Transdiaphragmatic pressure in quadriplegic individuals ventilated by diaphragmatic pacemaker

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Abstract
Background – Electrophrenic pacing can be used in the management of ventilatory failure in quadriplegic patients. A study was undertaken to determine the pattern of transdiaphragmatic pressure (Pdi) during the conditioning phase of electrophrenic pacing to see if it had a possible role in optimising the process of conditioning.

Methods – The tidal volume (TV) and Pdi were measured in a group of six quadriplegic patients commencing ventilation by low frequency pulse stimulation (7–10 Hz) and low respiratory rate stimulation (<10 breaths/min).

Results – Tidal volume increased between baseline and month 1 (4.33 ml/kg, p<0.001) and between months 1 and 2 (3.00 ml/kg, p<0.05) and then stabilised. Pdi was higher during bilateral diaphragmatic pacing (mean (SD) 1.73 (0.30) kPa) than with either left (1.15 (0.34) kPa) or right (0.86 (0.37) kPa) unilateral pacing. Pdi varied throughout the observation period, probably by interaction between recovery of the diaphragmatic fibres and the pacing regimen.

Conclusions – Patients with quadriplegia due to high spinal injury can be maintained with ventilation by continuous electrophrenic pacing. The control criteria used in this study for pacing were tidal volume and the patient’s tolerance, and the Pdi measurement did not contribute any additional information to help with managing the conditioning process.

Key words: diaphragmatic pacemaker, electrophrenic ventilation, quadriplegics, transdiaphragmatic pressure.

Methods
Six patients with quadriplegia due to accidental traumatic spinal injury at the C1–C2 level who were being started on ventilation by electrophrenic pacing were studied. The criteria for implantation were (1) chronic respiratory failure requiring artificial ventilation via a tracheostomy, (2) acceptable pulmonary function assessed clinically and by radiology, (3) normal arterial gases while mechanically ventilated on air, (4) normal level of consciousness, and (5) normal intrathoracic phrenic nerve conduction (that is, between 4 and 12 ms). The diaphragmatic response to electrical stimulation was evaluated by assessing diaphragmatic mobility on fluoroscopy or echography and by electromyography of the diaphragmatic action potentials evoked by supramaximal electrical stimulation of the phrenic nerve; the normal range of this measurement is very wide (80–1500 µV).

Two types of pacemaker were used: two patients received the S232 Avery (Farmingdale, New York) and four patients the Atrostim (Atrotech, Finland). The Avery pacemaker is monopolar and stimulates at 110 ms intervals and the Atrostim delivers multipolar stimulation at 160 ms intervals. Both systems are equipped with an external transmitter with antennae, an internal receptor, and electrodes. By means of the external transmitter, the amplitude, slope, or gradual pulse variation of the electrical stimulus can be modified, as can the respiratory rate, inspiration time, and pulse interval. The pulse interval is fixed in the Atrostim model. In every case the pacemaker was implanted using a thoracic approach and the surgical technique described by Glenn.

Diaphragm conditioning consisted of a progressive increase in the duration of pacing until exclusive pacemaker ventilation was attained. The conditioning period can be carried out by alternating mechanical ventilation with diaphragmatic pacing. In this series the duration of diaphragmatic pacing was increased gradually. Beginning two weeks after pacemaker implantation, the patient was paced bilaterally for 10–20 minutes every hour during the daylight hours at a respiratory rate of 15 breaths/
min and at a pulse interval of 90 ms with the Avery model or 160 ms with the Atrostim model.\(^1\) Impulse duration ranged from 0·5 to 1·3 s and the intensity of the current applied to each electrode configuration was just enough to elicit submaximal tidal volumes, as measured by spirometry. The pacing time was increased weekly until 30 min/hour was reached, after which pacing periods were programmed for additional increases followed by resting periods of mechanical ventilation of the same duration until the patient could be paced for 12 hours without signs of diaphragmatic fatigue. Resting periods during sleep were then reduced progressively until permanent pacemaker ventilation without need for mechanical ventilation was attained. As permanent pacing was established, the frequency of stimulation pulses was reduced to 7–10 Hz in the Avery model. The respiratory rate, which began at 15 breaths/min, was reduced to less than 10 as ventilation permitted. At the end of the conditioning period the tracheostomy cannula was replaced with a Teflon tube with a stopper that some patients removed during sleep.

Throughout the conditioning period we attempted gradually to reach an ideal pattern of stable exclusive pacemaker stimulation with the following characteristics: adequate tidal volume (TV) for the patient’s morphometric characteristics (15–20 ml/kg),\(^1\)\(^3\) low respiratory rate (below 10 beats/min), low stimulation pulse frequency (7–10 Hz), and absence of conditions suggesting muscular fatigue such as progressive reduction of TV during pacing or poor patient tolerance. The guiding criteria were progressive increase of a stable TV and patient tolerance of the pacing and ventilatory regimen.

