Vagus Nerve Stimulator Implantation in Children

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Background: Vagus nerve stimulation was approved in 1997 as an adjunctive treatment of partial-onset seizures refractory to medical therapy. Subsequent to the initial clinical trials, few studies have been published specifically addressing perioperative management issues.

Objectives: To review the operative technique and perioperative management of patients undergoing vagus nerve stimulator implantation and to analyze complications and their management.

Design: Retrospective medical record review and survey of patients who underwent implantation.

Setting: A tertiary care pediatric hospital in Kansas City, Mo.

Patients: One hundred two patients aged 21 months to 40 years.

Intervention: Vagus nerve stimulator implantation and lead placement.

Main Outcome Measures: The surgical technique of vagus nerve stimulator implantation is presented in detail. Perioperative complications are enumerated, and strategies for their management are described. A subjective patient survey addresses some quality-of-life issues and the effect on swallowing and voice.

Results: One hundred two patients successfully underwent vagus nerve stimulator implantation. Three patients experienced infection of the chest wound holding the generator and required explantation. These 3 patients underwent reimplantation within 2 months after the infection had cleared. Most patients experience some degree of hoarseness when the generator is activated, but this symptom usually does not significantly affect the ability to communicate. Responses to questions regarding quality of life are positive.

Conclusions: Vagus nerve stimulator implantation has a low incidence of serious complications. Quality of life seems to be improved for most patients. Modifications to the surgical procedure must be considered when performing the implantation on a young patient.


VAGUS NERVE stimulator (VNS) implantation was approved by the Food and Drug Administration in 1997 as an adjunctive treatment of partial-onset seizures refractory to medical therapy in patients 12 years and older. More than 17,000 prostheses (NeuroCybernetic Prostheses; Cyberonics, Inc, Houston, Tex) have been implanted for this purpose. The programmable device delivers periodic electrical stimulation to the left vagus nerve. Retrograde propagation of the current along the nerve travels to numerous areas in the brain, resulting in decreased seizure activity in many patients. The precise mechanism of seizure reduction using this modality is unknown. Vagus nerve stimulator implantation has also been approved for the management of treatment-resistant depression and bipolar disorder in Europe and Canada. Clinical trials are under way in the United States, studying its utility in the treatment of depression and obesity.

Since the initial clinical trials, much information has been published regarding success in treating refractory seizures using this novel approach. However, almost nothing has been published focusing on perioperative management, complications, and quality-of-life issues in this patient population. This article reviews our extensive surgical experience using VNS implantation in a predominantly pediatric population and reviews complications and adverse effects we have seen in our patients.
At this point, the operation is performed in the standard fashion using trichloromonofluoromethane (Freon 11). An iodine-paint, followed by the use of alcohol. The skin is dried using a povidone-iodine (Betadine) scrub and a 1:100,000 epinephrine solution.

Cisions are marked and infiltrated with 1% lidocaine with epinephrine. The left arm is then abducted 90° and attached to an arm board. A horizontal skin crease is chosen in the midneck for incision placement. Both vertical skin folds are noted and avoided for incision placement. The left arm is then abducted 90° and attached to an arm board. A horizontal skin crease is chosen in the midneck for incision placement. The left arm is then abducted 90° and attached to an arm board. A horizontal skin crease is chosen in the midneck for incision placement. The left arm is then abducted 90° and attached to an arm board. A horizontal skin crease is chosen in the midneck for incision placement. The left arm is then abducted 90° and attached to an arm board. A horizontal skin crease is chosen in the midneck for incision placement. The left arm is then abducted 90° and attached to an arm board. A horizontal skin crease is chosen in the midneck for incision placement. The left arm is then abducted 90° and attached to an arm board. A horizontal skin crease is chosen in the midneck for incision placement. The length of this incision varies depending on the size of the patient. However, the vagus nerve can usually be adequately explored in a child through a 4-cm incision. In the young patient, the incision is moved laterally 1 to 2 cm into the axilla to avoid placing the incision directly over the device. During patient positioning, the left arm is fully adducted and the natural vertical skin creases over the anterior axillary fold are noted and avoided for incision placement. The left arm is then abducted 90° and attached to an arm board. A horizontal skin crease is chosen in the midneck for incision placement. The length of this incision varies depending on the size of the patient. However, the vagus nerve can usually be adequately explored in a child through a 4-cm incision. Both incisions are marked and infiltrated with 1% lidocaine with 1:100,000 epinephrine solution (Figure 1). Sterile skin preparation is achieved using a povidone-iodine (Betadine) scrub and paint, followed by the use of alcohol. The skin is dried using trichloromonofluoromethane (Freon 11). An iodine-impregnated adherent drape is used to cover the skin. From this point, the operation is performed in the standard fashion (Figure 2). Bactracin is used to irrigate both wounds intraoperatively, and no drains are placed. All patients receive intravenous antibiotics before skin incision. Various antibiotic regimens have been used during the postoperative period at the discretion of the surgeon, ranging from a single dose of intravenous antibiotics to a short course of oral antibiotics. Nearly all patients have their VNS activated by a neurologist using a computer and telemetry wand before discharge from the hospital. Patients return for a single postoperative wound check 2 weeks later.

