Clinical assessment of diaphragm strength by cervical magnetic stimulation of the phrenic nerves

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Abstract

Background **– Accurate assessment of diaphragm strength can be difficult. Transdiaphragmatic pressure (PDI) measurements during volitional manoeuvres are useful but it may be difficult to ensure maximum patient effort. Magnetic stimulation of the phrenic nerves is easy to perform and the results are reproducible in normal subjects. The purpose of the present study was to evaluate the usefulness of magnetic stimulation of the phrenic nerves in the assessment of diaphragm weakness in patients.**

Methods **– Sixty six patients referred for assessment of respiratory muscle strength and 23 normal subjects were studied. Twitch PDI (TwPDI) following magnetic stimulation of the phrenic nerves and sniffPDI were obtained in all individuals. TwPDI following bilateral electrical stimulation of the phrenic nerves was also obtained in eight patients.**

Results **– Mean (SD) TwPdi for the normal subjects was 31 (6) cm H_2O and 18 (11) cm H_2O for the patients. TwPDI and sniffPDI were correlated ($r=0.77$). Seven of the 37 patients (19%) with a reduced sniffPDI had a TwPDI within the normal range whereas two of the 32 patients (6%) with a reduced TwPDI had a normal sniffPDI. TwPDI was similar with magnetic and electrical stimulation.**

Conclusions **– TwPDI following magnetic stimulation of the phrenic nerves is a clinically useful measurement when assessing diaphragm weakness.**

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Keywords: diaphragm strength, magnetic stimulation, phrenic nerves.

The diaphragm is the main inspiratory muscle[1] and it is important to be able to assess accurately diaphragm weakness. Patients with bilateral diaphragm paralysis or severe weakness present a striking clinical picture with orthopnoea as the major symptom. Lesser degrees of diaphragm weakness, however, are hard to detect and need specific testing. Vital capacity may be reduced, but this is a non-specific and relatively insensitive measure and diaphragm weakness has to be moderately severe before there is a substantial reduction.[2,3] Similarly, investigation using imaging techniques is not an adequate method for quantifying diaphragm strength.

Sniff transdiaphragmatic pressure (sniffPDI) is a useful measure of diaphragm strength.[3,4] However, the validity of sniff testing depends on the subject making a maximal effort and it is increasingly recognised that submaximal activation is common during volitional muscle testing.[5] Submaximal efforts are most likely to occur in patients who are ill or breathless. Nonvolitional testing by PDI measurement during bilateral electrical stimulation of the phrenic nerves overcomes this problem and can be useful. However, it may prove impossible to locate the phrenic nerves in some patients and it is sometimes difficult to maintain adequate simultaneous stimulation of both nerves. Repeated measurements may therefore be required to be sure that stimulation has been maximal. The technique can be uncomfortable, and if subjects are not relaxed twitch transdiaphragmatic pressure (TwPDI) can be misleadingly increased by muscle potentiation.[6]

Since it is less painful, cervical magnetic stimulation overcomes some of these difficulties and TwPDI is reproducible in normal subjects.[7,8] However, magnetic stimulation is different from electrical stimulation in that it activates some of the muscles that act on the upper thorax.[8] It is not clear whether this is an important problem when assessing patients. However since, like normal inspiration, cervical magnetic stimulation causes stabilisation of the upper thorax preventing the indrawing of the upper chest wall, it could be argued that it is no less physiological than electrical stimulation.

The purpose of the present study was to evaluate the clinical usefulness of cervical magnetic stimulation of the phrenic nerves when assessing diaphragm weakness in patients.

Methods

SUBJECTS

Twenty three normal subjects (five women) aged 20–54 years and 66 patients of mean age 48 (range 20–75) years referred for routine assessment of respiratory muscle function were studied. The protocol was approved by the hospital ethics committee and all subjects gave their informed consent.

PROCEDURES

Oesophageal and gastric pressures were recorded from latex balloon catheters (PK Morgan Rainham, Kent, UK) positioned and tested in the standard manner.[9,10] Pressures were

Table 1 General and clinical characteristics of the patients and normal subjects

Diagnosis/sympton	Total	Sex M	Sex F	Age (years)	Height (cm) Male	Height (cm) Female
Bilateral diaphragm paralysis	3	2	1	55 (42–72)	174 (172–177)	163
Diaphragm and phrenic nerve injury	4	4	0	39 (22–53)	176 (170–181)	
Dyspnoea of unknown origin	16	12	4	50 (23–72)	171 (157–191)	168 (158–175)
Hemidiaphragm paralysis	6	6	0	54 (34–75)	177 (170–193)	
Kyphoscoliosis	3	1	2	45 (43–46)	165	151 (147–156)
Motor neurone disease	3	2	1	47 (21–72)	171 (168–173)	165
Myopathy	5	3	2	45 (32–58)	178 (170–184)	168 (160–176)
Neuralgic amyotrophy	5	5	0	47 (42–57)	176 (172–184)	
Systemic lupus erythematosis	4	0	4	41 (37–43)		156 (150–163)
Miscellaneous	17	12	5	49 (23–68)	181 (173–193)	160 (152–175)
Normal subjects	23	18	5	33 (20–54)	179 (172–196)	168 (161–173)

