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EPIDURAL ANALGESIA DURING LABOR IN PATIENT WITH SCN5A GENE MUTATION

Sreenithi.J.J*1

*1Haritha Institute And Research Center, India.

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ABSTRACT

SCN5A gene mutations can lead to ion channel defects which can cause cardiac conduction disturbances. In the presence of specific ECG characteristics, this mutation is called Brugada syndrome (BrS). Other complications include Congenital hypothyroidism. Many drugs are associated with adverse events, making anaesthesia in patients with SCN5A gene mutations or Brugada syndrome challenging. This review article discusses the cases and the complication in performing epidural on BrS patient and its side effects.

I. INTRODUCTION

The SCN5A gene is a predominant sodium iodide symport (NIS) channel involved in the transport of iodide, a negatively charged version of iodine, into cells of certain tissues. The NIS protein is found primarily in the thyroid gland, a butterfly-shaped tissue in the lower neck. The thyroid gland produces and releases iodide-containing thyroid hormones that play an important role in regulating growth, brain development, and the rate of chemical reactions in the body (metabolism). In addition to the thyroid gland, the NIS protein is found in breast tissue during milk production (lactation), ovaries, salivary glands, certain stomach cells (parietal cells), tear glands (lacrimal glands), and a part of the brain called the choroid plexus. During lactation, the NIS protein transports iodide into the milk to supply breast-fed infants with this critical component of thyroid hormones.

Many drugs have been associated with arrhythmogenic events in BrS patients. Because of the unknown phenotype in patients with a SCN5A gene mutation, avoidance of arrhythmogenic medication is advised. Bupivacaine is one of the drugs that should be avoided while ropivacaine can be recommended for the same. Various cases of epidural medications with less concentration of ropivacaine has been used in BrS patients successfully.

BRUGADA SYNDROME:

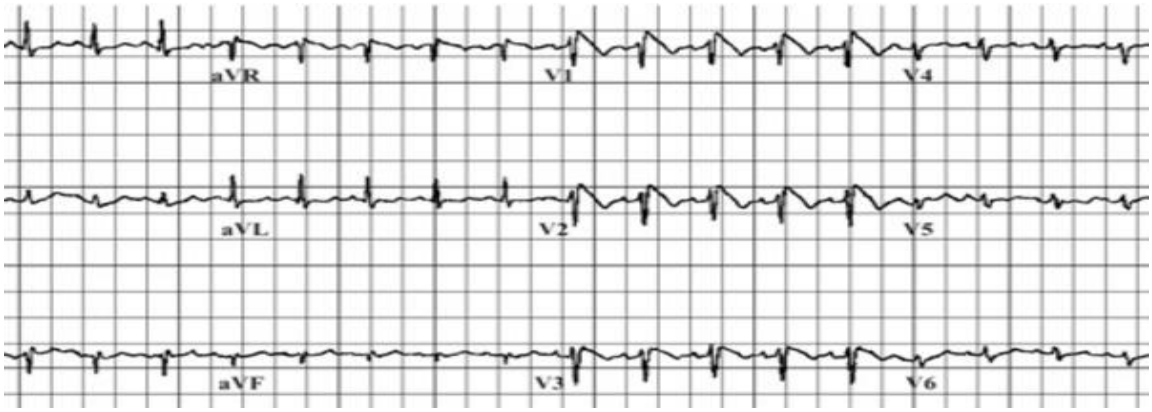

Figure 1: Characteristic measurement of the heart's electrical activity (electrocardiogram--ECG) in Brugada syndrome

Brugada syndrome is a condition that causes a disruption of the heart's normal rhythm. Specifically, this disorder can lead to irregular heartbeats in the heart's lower chambers (ventricles), which is an abnormality called ventricular arrhythmia. If untreated, the irregular heartbeats can cause fainting (syncope), seizures, difficulty breathing, or sudden death. These complications typically occur when an affected person is resting or asleep. Brugada syndrome usually becomes apparent in adulthood, although it can develop any time throughout life. Signs and symptoms related to arrhythmias, including sudden death, can occur from early infancy to late adulthood. Sudden death typically occurs around age 40. This condition may explain some cases of sudden infant death syndrome (SIDS), which is a major cause of death in babies younger than 1 year. SIDS is

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characterized by sudden and unexplained death, usually during sleep. Sudden unexplained nocturnal death syndrome (SUNDS) is a condition characterized by unexpected cardiac arrest in young adults, usually at night during sleep. This condition was originally described in Southeast Asian populations, where it is a major cause of death. Researchers have determined that SUNDS and Brugada syndrome are the same disorder.

