Vagus nerve stimulator in a patient with Angelman Syndrome. A challenge for the anaesthesiologist.

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14 year-old male with Epilepsy

- Angelman Syndrome
- Developmental delay, speech disorder, ataxia, microcephaly and myoclonus epilepsy.
- Levothyroxine, Valproic Acid, lamotrigine, clonazepam, brivaracetam, perampel, and primidone

Vagus nerve implantation surgery

General anaesthesia

- Premedication: 1 mg midazolam, 50 mcg fentanyl and 0,4 mg atropine .
- Induction: 150 mg propofol and 10 mg rocuronium
- Maintenance: propofol, remifentanyl and cisatracurium.
- Fentanyl 100 mcg, cefuroxime 1,5 g, dexamethasone, ondansetron 4 mg, ranitidine 50 mg, metamizole 2 g.
- Extubation: without reversal agents.

Angelman syndrome (AS) is a genetic disorder most commonly caused by a maternal deletion of the ubiquitin-protein ligase (UBE3A) gene at region 15q11-q13. This deletion affects the gamma-amino butyric acid (GABA) (A) beta-3 receptor subunit gene. It is characterized by a severe developmental disability, microcephaly, ataxia, seizures, sleep disturbances, idiosyncratic movements and behaviours, the dominance of the vagal tone with potential refractory bradyarrhythmia and airway difficulties.

The majority of currently used anaesthetics affect the CNS through the GABA system. These patients are at increased risk for complications during the administration of anaesthesia due to modified receptor kinetics and pharmacodynamics unpredictability. There are few studies with AS patients and they show different results and recommendations³. Discrepancies involve hypersensitivity versus insensitivity to hypnotics (both volatile and endovenous), benzodiazepines and neuromuscular blockers.

AEDs must be maintained perioperatively, which can alter the metabolism of drugs related with cytochrome p450 enzyme. Drugs have different effects on seizure threshold and those which predispose patients to seizures should be avoided, as ketamine² and enflurane. Benzodiazepines, propofol and thiopental can be useful due to the enhanced anticonvulsant effect that they have.

During the preoperative assessment we have to establish airway craniofacial anomalies, muscle atrophy and

hyperflexion of the extremities, which can make them be more susceptible to the effects of neuromuscular blocking agent.

We should not underestimate the dominance of vagal tone. It may be originated centrally and may be induced by changes in intrathoracic pressures and Valsalva-like maneuvers during the bouts of laughter. In extreme cases, patients have had bradycardia followed by ventricular asystole and cardiac arrest during surgery with general anesthesia. Preoperative treatment with atropine or glycopyrrolate dampens the vagal response of patients with Angelman syndrome. However, the administration of atropine in response to an unexpected arrhythmia is not always effective. Anesthesiologists should avoid medications that increase the patients' vagal tone, such as reversal agents.

Vagus Nerve Stimulation with surgical placement is a treatment modality for medically refractory epilepsy². Stimulation at high intensities has a chronotropic effect on the heart. Bradycardia, complete atrio-ventricular block and ventricular asystole after initial left vagus nerve intraoperative stimulation have been reported in literature. Postoperative complications include seizures, peritracheal hematoma, vocal cord paralysis, hoarseness and dyspnea. Seizures should be considered in patients with delayed awakening.

We must be cautious when we deal with an AS patient who has been programmed for a VNS implant. Pathology and surgery have different, but at the same time summative, mechanisms that can trigger the complications of this pathology more often than usual.

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