METHODS

SURGICAL TECHNIQUE

All surgeons (D.J.K., A.H.W., T.P.E., D.E.B., and G.W.H.) participating in this study used an identical intraoperative technique. Postoperative management strategies, however, had minor variations. Two incisions are used. The VNS’s generator is implanted in a subcutaneous pocket on the pectoralis fascia through a 4-cm incision on the anterior axillary fold. In the young patient, the incision is moved laterally 1 to 2 cm into the axilla to avoid placing the incision directly over the device. During patient positioning, the left arm is fully adducted and the natural vertical skin creases over the anterior axillary fold are noted and avoided for incision placement. The left arm is then abducted 90° and attached to an arm board. A horizontal skin crease is chosen in the midneck for incision placement. The length of this incision varies depending on the size of the patient. However, the vagus nerve can usually be adequately explored in a child through a 4-cm incision. Both incisions are marked and infiltrated with 1% lidocaine with 1:100,000 epinephrine solution (Figure 1). Sterile skin preparation is achieved using a povidone-iodine (Betadine) scrub and paint, followed by the use of alcohol. The skin is dried using trichloromonofluoromethane (Freon 11). An iodine-impregnated adherent drape is used to cover the skin. From this point, the operation is performed in the standard fashion (Figure 2). Bactracin is used to irrigate both wounds intraoperatively, and no drains are placed. All patients receive intravenous antibiotics before skin incision. Various antibiotic regimens have been used during the postoperative period at the discretion of the surgeon, ranging from a single dose of intravenous antibiotics to a short course of oral antibiotics. Nearly all patients have their VNS activated by a neurologist using a computer and telemetry wand before discharge from the hospital. Patients return for a single postoperative wound check 2 weeks later.

RESULTS

MEDICAL RECORD REVIEW

The medical records were obtained for all patients who underwent implantation at Children’s Mercy Hospitals and Clinics and the few patients who underwent implantation elsewhere and were subsequently followed up by our neurologists (J.V.M. and R.D.T.). A database was constructed focusing on patient demographics, operative times, perioperative patient management, intraoperative difficulties, and complications. Those patients who have had their devices removed or replaced were noted. The information was extracted from the medical records and analyzed descriptively.

PATIENT QUESTIONNAIRE

A questionnaire was compiled focusing on adverse effects, quality-of-life issues, and satisfaction with the device. A total of 18 questions were included on the document. Some questions were answered yes or no, and some required a graded response. In a cover letter that was sent with the questionnaire, the respondents were asked to make their responses to the questions independent from factors relating to the degree of seizure control obtained from the device. The questionnaire was mailed to all patients who underwent implantation in 1998, 1999, and 2000. Attempts were made to contact all patients and families receiving the questionnaire to encourage their participation. Participants were allowed to respond anonymously. All patients had at least 4 months of experience with the VNS. Data obtained from the questionnaire were analyzed for descriptive purposes.

Five questions pertained to speech issues. Questions were designed to ascertain how many children use speech as an effective form of communication and how VNS implantation affected this ability. Six questions were constructed to determine the normalcy of the swallowing mechanism and how this was affected by VNS implantation. Six further questions addressed quality-of-life issues, including stimulation of cough, pain related to the device, cosmesis, functional limitations, adverse effects from the use of the magnet, and level of alertness. A final question addressed overall satisfaction with the decision to pursue VNS implantation as an adjunctive treatment for the patient’s seizure disorder.

Figure 1. Incision placement and final position of the generator.

