Remifentanil slows more than seizures

Editor—A 22-year-old woman presented for vagal nerve stimulator (VNS) insertion by the neurosurgeons. She suffered intractable epilepsy with a large number of seizure types. She was practically unresponsive to medical therapy and had no demonstrable discharging cerebral focus suitable for resection.

Induction of anaesthesia was with propofol 1.5 mg kg$^{-1}$ supplemented by a remifentanil infusion initially at 0.5 µg kg$^{-1}$ min$^{-1}$, reduced to 0.25 µg kg$^{-1}$ min$^{-1}$ over the remainder of the case with sevoflurane 0.5 MAC maintenance. The device was placed around the left vagal trunk. Upon testing, immediate p-wave asystole was seen on the electrocardiograph with loss of the pulse oximeter and radial arterial line tracings, and the peripheral pulse. This lasted approximately 5 s until the device could be turned off, at which point sinus rhythm was restored with visible p-wave capture and a return to baseline haemodynamic variables.

The device was tested once more at the end of the procedure, when the remifentanil infusion had been turned off for approximately 5 min, and sinus rhythm was maintained. The patient was readmitted after 2 weeks for testing of the device under electrocardiographic monitoring, which was uneventful. She has had no apparent cardiovascular sequelae after 8 months of device usage, with a useful reduction in seizure frequency.

Although the VNS device is well known to neuroscience centres, there is little experience of it in the anaesthetic community. Approximately 11–12 000 devices have been inserted worldwide,$^1$ and VNS was granted FDA approval in 1997 to treat ‘adults with refractory focal epilepsies not candidates for epilepsy surgery’. While the mechanism of action is unknown, 50% of patients experience a 50% reduction in seizure frequency.$^2$

Despite stimulating the left vagal nerve directly, bradyarrhythmias and asystole are not frequently reported in the literature with this technique.$^3$ $^4$ All phenylpiperidines, and remifentanil in particular, are potent mediators of vagal bradycardia and have produced asystole in unrelated circumstances. The left vagal nerve is understood to innervate the atrioventricular node, and the right the vagus sinoatrial node; the occurrence of p-wave asystole on activating the device supports this. However, the fact that this bradycardia could not be reproduced in the absence of remifentanil, particularly after discontinuing the infusion for close to two context-sensitive half lives (approximately 5 min) would suggest that remifentanil at least facilitated ventricular asystole. It is likely that the vagotonic effects of remifentanil are dose dependent, at least for the individual patient.

At the Royal Victoria Hospital, Belfast, we have inserted 28 VNS devices with one case of asystole (incidence 3.6%), all in association with remifentanil. In contrast, a frequency of one case in 125 (0.8%) has been reported from King’s College, London,$^1$ but unfortunately the use of remifentanil was not detailed. It would be desirable to identify any risk factors at initial VNS testing that could identify subsequent bradyarrhythmias and syncope as it appears that asystole, at least in conjunction with remifentanil, may have a poor predictive value.

One concern with phenylpiperidines in this population is their well-recognized potential to lower the seizure threshold and promote EEG changes and frank seizures.$^5$ $^6$ It is possible that a proportion of this group of ‘brittle’ epileptic patients may suffer overt or occult seizures during anaesthesia potentiated by remifentanil, but masked in many cases by neuromuscular blockade.

The implications of this case are to consider carefully the risks of remifentanil when providing anaesthesia for VNS insertion or its use during subsequent anaesthetics in patients with a device in situ. Remifentanil has potent vagotonic effects which are desirable in many patients (e.g. those with ischaemic heart disease). However, the facilitation of bradyarrhythmias with VNS and the increased likelihood of seizures are two important factors to consider despite remifentanil’s ideal pharmacokinetic profile.

 Provision of anaesthesia for patients with a VNS in situ could include prophylactic antimuscarinic administration and requires immediate access to temporary ventricular pacing.

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