



CHOC Children's Hospital
Best Evidence and Recommendations

**Best Practices in Managing Ommaya Reservoirs to Reduce Risk of Infection
Associated with Brineura Infusion**

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PICO: In pediatric Batten disease patients with Ommaya reservoirs, what are best practices for management to reduce infection and standardize inpatient and home care?

P (Population/problem): In pediatric Batten disease patients with Ommaya reservoirs,
I (Intervention/issue) : what are best practices for management
C (Comparison): (compared to current practice)
O (Outcome): to reduce infection and standardize inpatient and home care?

Background:

Batten disease is a genetic, neurodegenerative disorder that results in a rapid regression of physical and cognitive development in the pediatric population. Also known as Neuronal Ceroid Lipofuscinosis (NCL), this genetic disorder has 14 known forms that are identified as CLN1-CLN14, and are differentiated by the type of genetic mutation. In the United States, it is estimated that 2-4 births per 100,000 are affected by Batten disease. The genetic mutations associated with this disorder disrupt the neurons' ability to dispose of wastes. Affected children typically function normally until age 2 to 4 years, followed by a rapid decline in cognitive, motor, visual, and language function over the subsequent 4 to 6 years (Schultz et al., 2018). Presentation includes seizures, unsteady gait, loss of vision, altered thought processes, movement disorders, and ultimately death by early adolescence.

In April of 2017, an enzyme replacement, Brineura, was approved by the FDA for use in symptomatic pediatric CLN2 Batten's patients. This strand of the disease is currently the only form of Batten disease that has an approved form of treatment. In this disorder, there is a deficiency of the lysosomal enzyme called tripeptidyl peptidase 1 or TPP1. Without this enzyme cellular function is affected, including an abnormal buildup of proteins and lipids that are not able to be disposed, causing cell death. This enzyme replacement, cerliponase alfa, known as Brineura, is a recombinant human TPP1 enzyme, and was developed by BioMarin Pharmaceuticals. Data demonstrate that patients treated with Brineura experienced a slower decline in function than historical controls (Schultz et al, 2018).

CHOC Children's Hospital was among the first in the nation to offer this promising treatment. Brineura is administered every two weeks through a surgically implanted intraventricular Ommaya reservoir, as this is the only way for the enzyme to cross the blood brain barrier. With bimonthly accessing of these devices, patients receiving treatment are at high risk of infection. Device-related complications such as infections have resulted in delayed treatment and have



detrimental effects on symptom management (Gerber et al, 2015; Mead, Safdieh, Nizza, Tuma & Sepkowitz, 2014; Peryl et al., 2014).

Slavc and colleagues (2018) recently synthesized the opinions and best practices of an international expert group of multidisciplinary healthcare professions on the use of intracerebroventricular drug delivery devices. Establishment of evidence-based protocols for safe management including accessing and deaccessing the Ommaya reservoir is necessary to reduce the rate of infection for Batten disease patients.

Search Strategies and Databases Reviewed:

- Due to the novelty of the Brineura infusion, there is a paucity of evidence specific to managing Ommaya reservoirs for Brineura infusions. For this reason, literature on adult and pediatric Ommaya reservoir management for other treatments (such as chemotherapy) was reviewed and applied to this unique population.
- Databases searched for this review included CINAHL, Medline in EBSCO and Pub Med. Key search words: Ommaya reservoirs, intraventricular infections, Propionibacterium acnes, preoperative hair removal, and antiseptic preoperative preparations. This search yielded 21 articles that were reviewed including retrospective, prospective analysis, case reports, comparison of randomized control trials, and literature reviews. Of these articles, 11 were found to have applicable information.
- Websites reviewed included: BioMarin Pharmaceuticals, CHOC Children's (choc.org), Batten Disease Support and Research Association (<https://bdsra.org>)
- Original process information and collaboration was completed with Nationwide Children's Hospital, Columbus, OH, and University Medical Center Hamburg-Eppendorf, Hamburg, Germany.