Figure 2. Operative field showing the strain-relief loop attached to the sternocleidomastoid muscle. The inset shows helical leads wrapped around the vagus nerve.
Operative times for primary VNS implantation ranged from 53 to 138 minutes (median, 85 minutes). Estimated blood loss was generally 5 to 10 mL. There were few intraoperative problems encountered. Variability of the vagus nerve location within the carotid sheath was occasionally noted by the surgeon. There was no incidence of major vascular injury or nerve trauma. In general, intraoperative testing of the generator and lead impedance testing proceeded without problems. However, there were 4 patients in whom intraoperative device testing was problematic. Three of these patients required the use of a second generator to correct the problem, and 1 required replacement of the leads. All of these problems were recognized intraoperatively, and easily corrected. There were no intraoperative cardiac problems encountered during device diagnostic testing in this cohort.

The first 48 patients who underwent implantation in this series were monitored in the hospital for 23 hours after surgery. Since then, all but 3 patients have been discharged after a 2- to 6-hour postoperative observation period. The 3 unexpected overnight admissions were necessary because of postoperative nausea and vomiting.

As noted earlier, all patients received a dose of intravenous antibiotics before incision. After surgery, 40 patients received multiple doses of intravenous antibiotics, 31 received a single dose of intravenous antibiotics, and 31 did not receive any intravenous antibiotics. Those patients not receiving intravenous antibiotics postoperatively were sent home with a short course of oral antibiotics.

Four patients experienced wound infections. Patient 1 developed cellulitis over the generator 3 weeks after surgery. He was treated with 5 days of intravenous vancomycin and cefazolin therapy, followed by oral antibiotics, and had resolution of the infection. Patient 2 was admitted 3 months after the original implantation because of infection at the generator site. This patient was treated with intravenous oxacillin sodium for 1 week without resolution. The patient then went to the operating room (OR) for removal of the generator and debridement of the pocket. Intraoperatively, no pus was encountered and a gram stain of the pocket failed to reveal any bacteria. A new generator was placed in the same pocket in the same operative setting. The patient was then sent home with an additional 4-week course of intravenous oxacillin. The patient returned to the OR for removal of the generator 4 months later because of persistent wound problems. The leads were also removed at this time because of tracking of the infection from the chest wound into the neck. The patient received additional antibiotic therapy and underwent successful reimplantation 6 weeks later. Patient 3 developed a small abscess over the generator 10 weeks after implantation. The patient went to the OR for incision and drainage of the abscess, and intravenous antibiotic therapy was started. Staphylococcus aureus was isolated. The generator soon became exposed, and the patient returned to the OR for removal of the generator (the leads were left in place). After a 2-week course of intravenous antibiotics and stabilization of the wound, the patient went back to the OR 2 months later for replacement of the generator. Patient 4 was readmitted to the hospital 11 days after implantation for intravenous antibiotic treatment of an infection located over the generator. This was believed to be related to the patient scratching her wound. An abscess was evident 2 days later, so the patient went to the OR for removal of the generator (the leads were left in place). No organism grew in aerobic or anaerobic culture. After a course of oral antibiotics, the patient returned to the OR 6 weeks later for replacement of the generator. The occurrence of infection in this group of patients did not correlate with the individual surgeon’s preference for perioperative antibiotic use.

One patient experienced a traumatic dehiscence of the chest wound secondary to wrestling 9 days after implantation. A small hematoma near the generator was drained at the bedside through the small wound dehiscence. There was no sign of infection. The patient was admitted for 48 hours of intravenous antibiotic therapy and monitoring of the wound. The patient was then discharged from the hospital, and oral antibiotic therapy was maintained until the wound closed secondarily. No signs of infection have become apparent 8 months following this injury.

Eight patients have returned to the OR for replacement of the generator because of routine depletion of the generator battery. Five patients have returned to the OR for replacement of the generator or leads because of device malfunction. Of these patients, we have encountered 1 with a grossly fractured lead and 2 in whom the lead loosened from its insertion in the generator. We noted relatively dense fibrosis around the vagus nerve in the area of the leads during a subsequent operation. When leads have required replacement, meticulous and atraumatic dissection of the leads from the vagus nerve is required to avoid injury to the nerve and surrounding vascular structures. None of the patients requiring lead replacement have experienced any recognized injuries to the vagus nerve.

Since starting the VNS program, we have removed 17 devices because of no perceptible benefit in seizure control. In these patients, we have usually elected to remove the generator and the portion of the lead coiled in the chest wound. Usually, the portion of the lead in the neck is not removed. The decision not to remove the portion of the lead in the neck must be discussed with the family, weighing the risk of potential injury to the vagus nerve from removing the lead against the risk of injury to the nerve if magnetic resonance imaging is per-
formed in the future with the helical lead still coiled around the nerve.

