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Treatment of chronic ventilatory failure using a diaphragmatic pacemaker

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We present our series of patients with chronic ventilatory failure treated with electrophrenic respiration: 13 males and nine females with a mean age of 12 ± 11.5 years. The etiology was, 13 tetraplegia, five sequelae of surgical treatment of intracranial lesions, and four central alveolar hypoventilation. The mean duration of the conditioning period were 3–4 months. Eighteen patients (81.8%) achieved permanent, diaphragmatically-paced breathing with bilateral stimulation and in four (18.2%) patients, pacing was only during sleep. Five patients died (22.7%): two during the hospital stay and three at home; two deaths had unknown cause and three were due respectively to, lack of at-home care, recurrence of an epidermoid tumor, and sequelae of accidental disconnection of the mechanical ventilation before beginning the conditioning period. Two cases were considered failures: One patient had transitory neurapraxia lasting 80 days, and the other had an ischemic spinal cord syndrome with progressive deterioration of the left-side response to stimulation. One patient had right phrenic nerve entrapment by scar tissue and four suffered infections. The follow-up periods since pacemaker implantation are currently: 1, 11 years; 4, 10 years, and 17, less than 5 years. The results of our experience demonstrate that complete stable ventilation can be achieved using diaphragmatic pacing and that it improves the prognosis and life quality of patients with severe chronic respiratory failure.

Keywords: pacing; diaphragmatic pacemaker; electrophrenic ventilation; tetraplegia; chronic ventilatory failure

Introduction

The experience of Glenn and colleagues with the use of the diaphragmatic pacemaker in treating chronic respiratory failure exemplifies progress in this field. In 1966[1] they began their first clinical experiments with the treatment of chronic respiratory failure using a diaphragmatic pacemaker; in 1984[2] they reported their results with continuous permanent bilateral ventilation of adults, in whom they achieved ventilation without diaphragmatic fatigue; in 1986[3] they summarized their 20 year experience; and in 1988[4] they presented the results of the first multicenter study of diaphragmatic pacing, which included 477 patients. Our own experience includes a 1987[5] report of the results obtained in three patients with traumatic tetraplegia treated with implantation of a diaphragmatic pacemaker for continuous, permanent bilateral stimulation.

In the current article we describe our experience from 1982–1995, with diaphragmatic pacemaker-assisted ventilation in a series of patients with chronic respiratory failure and discuss the indications, complications, and outcome of this attempt to improve the quality of life of these patients using continuous noninvasive regulation of ventilation.

Material and methods

Twenty-two patients with chronic respiratory failure (13 males and nine females) had a diaphragmatic pacemaker implanted. Their mean age was 12 ± 1.5 years (range 1–48 years); three patients were 1–3 years-old and five were 4–6 years-old.

The criteria for the implantation of the diaphragmatic pacemaker were: (1) Severe, chronic, respiratory failure requiring invasive mechanical ventilation via permanent tracheostomy on either a temporary, intermittent or continuous basis; (2) A central neurological cause: (a) alveolar hypoventilation, either primary or secondary to a brainstem disorder; (b) interruption of neuronal conduction at the upper cervical level, above the C_3 level; (3) Integrity of the intrathoracic section of the phrenic nerve; (4) Acceptable pulmonary function; (5) Normal level of consciousness.

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Chronic respiratory failure was always accompanied by severe hypoxemia and hypercapnia requiring mechanical ventilation usually on a continuous basis, but the need for ventilatory assistance sometimes was only partial or nocturnal.

The breakdown of diagnoses (Figure 1) was: 13 tetraplegia: 12 high spinal cord injuries (11 due to traffic accidents and one to a sports injury) and one anterior vertebral ischemia. Five sequelae of surgical treatment for, respectively, basilar impression, atlanto-axial dislocation, Arnold Chiari syndrome II with syringomyelia, reactive gliosis, and a bulbar epidermoid tumor. This group had unsystematized muscular paralysis and involvement of the cranial nerves. Four central alveolar hypoventilation, two of them having a history suggestive of encephalitis.

The viability of the phrenic nerves was explored preoperatively by measuring conduction time using the Newson-Davies[6] and Shaw[7] technique consisting of transcutaneous stimulation of the phrenic nerve in the neck. Conduction times of 4–12 m sec were considered normal; patients having longer conduction times were excluded from surgery. The response to electrical stimulation was evaluated by fluoroscopic or echographic study of diaphragmatic mobility and measurement of the action potentials elicited by supramaximal stimulation of the phrenic nerve; potentials of 80–1500 mV were considered normal.[8] Patients with preoperative action potentials under 90 mV were excluded from surgery.

