Management of Chronic Ventilatory Insufficiency with Electrical Diaphragm Pacing

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ABSTRACT: We have had experience with diaphragm pacing in 24 patients at the Toronto Western Hospital. Fourteen patients have undergone bilateral implants to treat chronic ventilatory insufficiency (CIV) caused by traumatic tetraplegia at the C1/2 level (eight patients), neurogenic apnea (five) and one case of neonatal apnea. Unilateral stimulators for nocturnal pacing have been implanted in five patients with central alveolar hypoventilation (sleep apnea) and five patients who suffered CIV resulting from various etiologies. Of the patients who were ventilator dependent, 80% were successfully weaned and in the entire series, 58% of the patients are living. Diaphragm pacing was successful in 67%, partially successful in 8% and ineffective in 25%. The major complications were: death by pneumonia, failure of the radio receivers, and infection. Diaphragm pacing is the treatment of choice for patients who are ventilator dependent and tetraplegic from upper cervical trauma or in some cases of neurogenic apnea; it may be life saving for patients who suffer central alveolar hypoventilation.

RESUME: Quatorze ans d’expérience avec la stimulation électrique du diaphragme. Nous avons fait l’expérience de la stimulation électrique du diaphragme chez 24 patients au Toronto Western Hospital. Quatorze patients ont subi une implantation bilatérale pour traiter une insuffisance ventilatoire chronique (IVC) causée par une quadriplégie traumatique au niveau de C1/2 (8 patients), une apnée neurogène (5) et un cas d’apnée néonatale. Des stimulateurs unilatéraux pour la stimulation nocturne ont été implantés chez 5 patients avec hypoventilation alvéolaire centrale (apnée du sommeil) et chez 5 patients qui souffraient d’IVC d’étiologies variées. Parmi les patients qui étaient dépendants d’un ventilateur. 80% ont été sevrés avec succès et, dans toute la série. 58% des patients sont toujours vivants. L’électrostimulation du diaphragme a été considérée comme un succès chez 67% partiellement efficace chez 8% et inefficace chez 25%. Les principales complications ont été les suivantes: décès par pneumonia, défaillance du récepteur radio nécessitant son remplacement après 4 ans et infection nécessitant le retrait de l’appareil. La stimulation électrique du diaphragme est le traitement de choix pour les patients qui sont dépendants d’un ventilateur et pour les patients devenus quadriplégiques à la suite d’un traumatisme cervical haut ou dans certains cas d’apnée neurogène; cette technique peut sauver la vie de patients qui souffrent d’hypoventilation alvéolaire d’origine centrale. Les patients qui ont une atteinte du nerf phrénique, du diaphragme ou des anomalies de la paroi thoracique ainsi qu’une maladie pulmonaire chronique ne sont pas appropriés à ce traitement coûteux.


The concept that intermittent stimulation of the phrenic nerve could produce diaphragmatic contractions and effect ventilation dates from 1783.1 The development of the modern technique of diaphragm pacing, however, was based upon the animal experiments of Sarnoff2 who coined the term “electrophrenic respiration”, and the work of Glenn3,4,5,6 who introduced transcutaneous radiofrequency transmission and suggested that this form of respiration be called “diaphragm pacing”. The first implantation of bilateral diaphragm pacemakers in a high tetraplegic patient was performed by Glenn7 in 1970 and the first in Canada was done in May 1973 at the Toronto Western Hospital.8 Both of these patients are well and continue to use diaphragm pacing as their sole means of respiration.

The purpose of this paper is to report the Toronto experience with the treatment of chronic ventilatory insufficiency (CIV) by diaphragm pacing. This series is part of an international,
multicentre, longterm study of 160 cases of diaphragm pacing headed by Glenn at Yale University.

