Safety of Ethmoid Sinus Drug-Eluting Catheter Insertion

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Objectives: We sought to evaluate an instrument that allows a drug-eluting catheter to be inserted into the ethmoid sinuses and to demonstrate its safety and reproducibility in a cadaver model.

Methods: A drug-eluting catheter was placed into 12 cadaveric anterior and posterior ethmoid sinuses by use of a trocar-based insertion device. The device’s position was analyzed with computed tomographic scans, and postprocedural dissection was performed.

Results: The drug-eluting catheter system was successfully inserted in all ethmoid sinuses without injury to the medial orbital wall, skull base, or sphenoid face. The final position of the distal tip of the catheter averaged 8.1 mm (root mean square [RMS], 3.3 mm) from the skull base, 5.6 mm (RMS, 3.5 mm) from the sphenoid face, and 5.0 mm (RMS, 3.5 mm) from the lamina papyracea; the proximal tip was at the face of the ethmoid bulla and 17.1 mm (RMS, 3.5 mm) below the skull base.

Conclusions: A trocar-based instrument can relatively safely and reproducibly introduce a drug-eluting catheter into the ethmoid sinuses without injuring the skull base, lamina papyracea, or sphenoid face. This device may allow safe topical drug delivery into the ethmoid sinuses and serve as a vehicle to treat chronic ethmoid sinusitis with direct and sustained topical therapy.

Key Words: chronic ethmoid sinusitis, chronic rhinosinusitis, device safety, drug-eluting catheter, minimally invasive procedure, topical therapy.

INTRODUCTION

Topical therapy for the treatment of chronic rhinosinusitis is limited by access to the involved sinuses. This is a particular challenge in patients who have never undergone sinus surgery, as the native anatomy and physiology of the sinonasal cavity allow no or minimal access of intranasal substances into the sinuses themselves. This is especially the case for the ethmoid sinuses, which communicate with the nasal cavity through a labyrinth of intricate connections and extraordinarily small ostia.

Topical delivery of medication (antibiotics, steroids, etc) is a common treatment for chronic rhinosinusitis in patients who have had sinus surgery. In fact, one of the benefits of functional endoscopic sinus surgery is that it allows postoperative access to the sinuses for these topical therapies. The creation of a system that can deliver these medications locally to a patient who has not had sinus surgery would be ideal, if the delivery could be done in a safe and reliable manner.

In chronic rhinosinusitis, topical steroids reduce inflammation by affecting the cytokine milieu in the sinonasal cavity. They reduce the mucosa’s expression of cytokines that promote a Th2 subset of T-helper cells that especially contribute to eosinophilic inflammation. Specifically, they have been shown to reduce the number of local eosinophils and T cells, as well as decrease the expression of interleukins 4 and 5. They are particularly useful in the topical management of patients who have undergone previous endoscopic sinus surgery.

The pharmacokinetics and pharmacodynamics of topical therapy depend on the substance used, the solvent in which the medication is delivered, and the contact time, absorption, clearance, and metabolism of the medication. Ideally, a medication that can be frequently delivered or continuously delivered would allow for the maximum amount of contact time for topical therapy. This is especially important in dealing with the sinonasal cavity, which has the ability to transport topical medication away from the target tissue with mucociliary flow. Delivering a drug-eluting catheter into the ethmoid sinuses should improve medical therapy via the delivery...
of topical medication directly into the diseased sinus; it does not rely on only treating the area into which the sinus drains. Using topical therapy in a patient with no history of sinus surgery will not reliably deliver the drug into the diseased sinus, especially the ethmoid sinus. The medication must overcome the anatomic barrier provided by the ethmoid cell walls, as well as the uncinate process and both the middle and superior turbinates. Also, the therapy must overcome the body’s natural mucociliary flow out of the sinus.

The ideal catheter and delivery system would be one that could be used safely and reliably. Also, it would cause minimal trauma to the sinus’s cell walls. After removal, the integrity and anatomy of the sinus should be minimally disturbed. A drug-eluting catheter and trocar-based delivery system has been developed by Acclarent, Inc (Menlo Park, California).

