To the Editor

Role of Midazolam in Parkinsonian Tremors: To Use or Not to Use

Resting tremors are one of the extremely disabling cardinal symptoms of Parkinson's disease (PD). The intraoperative precipitation of such a symptom during deep brain stimulation can impose many challenges for anesthesiologist as well as for the surgeon. Here we have highlighted the effect of midazolam during such an event.

Case 1- A 82-year-old patient with PD was posted for the battery replacement under monitored anesthesia care with remifentanil (0.05 mcg / kg / min) and propofol (25 mcg / kg / min) infusion. He had previously undergone deep brain stimulation (DBS) with bilateral sub thalamic nuclei (STN) electrode insertion and battery placement. During the skin closure, patient started tremors on left hand (same side of surgery). Though the patient was completely sedated at the time, 0.5 mg of intravenous midazolam was given and surprisingly tremors were abolished within a few minutes.

Case 2- A 43-year-old otherwise healthy PD patient was scheduled for DBS with bilateral STN electrode insertion and battery placement. Initial part of procedure was done in remifentanil (0.05 mcg / kg / min) and propofol (25 mcg / kg / min) infusion. She suddenly started tremors on left hand during left side electrode insertion. In this event too, patient was calm and mildly sedated. As these movements were distracting the surgical field, 0.5 mg of intravenous midazolam was given. Interestingly, hand tremors aborted within a few minutes.

The resting tremors of PD may precipitate during surgical stress or anxiety.[1] Though both patients seemed to be calm and mildly sedated, subtle surgical stress and anxiety coupled with off medications for prolonged time, might precipitate this distressing symptom. Occurrence of intraoperative tremors can interfere with patient's monitoring (electrocardiography, pulse oximeter and blood pressure measurement), chances of de-cannulation of intravenous or arterial lines and importantly slight movement at surgical field can distract the electrode insertion and produce catastrophic complications. The pathogenesis of PD tremors is a complex mechanism and still not fully understood. The proposed mechanisms include the dopamine - nor adrenaline interactions at substantia nigra, cerebello-thalamic circuit activation and role of locus coeruleus.[2,3] In animal experiments, midazolam has shown to produce its effect on many of the above mentioned sites or pathways thus likely to interfere with tremor genesis and treatment.[4] On the other hand, some reports suggested that midazolam used for sedation may augment or even precipitate extra pyramidal symptoms.[5] However, these cases were found in normal patients without PD. Thus it is likely that midazolam may produce different forms of interactions at different structures of brain of patients with or without PD. This hypothesis needs further research.

In conclusion, intraoperative tremors can be precipitated even in calm or sedated patients with PD. Low dose midazolam is effective to abort such an episode and hence may be used as first alternative.

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To the Editor

CT Perfusion in the Management of Acute Stroke

The phrase "time equals brain" is a well established mantra in stroke medicine. The quest to prolong the therapeutic window is just as crucial as identifying the appropriate patient population in which to begin the definitive therapy that can be fraught with hazards. It is well established that thrombolytic therapy can significantly reduce morbidity and mortality within a 4.5 hour window for some stroke patients[1]. The determination of this patient group is not as clear cut. In addition to evaluating the patient clinically, the choice of diagnostic imaging can be confusing to practitioners as the technology continues to evolve at a pace faster than our understanding of the disease. The most up to date guidelines by the American Stroke Association[2] and the Canadian Stroke Strategy Best Practices and Standards Writing Group[3] both agree that obtaining a non-enhanced head CT and when available and indicated, MRI diffusion weighted and fluid attenuated inversion recovery sequences. Until this writing, CT Perfusion (CTP) investigations are absent from the Canadian recommendations and the Americans only recommend CTP for cases presenting more than three hours after onset.

In a retrospective institutional survey[4], we reviewed the clinical management decisions with one vascular neurologist and one general neurologist (who covers the stroke service on call) for 15 patients who presented with acute stroke and had CT

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perfusion done at the time of presentation. Two sets of managements were arrived at, one determined from only the clinical presentation and the plain head CT-ASPECT score. The second plan was determined with the added CTA and CTP findings. These retrospective management plans were then compared with the actual management of these patients. The reviewing neurologists did not alter the treatment decisions based on the CTP findings because to date, there has been no randomized clinical trial testing CTP findings in acute stroke. So in principle, there was no change in decision making based on CTP information. But in practice, management of two patients was changed based on the CTP results and other clinical findings. In two other patients in our group, treatment did not change the imaging outcome, which was predicted by CTP. CT Perfusion information is being used at our center to determine who might benefit from intra-arterial tPA on a case by case basis.

We believe that the dichotomy of the principle and practice in implementing CTP in the care of acute stroke patients is due to the following important reasons. Firstly, though the physiological basis of CTP imaging findings are theoretically sound, there is no level one evidence to support the extent to which CTP information can change patient management. Secondly, the experience and knowledge in interpreting CTP is still limited. CT Perfusion is currently useful for its qualitative evaluation of cerebral perfusion but limited in its quantitative evaluation. This is largely due to the different post processing algorithm followed by different vendors. Thirdly, there is no established universal standardized protocol for CTP imaging. Due to a lack of good evidence, no established methodology has been established and as a result, each institution has tailored their unique protocol.

When appropriately applied, CTP imaging can be a good predictor of the radiological outcome of stroke. Much has been dedicated to evaluating CTP's theoretical underpinnings, technical implementations and image interpretation. Clinically however, we cannot treat the image on the screen and currently, there is no good evidence of how CTP results can help clinicians manage acute stroke therapy. There is still a stark principle and practice dichotomy in its clinical application of the acute stroke patient care. Before this modality can be incorporated into routine clinical practice, a strong evidence base needs to be established from which decisions can be made. We ultimately need a well-designed randomized controlled trial. Most of the therapeutic trials are based on the time window and have not shown a huge benefit in terms of final outcome. We believe this was because patients were selected based on time window, but every patient has a unique time window.

With the wide-spread availability of CTP penumbra imaging, we should consider incorporating the viable tissue window in addition to (or perhaps even instead of) the time window alone when making treatment decisions[5]. A therapeutic trial based on treatment to salvage viable tissue based on CTP penumbra imaging instead of by time of onset is the need of the hour and in our opinion is a move towards improved patient management.

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To the Editor

Acute Neurological Complication in Awake Craniotomy; - A Diagnostic Dilemma

Perioperative neurological complications are less frequently associated with patients undergoing awake craniotomies.[1] However, sometimes intraoperative neurological events warrant alternate diagnosis and management especially, if the cause is not related to surgery. After obtaining written informed consent from the patient, we have highlighted this issue.

A previously healthy young man was admitted to our hospital for investigation and treatment of headache and seizures, for few months duration. Magnetic resonance imaging demonstrated a mass on left frontal lobe. As the lesion was near the speech center, the patient was scheduled for an awake craniotomy. Surgery proceeded under monitored anesthesia care (MAC), with intravenous infusions of remifentanil (0.05 mcg /kg /min) and propofol (25 - 30 mcg / kg / min). All standard monitors were attached. Cyclic measurement of noninvasive blood pressure (NIBP) on left arm was stopped after right radial arterial cannulation. Left sided scalp nerves block were performed. The patient's neck was tilted to his right side and a soft bolster was placed under the left shoulder to preventing excessive stretch of the brachial plexus. The patient was comfortable and mildly sedated. At the time of tumor resection, all infusions were