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PHRENIC NERVE STIMULATION IN TETRAPLEGIA

A New Regimen to Condition the Diaphragm for Full-time Respiration

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ABSTRACT. Unipolar phrenic nerve stimulation (diaphragm pacing) has been used for ventilation of patients with C2 tetraplegia. Four-pole sequential nerve stimulation delays muscle fatigue when compared with unipolar stimulation. This may help to achieve more frequently long-term full-time bilateral electroventilation. Four-pole sequential nerve stimulation also offers an opportunity to shorten the conditioning phase of the hypotrophic diaphragm from about 6 to 2 months. The new conditioning regimen was tested successfully in two patients with C_2 tetraplegia. The new stimulation method and conditioning regimen remarkably shorten the time after injury during which mechanical ventilation is needed. This will give the patients earlier access to rehabilitation centres for spinal cord injuries and will diminish the work load of the personnel.

Key words: tetraplegia, respiratory failure, rehabilitation, diaphragm pacing, electric stimulation, phrenic nerve.

Modern rehabilitation and modern technical aids may enable a patient with high tetraplegia, i.e. tetraplegia including loss of respiration due to a C2 lesion, to care for himself, and to work. The possibility to achieve these goals worsens when the early period after trauma is lost without any attempts at rehabilitation. Rehabilitation is best performed at special rehabilitation centres which care for patients with spinal cord injuries.

However, in most countries these centres are not prepared to treat patients who need a mechanical ventilator permanently. This is because such patients cause a heavy load on personnel. In Finland it has been calculated (4) that up to five persons may be engaged to care for a patient in permanent need of a respiratory device. Three of them should be nurses, whether the patient lives at home or in an institution.

Phrenic nerve stimulation for treatment of central respiratory insufficiency is achieved by means of implanted nerve stimulators. Successful ventilation has been reported in about one hundred published cases of high tetraplegia. Total independence from mechanical ventilators, i.e. full-time stimulation, has been achieved with different rates of success (Table I). When full-time electroventilated, a patient with high tetraplegia achieves the nursing level of a patient with low tetraplegia, i.e., with his own diaphragmatic ventilation. Full-time electroventilation thus could be the key for early effective rehabilitation.

However, before full-time electroventilation is possible, the hypotrophic diaphragm has to be trained to produce a sufficient tidal volume. The diaphragm also has to be changed by electrostimulation into a fatigue-resistant muscle. With unipolar diaphragm pacers, this change (or conditioning) (3) takes 3 to 6 months in adults with uncomplicated high tetraplegia (8). In children, even longer conditioning phases are needed (6).

To delay muscle fatigue during electroventilation, we developed our bipolar phrenic nerve stimulation system (19) into a sequential four-pole (SFP) system (20). Discussion during a symposium on phrenic nerve stimulation (1) also revealed the possibility to shorten the conditioning phase by use of SFP stimulation (15, 16).

Neurophysiologic and technical background

Electroventilation by phrenic nerve stimulation is possible only with an intact peripheral nerve and muscle. Muscle hypotrophy is not a contraindication. However, it is a factor which increases the duration of the conditioning phase because of the time needed to retrain the muscle.

Human skeletal muscles contain slow twitch fatigue-resistant (SR) and fast twitch fatiguable (FF) muscle fibres of different compositions (18). The fibres of one motor unit, i.e. the fibres controlled by one axon, contain fibres of one type. It is possible to change all fibres of a muscle into SR-fibres by continuous electrical stimulation at low frequencies

Table I. *Results from several groups with phrenic nerve stimulation in patients with high (C2) tetraplegia after conditioning had been completed*

More than one hundred cases have been published. However, only 88 cases are included because in several publications data which are presented here are not given or are mixed with those of other patients

