

Use of dexmedetomidine during deep brain stimulation for Tourette Syndrome

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Use of dexmedetomidine during deep brain stimulation for Tourette Syndrome: a case report and review of the literature

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Summary

Deep brain stimulation is invasive and used in selected patients with intractable Tourette Syndrome. The anaesthetic technique of first choice during implantation of the electrodes is an awake technique with local anaesthetics and conscious sedation. The anaesthetic management can be challenging, especially in Tourette Syndrome patients due to sudden movements. The anaesthetic goal is to have a comfortable patient during the procedure with minimal influence of pharmacological agents on microelectrode recordings. Here, we describe our experience with the use of an intravenous dexmedetomidine infusion during deep brain stimulation in a patient with Tourette Syndrome. We discuss the effects on the microelectrode recordings and clinical testing. Finally, we describe the advantages of dexmedetomidine as a sedative agent in Tourette Syndrome patients during deep brain stimulation and the pharmacological effects of dexmedetomidine on the basal ganglia.

Introduction

Tourette Syndrome (TS) is a childhood-onset chronic complex neuropsychiatric disorder characterised by multiple motor tics plus one or more vocal tics and is associated with psychiatric co-morbidities. A small proportion of patients are refractory to pharmacological or behavioural therapy. Deep brain stimulation (DBS) has been introduced as a therapeutic approach for addressing some of the intractable tics of TS [1].

A successful outcome from DBS depends on the correct positioning of the electrodes on a specific target. Placement of the electrodes is by means of radiological images, or with the use of microelectrode recordings (MER) and macro-stimulation testing [2]. In our hospital, we use MER routinely for positioning of the electrodes.

A variety of anaesthetic techniques have been described for DBS and largely depend on the clinical experience of the surgical and anaesthesia team. The most commonly used technique is the "awake technique," whereby local anaesthesia is used in combination with conscious sedation [3].

The anaesthetist is confronted with several challenges: creating a comfortable patient with suppression of sudden movements, minimising interference of anaesthetic agents with electrophysiological testing and having an appropriately lucid patient to allow for clinical testing. In the literature, various anaesthetics have been used for conscious sedation in patients undergoing DBS surgery, however the majority of these affect neuronal activity of the basal ganglia neurons due to activation of gamma-aminobutyric acid (GABA) receptors [4].

Dexmedetomidine, an α_2 -agonist with sedative properties, does not influence GABA receptors. Little is known regarding the clinical and neurophysiological effects of continuous infusions of dexmedetomidine during DBS procedures in patients with TS. We describe our experience in a patient with TS who underwent DBS insertion using dexmedetomidine and review the literature of its effects on the basal ganglia.

Report

A 19-year-old male presented for bilateral DBS insertion following an 11 year history of TS. The condition initially presented with simple motor tics such as head shaking that later progressed to involve the rest of his body. They became more severe during childhood and adolescence. At the time of the surgery, he suffered from severe and almost continuously present motor tics, including eye blinking, head shaking and jerks of shoulders, arms, abdomen and legs. Moreover, he had mild vocal tics such as sniffing and coughing. Medication (clonidine, pimozide, haloperidol, quetiapine) and behavioural therapy (exposure, habit reversal, relaxation techniques) had been ineffective in the past. Pre-operatively, the patient scored 28 on the Yale Global Tic Severity Scale which is a clinical rating instrument to evaluate tic severity, and was thus deemed suitable by a multidisciplinary team for bilateral DBS insertion of the anterior segment of the internal globus pallidus.