**PATIENT QUESTIONNAIRE**

For all related graphs, responses are graded as follows: strongly disagree, disagree, neutral, agree, and strongly agree.

Of 73 questionnaires, 46 were returned and are included in this analysis. Twenty-two patients noted hoarseness when the VNS is stimulating. Sixteen of these patients were using speech as an effective form of communication. Of these 16 patients, 4 (25%) were believed to have significant problems with communication after VNS implantation (Figure 4). Reprogramming the device did not seem to affect the degree of speech problems.

Of the 46 patients, 45 had a relatively normal ability to swallow before VNS implantation. However, 4 patients have gastrostomy tubes and receive at least part of their diet by this route. Of the 46 patients, 4 agreed to the following statement: “When the VNS is stimulating, the patient experiences significant difficulty with swallowing” (Figure 4). Again, reprogramming the device seemed to have little effect on swallowing.

Five patients experienced an occasional cough when the device was stimulating. Three patients experienced mild pain related to the device, but no details were given regarding the nature of the pain. Five patients experienced adverse effects specifically related to use of the magnet to activate the device.

There seems to be little concern regarding cosmesis related to the generator and surgical incisions (Figure 5). Responses to the following statement, “The position of the VNS device on the upper chest has caused significant activity limitations for the patient,” are depicted in Figure 5. More than half of the respondents agreed or strongly agreed with the following statement: “The patient’s overall level of alertness has improved since VNS implantation” (Figure 5). The responses to the question regarding overall satisfaction with the VNS were quite positive (Figure 6).

**COMMENT**

The management of infections related to implantable devices is a complex issue. Because of the anatomical location of the VNS’s generator, guidelines on the management of pocket infections can be obtained from examining the pertinent literature regarding cardiac pacemaker and cardioversion device infections. The important difference between these devices and the VNS system is that the cardiac devices have a lead that goes into the intravascular space. This creates the possibility for the spread of infection from the pocket, leading to immediate septicemia and the risk of life-threatening bacterial endocarditis. Tracking of the infection along the VNS lead into the neck, as encountered in one of our patients, is much less of an issue. Otolaryngologists are more familiar with the cochlear implant device. Infections involving a cochlear implant can successfully be treated without explantation with greater frequency compared with the cardiac devices. This is probably because of the greater vascularity of the scalp region compared with the chest and the resulting ability to resist uncontrolled infection.

We have demonstrated that an infection, if identified in the early phase before suppuration, can be treated successfully with antibiotics and avoidance of explantation. However, this is probably the exception to the rule. Of the 4 patients with pocket infections, 3 required ex-
plantation. This is more consistent with the literature regarding pacemaker infections. Nearly all articles re-viewing this topic recommend that early and aggressive treatment of pocket infections is necessary to avoid additional morbidity. This includes early explantation of the device. It has been recommended that optimal treatment of an infected generator requires immediate explantation followed by 2 weeks of intravenous antibiotic therapy, reimplantation of a new device, and an additional 10 days of intravenous antibiotic therapy. This approach has demonstrated 100% success in the management of infected cardiac pacemakers. The same series demonstrated that attempts to manage the infected pacemaker without explantation failed in every instance, with occasional mortality and eventual explantation when medical therapy failed.

Of our patients with suppurative infections involving the generator site, 2 were cared for without removal of the leads. This might be unexpected given that there is at least 8 cm of lead and that the bulkier lead termin- als coiled in the generator pocket are left behind in the infected field once the generator is removed.

Infections involving implantable devices follow a different time course than other surgical infections. The typical wound infection when an implantable device is not used is usually manifest within the first week or two after surgery. When an implantable device is used, an early infection is defined as occurring within 28 days of surgery, a late infection occurs within the first year of implantation, and a delayed infection occurs longer than 1 year after surgery.2 Our patients who experienced infection certainly reflected this trend, with infections becoming evident 11 days, 3 weeks, 10 weeks, and 3 months postoperatively.

We have routinely used antibiotic prophylaxis on all of our patients who undergo implantation, albeit varying protocols depending on the surgeon’s preference. All patients received intraoperative intravenous antibiotics. Some patients received 1 to 3 doses of intravenous antibiotics postoperatively and no oral antibiotics. Some patients received only oral antibiotics postoperatively. The exact protocol for antibiotic use did not correlate with the occurrence of infection in our patient set. Examination of the published recommendations regarding antibiotic prophylaxis at cardiac pacemaker placement is varied. Most researchers support the use of perioperative antibiotics. However, at least one study showed no obvious benefit from antibiotic prophylaxis.