Electrical Apparatus

The principal component of the diaphragm pacer is a battery powered radiofrequency (RF) transmitter (Avery Laboratories, Farmingdale, N.Y.) that emits a series of repetitive trains of 34 square wave pulses of increasing amplitude over an inspiration duration of 1.35 seconds. Following a pause of 2.5 to 4 seconds during which the diaphragm relaxes and expiration takes place, the cycle is repeated to simulate normal breathing. The stimulus slope, pulse width, breathing rate, inspiration duration and amplitude of stimulation are adjustable to the patient’s comfort. The pulses are broadcast over a multistrand wire loop antenna which is taped to the skin overlaying the second component, a hermetically sealed, integrated circuit receiver that is implanted in a subcutaneous pocket on the patient’s chest wall. The receiver detects the pulse-modulated RF energy which is generated by the transmitter and passes the signal along a lead wire to a bipolar platinum electrode that is wrapped around the phrenic nerve in the neck or mediastinum. More recently, a unipolar cathode may be implanted beneath the phrenic nerve while the anode disk is placed in the subcutaneous pocket with the receiver.

Selection Criteria

The most important factor in considering a patient’s suitability for diaphragm pacing is the integrity of the phrenic nerves and diaphragm. They may be assessed simply by observing voluntary movement of the diaphragm under fluoroscopy. In patients who don’t possess voluntary respiration, the phrenic nerves may be stimulated by a cardiac pacemaker inserted transvenously. This technique has been supplanted in the past decade by transcervical stimulation of the phrenic nerves in the neck while recording diaphragmatic electromyographic responses along the costal margin.

Secondly, the function of the lungs and chest wall must be examined. This includes measuring resting lung volumes, time volume and flow volume curves, and performing exercise studies. Breath-holding responses as well as ventilation and perfusion scans, can provide valuable data.

Thirdly, the medullary respiratory centre should be evaluated by measuring arterial blood gas levels at rest and during sleep. The ventilatory response to normocapnic hypoxia and hypercapnic hyperoxia is also important.

Operative Technique

Many of the patients will have tracheostomies. The proximity of the supraclavicular incision to the tracheostomy site favours endotracheal intubation so that the tracheal stoma can be thoroughly cleansed and sealed off with sterile gauze and vidrape. Trans-tracheostomy intubation, however, is feasible when the endotracheal approach is difficult, but the risk of wound infection is increased. Some patients need to be thoroughly cleansed and sealed off with sterile gauze and vidrape. There may be complications in performing this procedure. The anesthesiologist should not employ neuromuscular blocking agents. A one centimetre length of the nerve is mobilized and the platinum electrode placed beneath and sutured to the underlying muscle. Great care is taken to avoid iatrogenic injury to the phrenic nerve which occurred in 3.7% of cases in Glenn’s series. The lowest current amplitude to produce visible and palpable diaphragmatic contractions is the threshold stimulation and measured 1.2 to 3.0 milliAmperes (mA). The lead wire is passed subcutaneously to an infracavicular pocket developed to contain the radioreceiver and the disk anode. Bilateral implants are necessary in tetraplegic patients and early in the series, each hemidiaphragm was paced for 12 hours only in order to prevent fatigue of the nerve or diaphragm which usually occurred after 16 hours of phrenic nerve stimulation. A weaning schedule was not begun until 10 days postoperatively to allow swelling to subside around the nerve and receiver sites. An initial five minutes of stimulation every hour was increased by five minutes every five to seven days until weaning was achieved, usually in six to eight weeks.

Since 1984 we have followed the technique advocated by Glenn to condition the diaphragm muscle by using low frequency, bilateral synchronous stimulation and a respiratory rate of eight to 10 breaths per minute. This method of pacing increases the strength and endurance of diaphragmatic contraction but it may take as long as four to six months of this schedule to achieve full time pacing.

Clinical Series

The Toronto series of 24 patients was divided into five groups; the first three groups received bilateral implants and the last two, unilateral.

(1) Traumatic tetraplegia — 8
(2) Neurogenic apnea — 5
(3) Neonatal apnea — 1
(4) Central alveolar hypoventilation — 5
(5) Miscellaneous respiratory failure — 5

The details for patients in each group are listed in Tables 1 to 4. Of the 16 patients who were ventilatory dependent, 13 (81%) were successfully weaned. The three failures included two patients, aged 69 and 81, who had suffered strokes in addition to chronic obstructive lung disease, and another 81-year-old man with brainstem hypoxia associated with a neurodegenerative disorder. At the present time, eight (50%) of these 16 patients are alive. The other patients died of pneumonia (three), myocardial infarction (two), and brainstem hemorrhage (one). There were also three cases of sudden death, perhaps the result of hypoxia from inadequate pacing. In the entire series, 14 patients (58%) are living and 10 (42%) have died.