In the first phase, a Leksell frame was placed. Local anaesthesia was achieved with a combination of levobupivacaine 2.5 mg.ml^{-1} and lidocaine 5 mg.ml^{-1} (a total volume of 20 ml) with epinephrine. During positioning of the frame, no sedation was administered. The patient was transported to the operating room and standard AAGBI monitoring applied (three-lead electrocardiogram, non-invasive blood pressure monitoring, and pulse oximetry). Oxygen 3 l.min^{-1} was administered via a nasal cannula with capnography monitoring. Intravenous access was obtained and invasive arterial blood pressure monitoring commenced. After positioning of the patient on the operating table, an infusion of dexmedetomidine $0.5 \text{ }\mu\text{g.kg}^{-1}.\text{h}^{-1}$ was started. Acetaminophen and cefazolin were given. During the surgical procedure, including MER and clinical testing, the patient received the same amount of dexmedetomidine. The patient was calm and comfortable with a modified Observer's Assessment of Alertness/Sedation score (OAA/S) between 4 and 5. Good quality multi-unit recordings were available to define the internal globus pallidus borders (Figure 1). The total duration of the MER was 20 minutes per side. A stimulation test was performed; no side effects were observed at a maximum stimulation amplitude of 4 mA. Based on the absence of side effects and the length of the trajectory in the internal globus pallidus, the final electrode position was chosen. A more detailed description of the surgical procedure has been described previously [1].

During the procedure, the maximum systolic blood pressure was between 90 and 125 mmHg and a heart rate between 60 and 85 beats per minute. The respiratory rate was between 15 and 23 breathes per minute with oxygen saturations of 100%.

In the second phase, in which the pulse generator was implanted, dexmedetomidine was discontinued. General anaesthesia was induced with propofol 2 mg.kg^{-1} and sufentanil $0.7 \text{ }\mu\text{g.kg}^{-1}$

¹ and the airway was secured with a laryngeal mask and intermittent positive pressure ventilation was initiated. Anaesthesia was maintained with an end-tidal sevoflurane concentration of 2.5-3.0% until the pulse generator was implanted in a subcutaneous pocket in the right lower abdominal quadrant.

Discussion

Studies have demonstrated that α_2 -adrenoreceptor agonists are a therapeutic option for TS patients with mild to severe tics. Therefore, the choice of dexmedetomidine appears to be a sensible choice for sedation in TS patients. In addition to its sedative and analgesic properties, it suppresses tics effectively. Several small studies have been published in which dexmedetomidine was used during DBS surgery. Most of these studies have been performed in patients with Parkinson's disease or other movement disorders. It has been suggested that low-dose dexmedetomidine does not impact on the quality of MER of the subthalamic nucleus and internal globus pallidus [5]. Other reports, however, suggest that dexmedetomidine does influence the MER, even at low dose [1,4]. Yet another report demonstrated that dexmedetomidine did not interfere with the MER, although it was not clear which concentration was used [5]. In our patient, we did not use a loading dose of dexmedetomidine because this is associated with more side effects. For procedural sedation, it is advised to use dexmedetomidine in a range of $0.2 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ to $1.0 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ until a desired clinical effect is achieved, although the effects of high dose dexmedetomidine on the MER are not clear.

A dexmedetomidine infusion was commenced after patient positioning at a continuous rate of $0.5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ until induction of general anaesthesia for pulse generator implantation, obtaining good quality MER in the internal globus pallidus. Clinical testing was possible, although at the end of the procedure it took longer to awaken our patient, probably due to accumulation of dexmedetomidine.

Dexmedetomidine is a selective α_2 agonist, similar to clonidine, but with a greater affinity for the α_2 receptor ($\alpha_1:\alpha_2$ ratio of 1:1620 vs. 1:220 respectively). It has a rapid onset of action with a distribution half-life of 6 minutes and a terminal half-life of 2 hours (compared with 12-16 hours for clonidine). Due to its short half-life, the clinical effect is short following discontinuation and, theoretically, this should lead to a reliable MER registration and clinical testing. However, following prolonged use clinical recovery may take longer.

As a sedative agent, dexmedetomidine has a favourable working profile. A major advantage is the minimal respiratory depressant effect. Administration of dexmedetomidine initially causes an increase in PaCO_2 , but is followed by an increase in the respiratory rate, known as the hypercapnic arousal phenomenon.

