GORE® Septal Occluder and Nickel Allergy
Septal Occluders and Nickel Allergy

Introduction

Patient sensitivity to the nickel present in septal occluder devices continues to be a topic of interest. The clinical outcomes associated with nickel sensitivity are poorly defined, and may include systemic adverse side effects, pericarditis, and increasing migraine headache. This hypersensitivity has been shown to cause “device syndrome” in a majority of patients with known allergies to nickel who undergo closure with various septal occluders. Since a majority of the Nitinol wire of the GORE® Septal Occluder and the GORE® HELEX® Septal Occluder is encased within ePTFE material, physicians often perceive the device as carrying a smaller risk for inducing an allergic reaction than other occluders. This is borne out by the data available, which, although admittedly limited, clearly distinguishes between free nickel (not present in any Gore device), Nitinol alloys that include nickel, and the Nitinol alloy used in the Gore septal occluders and other Gore Medical devices following electropolishing (which imparts a titanium oxide passivation layer to the Nitinol wire surface).

Clinical History of Nickel Allergy and the GORE® HELEX® Septal Occluder

A summary of reported clinical data regarding the GORE® HELEX® Septal Occluder and nickel allergic reactions follows in Table 1. Only two patients reported symptoms (itching) that would be consistent with an allergic reaction to nickel. Furthermore, symptoms did not correlate with reported nickel allergy status. Clinical reports of possible allergic reactions to GORE® HELEX® Device implants are extremely rare and lack evidence supporting a true allergic reaction: Five reported cases out of approximately 16,000 implanted devices. One reported case of an allergic reaction to a GORE® HELEX® Device is included in the peer-reviewed literature. This single case has been reported twice (Dasika et al., 2003; Vincent et al., 2003).

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Time of Onset</th>
<th>Treatment / Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itching, sore feet*</td>
<td>unknown</td>
<td>Explant after four months, symptoms did not resolve, sternal sutures removed</td>
<td>Continued reaction after device removal does not support an on-going allergic reaction to the device; no signs of allergic reaction from histology of explant</td>
</tr>
<tr>
<td>Fever, sweating, migraine</td>
<td>One - three days after implantation</td>
<td>Spontaneously resolved</td>
<td>Symptoms are not specific for allergic reaction; Spontaneous resolution is not consistent with long term allergic reaction to the device</td>
</tr>
<tr>
<td>Chest pains**</td>
<td>Within 24 hours of implantation</td>
<td>Device left in place. Patient doing much better.</td>
<td>Symptoms are not specific for allergic reaction; Spontaneous resolution is not consistent with long term allergic reaction to the device</td>
</tr>
<tr>
<td>Near syncope, palpitations; headaches, itchy palms; shortness of breath on exertion***</td>
<td>Within one week of implantation; between one and two weeks after implantation; within two - three weeks of implantation</td>
<td>Skin itching resolved after two - three weeks taking antihistamine as needed; shortness of breath on exertion “is not getting worse”</td>
<td>Resolution with short-term antihistamine therapy is not consistent with long-term allergic reaction to the device</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Within two days of implantation</td>
<td>Steroids prescribed. Pain persisted. Device removed three weeks after implantation</td>
<td>Symptoms are not specific for allergic reaction; Follow up data not available</td>
</tr>
</tbody>
</table>

* Patient tested positive in nickel patch test after implantation
** Patient had “known nickel sensitivity”
*** Patient had “documented nickel allergy but refused surgery without an attempt at device closure”
GORE® Septal Occluder and Nickel Allergy

Reddy et al. published the first paper on clinical outcomes in known nickel allergy patients treated with the GORE® HELEX® Septal Occluder. Results from three types of patients are compared in this study: the authors' single-center experience with the GORE® HELEX® Septal Occluder in patients with known nickel allergies, the authors' experience with the AMPLATZER® Septal Occluder in patients with no known pre-procedure nickel allergy, and 3) the reported experience of the AMPLATZER® Septal Occluder and PREMERE PFO Closure System in nickel allergic patients.