The results of diaphragm pacing were classified as follows:

(1) Success, meaning adequate ventilation, weaning from ventilator or control of sleep apnea. [16 patients (67%)] (2) Partial success, meaning some benefit derived from pacing but other methods of ventilatory support required. [two patients (8%)] (3) Failure, meaning pacing was ineffective. [six patients (25%)]

Complications

The major complication in this series was failure of the radioreceivers. This is caused by body fluid penetration of the leads and epoxy coating, resulting in a power supply failure. The receiver viability varied from two to nine years with an average life expectancy of four years. The most common clinical symptom warning of receiver failure was a sensation of...
"thumping" caused by a hiccup-like diaphragm contraction when the power output was becoming erratic. One patient (case 15) began to feel unpleasant shocks radiating into the shoulder and arm when the current spread to the neighbouring brachial plexus. She was able to eliminate this effect by turning down the stimulating power but then diaphragm pacing was inadequate and she developed right heart failure. Replacing the receiver led to smooth stimulation again and correction of the cor pulmonale. Regular measurement and analysis of the receiver output waveform after four years of implantation would anticipate failure and allow replacement before a potentially fatal outcome developed.

External component failure was caused either by breakage of the battery connector wire in the transmitter or wear in the antenna as shown by a green discoloration. A major problem occurred when the antenna loop (case 10), which had been secured by opaque paper tape, slipped down from the receiver site and pacing abruptly ceased. The patient lapsed into coma but fortunately responded quickly to the resumption of phrenic nerve stimulation. This serious situation could have been prevented by the use of transparent tape and an apnea alarm. Wound infection occurred in one receiver site of each of three patients and required removal of the units. A new implantation on the intra-thoracic phrenic nerve (case 10) has been successful after the patient was maintained on a ventilator for four months.

DISCUSSION

Patients who suffer CVI from traumatic tetraplegia at the C1/2 level (Group I) are ideal candidates for diaphragm pacing provided the phrenic nerves, diaphragm and lungs are normal.15

Table 1: Traumatic Tetraplegia — Bilateral Implants

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Date Implant</th>
<th>Complications</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>(2)</td>
<td>18</td>
<td>F</td>
<td>C1/2 Traumatic Infarct</td>
<td>Jan. 1974</td>
<td>Receivers replaced: Mar. 1980</td>
<td>Success</td>
</tr>
<tr>
<td>(3)</td>
<td>21</td>
<td>M</td>
<td>C1/2 Fracture — Dislocation</td>
<td>Dec. 1977</td>
<td>No Follow-up</td>
<td>Initial Success</td>
</tr>
<tr>
<td>(7)</td>
<td>71</td>
<td>M</td>
<td>C1/2 Fracture — Dislocation</td>
<td>Feb. 1985</td>
<td>Died M.I. May 1985</td>
<td>Successful wean</td>
</tr>
<tr>
<td>(8)</td>
<td>40</td>
<td>M</td>
<td>C1/2 Fracture — Dislocation</td>
<td>Aug. 1986</td>
<td>Replaced [R] receiver May 1987</td>
<td>Success</td>
</tr>
</tbody>
</table>