Phrenic nerve stimulation (no. of patients)								
Hours per day								
24 h	>12 h	<12 h	Failed[a]	Not needed[b]	Pt. lost[c]	Pts total	Source	Reference
13	10	14				37	Glenn et al.	1976 (7)
5						5	Glenn et al.	1984 (9)
7	3		1			11	Carter et al.	1987 (2)
5	2		3			10	Fodstad	1987 (5)
3						3	Garrido et al.	1987 (6)
		1				1	Ilbawi et al.	1985 (10)
2	3		1	2		8	Oakes et al.	1980 (11)
7					1	8	Vanderlinden et al.	1988 (22)
4	1					5	This presentation	
46 (53%)	19 (22%)	15 (16%)	5 (6%)	2 (2%)	1 (1%)	88 (100%)		

[a] Failure, disliked.
[b] Regained diaphragm function.
[c] Patient lost from follow-up.

(5–10 Hz) (15, 16). Fatigue of a muscle is delayed when low stimulation frequencies are used (3).

For long-term electroventilation of C_2 tetraplegic patients fatigue resistance of the diaphragm is more important than its ability to quickly produce large tidal volumes. To increase fatigue resistance of the diaphragm, all muscle fibres should be transformed into SR-fibres (9). This is best achieved by continuous stimulation at frequencies below 5 Hz (14). Such low frequencies would cause disturbing vibrations. When stimulation frequency is increased, vibrations disappear at a certain frequency, the fusion frequency, which is specific for each muscle (18). The fusion frequency of the human diaphragm is between 30 and 50 Hz (3). However, a slow decrease of the stimulation frequency over 3–6 months also causes the fusion frequency to decrease. At the end point fusion frequencies as low as 7 Hz may be achieved. For clinical purposes a compromise regimen of stimulation has to be used (9). Since continuous stimulation of a hypotrophic muscle even at low frequencies will soon cause fatigue, permanent damage may occur (13, 17) and no muscle growth can be demonstrated.

During natural contractions, only a minor part of all muscle units is in use at a time. Activation of motor units changes during each contraction in a randomized fashion. This part-time use of motor units during contraction provides rest for recovery of contractability even during labour (18).

Sequential four-pole stimulation (SFP) mimics the natural activation of skeletal muscle and thus helps to delay the onset of fatigue (20). Four electrodes are positioned around the nerve. With the four electrodes it is possible to create four stimulation compartments, which can be adjusted to avoid overlap (21). These compartments are stimulated in a sequential manner during each muscle contraction. The muscle contracts smoothly at fusion frequency, but the individual compartments are stimulated at a frequency which is one fourth of the fusion frequency (20).

METHODS AND PROCEDURES

On the basis of these considerations we developed the following regimen for the conditioning phase in adult patients with high tetraplegia but a well preserved peripheral nerve. The time elapsing between injury and implantation may be up to twelve months. After implantation of the phrenic nerve stimulation system ten to fourteen days are needed for wound healing (9). During the first stimulation period appropriate threshold and tidal volume currents are set up for the four electrode combinations (20). Then, the stimulator is used for ventilation at the lower threshold of the fusion frequency. Electroventilation continues until carbon dioxide retention is detected, which is a sign of muscle fatigue. This will take 20

Table II. *Development of conditioning regimen for hypotrophic diaphragm muscle in patients with high (C2) tetraplegia*

Bip.: bipolar electrode; 4-p.: quadripolar electrode; ms: milliseconds; cont.: continuous; Pulse interval: time between stimulus pulses; for convenience the reciprocal, stimulation frequency is also given. Conditioning periods, second and last third: resting time between the continuous periods was one hour