Values are mean (range).

measured by Validyne MP45-1 differential pressure transducers, range ± 150 cm H_2O, and amplified by carrier amplifiers (Validyne Co, Northridge, California, USA). These were calibrated before each study with a Universal Pressure Meter (BIO-TEK Instruments Inc., USA) which was regularly tested for accuracy with a water manometer.[11] All signals were passed into a 12-bit NB-MIO-16 analog-digital board and a Macintosh Centris 650 computer (Apple Computer Inc, Cupertino, California, USA) running LabVIEW software (National Instruments, Austin, Texas, USA). All signals were sampled at 100 Hz. Transdiaphragmatic pressure (PDI) was obtained by digital subtraction of oesophageal from gastric pressure using PDI at resting end-expiration as the reference point.

Magnetic stimulation was performed using a Magstim 200 (HP) (Magstim Co. Ltd, Whitland, Dyfed, UK) with a circular 90 mm coil.[7 8 12] To find the optimal site for magnetic stimulation of the phrenic nerve roots in both normal subjects and patients the neck was flexed and the coil was placed over the spinous process of C7. The coil was then moved up and down the cervical spine in the midline until the maximum response was obtained at 80% power output. Having found and marked the optimal site for stimulation, the subjects rested for 20 minutes to avoid twitch potentiation.[6] TwPDI was then measured at 100% Magstim output as the mean of five twitches performed at least 30 seconds apart.

In eight patients TwPDI was also measured following bilateral supramaximal electrical stimulation. The phrenic nerves were stimulated percutaneously at the posterior border of the sternomastoid muscle at the level of the cricoid cartilage.[13] Two pairs of bipolar electrodes (Medelec Ltd, Old Woking, Surrey, UK) with saline soaked felt tips were connected to a constant voltage stimulator (Digitimer type 3072) and a gated pulse generator (Digitimer type 2521, Welwyn Garden City, Herts, UK) which produced square wave impulses of 100 ms duration. The stimulation intensity was increased until supramaximal stimulation, as judged by surface electromyography and PDI, was achieved.

In all subjects maximal sniffs were performed after the magnetic or electrical stimulation to avoid twitch potentiation. Subjects were allowed to sniff at will and were given visual feedback of sniffPDI on the computer monitor. Usually 10 sniffs were obtained. SniffPDI was taken as the largest PDI.[4]

All sniffs and twitches were performed at relaxed functional residual capacity (FRC) as judged by oesophageal and transdiaphragmatic pressure traces immediately prior to the manoeuvre.

Since sniffs are a volitional test the largest sniff for each subject was accepted for analysis, whereas for twitches the mean of all acceptable twitches was used. Correlations between TwPDI and sniffPDI were sought using simple regression analysis. The lower limit of normal for both TwPDI and sniffPDI was defined as two standard deviations less than the mean observed in normal subjects.

Results

The general characteristics of all subjects and clinical diagnoses of the patients are given in table 1. Mean (SD) TwPDI following magnetic stimulation of the phrenic nerves was 31 (6) cm H_2O (range 18–45) for the normal subjects and 18 (11) cm H_2O (range 0–37) for the patients. Mean (SD) sniffPDI was 132 (22) cm H_2O (range 95–160) for the normal subjects and 73 (38) cm H_2O (range 8–169) for the patients. The relationship between TwPDI and sniffPDI in normal subjects and patients is shown in fig 1 ($r=0.77$).

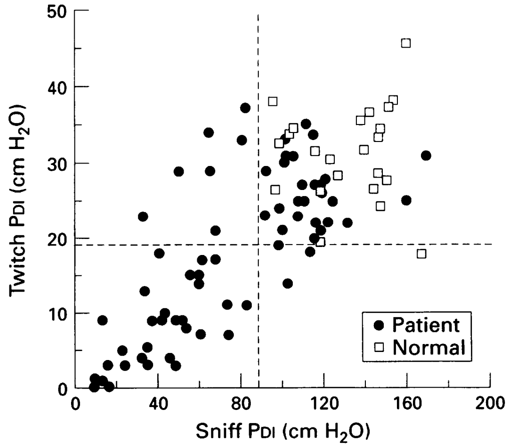

Figure 1 Relationship between transdiaphragmatic pressures obtained following magnetic stimulation of the phrenic nerves (twitch PDI) and during the sniff manoeuvre (sniff PDI) in 66 patients and 23 normal subjects (r=0.77). The dashed lines indicate -2 SD from the mean value of the normal subjects.