The pacemaker indication was established after assessing pulmonary function by measuring TV and arterial blood gases. During the conditioning period TV was measured by connecting a cannula fitted with an inflatable cuff to the tracheostomy present in all patients. An Ohmeda 5410 spirometer was used to measure digitally the TV, respiratory rate, and minute volume. These measurements were made at the end of every daily stimulation period during the conditioning period and were used as a guide for pacing adjustments. All measurements were made in the same position for each patient.

PDI was determined using polyethylene balloon catheters and the technique described by Agostoni et al\(^1\)\(^4\) and Roussos and Macklem,\(^1\) the catheters were inserted through the nose and the balloon was inflated with 2 or 3 ml of air, a volume that provides very sensitive tracings. Successive pressure measurements were made in the lower third of the oesophagus, in the stomach, and again in the oesophagus using a Jaeger Pneumotest Bodytest device. The stability of the oesophageal pressure before and after measurement of the gastric pressure was confirmed by excluding oesophageal contractions or abdominal muscle spasms. Pressures were measured during bilateral diaphragmatic pacing and with individual left and right hemidiaphragmatic pacing. During bilateral diaphragmatic pacing the tracing was recorded for two minutes or longer if the tracing was not very stable. Patients were more tolerant of unilateral diaphragmatic pacing so the tracing was recorded for a shorter time period, although at least three respiratory cycles were always included. No attempt was made to measure the patient’s tolerance of unilateral pacing, but the patient quickly (15–30 s) felt the change from bilateral to unilateral pacing. The measurements were always made at noon during diaphragmatically paced ventilation. During the conditioning period patients were ventilated diaphragmatically for at least three hours before measurements were made. Manometric studies were made at varying intervals, depending on the conditions of care, starting two months after pacemaker implantation.

### Results

The six patients were consecutive in a series of patients who had undergone electrophrenic pacemaker implantation since 1989. All were men and achieved permanent simultaneous bilateral ventilation by diaphragmatic pacing and could forego mechanical ventilation, reside at home, and perform light daily activities such as feeding and running a household. Table 1 shows details of the six patients. A good correlation was found between the subject’s height and phrenic nerve conduction time on the right side (Pearson correlation \(r=0·85, p<0·05\)) but not on the left (\(r=0·54, p=NS\)).

The conditioning period lasted about three months in the adults and four months in the children. The evolution of TV in the first five months is shown in fig 1. There was a significant increase in mean TV between baseline and month 1 (4·33 ml/kg, \(p<0·001\), 95% confidence interval (CI) 6·05 to 2·62) and between months 1 and 2 (3·00 ml/kg, \(p<0·05\), 95% CI 5·48 to 0·52) with no significant change thereafter. The two largest increases in TV were seen in the two babies.

The mean (SD) PDI elicited by bilateral stimulation (1·73 (0·30) kPa) was, for the whole group, significantly greater (\(p<0·001\)) than that achieved by unilateral stimulation of either hemidiaphragm, with the PDI achieved by left hemidiaphragmatic stimulation (1·15 (0·34) kPa) being significantly greater (\(p<0·01\)) than that

### Table 1 Characteristics of patients

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Weight (kg)</th>
<th>Height (m)</th>
<th>Conduction time (ms)</th>
<th>Action potential (mV)</th>
<th>Pacemaker</th>
<th>Time (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>M</td>
<td>14</td>
<td>1·27</td>
<td>4·5</td>
<td>4·5</td>
<td>AV</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>M</td>
<td>14</td>
<td>1·30</td>
<td>6·5</td>
<td>6·5</td>
<td>AT</td>
<td>13</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>M</td>
<td>14</td>
<td>1·60</td>
<td>8·5</td>
<td>8·5</td>
<td>AT</td>
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<td>4</td>
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<td>1·64</td>
<td>8·0</td>
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<td>AT</td>
<td>17</td>
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<tr>
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<td>M</td>
<td>14</td>
<td>1·68</td>
<td>6·0</td>
<td>6·0</td>
<td>AT</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>17</td>
<td>M</td>
<td>14</td>
<td>1·80</td>
<td>11·0</td>
<td>11·0</td>
<td>AT</td>
<td>29</td>
</tr>
</tbody>
</table>

\(AV = \) Avery pacemaker; \(AT = \) Atrostim pacemaker; \(t=\) interval between accident causing quadriplegia and pacemaker implantation.

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\(\text{PDI} = \) determined using polyethylene balloon catheters and the technique described by Agostoni et al\(^1\)\(^4\) and Roussos and Macklem,\(^1\) the catheters were inserted through the nose and the balloon was inflated with 2 or 3 ml of air, a volume that provides very sensitive tracings. Successive pressure measurements were made in the lower third of the oesophagus, in the stomach, and again in the oesophagus using a Jaeger Pneumotest Bodytest device. The stability of the oesophageal pressure before and after measurement of the gastric pressure was confirmed by excluding oesophageal contractions or abdominal muscle spasms. Pressures were measured during bilateral diaphragmatic pacing and with individual left and right hemidiaphragmatic pacing. During bilateral diaphragmatic pacing the tracing was recorded for two minutes or longer if the tracing was not very stable. Patients were more tolerant of unilateral diaphragmatic pacing so the tracing was recorded for a shorter time period, although at least three respiratory cycles were always included. No attempt was made to measure the patient’s tolerance of unilateral pacing, but the patient quickly (15–30 s) felt the change from bilateral to unilateral pacing. The measurements were always made at noon during diaphragmatically paced ventilation. During the conditioning period patients were ventilated diaphragmatically for at least three hours before measurements were made. Manometric studies were made at varying intervals, depending on the conditions of care, starting two months after pacemaker implantation.

