

Tympanostomy Tube Insertion System for Children With Otitis Media

Issue 127 • October 2014

Summary

- ✓ **The TULA System is a new technology for the placement of tympanostomy tubes in children with otitis media. The procedure is performed using local anesthesia in an outpatient setting.**
- ✓ **Traditional tympanostomy tube placement is performed by surgeons in an operating room under general anesthesia, resulting in the substantial use of health care resources, patient and caregiver anxiety, and caregiver absence from work.**
- ✓ **Using general anesthesia in children is not without risks including the potential for adverse drug reactions and aspiration events. There is also concern that using general anesthesia in young children may adversely affect neurological, cognitive, and social development.**
- ✓ **Results from three prospective, open-label, single group assignment clinical studies indicate that the TULA System is effective and tolerable for the delivery of local anesthetic to the tympanic membrane and the placement of tympanostomy tubes in children as young as 12 months. Reasons for procedure failure included children who were not comfortable undergoing the procedure using local anesthesia, failure to achieve anesthesia, the tube falling short of the tympanic membrane, and the tube being retained in the device.**
- ✓ **Few procedural complications were noted in the studies. These included tube occlusion and earache. None of the studies followed patients beyond two weeks.**
- ✓ **The TULA System is anticipated to result in health care savings for use in an outpatient setting instead of an operating room. However, the long-term safety and efficacy of the TULA System needs to be clarified to determine the extent of uptake in the clinical management of otitis media in children.**

Background

Otitis media (middle ear inflammation) is one of the most common early childhood infections in Canada resulting in the substantial use of health care resources and caregiver absence from work.¹ An estimated 20% to 40% of children suffer from recurrent acute otitis media (defined as three or more episodes in six months or four or more episodes in 12 months).²⁻⁴ Otitis media with effusion occurs when long-standing fluid in the middle ear becomes thick and glue-like.⁵ Otitis media with effusion commonly follows an episode of acute otitis media, but may also occur when the eustachian tube is obstructed. Approximately 90% of children experience at least one episode of otitis media with effusion by the age of four.⁶ Clinical manifestations of otitis media may include hearing loss, ear pain, sleep disturbance, tinnitus, and balance problems.⁷⁻¹² Although there is concern that prolonged hearing loss may lead to long-term impairment of speech and cognitive abilities, the clinical significance of the hearing loss associated with otitis media is still debated.¹³⁻¹⁵

A surgical procedure consisting of making an incision in the tympanic membrane (myringotomy) and placing a tympanostomy tube in the incision is used to drain fluid from the middle ear and provide ventilation of the middle ear space.⁵ Tympanostomy tubes improve hearing and reduce the risk for effusion and recurrent infections in children with otitis media.⁵ Tympanostomy tube insertion in young children is generally performed under general anesthesia by surgeons in an operating room and is the most common reason for a child to receive general anesthesia in the United States (US).¹⁶ Using general anesthesia in children is not without risks including the potential for adverse drug reactions and aspiration events. Although there is currently not enough information to draw firm conclusions regarding an association between anesthetic exposure and learning disabilities, there is concern that general anesthesia may adversely affect neurological, cognitive, and social development in children.¹⁷ Results from a recent study suggest that using general anesthesia in children before the age of one may lead to lifelong problems with short-term memory.¹⁸ The ability to shift tympanostomy tube placement from the operating room to an outpatient setting using local anesthesia would address concerns about the safety of

general anesthesia in children, reduce caregiver and patient anxiety, limit caregiver absence from work, allow more scheduling flexibility for surgeons, and shift care into a lower cost-setting.

The Technology

The TULA System (Acclarent, Inc., Menlo Park, California) is made up of two devices and coaching tools.¹⁹ The TULA IONTOPHORESIS SYSTEM is a headset equipped with single-use earplugs.²⁰

Iontophoresis is a method to actively move charged drug molecules through the skin using low levels of electrical current.²⁰ Ear electrodes within the earplugs connect to a control unit to deliver bilateral local anesthetic over ten minutes to the tympanic membrane.¹⁹ The TULA Tube Delivery System is used to make an incision in the tympanic membrane and insert a pre-loaded tympanostomy tube in a single automated motion.²¹ The entire procedure can be performed in an outpatient setting such as a clinic or doctor's office.

Regulatory Status

Health Canada issued a Class II Licence to Acclarent Inc. for the TULA IONTOPHORESIS SYSTEM in May 2014.²² This is the first iontophoresis device on the market that is specifically intended for simultaneous bilateral drug delivery to the ear canal for local anesthesia of the tympanic membrane. Health Canada has not yet granted approval for the TULA Tube Delivery System. Food and Drug Administration (FDA) clearance for sale in the US was received for the TULA Tube Delivery System and TULA IONTOPHORESIS SYSTEM in April 2011 and June 2011, respectively.^{20,21}

Patient Group

A population-based study estimated the rate of tympanostomy tube placement in Calgary, Alberta at 11 per thousand children aged 0 to 15 years.²³ The majority of the procedures were performed in children less than four years of age, with the highest rate occurring in the second year of life. Given the current population in Canada of 5.7 million children under 15, this represents a potential patient population of approximately 62,000.²⁴