The microbiological features of infections involving implantable devices are characterized by a preponderance of *S aureus* and *Staphylococcus epidermidis*. When considering infections in the pectoral area, however, the flora unique to the axillary region must also be considered. *Staphylococcus schleiferi* has recently been identified as a potential important contributor to infections in this region. Anaerobic organisms are being recovered with increasing frequency, probably because of refined transport of culture material and improved culture techniques.

Removal of the helical leads from the vagus nerve has been performed on multiple occasions in our series. This is met with varying degrees of difficulty depending on the amount of fibrosis encountered around the nerve. Intu-

itively, a subsequent operation on the vagus nerve to remove the leads would put the patient at risk for temporary or permanent injury to the nerve. We have not encountered any vagus nerve injuries in our experience. One prior article relates successful removal of 7 of 10 leads in patients without incidence of any permanent injury to the nerve or surrounding vascular structures. The potential risk of injury to the structures in the carotid sheath must be considered when counseling a patient for explantation of the VNS generator and leads. Leaving the helical leads in situ may place the vagus nerve at risk if the patient requires magnetic resonance imaging using the body coil because of potential heating of the leads induced by the strong magnetic field. Magnetic resonance imaging with the helical leads in place using a head coil, however, is considered safe by the Food and Drug Administration because of limitation of the magnetic field.

It has recently been suggested that the VNS’s generator and leads can be placed through a single incision in the lower neck, with the generator located beneath the pectoralis major muscle. The potential for a more satisfying cosmetic result must be weighed against issues. Bridging vessels from the chest wall to the pectoralis muscle can be avulsed when developing this plane of dissection. Control of these vessels may be difficult in this limited exposure approach. Also, the ramifications of infection must be considered. If an infection occurs beneath the pectoral muscle, recognition of this would be more difficult than if the infection were located closer to the skin. This may lead to a delay in diagnosis of the infection, leading to greater morbidity for the patient. Also, if an infection were to occur with this new approach, the leads would likely need to be removed because the neck cavity is in wide communication with the generator pocket. This may place the vagus nerve at significant risk. With the traditional 2-incision approach, the generator pocket is relatively isolated from the neck because the leads are tunneled in a subcutaneous plane. This would tend to isolate the neck cavity to a greater degree should a generator pocket infection occur.

Periodic stimulation of the vagus nerve to achieve therapeutic results is expected to cause some adverse effects. The most frequent of these is hoarseness, as demonstrated in our series. The degree of hoarseness has been related to the intensity level of current delivered to the vagus nerve. One researcher has noted varying degrees of vocal cord adduction and abduction by laryngeal stroboscopy depending on the frequency of the stimulation current.

Aspiration has rarely been encountered by others after VNS implantation. Schallert et al conducted video swallow studies on 8 patients following VNS implantation, demonstrating an increased incidence of laryngeal penetration but no frank aspiration. We encountered varying responses regarding the impact of VNS implantation on swallowing; overall, the effects seemed to be limited. We have not encountered any problems with chronic or repeated aspiration in our series of patients.

Quality-of-life issues have infrequently been evaluated in patients undergoing VNS implantation. Hornig et al used a global evaluation score as a longitudinal ordinate to score overall patient satisfaction with the VNS.
This evaluation score was positive over time, and did not always correspond with satisfaction related to seizure control after VNS implantation. In the present series, we tried to separate various factors that may be involved with the patient's overall satisfaction with the device unrelated to seizure control and expected adverse effects (eg, hoarseness). The results show that patients were generally pleased regarding limited surgical scarring, lack of activity limitations, and an increased level of alertness. Most patients and parents were pleased with their decision to pursue VNS implantation as a treatment option for seizures.

**CONCLUSIONS**

Vagus nerve stimulator implantation in children seems to be well tolerated. Control of seizures in this patient population is similar to that of adults following VNS implantation. Infection rates have been similar to established norms compared with pacemaker implantation, and guidelines regarding management of these problems are applicable to patients undergoing VNS implantation. As demonstrated by responses to our questionnaire, the impact of postimplantation hoarseness and swallowing is limited. Subjective quality-of-life and overall satisfaction scores related to the VNS are quite positive.

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