Pulmonary anatomy and function were evaluated clinically, radiologically, and functionally. Patients were considered eligible for surgery if chronic lung disease was excluded by clinical and radiologic findings and PaO_2 and $PaCO_2$ values were normal during mechanical ventilation.

Two types of diaphragmatic pacemaker were used: (1) A monopolar stimulation model (Avery lab., Farmingdale, NY) equipped with either an S 242 transmitter (two cases) or an S 232 transmitter (six cases); one was implanted unilaterally and the others were implanted bilaterally; (2) An Atrostim (Atrotech, Finland) multipolar sequential stimulation model[9,10] with either a Pekka transmitter (three cases) or a Jukka transmitter (11 cases). Both models had an external transmitter, antenna, an internal receiver, and electrodes, which were of different designs. In the Avery diaphragmatic pacemaker the cathode was placed on the phrenic nerve and the anode was remote; in the Atrostim diaphragmatic pacemaker a single electrode incorporated both. The transmitter emits a radiofrequency signal through an antenna located on the skin located above the subcutaneously implanted internal receiver. The Avery model stimulated at a pulse rate of 9.1 Hz, while the Atrostim produced sequential multipolar stimulation at 6.25 Hz. The receiver converts the radiofrequency signal into an electrical impulse that is conducted to the electrode on the phrenic nerve. The intensity, gradual variation of the impulse interval regulating the nerve impulse, respiratory rate, and inspiratory time can be programmed via the external transmitter.

The electrode was implanted via a thoracic approach and using the technique described by Glenn; reimplantations were performed via a cervical approach as described by Glenn.[11]

A diaphragmatic conditioning program was carried out. Beginning 15 days after pacemaker implantation, the diaphragm was stimulated for 10 min every hour of the day; the initial schedule was 15 breaths per min with either a 90 ms (Avery) or a 160 ms (Atrostim)

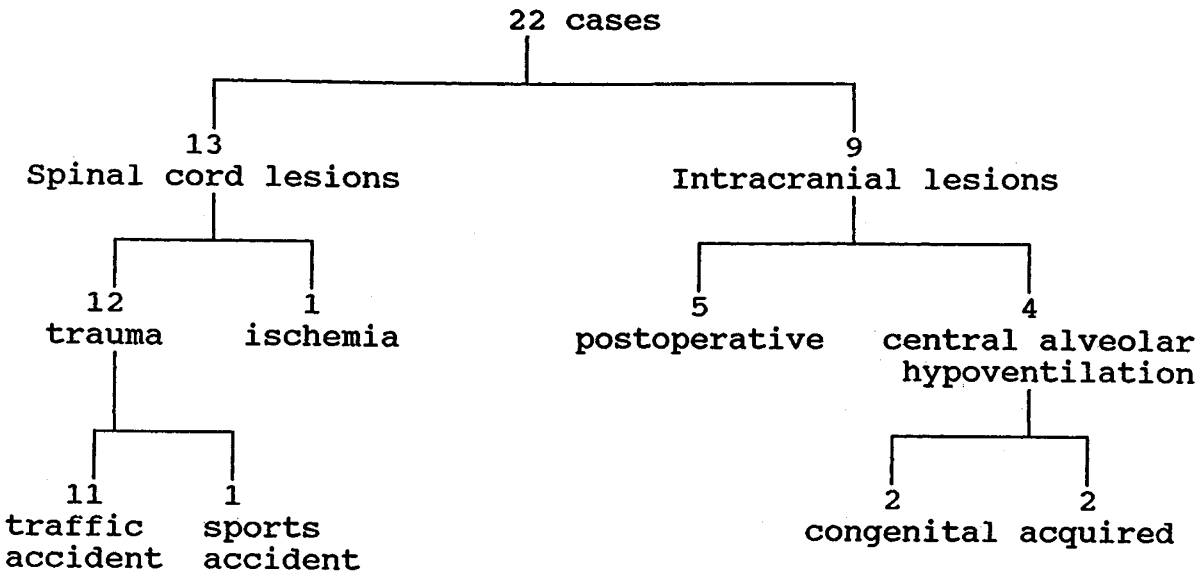

Figure 1 Cause of chronic ventilatory failure in 22 patients undergoing diaphragmatic pacing

pulse interval, an inspiratory time from 0.5 to 1.5 s, and submaximal intensity. Progressively higher intensities were used until achieving maximum tidal volume, as measured by spirometry. The stimulation time was increased weekly, alternating periods of mechanical ventilation and of diaphragmatic pacing of similar duration. Once 12 h of diurnal diaphragmatic pacing were attained without signs of fatigue, the periods of nocturnal mechanical ventilation were reduced each week until diaphragmatic ventilation was used 24 h a day. During this period, the respiratory rate was reduced to 8–10 breaths per minute as determined by the patient's tracheostomy by connecting the cannula with an inflatable balloon to an Ohmeda 5410 spirometer.