Current Practice

Current guidelines recommend that myringotomy with tympanostomy tube insertion should be reserved for children experiencing recurrent acute otitis media with effusion, or children having chronic otitis media with effusion persisting at least three months and exhibiting hearing difficulties or other symptoms including ear discomfort, balance problems, poor school performance, behavioural problems, or reduced quality of life.^{5,25} Other indications for tympanostomy tube insertion include children with otitis media with effusion of any duration who are at increased risk for speech, language, or learning problems — such as those with autism spectrum disorders, cleft palate, craniofacial disorders, and Down syndrome.⁵ During the conventional surgical procedure, the surgeon uses a surgical knife to create the incision, and different surgical instruments to pick up the tube and insert it into the incision.¹⁹ The entire procedure takes less than ten minutes but requires general anesthesia in young children who may not lie still or who may not tolerate the injection of local anesthetic to numb the tympanic membrane.²⁶ The tympanostomy tubes typically stay in place for six to 12 months.

In addition to the potential adverse effects of general anesthesia, risks related to tympanostomy tube placement are related to the effect of the tube on the tympanic membrane and middle ear. The most common complications to occur after tympanostomy tube placement include otorrhea (discharge from the tympanostomy tube) and tube occlusion.^{16,27} Other sequelae of indwelling tubes include premature tube extrusion and tube dislocation into the middle ear space. Sequelae after tube extrusion include tympanosclerosis (calcification of tissue in the middle ear), persistent perforation of the tympanic membrane, focal atrophy of the tympanic membrane, and cholesteatoma (formation of a cyst in the middle ear), which may result in hearing loss.^{16,27}

Methods

A peer-reviewed literature search was conducted using the following bibliographic databases: MEDLINE, PubMed, Embase, and The Cochrane Library (2014, Issue 6). Grey literature was identified by searching relevant sections of the Grey Matters checklist (<http://www.cadth.ca/resources/grey-matters>). No methodological filters were applied. The search was limited to English language documents published between January 1, 2009 and July 7, 2014. Regular alerts were established to update the search until August 25, 2014.

Conference abstracts were excluded from the search results. Peer-reviewed published studies evaluating the clinical efficacy and safety of the TULA System for the placement of tympanostomy tubes under local anesthesia in an outpatient setting were considered for inclusion in the evidence section of this bulletin. Unpublished data was also included. Case reports, editorials, letters, and literature reviews were excluded.

The Evidence

Clinical data to support the use of the TULA System in an outpatient setting for the treatment of otitis media in children have been reported in three prospective, open-label, single group assignment clinical studies.^{26,28,29} One of these studies has been published.²⁶ All three studies were conducted in the US.

One study was presented as a poster at the Triological Society's 2012 annual meeting.²⁸ Inclusion criteria were patients more than six months of age scheduled to undergo tympanostomy tube placement and who had the behavioural capacity to tolerate the procedure. Outcome measures included surgical procedure success, tube retention, and postoperative hearing. The tolerability of the procedure was measured on the Wong-Baker FACES Pain Rating Scale. This standardized and validated scale is frequently used with children, with 0 indicating a painless procedure and 5 representing intolerable pain. Twenty-eight patients (43 ears) aged one to 95 years were enrolled at three sites. Eighteen ears (41.9%) belonged to children aged five years or younger. All patients received local anesthesia using the TULA IONTOPHORESIS SYSTEM. A novel iontophoresis solution mixture containing lidocaine, epinephrine, and sodium bicarbonate was used for local anesthesia over ten minutes. Following anesthesia, the TULA Tube Delivery System was used to insert tympanostomy tubes. Successful tympanostomy tube insertion was achieved in 38 ears (88.4%). The tympanostomy tube was placed manually by the surgeon in the remaining five ears (11.6%). In all five cases, the incision was made but the tube fell short of the tympanic membrane or was retained in the device. At the two-week follow-up visit, tympanostomy tubes placed using the device were retained in position in all 38 ears (100%). Postoperative audiometry showed improved hearing in 36 ears (83.7%). The remaining seven ears (16.3%) showed no change in hearing from preoperative audiometry testing. The average pain score during the procedure was 1.

Unpublished results from the INOVA study have been reported on the www.clinicaltrials.gov website.²⁹ The study enrolled patients aged six months to 21 years with otitis media who were scheduled to undergo tympanostomy tube insertion. Outcome measures included surgical procedure success, tube retention, and adverse effects up to two weeks following the procedure. A total of 70 participants (average age of 7.0 ± 3.9 years) were enrolled. Five patients did not complete the study due to failure to achieve anesthesia using the TULA IONTOPHORESIS SYSTEM. Of 128 ears analyzed, tympanostomy tube delivery across the tympanic membrane was successful in 114 ears (89.1%). Of 112 ears (63 participants) assessed at the two-week follow-up visit following successful tympanostomy tube placement, 111 ears (99.1%) still had the tube in place.

