



Drug Interactions: Considerations for Surgery, Imaging, & Other Procedures

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This information should not replace guidance from a health care professional managing the care of your child or loved one. Caregivers should use this guide to help inform conversations as part of the health care team, working with medical professionals to determine the best medications to use given the individual patient's medical history and the intended outcome from each procedure.

During surgery or other invasive procedures, a patient may be put on medications that they normally do not take. Some medications can interact and cause regular medications to work differently. This document lists many commonly utilized medications in the context of surgery and other procedures, as well as medication that may be commonly used in Dravet syndrome and discusses potential risks or interactions that may be of concern.

Patients with Dravet syndrome are often already on several daily medications.

On admission, give the surgical team a list of current medications.

Important information for your list includes:

- Name of medication (brand or generic)
- Dose (mg instead of mL will help prevent confusion)
- Frequency (how many times a day)
- Route (G-tube, J-tube, by mouth)
- Specific times administered
- Any special methods for administering

Some medications may increase the risk of seizures or make seizure medications act differently. For this reason, it is particularly important to have a **Seizure Action Plan (SAP)** developed with the patient's neurologist ahead of time. This SAP should include a section with explicit instructions for seizure rescue interventions within a medical setting, including which medications should be avoided and if a particular medication has worked better for the patient in previous seizure emergencies. Always carry a copy of the SAP with the individual with Dravet syndrome and be sure to share a copy of the SAP with the surgical or health care team. For more information on SAP's, visit the Seizure Action Plan Coalition website: www.seizureactionplans.org

Medications Commonly Used in Imaging Procedures

The following medications are commonly used in imaging procedures. This chart indicates the purpose for each of those medications and whether the medication may have the potential to lower the seizure threshold- meaning a seizure could be more likely to occur when this medication is used in any individual. Discuss any concerns you have with the medical team performing the procedure; the patient's medical team will choose the most appropriate medications based on their individual medical history and the type of procedure being performed. It is very important to have a Seizure Action Plan developed with the patient's neurologist with explicit instructions for rescue interventions within a medical setting (including which medications should be avoided). Carry a copy with the patient at all times and be sure to share a copy of the plan with the surgical or medical team.

Medication	Purpose	Potential to lower seizure threshold?
Benzodiazepines (<i>Ativan</i> ®, <i>Valium</i> ®, <i>Versed</i> ®)	Decrease agitation	No
Clonidine (<i>Catapres</i> ®)	Decrease agitation	No
Diphenhydramine (<i>Benadryl</i> ®)	Decrease agitation	Yes
Barium sulfate (<i>Baro-cat</i> ®)	Contrast agent	Yes
Diatrizoate meglumine (<i>Gastrografin</i> ®)	Contrast agent	No
Diatrizoate sodium (<i>Gastrografin</i> ®)	Contrast agent	No
Gadobutrol (<i>Gadovist</i> ®)	Contrast agent	Yes
Gadopentetate dimeglumine (<i>Magnevist</i> ®)	Contrast agent	Yes
Gadoterate meglumine (<i>Dotarem</i> ®)	Contrast agent	Yes
Gadoversetamide (<i>OptiMARK</i> ®)	Contrast agent	Yes
Gadoxetate (<i>Eovist</i> ®)	Contrast agent	No
Iodixanol (<i>Visipaque</i> ®)	Contrast agent	Yes
Iohexol (<i>Omnipaque</i> ®)	Contrast agent	Yes
Iopamidol (<i>Isovue</i> ®)	Contrast agent	Yes
Iopromide (<i>Ultravist</i> ®)	Contrast agent	Yes
Iothalamate meglumine (<i>Conray</i> ®)	Contrast agent	Yes
Ioxaglate meglumine /ioxaglate sodium (<i>Hexabrix</i> ®)	Contrast agent	Yes
Ioxilan (<i>Oxilan</i> ®)	Contrast agent	No
Ethiodized oil (<i>Lipiodol</i> ®)	Contrast agent	No
Nitrous oxide	Anesthesia	Yes
Propofol (<i>Diprivan</i> ®)	Anesthesia	Yes
Sevoflurane (<i>Ultane</i> ®)	Anesthesia	Yes

Anti-Seizure Medications and Potential Interactions with Contrast Agents

As discussed above, some contrast agents may lower the seizure threshold for any individual. In addition, some contrast agents may interact with medications that are commonly used in the treatment of epilepsy. The patient's health care team will make the decision with you based on the patient's full medical history and the procedure being done. If your physician determines the best contrast agent is one that does have an increased risk of seizures, they may recommend a supplementary dose of an anti-seizure medication prior to the procedure.