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attained by right hemidiaphragmatic stimulation (0.86 (0.37) kPa).

For bilateral and unilateral pacing there were no significant differences between the first Pdi values recorded after implantation of the pacemaker and those at the last follow up visit which ranged from four to 45 months after starting electrophrenic pacing. Figure 2 shows the changes with time in Pdi recorded with bilateral stimulation for each of the six subjects. Whilst there were quite large changes with time for some individuals, there was no consistent change with time for the group. No significant correlation was found between any Pdi values and either the conduction speed or the diaphragmatic action potentials recorded before pacemaker insertion, nor was there any correlation found between the interval from the spinal injury to the commencement of pacing and either TV or Pdi.

Table 2 shows the values for breathing frequency, TV, and arterial gases during electrophrenic pacing for each patient at their last follow up when they were considered to be in a stable and optimal state.

**Discussion**

Recovery of the diaphragmatic muscle fibres is the basis of the conditioning period following implantation of a pacemaker. The evolution of TV values suggests that after three months, when the conditioning period is ended, TV values become relatively stable. This sequence of improvement probably reflects the time needed for all diaphragmatic fibres to recover from the disuse atrophy that occurs in the months of mechanical ventilation after spinal injury. However, we found no correlation between either TV or Pdi and the time lapse between the accident that produced the quadriplegia and implantation of the pacemaker.

The pacing parameters and rate of progression during the conditioning phase were based on clinical observations of each patient’s tolerance of pacing and spirometric measurements made during the conditioning period; these parameters are simple and immediately perceptible. Pdi measurements are more complex and troublesome to make and cannot be repeated frequently. We found that Pdi values did not correlate well with the evolution of TV and, for this reason, we no longer include Pdi in the routine follow up methods for the conditioning period. The fact that diaphragmatic pacing could be maintained for prolonged periods of time allowed the possibility of diaphragmatic muscle fatigue to be excluded.

The Pdi values obtained in this study were slightly lower than those reported in studies of other types of patients. Aubier et al. studied muscular fatigue in non-quadruplegic subjects using supramaximal transcutaneous and puncture stimulation and obtained values of 3-14 and 3-27 kPa. Hubmayr et al. studied the influence of thoracoabdominal morphology on diaphragmatic pressure and obtained a value of 3-1 kPa. In a group of patients with quadriplegia Glenn et al. found similar Pdi values at the beginning of the conditioning period and higher Pdi values at the end of it.

Pdi after bilateral stimulation was always superior to that elicited by unilateral stimulation. Bilateral contraction is always more effective than unilateral contraction because contraction of a single hemidiaphragm can be accompanied by paradoxical movement of the opposite hemidiaphragm and because muscle shortening depends on the distensibility of the opposite hemidiaphragm. With regard to unilateral contraction, the Pdi generated by left hemidiaphragm pacing is generally greater than
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that produced by right, and Bellemare et al.22 noted these differences in 1986. Although the abdomen is conceptualised traditionally as a liquid-filled container, it has been shown in dogs23 that there may be considerable regional differences in the pressures recorded during spontaneous breathing, mechanical ventilation, abdominal compression, or diaphragmatic pacing. The gastric balloon is placed beneath the left diaphragm and pressure variations may be absorbed on the other side by the liver, or the right diaphragm is less susceptible to paradox because of the liver and so the left gives best TV.

Pdi varied only slightly throughout the observation period, from 1·1 to 2·5 kPa, and no tendency was seen toward a steady increase. Pdi is the result of a combination of two relatively independent variables: (1) recovery of the diaphragmatic muscular fibres after a period of disuse after spinal injury, and (2) the diaphragmatic pacing regimen which depends on the increase in TV sought and patient tolerance. On the other hand, TV is influenced by other factors apart from Pdi,24 one of which is the paradoxical inward movement of the chest wall above the contracting diaphragm as a result of uncoordinated contraction of accessory respiratory muscles.25 No significant correlation was found between concurrent Pdi and TV values; however, in cases 1 and 2, in whom the largest improvement in TV was seen, Pdi in fact decreased slightly. In all the other cases there was an initial increase in TV with Pdi remaining unchanged. These findings strongly suggest that in the first two cases the improvement in TV was, at least in part, due to improvement of the mechanical characteristics of the respiratory system.

We conclude that it is possible to successfully change quadriplegic patients from mechanical ventilation to electrophrenic pacing and to maintain satisfactory ventilation with an improved quality of life. During the three months or so of conditioning the TV increased progressively but not thereafter, whereas the Pdi did not change significantly at all. We therefore recommend that only TV measurement and patient tolerance are used in the management of the conditioning period when commencing electrophrenic pacing.

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