In general, the ethmoid sinuses have been nearly impossible to treat with topical medications. Application of such therapies via catheter delivery has been described, but is not commonplace. The purpose of this study was to test the safety and feasibility of a trocar-based system to insert a drug-eluting catheter into the ethmoid sinuses.

**METHODS**

Fresh cadaver specimens were obtained, and fine-cut (0.625 mm) axial computed tomographic (CT) scans were obtained with coronal and sagittal reconstruction. The CT data were reviewed, and the following data were noted: the distance from the face of the ethmoid bulla to the face of the sphenoid sinus, the height of the ethmoid bulla, the slope of the skull base, the position of the anterior ethmoid neurovascular bundle, and the integrity of the lamina papyracea.

A trocar-based insertion device was used for the placement of a drug-eluting catheter. It consists of 3 separate components: the trocar, the delivery sheath, and the drug-eluting catheter itself (Fig 1). Conceptually, the trocar is used to penetrate the cell walls of the anterior and posterior ethmoid sinuses. It enters the ethmoid sinuses through the face of the bulla and is passed into the posterior ethmoid sinuses to a final position just anterior to the face of the sphenoid sinus (Fig 2A). A soft delivery sheath is press-
ent around the outer diameter of the trocar and stays in place in the ethmoid sinuses after the trocar is withdrawn. The drug-eluting catheter is then passed through the delivery sheath to its final position (Fig 2B). The delivery sheath is then removed as the drug-eluting catheter stays in position — spanning the anterior and posterior ethmoid sinuses — and is retained here by flexible metallic wings that deploy just within the ethmoid bulla (Fig 2C).

Insertion of the system was performed endoscopically on 12 cadaveric ethmoid sinuses. The trocar was first gently placed on the center of the face of the ethmoid bulla (Fig 3A). Care was taken to insert the trocar at the proper angle in the parasagittal and axial planes. In order to confirm that the distal tip would rest in the correct position in the axial plane (that is, not too far medially or laterally), the trocar was held parallel to the midsagittal line during insertion (“straight up and down”). For confirmation of proper placement in the parasagittal plane (that is, not too far superior or inferior), the angle of entry into the ethmoid sinuses had to be correct. In this study, it was confirmed by fluoroscopy. After the tip of the trocar was placed on the face of the bulla, a posterior-to-anterior image was captured with the fluoroscopy unit to ascertain correct placement in the axial plane. This was confirmed by visualizing the shaft of the trocar to be medial to the orbit and to be directly in line with the plane of the x-ray beam,

Fig 3. Position to enter right ethmoid sinuses is chosen as trocar is placed on face of bulla. A) Freer is used to expose middle meatal contents. B) Instrument is placed above endoscope before insertion, to allow angle of insertion to flatten and more closely parallel skull base. C) Face of bulla after trocar and catheter removal. D) Placing tip of endoscope at opening at face of bulla reveals penetrated posterior wall of bulla and horizontal basal lamella of middle turbinate with opening into posterior ethmoid sinuses. Note lack of trauma surrounding tract of trocar.
as if one were looking down the barrel of a shotgun. In order to begin with the correct angle of insertion, we placed the instrument above the endoscope (Fig 3B), thereby allowing an angle of insertion more parallel to the angle of the skull base. This technique of passing an operative instrument above the nasal endoscope is opposite from the normal configuration used during endoscopic sinus surgery but is essential in keeping the distal tip of the trocar away from the skull base.

After the trocar was correctly positioned for insertion, it was advanced slowly and in a controlled fashion with the surgeon bracing his operative hand on the patient’s face. Live cross-table fluoroscopic images were continuously monitored. There was little resistance at the face of the ethmoid bulla; however, immediately after the tip passed into the retrobullar recess, there was an increase in resistance when it encountered the horizontal basal lamella of the middle turbinate. After penetrating this, the tip entered the posterior ethmoid air cells, in which there was also little resistance until the sphenoid face was met. After placement of the trocar was complete, another identical fine-cut CT scan was performed with the trocar in place (Fig 4).

