

Medications and Perioperative Considerations for MCAS



Generally well tolerated

Lower-risk medications that are often preferred in MCAS patients.



Use with caution

May be tolerated in some patients but require individualized assessment.



Avoid if possible

Higher-risk medications that may increase the likelihood of adverse reactions.

ANALGESICS: NON-OPIOIDS



- Acetaminophen
- Paracetamol
- Metamizole



NSAIDs

Best tolerated: Celecoxib/Celebrex and/or meloxicam

Less tolerated: ketorolac, etodolac, nefopam, aspirin, ibuprofen, nabumetone, indomethacin.

*NSAIDs can increase leukotrienes which is a mast cell mediator.

*Note that aspirin can sometimes be used therapeutically in MCAS for elevated prostaglandins.

OPIOIDS

All opioids can trigger mast cell mediator release. Avoid if possible. Listed in order of preference.



Lower-risk options

Fentanyl
Sufentanil
Alfentanil
Remifentanyl



Moderate-risk options

Piritramide
Tramadol
Buprenorphine
Hydromorphone
Oxycodone
Hydrocodone
Tapentadol
Oxymorphone



Avoid if possible

Morphine
Codeine
Meperidine (Pethidine)

*Note: may require adjunct treatment with Zofran/ondansetron due to nausea/vomiting risk.

ANTIBIOTICS



- Roxithromycin
- Penicillins
- cephalosporins
- sulfonamides
- clindamycin



- Cefuroxime
- Gyrase inhibitors
- Fluoroquinolones



- Vancomycin
- Polymyxin B

*Fluoroquinolones are contraindicated in connective tissue disorders due to increased risk of tendon rupture and aortic aneurysm/dissection.

LOCAL ANESTHETIC



Amide local anesthetics are generally preferred over ester-type. Amide options in order of preference:

- Bupivacaine
- Ropivacaine
- Lidocaine

*Opt for preservative free.



Ester-type more commonly cause reactions:

- Tetracaine
- Procaine
- Benzocaine

*Many reactions may occur from preservatives e.g. methylparaben, sulfites, epinephrine additives.

BENZODIAZEPINES



- Clonazepam
- Midazolam
- diazepam

ANTIDEPRESSANTS



- Doxepin
- Amitriptyline
- Clomipramine.
- Maprotiline

*doxepin, amitriptyline, and clomipramine are TCAs with antihistamine properties that are often beneficial.



- SSRIs
- Bupropion
- Duloxetine
- Venlafaxine

MUSCLE RELAXANTS



- cis-atracurium
- pancuronium
- vecuronium
- succinylcholine

*cis-atracurium is generally preferred.



- Rocuronium

*Rocuronium is one of the more common causes of perioperative anaphylaxis overall, but not necessarily associated with increased incidence in MCAS patients.



- Atracurium
- Mivacurium

ANTICONSULSANTS



- Clonazepam



- Carbamazepine
- Topiramate

PEPTIDERGIC DRUGS



- Icatibant
- Cetrorelix
- Sermorelin
- Octreotide
- Leuprolide

X-RAY AND MRI CONTRAST MEDIUM



Non-ionic contrast media preferred:

- Iohexol
- Iopamidol
- Iopromide
- Ioxilan
- Ioversol
- Iotrotran
- Iodixanol



Iodinated contrast medium, and gadolinium chelate (Gd33).

Macrocyclic gadolinium chelate may be a better option such as:

- Gadobutrol
- Gadoterate meglumine
- Gadoteridol

Ones that have a higher adverse incidence are linear gadolinium agents such as:

- gadopentate dimeglumine
- gadodiamide

*Consider premedication if these are necessary.

**Prior contrast reaction history is more predictive than diagnosis of MCAS alone.

INTRAVENOUS FLUIDS



- 0.9% NaCl solution
- Lactated Ringer's
- Plasma-Lyte
- D5W



- Albumin



- Hydroxyethyl starch
- Gelatine-based plasma substitutes

HYPNOTIC/SEDATIVE/ANESTHETIC AGENTS



- Dexmedetomidine
- Etomidate
- Propofol
- Ketamine



- Methohexital
- Thiopental
- Phenobarbital

REVERSAL OF NEUROMUSCULAR BLOCKADE



- Neostigmine
- Sugammadex

CARDIOVASCULAR DRUGS



- ARBs (sartans, such as Losartan)
- Calcium channel Antagonists
- Ivabradine
- and much else.
- Beta-blockers

*Beta-blockers should be used cautiously in patients at high risk for anaphylaxis because they may reduce responsiveness to epinephrine (propranolol has higher risk than metoprolol). Likewise ACE inhibitors may worsen anaphylaxis and increase risk of angioedema through bradykinin accumulation.