Patient	1	2	3	4	5	6
Sex	M	M	F	M	F	M
Age at implantation (years)	32	17	39	28	55	39
Interval since trauma (months)	3/5	4	48	11	4	5
Year of implantation	1980	1982	1984	1987	1987	1988
Implantation site	neck	neck	neck	thorax	thorax	thorax
Electrode type	bip.	bip.	bip.	4-p.	4-p.	4-p.
Respiratory rate (/min)	17	12–15	10–14	10–13	9–10	12–17
Pulse interval (ms)	37	40–50	40–50			
Combination interval (ms)				120–200	160–200	120–200
Interpulse interval (ms)				30–50	40–50	30–50
Motor unit stimulation frequency (Hz)	27	25–20	25–20	8.3–5	6.25–5	8.3–5
Muscle stimulation frequency (Hz)	27	25–20	25–20	33.3–20	25–20	33.3–20
Conditioning periods at beginning of						
First third						
min/h	5–45	2–15	2–60	10–30	10–20	5–20
h/24 h	0.7–6	0.5–3	0.5–7	2–6	1.5–3.5	1–2.3
Second third						
cont. min	45–180	15–70	60–180	30–120	20–60	20–60
h/24 h	6–10	3–10.5	7–10	6–7	3.5–8	2.3–3.7
Last third						
cont. h	2.5–6	1–4	2.5–14	2	1–2	1–3
h/24 h	10	10.5–24	10–23	7–10	8–24	3.7–24
of conditioning phase						
Stimulation h/day after conditioning	10	24	23–24	2–10	24	24
Duration of conditioning (months)	>3	3	3	4	2	1.5

to 40 min. The conditioning regimen can now begin with about 2/3 of the time which had elapsed up to beginning carbon dioxide retention, the "tolerable stimulation time". The patient is stimulated for this length of time every hour preferably 24 hours a day (14). In clinical practice 12 to 16 hours per day could be achieved. After one week or a shorter period another analysis is carried out to determine at which duration of stimulation fatigue occurs. A regimen with the new tolerable time is instituted for the next period. The programme continues in this manner until full-time stimulation during 12 hours of day-time is achieved.

After a pause of two hours in the evening, full-time stimulation is begun during the night and continued during the following morning. The time of stimulation is extended one hour each day with earlier start of stimulation in the evening. The patient should be watched carefully for any signs of fatigue. If in doubt, blood gas analysis or capnography should be used.

RESULTS

The new conditioning regimen was tested in two patients (Table I, cases 5 and 6). In both patients due to misunderstanding or to shortage of personnel, an ideal regimen could not be performed. The physicians in charge of the first patient did not really believe in the efficacy of sequential motor nerve stimulation, and they kept her on the ventilator part-time at a stage when full-time electroventilation might have been possible. During the conditioning phase in the second patient (case 6), the regimen could for several days not be changed as planned, due to interim shortage of nursing personnel. Otherwise the conditioning might have been performed in less than 6 weeks.

DISCUSSION

Electroventilation by means of implanted phrenic nerve stimulators has been used for more than 20 years (8). During the first period, fusion frequencies were used for stimulation. Conditioning was performed on an empirical basis and took 3 months. To avoid fatigue during long-term stimulation alternative stimulation of both sides of the diaphragm was used (7). With this regimen, one third of the patients achieved full-time long-term independence from mechanical ventilators (Table I).

Results of animal studies (3, 12, 14, 15) caused the development of a different conditioning regimen (9). After slowly lowering the fusion frequency over months, transformation of FF fibres into SR fibres, and thus development of fatigue resistance, is achieved at frequencies below 10 Hz (9, 16). The conditioning time takes 3 to 6 months (8). For results see Table I.

When the phrenic nerve is stimulated at fusion frequency with SFP stimulation, the four compartments of the nerve are stimulated at one fourth of that frequency. The frequency of a single compartment induces the transformation of FF-muscle fibres into SR-fibres already from the beginning of the conditioning period and onwards (see: Motor unit- and muscle stimulation frequency in Table II, cases 5 and 6).

The results from our last two patients show that, as predicted (14), the conditioning period in patients with high tetraplegia can be significantly shortened when SFP is used. It should be possible to achieve independence from a mechanical ventilator, and thus access to a spinal cord injury rehabilitation centre, within two months after implantation. In countries with special spinal cord injury centres, which provide full care from the day of injury, SFP could lessen the work load on the personnel.

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