Anti-Seizure Medication	Direct interaction with contrast agents?
Acetazolamide (<i>Diamox</i> ®)	Yes
Brivaracetam (<i>Briviact</i> ®)	No
Cannabidiol (<i>Epidiolex</i> ®)	No
Carbamazepine (<i>Tegretol</i> ®)	No
Clemizole*	no info
Clobazam (<i>Onfi</i> ®)	No
Clonazepam (<i>Klonopin</i> ®)	No
Diazepam (<i>Valium</i> ®)	No
Ethosuximide (<i>Zarontin</i> ®)	No
Fenfluramine** (<i>Fintepla</i> ®)	No
Lamotrigine (<i>Lamictal</i> ®)	No
Levetiracetam (<i>Keppra</i> ®)	No
Lorcaserin* (<i>Belviq</i> ®)	No
Lorazepam (<i>Ativan</i> ®)	No
Methsuximide (<i>Celontin</i> ®)	No
Perampanel (<i>Fycompa</i> ®)	No
Phenobarbital (<i>Luminal</i> ®)	No
Rufinamide (<i>Banzel</i> ®)	No
Soticlestat*	No
Stiripentol (<i>Diacomit</i> ®)	No
Topiramate (<i>Topamax</i> ®)	No
Valproic acid (<i>Depakote</i> ®)	No
Zonisamide (<i>Zonegran</i> ®)	No
*These medications are currently in clinical trials and information is currently limited	
**This medication was recently granted FDA approval and studies are still limited	

Other Medications That May Interact with Contrast Agents

There are some other commonly used medications (not specific to Dravet syndrome) that may have interactions with contrast agents. Make sure you discuss all medications the patient is taking with the medical team prior to any procedure.

Medication	Direct interaction with contrast agents?
Lithium (<i>Lithobid</i> ®)	Yes
NSAIDs (<i>Motrin</i> ®, <i>Toradol</i> ®, <i>Aleve</i> ®)	Yes
Propranolol (<i>Inderal</i> ®)	Yes
Phenothiazines (<i>Thorazine</i> ®, <i>Triavil</i> ®, <i>Compazine</i> ®, <i>Mellaril</i> ®)	Yes
Haloperidol (<i>Haldol</i> ®)	Yes
Amitriptyline (<i>Elavil</i> ®), Doxepin (<i>Silenor</i> ®)	Yes

Medications Commonly Used in Surgical Procedures That May Interact

During surgery, it is very important that patients are comfortable. Many medications are needed to achieve this level of comfort. Below you will find lists of commonly used medications in surgical procedures and any potential interactions that may be of concern.

The sections below cover: (1) pain medications, (2) sedation medications, (3) paralytics, (4) anti-seizure medications, (5) reversal agents, (6) antibiotics, (7) stabilizers, and (8) anti-inflammatory agents.

- 1. Pain Medications:** During surgery, IV pain medications are given to keep patients comfortable during the procedure. The following are commonly used IV pain medications.

Non-Opioids

Acetaminophen (*Tylenol*®)
 Dexmedetomidine (*Precedex*®)
 Ibuprofen (*Motrin*®)
 Ketorolac (*Toradol*®)
 Lidocaine (*Xylocaine*®)

Opioids

Fentanyl (*Duragesic*®)
 Hydromorphone (*Dilaudid*®)
 Morphine
 Remifentanil (*Ultiva*®)

Medication	Interacts with...	Explanation
Sufentanil (<i>Sufenta</i> ®)	Stiripentol (<i>Diacomit</i> ®)	Stiripentol will increase the amount of Sufentanil in the body
Lidocaine (<i>Xylocaine</i> ®)	Dravet syndrome	Lidocaine can worsen seizures in patients with Dravet syndrome. NOTE: This refers to <u>intravenous</u> lidocaine; worsened seizures with subcutaneous or topical lidocaine is rare and these routes should still be reasonable if warranted.

