvious promise. Thoracic and lumbar epidural catheters were placed, allowing both the stimulus and the conducted response to be applied to and recorded from the spinal cord itself. This avoids some of the problems that plague both standard SSEPs and MEPS. It can be argued that this method has no false negatives, because any loss of potentials should represent true spinal cord ischemia (even if this is not followed by paraplegia), and their data indicate that almost 70% of patients indeed have some degree of ischemia. More importantly, they showed that patients for whom the electrospinogram was lost within the first 15 minutes of aortic occlusion are at very high risk for clinical cord injury (30%). Given this, it might be reasonable to ask that the surgeon wait for 15 minutes after aortic clamping before “permanently” dividing the aorta—although it remains to be seen just what alternative surgical approach might be used in such a situation, particularly since the placement of an axillofemoral shunt did not appear to be of great benefit. Perhaps the method would be better used to define a patient population in which therapeutic interventions might be tried without the statistical “dilution” encountered when large numbers of low-risk patients are included in a study.

It is important to emphasize that the authors have not shown that the electrospinogram is “better” than traditional SSEPs (and it would have been helpful if standard SSEPs had been recorded simultaneously), nor have they shown a clear benefit from such monitoring, because they made no effort to intervene when the electrospinogram was lost and because their overall incidence of paraplegia is not clearly different from that reported by others. However, if this method were applied properly in the context of systematic trials of various treatments or protective maneuvers, it might aid in substantially reducing the number of catastrophic neurologic complications of otherwise lifesaving surgery.

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Effects of Inhalational Anesthetics on Biochemical Events in Growing Neuronal Tips

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ANESTHESIOLOGISTS have had a long-standing concern that inhaled anesthetics given during the developmental period might produce adverse outcomes. In well defined animal models, the administration of inhaled anesthetics during the perinatal period has been associated with morphologic and behavioral abnormalities. The type and severity of these teratogenic effects depend on the animal model examined and the anesthetic administered. For example, marked anomalies in the fetal central nervous and skeletal systems develop after exposure of pregnant rats (on the 9th day of gestation) to nitrous oxide. Pregnant rats given other gaseous and volatile anesthetics do not exhibit an increased incidence of fetal macroscopic lesions, although more subtle (e.g., behavioral) changes in the offspring remain possible.

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