Results

Eighteen patients (81.8%) achieved permanent, diaphragmatically-paced breathing with bilateral stimulation. In four (18.2%) patients, pacing was needed only during sleep: one 8-year-old girl with central alveolar hypoventilation; one 48-year-old male with tetraplegia due to spinal ischemia as a result of thrombosis of the anterior spinal artery; two cases of central alveolar hypoventilation with unilateral stimulation. Stimulation was unilateral in one patient, an 18-year-old male, because only one electrode was implanted and in another, a 2-year-old male, because one electrode produced phrenic nerve entrapment.

The mean duration of the conditioning period were 3 months for adults and older children and 4 months for small children.

Mean conduction times were: right phrenic nerve 6.46 m sec (SD 1.76, range 4–11 m sec); left phrenic nerve 6.56 m sec (SD 1.65, range 4–10 m sec). The differences between these times in the two hemidiaphragms were not statistically significant; the longest conduction time in the series was 11 m sec. The action potentials were confined to a narrow band of voltages, the mean values being: right diaphragm 524 mV (SD 280, range 85–1000 mV); left diaphragm 552 mV (SD 188, range 200–770 mV).

The tidal volumes found during diaphragmatically-paced breathing increased in the first months of pacing, then remained within normal limits for the subject's weight. In the most recent follow-ups of a subgroup of six patients in whom transdiaphragmatic pressure was measured, the following values were obtained during diaphragmatically-paced breathing: 8–10 breaths per minute; tidal volume 11–30 ml/kg body weight (mean 18 ± 6); PaO_2 11.3–12.3 Kpa (84–92 mm Hg); and PaCO2 3.7–5.6 Kpa (27–42 mm Hg).

Both diaphragmatic pacemaker models had a good performance, but some pacemaker-related complications appeared: antenna fractures occurred frequently in both models; the Avery receiver failed in 4 cases, probably as a result of defective sealing of the cable exit port; there was one fracture of the conducting wire from the battery in an Avery transmitter, and one Atrostim (Jukka) transmitter had to be repaired.

Ventilatory support	Spinal lesions	Postoperative disorders	Central alveolar hypoventilation	Total
Total	12	5	1	18 82%
Partial	1	-	3	4 18%
Bilateral	13	5	2	20 91%
Unilateral	-	-	2	2 9%

Figure 2 Levels of ventilatory support in chronic ventilatory failure of different origin

Five patients died (22.7%): two during the hospital stay and three at home. Two of these deaths were of unknown cause: one, a 4-year-old girl with permanent diaphragmatic ventilation and the other, a 48-year-old woman with alternating diaphragmatically paced ventilation and mechanical ventilation for 6 years. The three deaths of known cause were due to: one lack of at-home care; one recurrence of an epidermoid tumor 10 months after pacemaker implantation; and a 2-year-old girl with a reimplanted diaphragmatic pacemaker who suffered disconnection of the mechanical ventilation with severe neurological sequelae before beginning the conditioning period. Conditioning was carried out and she was paced diaphragmatically for a year, but the family eventually requested her discharge and she died at home a few weeks later. The other patients had permanent tracheostomies and lived at home, coming to the hospital only for scheduled follow-up visits or the treatment of complications.

Two cases were considered failures: One patient had transitory neurapraxia lasting 80 days; continuous, permanent bilateral diaphragmatic ventilation later was maintained for 9 years. The other patient had an ischemic spinal cord syndrome with progressive deterioration of the left-side response to stimulation.

A 3-year-old boy with central alveolar hypoventilation, presumably of congenital origin, and an Atrostim diaphragmatic pacemaker had right phrenic nerve entrapment by scar tissue proliferation around the electrode. Ninety days after implantation, the electrode and other implantable pacemaker elements were removed, the scar tissue was excised, the ends of the phrenic nerve were anastomosed using microsurgical techniques, and the pacemaker was reimplanted. Ten months after reimplantation the patient had recovered diaphragmatic mobility and had unilateral stimulation during sleep, which sufficed to control his central alveolar hypoventilation.

