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New Recommendations for Use of Heptavalent Botulinum Antitoxin (H-BAT)

Background

Botulism is a life-threatening neuroparalytic illness caused by the ingestion of botulinum toxin. The incidence of foodborne botulism in Alaska is among the highest in the world, and all Alaska cases have been associated with eating Alaska Native traditional foods, including fermented foods, dried foods, seal oil, and muktuk.[1,2]

There are seven different types of botulinum toxins: A, B, C, D, E, F, and G. While types A–F have been documented to cause human disease, botulism cases in the United States are mainly caused by toxin types A, B and E. For over 30 years, the Centers for Disease Control and Prevention (CDC) has supplied states with types A, B and E antitoxin for treating botulism patients. Prompt administration of types A, B and E antitoxin has been shown to increase survival rates and decrease the number of patient-days in the hospital, days on a ventilator, and days until sustained clinical improvement compared to standard-of-care alone.[3]

Heptavalent Botulism Antitoxin

A new heptavalent botulinum antitoxin (H-BAT) produced by Cangene Corporation contains antibodies specific for the seven toxin types (A–G). H-BAT is being phased-in by CDC to replace the types A, B and E antitoxin products, which are in short supply and will soon expire. *H-BAT is currently available for use in Alaska.* H-BAT is a sterile solution containing purified $F(ab')_2$/Fab immune globulin fragments derived from horses that have been immunized with botulism toxoids and toxins; the Fc fragments of the equine antibodies have been removed from the final product to minimize the risk of patients developing an allergic response. A vial of H-BAT contains no preservatives and is intended for single use by the intravenous route.[4] As is true for the monovalent type E antitoxin, H-BAT is an investigational new drug (IND).

Storage and Handling[4]

Due to high rates of botulism in Alaska, distances to medical facilities and the importance of prompt administration, the Section of Epidemiology (SOE) will be storing H-BAT kits at some hub hospital pharmacies statewide, as was done with the types A, B and E antitoxin products. H-BAT that is maintained frozen at -15°C (5°F) must be used within one year. Once thawed, H-BAT must be stored at 2°–8°C (35°–46°F) and must be used within 6 months; H-BAT should not be re-frozen.

Administration[4]

The recommended adult dosing is <u>one 20 mL vial</u> of H-BAT. Consult SOE for dosing children aged >12 months. Frozen H-BAT can be thawed at 37°C (99°F) in a water bath.

- Obtain patient consent prior to administration of H-BAT.
- *Sensitivity testing prior to H-BAT administration is not required.*
- Prepare infusion under aseptic conditions.
- *Do not shake vial;* avoid foaming.
- Visually assess for particulate matter and discoloration. Do not infuse unless it is clear, is not turbid, and contains no particulate matter.
- Dilute 1:10 in 0.9% Sodium Chloride, Injection, USP. The premixed, unused IV bag can be stored refrigerated for use within approximately 8 to 10 hours.
- Use of an in-line filter is optional. If chosen, an in-line filter (pore size 15 µ) is recommended; smaller pore sizes may slow the infusion rate.
- Have epinephrine, diphenhydramine and intubation capabilities immediately available to treat anaphylactic or anaphylactoid reactions.
- To minimize allergic reactions, administer slowly using a continuous infusion pump starting at 0.5 mL/min for the first 30 minutes.
- If no infusion-related safety concerns are evident, increase to 1 mL/min for the next 30 minutes.
- If no infusion-related safety concerns are evident, increase to 2 mL/min for the remainder of the infusion.
- Due to its IND status, H-BAT requires that providers track patient outcomes (paperwork is provided in the state-supplied H-BAT kit).

Allergic Reactions and Contraindications

There are no absolute contraindications to treatment of an individual with a definite high-risk exposure to botulinum toxin. Although allergic reactions are expected to be infrequent, immediate systemic reactions (allergic reactions or anaphylaxis) can occur whenever an equine product is administered. An immediate reaction (e.g., shock, anaphylaxis) usually occurs within 30 minutes. Milder allergic reactions such as mild bronchorestriction, hypotension, or hives may be more common.

Pregnant Women[4]

There is little experience giving H-BAT to pregnant women. However, A, B and E antitoxins have been given to pregnant women without causing harm to the mother or the fetus. Being pregnant is not a reason to avoid H-BAT administration for botulism. The benefit to the mother and the fetus from receiving H-BAT for botulism should be weighed against the risk of harm from the treatment; decisions should be made on a case-by-case basis by the treating physician.

Infant Botulism

For cases of infant botulism, health care providers should continue to consult the California Infant Botulism Program (510-231-7600) and obtain BabyBIG® if indicated.[5] BabyBIG® is effective against botulism toxin types A and B; however, H-BAT has been used to treat a case of type F infant botulism and, on a case-by-case basis, may be used for future cases of infant botulism.

Recommendations

1. Health care providers should notify SOE immediately when a patient is suspected to have botulism.
2. After stabilizing the patient, health care providers should collect 10cc of serum, vomitus and stool, and suspected food items for laboratory testing as directed by SOE.
3. Administer H-BAT antitoxin promptly to patients with a clinical syndrome compatible with botulism.
4. SOE staff (1-800-478-0084) and CDC's botulism experts (1-770-488-7100) are available 24/7 for consultation.

References

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4. IND Protocol: Use of NP-018 Heptavalent Equine-Based Botulinum Antitoxin (H-BAT) After Exposure to *Clostridium botulinum* Toxin or Other Closely-Related Botulinum Toxin-Producing *Clostridia* Species Due to a Naturally-Occurring Outbreak or Isolated Incident. CDC IRB # 4509. BB-IND 6750.
5. State of Alaska Epidemiology *Bulletin*. "Infant Botulism – Interior Alaska, March 2009. Number 17, July 15, 2009. Available at: http://www.epi.hss.state.ak.us/bulletins/docs/b2009_17.pdf

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