The haemodynamic stability in patients undergoing conscious sedation with dexmedetomidine is a result of a dose-dependent activation of the central and peripheral α_2 receptors, which leads to a reduction of heart rate and a decrease of the systemic vascular resistance. Another advantage is suppression of the stress response, leading to fewer fluctuations of systemic blood pressure, which is ideal during electrode insertion into brain parenchyma, in order to reduce the risk of intracranial haemorrhage. However at higher doses, or after bolus administration, this can lead to a transient episode of hypertension as a result of selective activation of the peripheral post-junctional α_1 -receptors or the peripheral α_{2B} -receptors [6].

The most common side effects include bradycardia, hypotension and nausea and vomiting. In addition, there are reports of paradoxical agitation when higher doses of dexmedetomidine are used which can lead to significant complications [4].

The successful use of dexmedetomidine during microelectrode recordings depends upon the effect of the selective α_2 agonist on the basal ganglia neuronal firing properties. In the rat basal ganglia only the α_{2c} -receptor is expressed. This receptor is mainly present in the caudate-putamen, nucleus accumbens and the islands of Calleja and probably only on nerve fibres in the pallidum [7]. In a post-mortem human brain study α_2 -adrenergic receptors were only found in the pars lateralis of the globus pallidus [8]. Dexmedetomidine thus has a sedative effect without

influencing the neuronal firing properties of pallidal neurons because the amount of α_2 -receptors is very low or even absent in the globus pallidus.

The working mechanism regarding the sedation and analgesic effects of dexmedetomidine on the basal ganglia has not been elucidated yet. It has been hypothesised that the sedative and analgesic effects are the result of stimulation of the α_{2A} and α_{2C} subtypes in the cortex and thalamus. Additionally, it is thought that the analgesic effects are a result of stimulation of the α_2 -receptors leading to inhibition of nociceptive neurons in the dorsal horn and reducing the release of substance P [6]. Another theory is that the sedative effect is achieved by a decreasing activity of neurons in the locus coeruleus, thereby increasing the activity of inhibitory GABAergic neurons in the ventrolateral preoptic nucleus [9]. The neuronal firing properties of the globus pallidus might therefore be indirectly influenced by the effect of dexmedetomidine on the striatal α_2 -receptors. In comparison, a very high expression of GABA receptors is present in the basal ganglia and globus pallidus. Therefore, GABAergic sedatives will have a much more profound effect on the firing properties of basal ganglia neurons than dexmedetomidine.

In summary, we evaluated the use of dexmedetomidine as a sedative agent during deep brain stimulation for a patient with TS. In this category of patients, it is important to create a safe environment with adequate tic reduction for the patient in which MER registration and clinical testing are possible. Dexmedetomidine is a beneficial sedative agent for DBS procedures due to a favourable mechanism of action and minimal interference with MER. We recommend not discontinuing dexmedetomidine during MER.

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Competing Interests

No external funding or competing interests declared.

Image

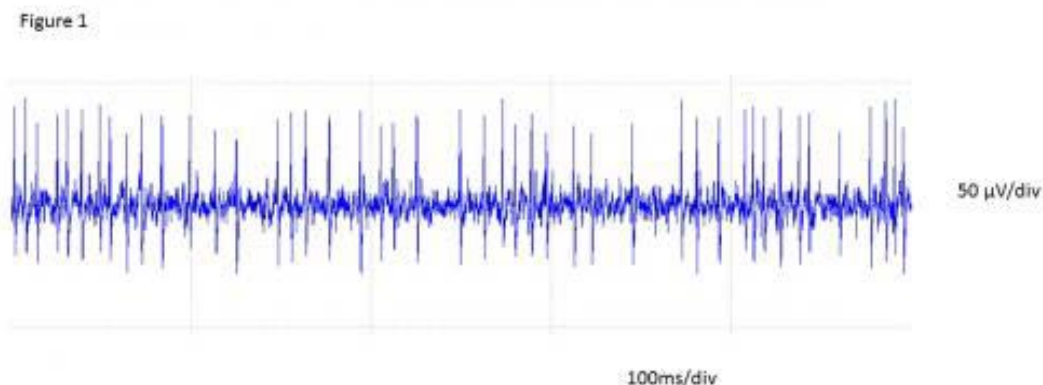


Figure 1. Microelectrode recordings of the globus pallidus.

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