- 2. Sedation Medications:** During surgery, it is important to keep patients asleep. The following medications are used to keep patients asleep during procedures

Barbiturates

Phenobarbital (*Luminal*®)
 Thiopental (*Phenothal*®)
 Pentobarbital (*Nembutal*®)
 Methohexital (*Brevital*®)

Inhaled anesthetics

Desflurane (*Suprane*®)
 Isoflurane (*Forane*®)
 Nitric oxide
 Sevoflurane (*Ultane*®)
 Propofol (*Diprivan*®)

Benzodiazepines

Lorazepam (*Ativan*®)
 Midazolam (*Versed*®)
 Remifentanil (*Ultiva*®)

Opioids

Fentanyl (*Duragesic*®)
 Hydromorphone (*Dilaudid*®)
 Morphine
 Remifentanil (*Ultiva*®)

Sedatives:

Sufentanil (*Sufenta*®)
 Dexmedetomidine (*Precedex*®)
 Ketamine (*Ketalar*®)

Medication	Interacts with...	Explanation
Thiopental (<i>Phenothal</i> [®])	EEG	Can produce an isoelectric EEG
Methohexital (<i>Brevital</i> [®])	Seizures	May worsen focal seizures
Phenobarbital (<i>Luminal</i> [®])	Stiripentol (<i>Diacomit</i> [®])	Use of phenobarbital with stiripentol is contraindicated. Phenobarbital can significantly reduce the efficacy of stiripentol and increase risk for seizures
Opioids	All anti-seizure medications	May further increase sleepiness
Ketamine (<i>Ketalar</i> [®])	Stiripentol (<i>Diacomit</i> [®])	Stiripentol can increase the amount of ketamine in the body
Lorazepam (<i>Ativan</i> [®])	Valproic acid (<i>Depakote</i> [®])	Valproate products can increase the amount of lorazepam in the body. Consider reducing lorazepam by 50% if coadministered with valproate.
Midazolam (<i>Versed</i> [®])	Phenobarbital (<i>Luminal</i> [®])	Can increase the amount of midazolam in the body
	Stiripentol (<i>Diacomit</i> [®])	
Inhaled anesthetics	Phenobarbital (<i>Luminal</i> [®])	Both increase risk for low blood pressure
Lidocaine (<i>Xylocaine</i> [®])	Phenobarbital (<i>Luminal</i> [®])	Risk for methemoglobinemia (hypoxia, cyanosis)
	Phenytoin (<i>Dilantin</i> [®])	

3. Paralytics: In order to have a successful procedure, patients have to stay still. The following are paralytics used to keep patients still.

Cisatracurium (*Nimbex*[®])
Mivacurium (*Mivacron*[®])
Rocuronium (*Zemuron*[®])

Succinylcholine (*Anectin*[®])
Vecuronium (*Nocuron*[®])
Pancuronium (*Pavulon*[®])

Medication	Interacts with...	Explanation
Rocuronium (<i>Zemuron</i> [®])	Carbamazepine * (<i>Tegretol</i> [®])	Increases clearance of rocuronium, pancuronium, vecuronium, and cisatracurium, and decreases their duration of action
Pancuronium (<i>Pavulon</i> [®])		
Vecuronium (<i>Nocuron</i> [®])		
Cisatracurium (<i>Nimbex</i> [®])		
*Carbamazepine is contraindicated for Dravet syndrome as it can worsen seizures		

4. Anti-Seizure Medications: During the surgery, IV anti-seizure medications may be needed to prevent seizing during longer procedures. The following are IV anti-epileptics commonly used for seizure prevention.

Fosphenytoin (*Cerebryx*[®])
Levetiracetam (*Keppra*[®])

Phenobarbital (*Luminal*[®])
Lacosamide (*Vimpat*[®])

Medication	Interacts with...	Explanation
Fosphenytoin (<i>Cerebryx</i> [®])	Dravet syndrome	Fosphenytoin can worsen seizures. Avoid use in Dravet syndrome.