Table 2: Neurogenic Apnea — Bilateral Implants

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Date Implant</th>
<th>Complications</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>(9)</td>
<td>25</td>
<td>F</td>
<td>Medially AVM Hematoma</td>
<td>1979</td>
<td>AVM Re-bled Died 1980</td>
<td>Success — Weaned off ventilator</td>
</tr>
<tr>
<td>(12)</td>
<td>82</td>
<td>M</td>
<td>Viral Neuropathy Brainstem Hypoxia</td>
<td>Mar. 1985</td>
<td>Unable to wean despite adequate diaphragmatic excursion Failure</td>
<td>Failure</td>
</tr>
<tr>
<td>(13)</td>
<td>36</td>
<td>F</td>
<td>Ant Spinal Arterial Thrombosis Cervical infarct Tetraplegia</td>
<td>Mar. 1987</td>
<td>None yet</td>
<td>Partial success — in process of weaning</td>
</tr>
</tbody>
</table>
The two eldest patients, aged 48 and 71, were successfully weaned from their ventilators but later died from myocardial infarctions while they were still in hospital. There is no evidence that the diaphragm pacing had a deleterious effect on the myocardium. Detailed pulmonary function tests in two other patients showed satisfactory gas exchange with unilateral phrenic nerve stimulation every 12 hours allowed successful weaning from the ventilator and enabled the child to leave the hospital. Unfortunately this manner of pacing was inadequate for him to survive a bout of pneumonia and he died five months later. Bilateral synchronous diaphragm pacing may have yielded a happier outcome.

Complete spinal cord lesions between C3 and C5 cause damage to the phrenic neurons or motor roots and the nerves cannot be stimulated. Many of these patients will recover voluntary respiration after three months, but some will require permanent mechanical ventilation. A partial lesion of the mid-cervical cord may impair rather than destroy phrenic nerve function; especially if the C5 roots are preserved below the level of the lesion, augmentation of ventilation by diaphragm pacing may be feasible. In these cases it may be necessary to expose the phrenic nerve and stimulate it directly to evaluate if tidal volume can be improved and thus, justify a permanent implant.

Neurogenic apnea patients (Group II) are less favourable candidates for diaphragm pacing. The underlying pathology may be a progressive condition or it might also affect phrenic nerve function. Careful evaluation of these patients and the use of bilateral synchronous respiration is particularly important in this group as successful weaning from the ventilator can improve their quality of life significantly.

The baby with neonatal apnea required implantation of the radio receivers within the pleural cavity as the skin was too thin to cover the bulky units. The pacing schedule of unilateral phrenic nerve stimulation have demonstrated normal ventilation: perfusion rates on the contralateral side despite slight paradoxic movement of the contralateral hemidiaphragm. Complete spinal cord lesions between C3 and C5 cause damage to the phrenic neurons or motor roots and the nerves cannot be stimulated. Many of these patients will recover voluntary respiration after three months, but some will require permanent mechanical ventilation. A partial lesion of the mid-cervical cord may impair rather than destroy phrenic nerve function; especially if the C5 roots are preserved below the level of the lesion, augmentation of ventilation by diaphragm pacing may be feasible. In these cases it may be necessary to expose the phrenic nerve and stimulate it directly to evaluate if tidal volume can be improved and thus, justify a permanent implant.

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who in retrospect were inappropriate candidates for phrenic nerve implants. One of these patients (case 21) had suffered damage to the phrenic nerves by polio; another (case 20) patient's diaphragms were weakened by mitochondrial myopathy. The anatomy of case 22, with severe congenital kyphoscoliosis, was so distorted that the phrenic nerve could not be found at surgery. The two patients with chronic obstructive pulmonary disease were paced but could not be weaned from the ventilator as adequate gas exchange was impossible. These patients both had serious neurological deficits from cerebral infarction and succumbed to pneumonia.

Although all the patients who suffered traumatic tetraplegia developed a profound depression as a result of their neurological deficit no new psychopathology arose as a result of the pacing. The patients welcomed pacing as the means to freedom from a ventilator. One patient lives in her own apartment and requires four hours nursing care a day; one patient lives at home and three patients live in a chronic care hospital. In the Central Alveolar Hypoventilation group, two patients are working and two are retired but leading normal lives.

It is probable that one of the limiting factors to widespread implantation of diaphragm pacers is the cost. At the time of writing, the cost of bilateral phrenic nerve implants, a bedside transmitter for bilateral synchronous stimulation and a back-up portable transmitter is approximately $25,000 (Cdn.).

We agree with Glenn that patients with implanted diaphragm pacers require continuing care by a team of dedicated physicians, nurses, technicians and electronic engineers, as well as support from the family. This commitment of time and financial resources is essential to achieve maximum rehabilitation benefits from this type of modern technology. 13,19

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References