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- β -Adrenoceptor antagonists
- Adenosine
- Protamine

ANTISEPTICS		WOUND CARE
✓ Alcohol(topical) • povidone-iodine	⚠ Chlorhexidine *Chlorhexidine can be a cause of perioperative anaphylaxis in the general population.	⚠ Adhesives/plasters *Avoid plasters or adhesives if have significant skin reactions (such as in cutaneous mastocytosis). If they must be used, use an adhesive removal and slow removal of plaster/adhesive. Consider protecting the skin with Mepitac or Mepilex.

COMMON LABOR AND DELIVERY DRUGS		
✓ Tocolytic agent (terbutaline) • Oxytocin (possible trigger in some, consider premedication with antihistamines)		⚠ Methylergonovine • prostaglandins

INHALANT ANESTHETICS	MISCELLANEOUS	
✓ Isoflurane • Sevoflurane • Desflurane • Nitrous oxide	✓ Atropine • Glycopyrrolate • Ondansetron • Aprotinin (fibrin glue) • Dyes • Latex (if no allergy)	⚠ Alcohol-containing medications • Alcoholic beverages • Blood transfusions

PREOPERATIVE CONSIDERATIONS

Excipients

- Excipients are inactive ingredients added to medications and are often the culprit in reactions to medications. These can be avoided by compounding the medication at a compounding pharmacy. Here is a tool that you can use to check for inactive ingredients in medications (search the specific drug name, scroll down to ingredients and appearance): <https://dailymed.nlm.nih.gov/dailymed/>
- Common excipients that can cause reactions in some individuals include: polyethylene glycol (PEG), polysorbate 80, dyes, titanium dioxide, lactose and corn starch. Past reaction or tolerance is the biggest clue to future reactions.

General Medication/Supplement advice

- Start one medication or supplement at a time to evaluate tolerance.
- If you are highly sensitive and starting a higher-risk medication or a new medication/supplement, consider introducing it at the lowest possible dose along with H1 and H2 antihistamines to help reduce the risk of reactions.

Other Considerations:

- Develop a preoperative plan with your doctor: It can be helpful to increase mast cell stabilizing medications prior to operations, and to take them until the day of surgery (if they need to be discontinued) and there may be premedication recommendations your doctor can recommend to discuss with the surgeon such as IV antihistamine use or steroids. It is common to use IV Benadryl or other antihistamines prior to other IV medications or contrast to reduce reaction risk.
- Avoid abrupt discontinuation of chronic antihistamines or mast cell stabilizers before surgery unless specifically instructed
- If you have had a reaction to a previous anesthetic, find out what it was and request a different anesthetic agent
- Inform staff of adhesive/fragrance sensitivities
- Discuss preferred medications with anesthesiologist and surgeon before surgery
- Request slow medication administration when possible
- Other triggers to consider: psychological stress and anxiety, pain, environmental factors (too cold/hot of operating room, or changes in temperature), pressure (tourniquet, BP cuff), friction (tape) or other mechanical irritation, trauma, dry skin, histamine rich foods and odors (perfumes). It helps to minimize operative time, have optimal positioning, a quiet environment, reduce stress, control pain, maintain moderate/normal room temperature (can use heat maintenance devices, warm intravenous and irrigation fluids), moisturize skin, avoid puncturing blisters, avoid pressure and friction during procedures, request fragrance-free and a single occupancy room. Avoid rapid IV medication administration, and opioids given as bolus.
- Depending on the severity of the Mast Cell Disorder, it may be helpful to get markers before the surgery such as tryptase levels (can be a helpful reference point).
- Patients with systemic mastocytosis generally carry higher perioperative anaphylaxis risk than typical MCAS patients.

Resources:

- Molderings GJ, Haenisch B, Brettner S, et al. Pharmacological treatment options for mast cell activation disease. *Naunyn Schmiedeberg's Arch Pharmacol*. 2016;389(7):671-694. doi:10.1007/s00210-016-1247-1
- Kumaraswami S, Farkas G. Management of a Parturient with Mast Cell Activation Syndrome: An Anesthesiologist's Experience. *Case Rep Anesthesiol*. 2018;2018:8920921. Published 2018 May 22. doi:10.1155/2018/8920921
- Hepner, David. Perioperative Management of Patient with MCD. TMS training August 5, 2024
- Pascale Dewachter, Mariana C. Castells, David L. Hepner, Claudie Mouton-Faivre; Perioperative Management of Patients with Mastocytosis. *Anesthesiology* 2014; 120:753–759 doi: <https://doi.org/10.1097/ALN.0000000000000031>