5. **Reversal Agents:** Everyone reacts differently to different medications. To prevent becoming too sleepy or too still, the surgery team will have reversal agents on hand.

Paralytic Reversal Agents

Glycopyrrolate (*Robinul*®)
 Neostigmine (*Prostigmin*®)
 Pyridostigmine (*Mestinon*®)
 Sugammadex (*Bridion*®)

Opioid & Benzodiazepine Reversal Agents:

Flumazenil (*Anexate*®)
 Naloxone (*Narcan*®)

Medication	Interacts with...	Explanation
Benzodiazepines	Flumazenil (<i>Anexate</i> ®)	Benzodiazepines are commonly used in the treatment of epilepsies. Use of flumazenil can reverse these actions and cause seizures to emerge or worsen.
Flumazenil (<i>Anexate</i> ®)	Seizures	This medication is generally contraindicated in patients with seizures unless emergently needed.

6. **Antibiotics:** Antibiotics are an extremely important way of preventing infections from complicating surgeries. They can be given before and after the surgery, either via IV or injected directly into the brain.

Cefazolin (*Ancef*®)
 Ceftazidime (*Fortaz*®)
 Clindamycin (*Cleocin*®)
 Vancomycin (*Vancocin*®)
 Gentamicin

There are no pertinent drug interactions with antibiotics and anti-seizure medications.

7. **Stabilizers:** A patient's body can react in many different ways to a surgical procedure. This is why the surgery team will have access to several stabilizers to keep vitals all in equilibrium.

Stabilizing Blood Pressure

Nicardipine (*Cardene*®)
 Dobutamine (*Dobutrex*®)
 Dopamine (*Intropin*®)
 Epinephrine (*Adrenalin*®)
 Ephedrine (*Cophedra*®)
 Esmolol (*Brevibloc*®)
 Hydralazine (*Apresoline*®)
 Labetalol (*Trandate*®)
 Nicardipine (*Cardene*®)
 Nitroglycerin (*Nitrostat*®)
 Nitroprusside (*Nitropress*®)
 Norepinephrine (*Levophed*®)
 Phenylephrine (*Vazculep*®)
 Vasopressin (*Pitressin*®)

Stabilizing Blood Sugar:

Insulin

Stabilizing Body Fluid/Hydration:

Albumin
 Furosemide (*Lasix*®)
 Dextrose containing fluids
 D5W +/- electrolytes
 D10W +/- electrolytes
 D20W
 Lactated Ringers (LR)
 Mannitol
 Plasma-Lyte®
 Sodium containing fluids
 ½ NS
 NS
 3% N

Medication	Interacts with...	Explanation
Nicardipine (<i>Cardene</i> ®)	Phenobarbital (<i>Luminal</i> ®)	Phenobarbital can reduce efficacy of nicardipine
Nicardipine (<i>Cardene</i> ®)	Stiripentol (<i>Diacomit</i> ®)	Stiripentol can increase the amount of nicardipine in the body
Ephedrine (<i>Cophedra</i> ®)	Acetazolamide (<i>Diamox</i> ®)	Can increase the amount of ephedrine in the body
	Topiramate (<i>Topamax</i> ®)	
	Zonisamide (<i>Zonegran</i> ®)	

- 8. Anti-inflammatory Agents:** During and after the procedure, the help of some steroids may be needed to decrease inflammation. They will typically start with a higher dose and slowly decrease down over time. These medications may be rough on the stomach, so they are typically given with some tummy protection (anti-acids).

Steroids:

Dexamethasone (*Decadron*®)
Hydrocortisone (*Solu-Cortef*®)
Methylprednisolone (*Solumedrol*®)

Acid Reducers:

Famotidine (*Pepcid*®)
Pantoprazole (*Protonix*®)
Esomeprazole (*Nexium*®)
Omeprazole (*Prilosec*®)
Lansoprazole (*Prevacid*®)

There are no pertinent drug interactions with steroids, anti-acids and anti-seizure medications.

Questions? Email: veronica@dravetfoundation.org

References

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