Four patients (three with an Avery pacemaker, one with an Atrostim) suffered infections as a result of ulceration around the cable and electrode connections, two in the immediate postoperative period and two later. None of the cases could be resolved by minor surgical interventions; all electrode elements had to be removed and a new electrode was reimplanted using a cervical approach.

The follow-up periods since pacemaker implantation are currently: 1, 11 years; 4, 10 years, and 17, less than 5 years.

Discussion

Our criteria for diaphragmatic pacemaker implantation, previously reported, are similar to those of other authors;[4,9,12] we kept to them from the onset and recommend them.

The contraindications for continuous bilateral ventilation in pediatric patients are the topic of ongoing discussion because of fear of possible diaphragmatic fatigue and phrenic nerve injury.[4,12] In our series, seven patients were under 5: three 4-year-olds, one 3-year-old, two 2-year-olds, and one 1-year-old. Five of these patients had tetraplegia and two had central alveolar hypoventilation; one of the five tetraplegics died of lack of at-home care and the other four have had diaphragmatic pacing for more than 2 years. In these cases, no signs of diaphragmatic fatigue have been detected in the 6 month follow-up visits and lung volumes and arterial blood gas findings are normal for their ages. We attribute these good results to the use of low respiratory rates and low pulse frequencies.

Our series compared to those of other authors[4,9,12] had more cases of traumatic origin and tetraplegics than patients with alveolar hypoventilation. Bulbar lesions with unilateral or bilateral paralysis of the upper and/or lower vagal muscles and associated reversible or irreversible injury of cranial nerves V, VI, IX and XII produce devastating effects on the vital functions related with swallowing, breathing, and phonation; a good understanding of anatomy and function helps to establish surgical priorities in the rehabilitation of neurological disorders of the aero-digestive tract. In these cases surgery can be life-saving.[13]

We found no logical explanation for the differences between hemidiaphragms in conduction time; in one case the conduction time was 11 m sec on the left side and 6 m sec on the right side.

Diaphragmatic conditioning is a process by which the fast-contracting fibers (anaerobic, highly glycolytic fibers), which are highly susceptible to get fatigued, are converted to slow-contracting fatigue-resistant fibers (aerobic oxidative fibers), which enable permanent ventilatory support using diaphragmatic pacing.[14,15] All the patients underwent conditioning and the most important difficulties occurred in patients with brainstem injuries, swallowing disorder, and respiratory aspiration.

Clinical observations of the tolerance of diaphragmatic pacing and spirometric findings during the conditioning period and over more prolonged periods allow diaphragmatic muscle fatigue to be excluded.[16–18] A study of the ventilatory parameters and transdiaphragmatic pressure is being carried out in a subgroup of these patients to improve the analysis and prevention of fatigue in this type of diaphragmatic pacing.

The most feared complication in the postoperative period of these patients is phrenic nerve entrapment. There have been few reports on phrenic nerve repair with recuperation of function;[19,29] in our case we describe the indication for time of repair, the use of microsurgical techniques, and the excellent result obtained.

It is difficult to compare the mortality rate observed in our series (22%) with other reports (28–51%).[4–12] The duration of the follow-up period after pacemaker implantation varies, as do the populations treated. For instance, in our series most of the patients had tetraplegia and were absolutely dependent on mechanical ventilation, whereas in the two series cited most of the patients had central alveolar hypoventilation without muscular paralysis and were ventilated part-time during sleep. We observed no death related directly with the diaphragmatic pacemaker implantation procedure.

Patients with tetraplegia due to a high spinal cord injury are faced with the prospect of indefinite dependence on invasive mechanical ventilation using manometric respirators. In patients with primary alveolar hypoventilation and severe respiratory failure, ventilator dependence is only partial, but mechanical ventilation is needed. In both cases, changing the type of ventilation improves the patient's prognosis by eliminating the risks of mechanical ventilation and enhances their quality of life by making at-home care possible. Moreover, the small size and autonomy of the pacemaker equipment allow it to be attached to the bed or wheelchair enabling the patient to move easily around the home or to leave home for social activities and relations.

The results of our experience demonstrate that complete stable ventilation can be achieved using diaphragmatic pacing and that it improves the prognosis and life quality of patients with severe chronic respiratory failure.

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