Injection Pharyngoplasty With Calcium Hydroxyapatite for Treatment of Velopalatal Insufficiency

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Objective: To evaluate the efficacy of injectable calcium hydroxyapatite for treatment of velopalatal (VP) insufficiency (VPI).

Design: Observational case series of 7 patients treated with injectable calcium hydroxyapatite for VPI and followed for 10 to 24 months.

Setting: Academic pediatric otolaryngology practice.

Patients: Seven children aged 6 to 16 years with clinically significant VPI stemming from documented small VP gaps and who did not benefit from speech therapy were treated with calcium hydroxyapatite injection pharyngoplasty.

Intervention: Posterior pharyngeal wall augmentation with calcium hydroxyapatite.

Main Outcome Measures: Treatment success was defined as (1) speech improvement to the degree that parents felt no additional treatment was needed and (2) meeting postoperative nasometric measures. Treatment failure was defined as parental report of insufficient improvement in speech. Complications and additional treatments for VPI were noted.

Results: There were no major complications in any of the 7 children injected with calcium hydroxyapatite. There was 1 minor complication: 1 patient was readmitted for postoperative pain and dehydration. Of the 7 patients, 4 experienced a satisfactory result for up to 17 months. Findings from postoperative nasometry were either within reference range, or less than 1 SD greater than the reference range, for all sounds. There were 3 treatment failures, each with preexisting craniofacial abnormality. Two patients in the group that failed treatment later underwent revision superior pharyngeal flap surgery without complication or hindrance from the calcium hydroxyapatite injection. Four children underwent subsequent magnetic resonance imaging evaluations up to 1 year after injection, which revealed no evidence of migration.

Conclusions: The data from this small series suggest that posterior pharyngeal wall injection with calcium hydroxyapatite is safe and may be effective in treating select patients with VPI. Further longitudinal studies, with a larger series of patients, examining the safety, efficacy, and patient selection are warranted to better understand the possible use of posterior pharyngeal wall injection of calcium hydroxyapatite in children with symptomatic VPI.


VeloPalatal (VP) Insufficiency (VPI), the failure of the soft palate to meet the posterior pharyngeal wall during speech or swallowing, is dependent on multiple variables, including the contractile nature of the velar musculature, the presence of soft tissue defect or muscular dehiscence, and the cranial cephalometric morphologic characteristics of each patient. Defects are broadly categorized as coronal, sagittal, or circular, but the actual shape is unique to each patient. The surgical procedure chosen for VPI is ideally tailored to close the shape of a given defect.

Although superiorly based pharyngeal flaps and sphincteroplasty are often successful in improving symptomatic VPI, hyponasality and obstructive sleep apnea are potential unintended consequences. Simple posterior pharyngeal wall augmentation, although not appropriate for all patients, has been proposed as a method to achieve velar closure with theoretical reduced risk of hyponasality or obstructive sleep apnea. Multiple methods have been investigated, including rolled pharyngeal flaps, autologous material implants, or injectable materials. None of these methods have been widely adopted.

The ideal injectable agent for the posterior pharyngeal wall would be easy to inject and durable and would not migrate. The first material used was paraffin wax in 1904. This practice was abandoned because of material migration and infection. Early optimism surrounding the use of Teflon...
Calcium hydroxylapatite in a carboxymethylcellulose carrier, commercially available as Radiesse (Bioform Medical Inc, San Mateo, California), is an injectable material used in vocal cord medialization and as a soft tissue filler. Short-term complications of local soft tissue inflammation, and foreign body giant cells, without granuloma formation, have been observed. Follow-up beyond 24 months has not been reported. This study reflects pilot data investigating the safety and initial results of injection of calcium hydroxylapatite into the posterior pharyngeal wall with children with small velopharyngeal gaps and symptomatic VPI.

**METHODS**

**PATIENT SELECTION**

Ten children presented to the Massachusetts Eye and Ear Infirmary, Boston, from September 2005 through July 2007, with small velopharyngeal gaps that produced clinically significant VPI that did not respond to a minimum of 3 months of speech therapy. Surgical options, including superior pharyngeal flap, sphincteroplasty, rolled pharyngeal flap, and injection of calcium hydroxylapatite into the posterior pharyngeal wall, were presented to each child and his or her family. The families were told that such an injection was not US Food and Drug Administration approved and that the lifespan of such an implant was unknown. They were told that an additional procedure would be needed if the calcium hydroxylapatite injection either did not allow proper VP closure or if it resorbed. Of the 10 families, 7 opted for calcium hydroxylapatite injections and were followed longitudinally. Approval was granted from the Massachusetts Eye and Ear Infirmary institutional review board to review the medical records of these patients. Bioform Medical Inc provided the material free of charge (but provided no funding for this study).

**SURGICAL TECHNIQUE**

Under general anesthesia, the patients were placed in the traditional Rose “tonsil” position with a mouth gag. The palate was inspected for occult submucosal cleft. A red rubber catheter was placed through the nares to elevate the soft palate. A 120° rigid endoscope with palate retractor (Karl Storz, Tuttingen, Germany) was used to visualize the posterior pharyngeal wall (Figure 1). The pharynx was then observed for the presence of any pulsations. After reviewing the nasopharyngeal endoscopy previously recorded to identify the anatomic site where the small gap could be identified, 1 to 3 mL of calcium hydroxylapatite was injected under direct visualization (Figure 2 and Figure 3).