CONGENITAL HYPOTHYROIDISM:

Several SLC5A5 gene mutations have been identified in people with congenital hypothyroidism, a condition characterized by abnormally low levels of thyroid hormones starting from birth. About half of these mutations delete part of the SLC5A5 gene or disrupt protein production, resulting in an abnormally small, non-functional protein. The remaining mutations change one of the building blocks (amino acids) used to make the NIS protein. Some amino acid substitutions prevent the NIS protein from being positioned in the cell membrane, disabling iodide transport. Other amino acid substitutions do not affect the membrane location of the NIS protein but change the protein's 3-dimensional shape, which impairs its function. SLC5A5 gene mutations reduce or prevent iodide transport. As a result, the thyroid gland cannot accumulate iodide efficiently, which decreases the production of thyroid hormones. The signs and symptoms of congenital hypothyroidism associated with these gene mutations range from mild to severe depending on the level of hormone production remaining. In many cases, the thyroid gland is enlarged (goiter) in an attempt to compensate for reduced hormone production. Because cases caused by SLC5A5 gene mutations are due to a disruption of thyroid hormone synthesis, they are classified as thyroid dyshormonogenesis.

ROPIVACAINE AS EPIDURAL ANALGESIC AND ANAESTHESIA:

An epidural is a procedure that involves injecting a medication either an anaesthetic or a steroid into the space around your spinal nerves known as the epidural space. The goal of an epidural procedure is to provide pain relief (analgesia) or a complete lack of feeling (anaesthesia) for one region of your body, such as your legs or belly. Epidural medications fall into a class of drugs called local anaesthetics (examples include: bupivacaine, chloroprocaine, and lidocaine) and can be delivered in combination with narcotics (examples include: fentanyl and sufentanil) in order to decrease the required dose of local anesthetic.

Ropivacaine is a long-acting amide local anaesthetic, related structurally to bupivacaine, that has been introduced for use in epidural analgesia in labor. Currently, the optimum dosage regimen for ropivacaine in this setting has not been determined, and recommended initial doses have ranged from 20 to 40 mg. Because there have been few formal investigations of dose requirements for epidural ropivacaine, we performed a prospective, randomized, double-blind study to determine the dose–response of ropivacaine to establish epidural analgesia in early labor.

MECHANISM OF ACTION AND CARDIOTOXICITY:

Ropivacaine causes reversible inhibition of sodium ion influx, and thereby blocks impulse conduction in nerve fibres. This action is potentiated by dose-dependent inhibition of potassium channels. Ropivacaine is less lipophilic than bupivacaine and is less likely to penetrate large myelinated motor fibres; therefore, it has selective action on the pain-transmitting α, β and C nerves rather than Aβ fibres, which are involved in motor function. The incidence of cardio toxicity and central nervous system (CNS) toxicity as a result of inadvertent intravascular injection of ropivacaine appears to be low. According to a pooled analysis of data from ≈3000 patients in 60 clinical studies, the incidence of probable accidental IV injection of ropivacaine was ≈0.2% (six patients) and only one patient experienced convulsions; no patient showed symptoms of cardio toxicity. The convulsive local anaesthetic doses of bupivacaine and ropivacaine were studied in different animal models; bupivacaine has a 1.5- to 2.5-fold lower convulsive threshold when compared to ropivacaine. On the basis of animal and volunteer studies, it can be concluded that ropivacaine seems to be less neurotoxic and cardiotoxic than bupivacaine.

CASE REPORT:

A 31-year-old patient, carrier of SCN5A mutation, with no history of syncope or aborted sudden cardiac arrest, presented at the preoperative assessment clinic of our anaesthetic department at 27 weeks of gestation. She used no medication. Past medical history included surgical correction of an atrial ventricular septum defect at the age of 8. Cardiac ultrasound showed mild left sided atrioventricular valve regurgitation and a good left ventricular function. An ECG showed a first degree heart block with an intraventricular conduction delay.

