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Idiopathic Chronic Hiccup (ICH): Phrenic Nerve Block Is Not the Way to Go

Letter to the Editor:—We read with interest the case reports by Okuda et al. regarding the use of a nerve stimulator for phrenic nerve block in the treatment of hiccups. We agree with the authors (and the literature) that phrenic nerve block may not (and most probably will not) be effective and that it might (and most probably will) cause not only a reduction in vital capacity, but also dyspnea and hypoxia. However, we strongly object to their (implied) opening statement that failure of such simple therapeutic attempts as stimulation of the pharynx, compression of the eyeballs, gastric lavage, and sedation or inhalation of carbon dioxide warrants such heroic trials of "last resort" as phrenic nerve block.

During adult life, transient hiccuping is a common (albeit irrelevant) occurrence, associated most often with gastric distention, sudden temperature changes, or emotion.^{2,3} The transient hiccuping either resolves spontaneously or responds to simple nonpharmacologic measures. Hundreds of these simple hiccup-terminating maneuvers have been described, and for some of them a physiologic explanation can be given. It seems that activation of the vagus nerve is therapeutic in cases of transient hiccuping, as opposed to vagal interruption, which potentiates such episodes.^{4,5}

The hiccup can, however, become a "fixed-action pattern" and thus persist. Despite the finding that more than 100 medical conditions have been associated with hiccup, more often than not an organic cause will not be discovered. For this idiopathic chronic hiccup (ICH), the simple hiccup-terminating maneuvers are not effective, and pharmacologic therapy is needed.

Although virtually all available drugs have been used more or less

GABA

H₂N COOH

H₂N COOH

H₂N COOH

Gabapentin

Baclofen

The shaded area represents the gamma-amino-butyric acid (GABA) molecule. Gabapentin consists of a GABA molecule covalently bound to a lipophilic cyclohexane ring. The substance does not have any intrinsic GABAmimetic activity but seems to promote the release of endogenous GABA. Baclofen, while chemically a very simmilar compound, it has direct GABAmimetic activity restricted however to postsynaptic GABA type B receptors.

Fig. 1.

successfully to suppress hiccuping,^{7,8} more recently Baclofen, a gamma-aminobutyric acid (GABA)-agonist used in the therapy of muscle spasticity, has been suggested as a hiccup therapy.^{9,10,11,12,13,14} Baclofen is believed to exert its antispastic effects by increasing the threshold for excitation (cell hyperpolarization), which depresses synaptic transmission in the spinal cord. Recently, two ICH studies reported similar results produced by a combination therapy using cisapride, omeprazole and Baclofen (COB).^{13,15} Cisapride, omeprazole, and Baclofen produced at least significant hiccup relief in 60% of all patients with ICH treated.

In those cases in which the hiccup is not responding to Baclofen, Gabapentin, a GABA-derivative used in the therapy of seizures and spasticity, also can be effective. ¹⁶ Our ongoing trials in which cisapride, omeprazole, and Baclofen therapy nonresponders are either switched to Gabapentin (COG) or receive Gabapentin in addition (COBG) seem extremely promising. ¹⁷

Although pharmacologic therapy will not always cure ICH, substantial relief is most often achievable. It is true that simple hiccupterminating maneuvers such as the ones described in the case report, although very popular, are not likely to be effective for ICH. Their failure does not, however, warrant proceeding directly to potentially damaging "last-resort" maneuvers, such as phrenic nerve interruptions. The logical next step is the use of appropriate drugs in an appropriate dosage for an appropriate duration of time.

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In Reply:—We did not claim that "the failure of simple hiccupterminating maneuvers warrants proceeding directly to potentially damaging 'last-resort' maneuvers such as phrenic nerve interruptions." Instead, we fully agree with Dr. Petroianu's claim that "the logical next step (after failure of simple maneuvers) is the use of appropriate drugs." Our statement, "block of the phrenic nerve has been suggested as 'the last resort," *1 means that the use of this block should be considered if other less-invasive methods, including the use of potentially effective drugs, have failed. Most patients with intractable hiccups are referred from other departments in which a variety of methods, including potentially effective drugs such as baclofen, have been used in vain, although we did not described these explicitly.

The main point we made in our report¹ was not advocating the phrenic nerve block but that the use of electric nerve stimulation enables one to avoid unnecessary attempts at repeated blocks. In fact, in one of our patients, we judged that a successful block of the phrenic nerve would not decrease hiccups and abandoned this method. There is no "holy grail" for intractable hiccups: neither baclofen nor phrenic nerve block is always effective. The importance—we believe—is to judge whether each treatment method is effective in each patient and to stop ineffective methods at an early

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Hypoxic Apnea, Epidural Anesthesia, and Infants

To the Editor:—In reviewing the recent report by Hogan *et al.*¹ regarding hypoxic apnea in rabbits receiving epidural anesthesia, I was struck by the similarity of their report to a phenomenon seen in hypoxic newborn and premature infants: to wit, a brief hyperventilatory response followed by hypoventilation and apnea.² In many ways, the newborn or premature infant is similar to the authors' rabbit-with-epidural-anesthesia model. Obviously, the blood pressure of the newborn or premature infant is much lower than that in an older child or adult. At the same time, infants

exhibit primarily parasympathetic tone; this is seen in their exaggerated bradycardic responses to laryngoscopy, anesthetics, and succinylcholine, and in the absence of hypotension after pharmacologic sympathectomy with spinal or epidural anesthesia. These similarities between the rabbit-with-epidural-anesthesia model and the newborn or premature infant led me to wonder whether there might be a common mechanism for hypoxic apnea and a role for blood pressure augmentation, adrenergic agonists, or vagolytics in the prevention or treatment of infant apnea.