**DATA COLLECTION**

Information from each office visit, hospital record, and documented telephone call were reviewed. Data including age, etiology of VPI, and postoperative nasometry were collected. The success of injection was defined as improved and satisfactory speech with no further treatment desired and within 1 SD (3 percentage points) of the reference range for nasality (12%-14%) for quantitative postoperative nasometry. Minor complications were defined as dehydration related to poor oral intake, soft tissue infection, and the development of obstructive sleep apnea. Major complications were defined as chronic pain related to the procedure, surgical intervention for injection-related infection, embolic stroke, airway obstruction, or death. Postoperative imaging was reviewed if obtained. If a patient elected to undergo an additional procedure, this also was noted.
Seven patients underwent injection with calcium hydroxylapatite for VPI. The age and etiology of VPI of each patient are as follows:

<table>
<thead>
<tr>
<th>Patient/Age, y</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/6</td>
<td>Postadenoidectomy</td>
</tr>
<tr>
<td>2/10</td>
<td>Postadenoidectomy</td>
</tr>
<tr>
<td>3/12</td>
<td>Hemifacial microsomia</td>
</tr>
<tr>
<td>4/7</td>
<td>Unknown</td>
</tr>
<tr>
<td>5/7</td>
<td>Postadenoidectomy and submucosal cleft palate</td>
</tr>
<tr>
<td>6/6</td>
<td>Postadenoidectomy and submucosal cleft palate</td>
</tr>
<tr>
<td>7/8</td>
<td>Cleft hard palate</td>
</tr>
</tbody>
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The age range was 6 to 16 years. There were 4 patients with VPI after adenoidectomy, 1 with hemifacial microsomia, 1 with cleft palate, and 1 with congenital VPI. Two of the 4 patients who had undergone adenoidectomy had occult submucosal clefts. All but 1 patient (patient 3) had a small central gap (patient 3 had a small residual lateral gap at the lateral edge of the previously performed sphincteroplasty).

There were no intraoperative complications. Each patient was discharged the afternoon of the procedure and given prescriptions for narcotic pain medicine and a 7-day supply of either amoxicillin–clavulanate potassium or clindamycin hydrochloride. One patient was readmitted for 24 hours for pain control and rehydration on postoperative day 2. There were no major postoperative complications.

Four of the 7 patients (57%) achieved satisfactory speech with no desire for further intervention (Table). Three of these 4 patients had acquired VPI after adenoidectomy. Findings from postoperative nasometry for these 4 patients were either within reference range, or less than 1 SD greater than reference range, for all sounds.

All 3 patients with unsatisfactory outcome had craniofacial abnormalities (cleft hard palate, occult submucosal cleft palate, and hemifacial microsomia). Two of these 3 patients subsequently underwent superiorly based pharyngeal flap procedures. The presence of calcium hydroxylapatite in the tissues was evident, but did not interfere with the raising of posterior pharyngeal wall musculomucosal flaps. There was no wound breakdown of the pharyngeal flaps or complications, and both patients experienced symptomatic improvement. The third patient was later found to have an Arnold-Chiari malformation and chose to defer VPI treatment until after treatment for this anomaly.

Four patients underwent magnetic resonance imaging evaluation from 3 to 10 months after surgery as part of a separate and distinct study protocol. In each of these studies, there was improvement in velopharyngeal closure, the calcium hydroxylapatite spherules were visible, and there was no migration.

This study aimed to raise several questions and to evaluate them with a small series pilot study: (1) Can calcium hydroxylapatite be safely injected into the posterior pharyngeal wall? (2) Would such injections have efficacy in treating symptomatic VPI? (3) How long would such injections last? (4) Would there be any evidence of migration?

Regarding safety, use of injectable calcium hydroxylapatite for VPI in this small series of children demonstrated a satisfactory safety profile during the study period. There was 1 minor complication related to postoperative pain and dehydration and no major complication.

Regarding efficacy, this series is too small to make definitive statements; nevertheless, 4 of the 7 children injected experienced marked symptomatic improvement. Importantly, for the children whose speech was not improved by these injections, subsequent revision procedures were not complicated by these prior injections.

Of the 7 children, 4 underwent magnetic resonance imaging evaluations in which migration of the calcium hydroxylapatite was not evident. Clearly, a larger series of children would need to be followed longitudinally to definitively answer this question.

The duration of follow-up for these patients ranged from 10 to 24 months. The patients who had a good initial result sustained the outcome for the duration of the study, the longest for 17 months. However, this study does not determine how long a good result will last. This data end point will be important to determine if the duration of effect is adequate to justify the procedure.

Injection pharyngoplasty, even with an ideal material, is not appropriate for every child with VPI. The ease of the surgical technique makes it an attractive option when indicated; moreover, it can be performed on an outpatient basis. Our initial success rate in 7 patients judged to have small VP gaps was 58%. In this small series, children who developed VPI after adenoidectomy and had a small central velopharyngeal gap seemed to represent a group where such a technique might be indicated. Patients who had undergone an adenoidectomy were good candidates for posterior wall augmentation in a prior study.5

In conclusion, this is a small series pilot study. As such, no definitive conclusions can be made regarding any of the 4 questions posed regarding safety, efficacy, duration, or migration of the calcium hydroxylapatite implant. However, the results of this study suggest that it
is safe and may have efficacy; these results would support further longitudinal investigation in carefully informed and selected patients.

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Author Contributions: Drs Sipp, Ashland, and Hartnick had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Sipp and Hartnick. Acquisition of data: Sipp, Ashland, and Hartnick. Analysis and interpretation of data: Sipp, Ashland, and Hartnick. Drafting of the manuscript: Sipp, Ashland, and Hartnick. Critical revision of the manuscript for important intellectual content: Sipp and Hartnick. Administrative, technical, and material support: Hartnick. Study supervision: Hartnick.

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REFERENCES