Infant botulism in Australia: availability of human botulinum antitoxin for treatment

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We report the first Australian case of treatment of infant botulism with a human botulinum antitoxin developed in the United States by the California Department of Public Health. Our patient's clinical improvement was rapid, and although the product is expensive, cost-analysis supports the economical viability of its use. In future cases of suspected infant botulism, we recommend that Australian clinicians promptly obtain and administer this antitoxin to their patient. **(MJA 2010; 193: 614-615)**

Clinical record

A 5-month-old girl who was fully breastfed presented to the emergency department at a tertiary children's hospital with poor feeding and lethargy. She was afebrile and mildly dehydrated, with a poor suck and a weak cry. Laboratory testing revealed a normal full blood examination and mild derangement of electrolytes consistent with dehydration. Blood cultures were sterile, and cerebrospinal fluid examination was normal.

Formal neurological examination revealed bilateral ptosis, low muscle tone, globally reduced muscle strength and no gag reflex. Deep tendon reflexes were absent, and pupillary reflexes were preserved. Nerve conduction velocities and electromyography were normal. Further history revealed no recent ingestion of honey and no passage of bowel motions for 10 days. She had not received oral polio vaccine and had no history of overseas travel.

The patient was transferred to the hospital's paediatric intensive care unit (PICU), where we established a working diagnosis of infant botulism, pending confirmatory investigations. The patient was electively intubated and ventilated on Day 3 of her hospital admission. Faecal fluid was obtained per rectum for a mouse toxin bioassay.

We telephoned the California Department of Public Health's Infant Botulism Treatment and Prevention Program (IBTPP) in the United States to purchase BabyBIG (botulism immune globulin [intravenous human]) (Massachusetts Public Health Biologic Laboratories and Cangene Corporation, Boston, Mass, USA), which we received 48 hours later. A single infusion of BabyBIG was administered on Day 7 of the child's admission to hospital, with no adverse consequences. The product cost US$43 500.

The diagnosis of infant botulism was confirmed by the mouse bioassay, with growth of toxin B-producing *Clostridium botulinum* from faeces. The child was extubated on Day 10 of her PICU admission, discharged from the PICU on Day 16, and discharged home on full enteral feeds on Day 24. Follow-up physiotherapy showed gross motor delay with postural weakness, which had resolved by 2 months after discharge.

Discussion

This is the first case of infant botulism in Australia in which BabyBIG has been used (personal communication, Dr Stephen Arnon, Chief, IBTPP, California Department of Public Health, 21 March 2009). While an uncommon disease, Australia has had about one case per year since 1999.[1]

Infant botulism arises from ingestion of *C. botulinum* spores and growth of the organism in the gastrointestinal tract, producing botulinum toxin, which binds irreversibly to receptors at the neuromuscular junction, producing flaccid paralysis. Ingestion of honey is a classic risk factor, although frequently no specific source of the infection is found. Intensive supportive care is required until muscular function recovers — a process which takes weeks to months, usually with extended hospitalisation and artificial ventilation.

BabyBIG was developed by the California Department of Public Health and registered with the US Food and Drug Administration (FDA).[2] The product is derived from serum donations from individuals immunised with pentavalent botulinum toxoid, a vaccine developed by the US military. Purification and preparation of the product is in line with FDA licensing requirements for processing human plasma, including screening of donors and testing plasma for transmissible diseases. The product comes as a lyophilised powder of immunoglobulin G, stabilised with 5% sucrose and 1% human albumin, and contains neutralising antibodies against botulinum toxins A and B. The product has a half-life of about 28 days, and a single infusion is calculated to neutralise all absorbed botulinum toxin for at least 6 months.

BabyBIG was initially assessed in a randomised, double-blind, placebo-controlled trial conducted between 1993 and 1997.[3] The trial involved 129 Californian infants with botulism, treated on Days 0–3 of hospital admission, and showed significant decreases in duration of ventilation (by 2.6 weeks [$P = 0.01$]), length of PICU stay (by 3.2 weeks [$P < 0.001$]), length of hospital stay (from 5.7 weeks down to 2.6 weeks, [$P < 0.001$]), and mean hospital costs per patient (of US$88 600 [$P < 0.0001$]). Subsequent open-label, US-wide use of the product on 382 infants showed similar results in the 366 infants who received BabyBIG within 7 days of admission.[3] The product was initially only available to infants in North America, but since 2003 has been exported internationally on a case-by-case basis. A subsequent review has shown that only 5% (32) of 681 cases treated with BabyBIG since 2003 have been misdiagnoses, with no adverse events occurring as a consequence of the infusion in any infants.[4]

Although the cost of the treatment is substantial, evidence has shown the intervention to be economically sound. In our case, a conservative estimate of costs saved just from reduced requirement for intensive care ranged from A$28 000 to A$117 600, based on an estimate of A$4000 per intensive care day. The social and emotional benefits of early discharge and recovery to the child and her family are obvious.

In cases of suspected infant botulism, we recommend that Australian intensive care physicians and paediatricians promptly obtain and administer BabyBIG to their patient. All experience to

date encourages pre-emptive treatment without waiting for confirmation by diagnostic testing. Despite long distances in sourcing the product, with good communication, this process can provide a timely, safe, effective and cost-saving treatment for infant botulism.

Competing interests

None identified.

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