## Background

In July 2014, Ryanodex was introduced as an alternative to traditional dantrolene sodium for the treatment of Malignant Hyperthermia (MH). MH is a pharmacogenetic disorder characterized by hypercapnia, tachycardia, hyperthermia, muscle rigidity, rhabdomyolysis, and possibly hyperkalemic cardiac arrest. Ryanodex is a hyperconcentrated (250 mg/vial) form of dantrolene that requires only 5 mL sterile water per vial, in contrast to generic formulations, which require 60 mL sterile water per 20 mg vial, and therefore, a greater resource need at the time of the acute MH event.

## Methods

The call log database of the Malignant Hyperthermia Association of the U.S. (MHAUS) was examined to determine the characteristics of those cases in which Ryanodex was used to treat MH. We queried cases of MH that occurred between July 2016 and March 2016.

## Case 1

- **2yo female, nasal fistula repair**
- Administered volatile anesthetic agents
- Intraoperatively developed:
  - Hypercapnia
  - Tachycardia
  - Hyperthermia
- Blood gas: pH 7.12 and pCO₂ 93
- Anesthetic was discontinued
- Patient received 3 mg/kg Ryanodex and external cooling
- Response to Ryanodex administration:
  - Rapid decrease in P₅₅CO₂
  - Decreased body temperature.
- Follow-up and diagnostic studies pending.

## Case 2

- **47 yo male, lumbar laminectomy**
- Intraoperatively developed:
  - Hypercapnia
  - Tachycardia
  - Hyperthermia
  - Hypotension
- Sevoflurane was discontinued.
- Ryanodex was administered although the patient’s symptoms began to resolve after discontinuing sevoflurane.
- Patient recovered without additional Ryanodex
- Revealed later that he had a family history of MH
- Diagnostic testing revealed an RYR1 variant of unknown significance: [c.14806C>A p.Leu4936 Met, Heterozygous, Inheritance AD,AR]

## Case 3

- **42 yo male**
- Administered succinylcholine and isoflurane
- Developed:
  - Hypercapnia
  - Hyperthermia
- Isoflurane was discontinued
- Patient was administered 2.5 mg/kg of Ryanodex
- Patient appeared to respond favorably to these treatments
- Transferred to the ICU
- CK was later measured to be >100,000
- Normal K
- Normothermic
- Generalized weakness was reported following administration of Ryanodex.
- The patient recovered and diagnostic tests are pending.

## Case 4

- **60 yo male with a family history of MH**
- **POD 2 after bronchoscopy for advanced lung cancer**
- Non-triggering anesthetic
- Postoperatively developed:
  - Rhabdomyolysis
  - Hyperthermia to 107 F.
- Two days later the ICU physician called the MHAUS hotline for treatment advice
- Ryanodex was administered without apparent effect and the patient expired
- Diagnostic studies are pending.
- Unclear if episode represented true MH or other entity causing muscle breakdown.

## Conclusions

We report the first uses of Ryanodex to treat MH in humans. In this limited population, Ryanodex appears to be equally efficacious with similar side effects as generic dantrolene formulations.