

# HOW MUCH DANTROLENE SHOULD BE AVAILABLE IN FACILITIES WHERE VOLATILE AGENTS ARE NOT AVAILABLE OR ADMINISTERED, AND SUCCINYLCOLINE IS ONLY STOCKED ON SITE FOR EMERGENCY PURPOSES?

Developed 2018

## Supporting Evidence

### Background:

Most MH cases are triggered by the administration of a volatile anesthetic agent with or without succinylcholine, but in a small percentage of cases MH appears to be triggered by succinylcholine alone in the absence of a volatile agent.<sup>1,2</sup> For example, 1.4% of “very likely” or “almost certain” (terms derived from the MH clinical grading scale<sup>3</sup>) MH events reported to the North American Malignant Hyperthermia Registry (NAMHR) were triggered by succinylcholine alone (personal communication, Michael Young, M.S., NAMHR, February 9, 2017).<sup>1,4</sup> In a report from the University of Toronto MH testing center, 20 of 129 (15.5%) biopsy-proven MH events were triggered by succinylcholine alone.<sup>2</sup> In Europe, 2 of 200 (1%) biopsy proven MH events were due to succinylcholine alone.<sup>5</sup> As a patient safety and advocacy organization, MHAUS has recommended “Dantrolene must be available for all anesthetizing locations where MH trigger agents are used.” Furthermore, MHAUS recommends that centers stock a minimum of 36 20-mg vials of Dantrium or Revonto (total dose 720-mg), or three 250-mg vials of Ryanodex (total dose 750-mg). These amounts of dantrolene were originally determined by the analysis of MH event data showing that some cases of acute MH required up to or more than 10-mg/kg body weight, and therefore, these total dose amounts would suffice for the majority of average-sized patients that develop MH.<sup>1</sup>

Over the past several decades there has been steady growth of free-standing or office-based surgery facilities that use intravenous anesthesia techniques without inhalational agents, and stock succinylcholine to treat life-threatening airway emergencies only. Over this period MHAUS has received numerous requests from anesthesiologists at many of these centers, as well as from representatives of the Ambulatory Surgery Committee of the American Society of Anesthesiologists, and the Society of Ambulatory Anesthesia, to amend our recommendations for stocking dantrolene in these facilities. These requests have been based on three main arguments. The first is the assumption that since the incidence of MH susceptibility in the general population is low, and the need for succinylcholine to treat an airway emergency in these centers is uncommon, then the likelihood of the above two events happening to the same patient is so low that it renders the cost of stocking dantrolene prohibitively high when compared to its potential usefulness.<sup>†</sup> The second is that accrediting agencies such as The Joint Commission and others have traditionally relied on the expert opinion of patient safety organizations such as MHAUS to determine accreditation criteria. These accreditation organizations, in line with MHAUS recommendations, have taken the

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\* <http://www.mhaus.org/faqs/dantrolene>

† At the time of this writing, there are three dantrolene products on the market. Dantrium (Par Pharmaceuticals, Woodcliff Lake, NJ, USA) is one of the generic dantrolene products, is supplied as 20-mg vials (each mixed with 60 mL sterile water), has an approved shelf-life of 36 months, and costs \$1,063 per year to stock. Revonto (US World Meds, Louisville, KY, USA) is one of the generic dantrolene products, is supplied as 20-mg vials (each mixed with 60 mL sterile water), has an approved shelf-life of 36 months, and costs \$840 per year to stock. Ryanodex (Eagle Pharmaceuticals, Woodcliff Lake, NJ, USA) is the newer hyperconcentrated form of dantrolene, is supplied as 250-mg vials (each mixed with 5 mL sterile water), has an approved shelf-life of 24 months, and costs \$3,450 per year to stock.