The drug-eluting catheter was put into its final position as detailed above and filled with liquid contrast agent through a port on the proximal end of the catheter’s shaft (Fig 1C). A 1-way valve keeps the liquid in the distal tip of the catheter, in which it fills a very narrow balloon-like reservoir with small micropores that allow liquid medication to diffuse out of the catheter over a prolonged period of time (Fig 5). A third fine-cut CT scan was performed with only the catheter in place.

The catheter was easily removed endoscopically by simply grasping and withdrawing it. After removal, a final (postprocedure) fine-cut CT scan was obtained. All 4 CT scans were reviewed for proper positioning and to rule out injury to the skull base, lamina papyracea, sphenoid face, and the middle and superior turbinates. The walls of the ethmoid air cells were also studied in 3 planes to look for any undue trauma, that is, whether the trocar penetrated them or crushed them. Measurements were taken on the postprocedure CT scan from the proximal and distal tips of the device to the skull base, lamina papyracea, and sphenoid face.

After removal, complete ethmoidectomy was performed endoscopically to trace the path through which the trocar and catheter passed (Fig 3C,D). The skull base and lamina papyracea were skeletonized and the sphenoid face was fully exposed to look for trauma to any of these structures.

RESULTS

The drug-eluting catheter system was successfully inserted into the ethmoid sinuses of all 12 cadaver sides without injury to the medial orbital wall, skull base, or sphenoid face as confirmed by postprocedure CT scan and dissection. The final position of the distal tip of the stent averaged 8.1 mm (root mean square [RMS], 3.3 mm) from the skull base, 5.6 mm (RMS, 3.5 mm) from the sphenoid face, and 5.0 mm (RMS, 3.5 mm) from the lamina papyracea; the proximal tip was at the face of the ethmoid bulla and 17.1 mm (RMS, 3.5 mm) below the skull base. In the axial plane, the final resting place of the distal tip of the catheter was within the posterior ethmoid...
sinuses between the superior turbinate and the lamina papyracea.

Also, the architecture of the ethmoid air cells was preserved as seen by CT scanning and endoscopic dissection; that is, the cells were penetrated but not crushed by the trocar. The diameter of the resultant opening that remained in the ethmoid air cells was the same as the diameter of the trocar.

**DISCUSSION**

The mainstay of medical therapy for chronic ethmoid sinusitis is the use of systemic antibiotics, usually combined with either topical or systemic steroids. In patients with no history of endoscopic sinus surgery, topical treatments may not adequately reach the target tissue. Surgical therapy for chronic ethmoid sinusitis is reserved for disease that is refractory to maximal medical management; the primary surgical therapy is extirpative and consists of ethmoidectomy. This study shows that a drug-eluting catheter can be relatively safely and reliably inserted into virgin ethmoid sinuses in order to allow the topical elution of medications into the ethmoid sinuses without ethmoidectomy.

There has been previous interest in treating chronic ethmoid sinusitis with a temporary implantable device — an irrigation catheter. Lavigne et al. used a trocar-based insertion device to deliver a "tube for irrigation of the ethmoid" through which saline solution, topical antibiotics, and topical steroids were administered. This required the patient to cannulate the catheter and instill saline solution and medication several times a day for 21 to 30 days. The only end point for follow-up in that study was treatment in nonvalidated symptom scores. Three of 20 patients (15%) had persistent disease and eventually required surgery; 85% of patients in whom systemic therapy alone had previously failed improved when topical therapy was added via an implantable device into the ethmoid sinuses.

In contrast to the above-mentioned catheter that the patient has to access, a drug-eluting catheter in the ethmoid sinuses can continuously deliver medication to the interior of diseased ethmoid cells in the hope of treating chronic ethmoid sinusitis. The purpose of this study was to determine the safety and feasibility of a system to insert such a catheter. This system was inserted without incident in 12 cadaveric ethmoid sinuses without injury to the skull base, lamina papyracea, or sphenoid face.

Pushing a trocar through the ethmoid sinuses seems antithetical to many common concepts of sinus surgery in which landmarks are carefully sought and followed. According to the standard endoscopic sinus surgery principles of Wigand, Stammbberger, and Kennedy et al., the ethmoid sinuses are entered low and medially to avoid injury to vital structures. These tenets are followed with the use of the trocar for the delivery of the drug-eluting stent. The tip of the device is positioned on the middle to lower third of the bulla and is then advanced (pushed) blindly into the remainder of the ethmoid sinus, staying low and medial in the ethmoid cavity. Although insertion of this device is quicker than performing an ethmoidectomy, the potential risks are no different.