Synthesis of Evidence:

Accessing Ommaya Reservoirs

- Gerber et al. (2015) completed a retrospective analysis of Ommaya reservoir related complications in pediatric patients, finding a high rate of infection, requiring removal of over half of the reservoirs (17 of 31). This study, although questionable in reliability and validity due to retrospective nature, led to the recommendation of standard operating procedures for intracerebroventricular device placement and use.
- Peryl et al. (2014) examined 98 pediatric oncology patients with Ommaya reservoirs, and documented device related complications. In contrast to the Gerber et al. study, only one incidence of infection was reported related to the Ommaya reservoir. This study recognized the importance of procedures, and established guidelines for administration of intraventricular chemotherapy via the Ommaya reservoir. This study also stressed the need for specially trained neurosurgeons and nurses to perform these procedures.
- A more recent literature review and analysis by Cohen-Pfeffer et al., (2016) confirms the findings of the above studies, and recognizes and recommends the need for best practice guidelines for the management of these intracerebral devices in order to minimize infectious complications.



- The work of Slavic et al, 2018, has synthesized the opinions of an international expert group of multidisciplinary healthcare professions and the procedures utilized at their institutions. Consensus is that the development of a best practice protocol for use of intracerebroventricular drug delivery devices or Ommaya reservoirs is necessary to reduce the rate of CNS infection and minimize related complications

Infection Prevention/Identified Organisms

- Frequent skin flora organisms found to infect Ommaya reservoirs include: Propionibacterium acnes, Staph aureus, and Staph epidermis (Jakab, Zbinden, Gubler, Ruef, Von Graevenitz, & Krause, 1996; Mechleb, Khater, Eid, David, & Moorman, 2003; Viraraghavan, Jantausch, & Campos, 2004).

Ommaya Site Maintenance:

In an effort to understand the safest method for preparing the catheter site for infusion, studies were examined related to best practice for hair removal.

- Hair clipping is documented as the preferred method of hair removal, versus shaving which can introduce microscopic cuts and abrasions allowing for the introduction of bacteria (Tanner, Norrie, & Melen, 2011).
- There has been no definitive research that suggests depilatory creams are less effective than clipping yet many patients have reported irritation at the port site (Tanner et al., 2011).
- Home care for the infusion sites between infusions has been considered, with research suggesting use of a pH-neutral or bacteriostatic shampoo the night before access (Slavic et al., 2018).

Practice Recommendations:

- To optimize outcome, organizations providing Brineura for treatment of Batten disease should establish formal clinical guidelines and policy/procedures to address safe management including accessing and deaccessing the Ommaya reservoir. Guidelines should include the following best practices:

Accessing:

- The reservoir port should not be accessed until 5 days after Ommaya placement for reduction of infection (Gerber et al., 2015; Peryl et al., 2014; Slavic et al., 2018).
- Each infusion must be performed as a sterile procedure. No person to enter or leave the room during procedure, door and windows closed during the entire access process (Gerber et al., 2015; Peryl et al., 2014). All persons in room wear mask, gown, hat, and gloves, including caregivers; those accessing patient must use sterile technique (Gerber et al., 2015; Peryl et al., 2014; Slavic et al., 2018).
- Immediately prior to access, hair around the Ommaya site should be clipped, not shaved, to reduce surgical site infections and introduction of microscopic cuts and abrasions (Slavic et al., 2018; Tanner et al., 2011).
- The reservoir site should be cleaned 3 times with Chloraprep (Chlorhexidine with alcohol) utilizing sufficient cleaning, scrubbing with circular motion, and dry time



of at least 2 minutes for each application. Recommended iodine-based or alcohol-based with chlorhexidine, cleaning 3-5 times with applicator (Slavc et al., 2018). International studies use Propanol plus octenidine dihydrochloride (not used in US). The product is less expensive and comparison studies have shown same efficacy.

- Reservoir site should be accessed with a 22 G Huber needle by neurosurgeon (size supplied by manufacturer), and 3-5mL CSF sample is drawn, for testing of CSF cultures, protein, glucose, and cell count. Aspiration ensures patency as well as isovolumetric purposes to reduce the risk of increased ICP (Slavc et al., 2018).

Deaccessing:

- Before removal of needle, RN dons sterile gloves and mask for deaccess. Port is removed by pulling needle straight up, avoiding any angle. Sterile 2X2 gauze is utilized, placing pressure on port access site, rubbing gently, and avoiding pumping the reservoir (Slavc et al., 2018). A band-aid should be applied to help prevent infection (Gerber et al., 2015; Peryl et al., 2014; Slavc et al., 2018).

Home Management:

- Family is provided instruction on signs of infection and the HibacLens shampoo (or pH-neutral shampoo) to be used on evening prior to infusion (Slavc et al., 2018).

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