stance that surgical facilities must stock dantrolene if they also stock succinylcholine as a requirement to become accredited by the Center for Medicare and Medicaid Services (CMS).<sup>‡</sup> The third is that to acquire accreditation, some ambulatory surgery facilities that do not want to incur the cost of dantrolene will not stock succinylcholine, thus putting their patients' lives at risk in the event of a life-threatening airway obstruction.<sup>§</sup>

## Discussion:

MHAUS hotline consultants, members of our board of directors, and professional advisory council discussed at length the advantages and disadvantages of stocking dantrolene in these types of facilities and whether or not we should amend our existing recommendations. Opinions varied widely and generally fell into one of two approaches. The majority group of MH experts believes that as a patient advocacy organization that was originally chartered by MH susceptible patients and has MH susceptible families on our board of directors, the primary responsibility of MHAUS is to protect the health of our patients, both known MH susceptibles, and those who will subsequently develop MH, but are as yet unaware of their MH susceptible status. Experts in this group feel that the cost of stocking dantrolene, even if never used, is a relatively small price to pay for the security and confidence of knowing that anesthesiologists can be free to stock and administer succinylcholine for life-threatening airway obstruction without fear of patients developing MH without the only known antidote immediately available. These experts hold strong beliefs that one of the missions of MHAUS is to make an MH death a “never event”, and that having an adequate supply of dantrolene wherever triggering agents are administered is crucial to this mission, especially in light of data that demonstrates a convincing relationship between the length of time it takes to administer dantrolene and subsequent patient outcomes. Data from the NAMHR indicate that the likelihood of an MH complication increased 1.6 times for every 30-minute increase in time between the first MH sign and the first dantrolene dose.<sup>1</sup> In data from Canada, the time between onset of the first clinical sign and dantrolene administration was longer in patients who experienced complications compared with those who did not (23.5 vs. 15.0 minutes,  $P = 0.005$ ) and for each 10-minute delay in administration of dantrolene, complications increased substantially. When dantrolene administration was delayed beyond 50 minutes, complication rates increased to 100%.<sup>2</sup> Furthermore, there is an absence of existing reliable data on the incidence of MH susceptibility in different geographical areas, and on the incidence of the use of succinylcholine during administration of total intravenous anesthesia. Therefore, there is no way to approximate the true risk of MH in this clinical situation.

Other MHAUS experts, however, acknowledge the low incidence of MH caused by succinylcholine alone and the cost to health expenditures on a more global basis if every surgical facility was required to continuously buy and stock a dantrolene supply that is never used. This group of experts also worry about the health consequences of anesthetized patients if these surgical facilities choose not to stock succinylcholine solely for the reason to avoid the obligation of purchasing dantrolene, and they strongly oppose a recommendation that is not evidence-based. Some experts in this latter group thought that another reasonable option would be to require less than a full recommended dose (10 mg/kg) of dantrolene, reasoning that a “starter” dose would be useful prior to transferring the patient to a full service medical center.

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<sup>‡</sup> [https://www.ashp.org/news/2016/05/20/readiness\\_for\\_malignant\\_hyperthermia\\_can\\_be\\_survey\\_stumbling\\_block](https://www.ashp.org/news/2016/05/20/readiness_for_malignant_hyperthermia_can_be_survey_stumbling_block), Accessed December 11, 2017.

<sup>§</sup> This does not take into account the recent availability of sugammadex, which may facilitate the use of high-dose intravenous rocuronium to treat life-threatening airway obstruction.

## Conclusions:

The consensus of our experts was that the incidence of MH induced by succinylcholine alone is not rare enough to justify the absence of dantrolene wherever succinylcholine may potentially be administered. Facilities that stock and have the potential to administer any triggering agent, including succinylcholine without volatile agents, should have dantrolene immediately available (i.e., the ability to administer dantrolene within 10 minutes of the first sign of MH) in the event that a patient in that facility develops MH. Organizations that inspect healthcare facilities on behalf of CMS, as well as individual state-based licensing and inspection agencies should be the purveyors of decisions that involve healthcare costs to society.

## References

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