One published, peer-reviewed study examined the safety and effectiveness of the TULA System in an outpatient setting.²⁶ The study population was composed of 50 patients (86 ears) who met the standard indications for myringotomy with tympanostomy tube insertion or myringotomy alone. The age range was 12 months to 84 years, with 17 patients (34.0%) being less than three years of age. All procedures were performed at a single clinic by the same physician. All patients received local anesthesia using the TULA IONTOPHORESIS SYSTEM. Age-appropriate distraction was used during the procedure but no preoperative restraints or medications were used. Outcome measures included iontophoresis success (defined as an anesthetized tympanic membrane at the conclusion of iontophoresis), surgical procedure success, and pain measured on the Wong-Baker FACES Pain Rating Scale. Iontophoresis was successful in 78 ears (90.7%). Reasons for iontophoresis failure included children whose ear plugs failed to make a good seal ($n = 2$) and children who did not tolerate iontophoresis and were scheduled for surgery under general anesthesia ($n = 4$). The average pain score during iontophoresis was 1.07. Of the ears that completed iontophoresis, the surgical procedure was performed successfully in 70 ears (89.7%). Reasons for surgical procedure failure included children who were not comfortable undergoing the procedure under local anesthesia ($n = 1$), children who felt discomfort with palpation of the tympanic membrane prior to surgery ($n = 1$), and children who reported discomfort upon myringotomy, leading to cancellation of tympanostomy tube placement ($n = 2$). Three of these children were scheduled for tympanostomy tube insertion under general anesthesia. The average pain score during the surgical procedure was 1.19.

Adverse Effects

No serious adverse effects relating to the TULA Tube Delivery System were reported in any of the studies.^{26,28,29} One study reported tube occlusion in two participants (2.86%) and otalgia (earache) in one participant (1.43%).²⁹ No safety issues or complications associated with the TULA IONTOPHORESIS SYSTEM or the local anesthetic mixture were noted.²⁶ None of the studies reported long-term safety outcomes.

Cost

The manufacturer's price for the TULA IONTOPHORESIS SYSTEM in Canada is currently unavailable.

Concurrent Developments

The Hummingbird TTS tympanostomy tube system (Preceptis Medical Inc., Minneapolis, Minnesota) for the insertion of tympanostomy tubes under conscious sedation using nitrous oxide^{30,31} is in development. The device is made up of a surgical scalpel, ear tube injector, and a suction mechanism.³² An open-label, single group assignment clinical trial is currently investigating if the Hummingbird TTS device is safe and effective for tympanostomy tube insertion in children with otitis media³³ six months of age or older. Study completion is anticipated in December 2016. The KINETUBE (La Diffusion Technique Française Fabricant, Saint-Étienne, France) is also under investigation for otitis media in children.³⁴ The device is made up of a pressure generator and a patient interface equipped with a sensor that detects swallowing. This device is designed to equalize pressure in the middle ear by improving the opening of the eustachian tube during swallowing. A randomized clinical trial is comparing the efficacy of tympanostomy tubes with the KINETUBE device for the treatment of recurrent otitis media with effusion in children aged seven to 15 years.³⁴ The primary outcome measure is a difference in hearing at three years. Study completion is expected in July 2016.

Rate of Technology Diffusion

Current evidence to support the safety and efficacy of the TULA System for otitis media in children is limited by the number of very young children enrolled in each study (less than 50% of each study population was four years of age or younger), lack of comparative evidence with standard treatments, and the absence of long-term safety data. Other open-label, single arm studies investigating the TULA System for the treatment of otitis media under local anesthesia have been completed but no results have been reported.^{35,36} No new, ongoing studies evaluating the TULA System were identified. The long-term safety and efficacy of the TULA System needs to be clarified to determine the extent of uptake in the clinical management of otitis media in children.

Implementation Issues

There is preliminary evidence that the use of the TULA System in children with otitis media is safe and effective for the placement of tympanostomy tubes in an outpatient setting in children as young as 12 months. Although use of the TULA System will necessitate using health care resources in terms of the associated cost of the device and the training of staff, it is anticipated to result in health care savings for use in an outpatient setting instead of an operating room. According to the Ontario Case Costing Initiative, the average overhead associated with an operating room for myringotomy and tympanostomy tube placement in pediatric patients was \$861 in 2011.³⁷ A US study reported that performing the tympanostomy tube procedure in an operating room cost US\$1,850 more per patient than performing the procedure in an outpatient treatment suite.³⁸

More studies are required to clarify several knowledge gaps. The long-term impact of the TULA System on outcomes such as hearing loss, acute otitis media and effusion recurrence, caregiver absence from work, and quality of life in comparison to conventional tympanostomy tube placement has yet to be determined. More studies are required to ascertain the need for repeat or manual procedures and to support treatment decisions in subpopulations, particularly those with comorbidities. While the TULA coaching tools may help facilitate patient cooperation, children will need to have the appropriate disposition to tolerate the procedure, and general anesthesia may be safer in some children.

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Cite as: Ndegwa S. Tympanostomy tube insertion system for children with otitis media. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2014. (Issues in emerging health technologies; issue 127).

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ISSN: 1488-6324 (online)