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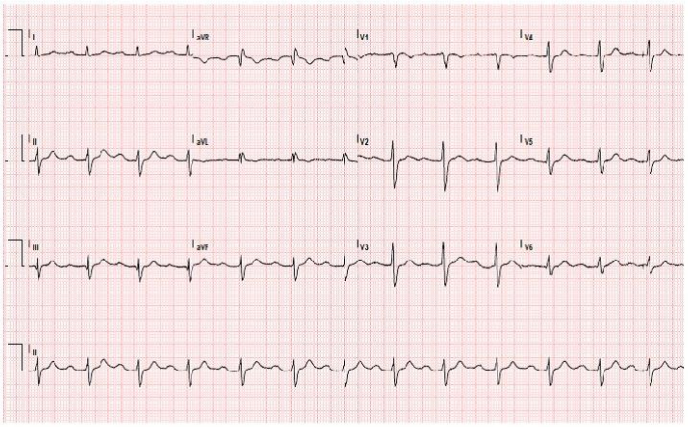
Because of these findings, she was included in a clinical research project relating to the association of cardiac septum defects, conduction disturbances, and SCN5A mutations. This rare mutation, which was only once found in another patient in Netherlands, is the most likely cause of her cardiac conduction disturbances. The father of our patient who also has cardiac conduction disturbances was found to have the same gene mutation.



The obstetric history included one spontaneous abortion and one instrumental vaginal delivery of a healthy male neonate complicated by a retained placenta requiring manual removal under uncomplicated general anesthesia. With regard to the SCN5A mutation and local anesthetics at her first labour, epidural analgesia was considered a relative contraindication due to the possibility of arrhythmias and she was offered patient-controlled analgesia using remifentanil. Having experienced her previous delivery as being very traumatic, she specifically requested epidural analgesia during labour in her current pregnancy. After a multidisciplinary discussion with our cardiologists, gynaecologists, and anesthesiologists, it was agreed to induce labour at 38 weeks of gestation with early titrated epidural analgesia under continuous rhythm monitoring. Ropivacaine 0.1% with sufentanil 1 µg/mL was considered the safest anaesthetic medication. The patient was fully informed about the risks and possible adverse events. At 38 weeks of pregnancy, she was admitted at the department of obstetrics. Monitoring consisted of continuous ECG, saturation, and non-invasive blood pressure monitoring and the presence of a resident cardiologist. The epidural space was located at 5 cm using 18-gauge Tuohy needle at the L3-4 intervertebral space. An epidural catheter was inserted and a test dose of 2.5 mL ropivacaine 0.1% with sufentanil 1 µg/mL was administered resulting in no changes in ECG, heart rate, blood pressure, or sensory block. Ten minutes later, a loading dose of 8 mL of the same mixture was given through the epidural catheter. After 20 minutes, a bilateral sensory block (to ice) to the T10 dermatome level was achieved. Patient-controlled epidural analgesia (PCEA) was started using an infusion of ropivacaine 0.1% with sufentanil 1 µg/mL 5 mL/h with a patient-controlled bolus dose of 5 mL with a lockout interval of 30 minutes. Labour was induced by amniotomy and an intravenous oxytocin infusion in increasing dosage, and the first stage progressed uneventfully. At 9 cm dilatation, the patient experienced increasing pain which was managed by injection of 5 mL of lidocaine 1% through the epidural catheter, because of the pharmacologic profile of the fast onset and intensive blockade. A healthy male neonate was spontaneously delivered 6.5 hours after starting the epidural. No hypotension or cardiac arrhythmias were recorded during this period, neither was a change in her heart block noted by the resident cardiologist. The patient was continuously monitored for 24 hours postpartum on the obstetric high care unit; during this period no arrhythmias occurred.

II. CONCLUSION

Collaboration between interprofessional and multidisciplinary teams is essential in the choice of the locoregional anesthesia technique as the chosen technique must take into account various factors, in particular, the opinion of the patient, the surgeon, and the preferences of the anesthesiology clinician who must be able to perform the nerve block without difficulty for patient safety it is advisable to follow specific guidelines and protocols to conduct adequate regional anesthesia procedures. Furthermore, maintaining continuous closed-loop communication between all members of the perioperative care team regarding the need, technique, and potential management issues associated with the regional anesthetic utilized is essential to optimizing patient outcomes. In addition to obtaining thorough informed consent from either the patient or their authorized legal

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guardian before the placement of any regional anesthesia, all health team members are responsible for voicing their concerns as needed throughout the perioperative period based on their professional discretion.

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