82 Infant Botulism

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Botulism is a disease caused by *Clostridium botulinum* (*C. botulinum*). Three manifestations are known: food botulism, wound botulism, and infant botulism. Food botulism occurs as a result of exposure to botulinum toxin whereas infant botulism and wound botulism occur as a result to exposure to botulinum spores. Infant botulism is the most concerning for pediatricians. Infant botulism was first known in 1976 after Pickett et al. described an infant with hypotonia.

Causative Agent

C. botulinum is a Gram positive, spore forming, and nonmotile bacillus. It grows under anaerobic conditions and is distributed widely in the environment (soil, water, etc.). It produces very lethal toxins of many types, A through G. A and B are the most common toxins causing infantile botulism. Rare cases of toxin E disease due to *C. butyricum* and type F due to *C. baratii* have been reported. Type F toxin tend to produce disease in the very young infant and tend to be more severe. The only confirmed source of acquiring *C. botulinum* spores by an infant is ingestion of honey although this history is positive in only 20–35% of the cases.

Pathogenesis

Although honey is a known source of the spores, it is now rarely consumed by infants. Therefore the main source of botulinum spores is the environment, mainly the soil. Disruption of soil by farming or construction transmits the spores in dust particles to foods or water. Once consumed by the baby, spores germinate in the gastrointestinal tract producing the organisms which in turn produce the toxin. The toxin is absorbed and reaches the blood. From the blood it is distributed to cholinergic terminals including neuromuscular junction, ganglionic synapses, and parasympathetic postganglionic terminals. It binds to acetylcholine vesicles and thus prevents its secretion. This results in paralysis and hypotonia.

Clinical Manifestation

Infant botulism occurs in infants 6 days to 12 months of age and not later. Risk factors for acquiring botulism include consumption of honey, and constipation. The classic presentation is manifested by weak cry, poor oral intake, profound hypotonia, and constipation. Constipation usually precedes the other manifestations by 3 days to few weeks.

The hallmark of the disease is profound hypotonia. Characteristically it is descending in nature starting in the neck and proceeding caudally. In addition cranial nerves may be involved resulting in weakening of the pharyngeal muscles. This in turn results in weak, feeble cry, difficulty in swallowing, and regurgitation. Ophthalmoplegia and poor pupillary reaction to light may also occur.

Autonomic dysfunction may result in mucus membrane dryness and fluctuation in blood pressure and pulse rate.

Clinical diagnosis can be reached with certainty when full complement of symptoms and signs are present; however, infant botulism may present with a myriad of pictures ranging from asymptomatic disease to fulminant fatal disease.

Infantile botulism should be differentiated from other diseases that may present with similar picture including sepsis, Gullain-Barre disease, poliomyelitis, myasthenia gravis, heavy metal toxicity, organophosphorus toxicity, and metabolic diseases.

Lab Diagnosis

It is very rare to isolate *C. botulinum* from stool of normal infants; therefore isolating it from stool of an infant with clinical findings of botulism is regarded highly suggestive of infant botulism. *C. botulinum* can be isolated from the stool up to 150 days after infection. However, biologic mouse toxin assay is the only clinically evaluated diagnostic test. Recently ELISA has been developed for rapid detection of toxin A and B in the serum or fecal filtrate. This test allows detection in 24 h as compared to 4 days that are required for mouse assay.

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Table 82.1
Management targets to optimize outcome (in addition to use of BabyBIG®) (From: Long S (March 2007) Infant botulism and treatment with BIG-IV (BabyBIG_). The Pediatric Infectious Disease Journal • vol 26(3))

• Perform preemptive intubation when protection of airway is compromised; extubate when gag reflex, swallow, and sustained activity against gravity is restored
• Perform ventilator-associated pneumonia prevention "bundle"
• Differentiate hyponatremia due to dehydration vs. SIADH
• Position supine with head of planar mattress (not head of infant) raised 30°; small (washcloth size) roll behind neck; roll behind thighs (to minimize venous pooling & SIADH); smooth infant and bed clothing to avoid pressure from folds
• Institute nasojejunal feedings (continuous initially) within 48 h of admission, and remove intravenous catheter(s)
• Avoid use of unnecessary antibiotics, Foley catheters

Table 82.2
Differences in outcomes of infants treated with BIG-IV* (From: Arnon SS et al (2006) Human botulism immune globulin for infant botulism. N Engl J Med 354:462–471)

Randomized placebo-controlled trial (129 infants)[a]		
Duration of	Placebo	BIG-IV
Hospitalization	5.7 weeks	2.6 weeks
ICU care	5.0 weeks	1.8 weeks
Mechanical ventilation	4.4 weeks	1.8 weeks
Tube feeding	10.0 weeks	3.6 weeks
Total hospital charges	$163,000	$74,800
Open-label use (366 infants)		
Duration of hospitalization	BIG-IV @ 4–7 days hosp 2.9 weeks	BIG-IV @ <4 days hosp 2.0 weeks

*All differences statistically significant; *P* values ≤ 0.001
[a]Infants eligible only if <3 hospital days

Supportive tests include characteristic EMG picture of brief, small, abundant motor-unit potentials (BSAP). This can be observed in 90% of affected infants. Nerve conduction is usually normal.

Treatment

Management of infantile botulism relies mainly on supportive care (*Table 82.1*). This means supplying oxygen or artificial ventilation if needed. Two important factors have been associated with respiratory decompensation in these patients; administration of aminoglycoside antibiotics and neck flexion during positioning for lumbar puncture of computerized tomography. Aminoglycosides may potentiate neuromuscular blockade and therefore should be avoided in these patients. Most of the affected infants have poor suck and swallowing and therefore need nasogastric or nasojejunal feedings and occasionally parenteral nutrition. Care should be provided to prevent aspiration. Antibiotics have no room in treatment except for secondary bacterial infections. Botulism immunoglobulin intravenous (BIG-IV) is now available and has revolutionized therapy of infant botulism. It is derived from pooled human plasma of immunized adult volunteers and it neutralizes free toxin. Its use has improved morbidity significantly (*Table 82.2*). It should be given immediately based on clinical diagnosis without awaiting confirmatory test. It is most effective if given within the first 72 h of illness; however, it should be offered even after 72 h. With appropriate supportive management, the outcome is usually excellent with a mortality rate of less than 2%. The only preventive measure is avoiding honey in infant feeding. Relapse is rare and there are no special infection control issues.

References

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