On follow-up, none of the patients receiving the GORE® HELEX® Device developed an allergic reaction, significant chest pain, or arrhythmia. In contrast, patients without pre-procedural known nickel allergy (who were primarily implanted with AGA Medical occluders) had an incidence of palpitations (12%), atrial fibrillation (5%), and chest pain (13%). The authors also compared the results from the patients implanted with the GORE® HELEX® Septal Occluder to published reports of allergic reactions in patients having a known nickel allergy and implanted with either the AMPLATZER® Septal Occluder or PREMERE PFO Closure System. In those case series, 89% of the patients developed an allergic reaction. Reddy et al. concluded that the absence of allergic reactions in the GORE® HELEX® Septal Occluder group in their series is suggestive that the GORE® HELEX® Septal Occluder appears to present a lower risk in nickel allergic patients.

Nickel allergy continues to be a poorly understood phenomenon. Although this study is suggestive that the GORE® HELEX® Device presents less risk for patients with a known allergy or hypersensitivity to nickel for percutaneous interatrial shunt closure, the authors concede that future research is needed to investigate the frequency of nickel allergic syndromes for septal occluders. Gore’s position remains consistent with what is published in the GORE® Septal Occluder IFU, i.e., that physicians and patients should be warned that those with a known nickel allergy may suffer a reaction to the device. Specifically, the IFU states:

“Patients allergic to nickel may suffer an allergic reaction to this device. Certain allergic reactions can be serious; patients should be instructed to notify their physicians immediately if they suspect they are experiencing an allergic reaction such as difficulty breathing or inflammation of the face or throat. Some patients may also develop an allergy to nickel if this device is implanted.”

GORE® Septal Occluder Nickel Elution

It is suspected that the severity of an allergic reaction to nickel is directly related to the quantity of nickel potentially eluted into the bloodstream from an implanted device. Multiple factors, including nickel mass, exposed surface area, and the quality of the wire, may affect the potential amount of nickel elution. Although an allergic reaction to the metal contained in the GORE® Septal Occluder is possible, there are several design elements of the device that may reduce this risk. Specifically, the GORE® Septal Occluder is comprised of only five wires, which are predominately encased within ePTFE material. Secondly, the wire utilized in the device is prepared with a proprietary wire surface treatment process, that significantly reduces the amount of available nickel on the surface of the wire.

To investigate the impact of these design characteristics of the GORE® Septal Occluder, a head-to-head comparison was performed with the AMPLATZER® PFO Occluder to assess potential differences in nickel elution rates. In this study, the amount of nickel eluted from the AMPLATZER® PFO Occluder (one 18 mm and one 25 mm device) and the GORE® Septal Occluder (four 30mm devices) was determined. For further comparison, nickel eluted from the GORE® HELEX® Septal Occluder (ten 35mm devices) was also determined. The devices were placed into vials containing phosphate buffered saline maintained at 37°. Over the 60 day test period, the samples were removed from each test vial and placed into new test vials containing fresh phosphate buffered saline. At the end of the 60 day immersion test, the amount of nickel present in each test sample was measured using inductively coupled plasma atomic emission spectroscopy. The GORE® Septal Occluder had undetectable nickel levels (< 0.01 μg / ml saline) at
all timepoints, whereas the AMPLATZER® PFO Occluder eluted on average nearly 50 μg per device over the 60 day test period. The GORE® HELEX® Septal Occluder eluted on average 0.174 μg per device over the 60 day test period. Figure 1 illustrates the average cumulative nickel elution per device over the duration of the test.

Although the clinical ramifications of these differences in eluted nickel are unknown, it was noted that the design of the GORE® Septal Occluder and the GORE® HELEX® Septal Occluder yields significantly less eluted nickel than the AMPLATZER® PFO Occluder.

**Conclusion**

The clinical presentation of nickel allergy in patients treated with the GORE® HELEX® Septal Occluder is rare. Given the design similarities between the GORE® Septal Occluder and the GORE® HELEX® Septal Occluder, the clinical manifestation of nickel allergy due to the GORE® Septal Occluder is also expected to be minimal. In addition, in vitro testing demonstrated undetectable levels of nickel eluting from the GORE® Septal Occluder compared to nearly 50 ug per device for the AMPLATZER® PFO Occluder.

**References**

