Anesthetic considerations in Dravet syndrome

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INTRODUCTION

Dravet syndrome is one of the most common severe genetic epilepsies, occurring at an incidence of approximately 1/15000.¹ Children with Dravet syndrome typically present in the first year of life with prolonged tonic-clonic seizures triggered by febrile illness or vaccines. Afebrile seizures later develop and epilepsy remains treatment-resistant into adulthood. Approximately 90% of individuals with Dravet syndrome have a pathogenic variant in the SCN1A gene, with resultant loss of function in the neuronal sodium channel Nav1.1. Use of sodium channel blocking antiseizure medications can aggravate seizures in Dravet Syndrome.²

Lidocaine is a class 1b antiarrhythmic and local anesthetic drug that is frequently used during intravenous induction of anesthesia with propofol to reduce injection pain. Lidocaine is a sodium channel blocker and, although not described in the Dravet literature, presumably has the potential to exacerbate seizures.

We describe a child with Dravet syndrome, on multiple anti-seizure medications known to inhibit clearance of hepatically metabolized drugs, who had a generalized tonic-clonic seizure immediately following intravenous administration of lidocaine. The patient’s mother provided informed consent.

CASE SUMMARY

The child is a two-year-two-month-old 12.5 kg boy with Dravet syndrome, diagnosed aged 9 months, due to a pathogenic SCN1A variant. In the year prior, he had had four febrile tonic-clonic seizures, three being prolonged. He also had infrequent afebrile focal seizures. His regular antiseizure medications were cannabidiol, sodium valproate, clobazam, and stiripentol. Previously he had used topical EMLA cream without adverse event.

Following a croup-like illness 10 days prior, for which he was treated with 2 days of prednisolone and ibuprofen, he presented with hematemesis and melena. He was afebrile and, apart from mild rhinorrhea, had no symptoms of infection. His hemoglobin
was 68g/L (normal range: 110–160g/L) and he received a red
blood cell transfusion and intravenous pantoprazole prior to trans-
fer to our hospital for gastroscopy. None of his usual antiseizure
medications were omitted. Due to the history of hematemesis, an
intravenous rather than inhalational induction of anesthesia was
performed. Doses were determined based on actual body weight.
Blood taken 10 min prior to anesthesia showed a hemoglobin of
113g/L, normal hematocrit, electrolytes, and glucose. An injec-
tion of 1 ml of 1% lidocaine (0.8 mg/kg) was given intravenously
for propofol pain amelioration into a peripheral vein with a brief
proximal tourniquet, after which the child developed a tonic–clonic
seizure. The seizure terminated with 0.1 mg/kg of intravenous
midazolam followed by a rapid induction using propofol and
remifentanil. The remaining anesthesia was uneventful without
signs of cardiac dysfunction.

No further seizures occurred during the admission.

DISCUSSION

Most individuals with Dravet syndrome survive into adulthood and
are likely to require multiple anesthesia, for example, during emer-
gent management of status epilepticus, dental examination, and
gastrostomy insertion. Intravenous lidocaine is used for a variety of
indications including nerve blocks, perioperative pain management,
and cardiac arrhythmias. Given that our patient’s seizure occurred
while he was afebrile, and unlike his usual seizures was brief and eas-
ily terminated with midazolam, it is plausible that it was precipitated
by lidocaine use.

The SCN1A gene encodes the alpha protein subunit of the
voltage-gated sodium channel Nav1.1, which is the major sodium
channel on inhibitory (GABAergic) interneurons. SCN1A mutations
impair channel and interneuron function, resulting in a hyperex-
citable state. Sodium channel blockers further reduce GABAergic
inhibition, increasing seizure propensity. Literature suggests that
carbamazepine, oxcarbazepine, and lamotrigine should be avoided
in Dravet syndrome due to exacerbation of seizures and poorer long-
term cognitive outcomes. Use of lidocaine for anesthesia therefore,
might similarly increase seizure risk.

Multiple factors may have contributed to our patient’s sei-
zure following the lidocaine injection. Usually, lung uptake of
lidocaine results in lower arterial versus venous plasma con-
centrations protecting against neurotoxicity following injection,
including in patients with epilepsy. With tourniquet use the cen-
tral bolus rate may have been augmented, resulting in a brief but
significant elevation in arterial lidocaine concentration; how-
ever, even a slow injection mixed with propofol could potentially
cause a seizure in Dravet syndrome. An increased free fraction
of lidocaine due to changes in plasma protein content following
the gastrointestinal bleed and transfusion may also have contrib-
uted, while the gastric ulcers themselves could reduce antisei-
zure medication absorption. Finally, drug error is a possibility to
consider, however both the strength and dose administered were
carefully checked.

Anesthetic management in Dravet syndrome should consider
potential drug interactions. Some drugs used in Dravet syndrome in-
cluding stiripentol, cannabidiol, and fenfluramine result in inhibition
of cytochrome P450 enzymes. Given the child’s seizure occurred
after a bolus of lidocaine, hepatic drug metabolism is unlikely to have
contributed. However, in other circumstances, decreased clearance
of hepatically metabolized drugs, for example, midazolam when used
as an oral premedication, may result in excessive sedation or need
for airway protection.

Intravenous lidocaine, particularly administered as a bolus,
should be avoided in Dravet syndrome. Potential interactions of an-
esthetic drugs with antiseizure medications should be considered.

LEARNING POINTS

• Dravet syndrome is a common genetic epilepsy and remains
treatment-resistant into adulthood.
• Lidocaine, and other sodium channel blockers, should be avoided
in Dravet syndrome.
• Be cautious of reduced midazolam clearance in patients taking
enzyme-inducing antiseizure medications.

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CONFLICT OF INTEREST

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DATA AVAILABILITY STATEMENT

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ated or analyzed in this study.

ETHICAL APPROVAL

The Royal Children’s Hospital’s Human Research Ethics Committee
(HREC)’s policy is that case reports are exempt from HREC review.
INFORMED CONSENT
Informed written consent was given by the patient's parents who have read and approved of the case report.

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