One complication of insertion is skull base injury. This may occur when the trocar is passed through the ethmoid sinuses at an incorrect angle. The shaft of the trocar should be as flat as possible so that the angle is parallel to that of the skull base. To obtain the proper angle of insertion, the surgeon has to raise his or her wrists after placement of the tip of the trocar on the face of the bulla. This is facilitated by placement of the instrument in the nasal cavity above (rather than below) the scope, which may seem awkward to the surgeon. Fluoroscopy is crucial, not only for checking this initial position, but also for following the distal tip of the trocar during insertion, especially as the height of the skull base decreases posteriorly.

Another potential complication would be injury to the sphenoid face. Entering the sphenoid sinus could increase the risk of injury to the internal carotid artery, optic nerve, pituitary gland, or other intracranial structures. The length of the drug-eluting catheter and the length of the distal tip of the trocar is such that this injury should not be likely if the distance between the face of the bulla and the sphenoid face is greater than 25 mm. Also, the surgeon should brace his or her operative hand on the patient’s face during insertion. This helps to steady the hand and prevent a deep insertion into the sphenoid sinus.

Penetration of the lamina papyracea may occur if the trocar is not inserted parallel to the parasagittal plane. If this occurred, it could cause damage to several intraorbital structures such as the medial rectus muscle, optic nerve, or blood vessels. An injury to the optic nerve could result in blindness. Orbital injury is best avoided by keeping the shaft of the trocar parallel to the sagittal midline. In this study, intraoperative fluoroscopy was used to confirm that placement was medial to the orbit with a posterior-anterior image from the fluoroscopy unit. The device was placed on the face of the bulla, and the image was captured; the correct orientation was
confirmed by a radiographic image showing that the shaft of the trocar was coaxial with the plane of the x-ray beam, as if one were looking down the barrel of a shotgun. This angle of orientation in the axial plane had to be maintained by the surgeon as the fluoroscopy unit was turned to the cross-table lateral position to view the skull base during insertion.

Although no complications were incurred during this study, there are, as during any ethmoid procedure, multiple risks to neighboring vital structures. This device is advanced (pushed) into virgin ethmoid sinuses; standard Wigand-style ethmoidectomy removes skull base partitions in a posterior-to-anterior fashion. If an inadvertent injury occurs with insertion of this device, the area that has been penetrated has not been exposed, and an ethmoidectomy will need to be performed to expose and manage the injury. Meticulous technique is mandatory for safe and proper insertion; pitfalls exist if incorrect technique is used and may lead to complications. One potential pitfall is skull base penetration, which may occur if the trocar is advanced at an incorrect angle, ie, with an angle of insertion directed toward rather than parallel to the skull base. This risk can be minimized by placing the instrument above the endoscope, rather than below, as is more common. Placing the instrument above the endoscope “flattens” the angle of insertion, allowing placement at an angle parallel to the skull base.

Overall, this concept may be a bit foreign to sinus surgeons. However, attention to detail, endoscopic visualization, and fluoroscopic images allow this catheter system to be safely inserted. This study shows that cadaver training and proper technique may allow a drug-eluting catheter to be safely inserted into virgin ethmoid sinuses. This catheter may serve as a vehicle to provide treatment for chronic ethmoid sinusitis in which maximal medical management has failed, by delivering topical medications directly to the diseased ethmoid sinuses without the need for ethmoidectomy.

CONCLUSIONS

This study demonstrates that insertion of a drug-eluting catheter into the ethmoid sinuses is feasible and relatively safe in the hands of a trained otolaryngologist. A trocar-based instrument can safely and reproducibly introduce a drug-eluting catheter into the ethmoid sinuses without injury to the skull base, lamina papyracea, or sphenoid face. This device may allow relatively safe topical drug delivery directly inside diseased ethmoid sinuses without ethmoidectomy.

REFERENCES