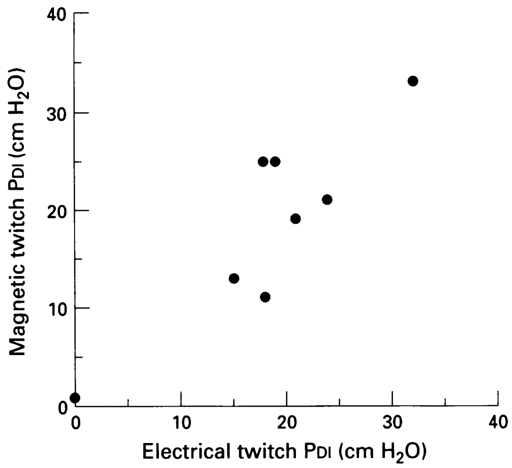

Figure 2 Comparison between magnetic and electrical twitch PDI in eight patients.

For purposes of comparison we took the lower limit of normal to be two standard deviations below the mean in the 23 normal subjects. This yielded values of 88 cm H_2O for sniffPDI and 19 cm H_2O for TwPDI. Using these criteria seven patients had a low sniffPDI but a normal TwPDI (this was 19% of those with a low sniffPDI and 11% of the total) whereas two patients had a low TwPDI and a normal sniffPDI (6% of those with a low TwPDI and 3% of the total).

Mean (SD) TwPDI following bilateral electrical stimulation of the phrenic nerves in eight patients was 18 (9) cm H_2O and following magnetic stimulation was 19 (10) cm H_2O. The relationship between TwPDI following electrical stimulation and magnetic stimulation in these eight patients is shown in fig 2.

Discussion

The main finding of the present study is that TwPDI produced by cervical magnetic stimulation is sufficiently practical to permit study of diaphragm strength in unselected patients with suspected respiratory muscle weakness. The results obtained closely correlated with established tests of diaphragm strength – namely, the sniffPDI and PDI by electrical stimulation. Before enlarging on these findings some methodological issues will be addressed.

Twitch potentiation is a potential problem during assessment of diaphragm strength irrespective of the method of stimulation.[6 14] After a maximal voluntary contraction of the diaphragm the TwPDI at FRC can increase by 70%.[6] To ensure that potentiation is avoided, subjects should rest, breathing quietly for 10–20 minutes before testing.[6] This problem is harder to avoid with electrical stimulation because repeated stimulations are often required to find the optimum electrode position. Twitch potentiation may have misleadingly increased the TwPDI obtained in the eight patients submitted to electrical stimulation. This could explain why the TwPDI obtained with electrical stimulation was the same as that obtained with cervical magnetic stimulation, unlike trained normal subjects in which the TwPDI obtained with cervical magnetic stimulation is usually slightly bigger.[8]

The effect of lung volume on TwPDI also needs to be considered. TwPDI changes by approximately 5 cm H_2O per litre acute change in lung volume[15] and preliminary data suggest that patients with chronic hyperinflation also have a reduced TwPDI when assessed by cervical magnetic stimulation.[16] Lung volume was not measured directly in the present study but all stimulations were undertaken at FRC as judged by the oesophageal and transdiaphragmatic pressure tracings during tidal breaths. Only TwPDI responses obtained at FRC were accepted for analysis. Clearly, if cervical magnetic stimulation were to be used for repeated measurements in the same patient, it would be important to ensure that the FRC was the same on each occasion.

A further potential drawback of magnetic stimulation is the activation of other muscles acting on the upper rib cage which may cause a somewhat higher magnetic than electrical TwPDI.[8] In patients with bilateral diaphragm paralysis (as judged by sniffPDI and electrically stimulated TwPDI) cervical magnetic stimulation does not cause a negative oesophageal pressure, suggesting that the mechanism whereby magnetic stimulation produces a greater PDI is largely stiffening of the upper rib cage.[17] In practice, a good correlation was found between TwPDI and sniffPDI, suggesting that activation of the muscles of the upper thorax does not detract to any extent from the value of cervical magnetic stimulation in the clinical assessment of diaphragm strength.

In most patients, as expected, we observed a good correlation between cervical magnetic stimulation and sniffPDI. However, 19% (seven of 37 patients) with reduced sniffPDI proved to have normal diaphragm strength when assessed by magnetic stimulation, suggesting that they may have made a submaximal effort during the sniff. Use of cervical magnetic stimulation in these patients enabled diaphragm weakness to be excluded, thus avoiding both anxiety and further investigation.

Equally, two patients (6% of those with a low TwPDI) who had a mild weakness when judged by TwPDI had normal sniffPDI. This was possibly due to submaximal magnetic stimulation of the phrenic nerves. Submaximal stimulation can occur if the coil cannot be placed close enough to the phrenic nerves. One of the two patients had ankylosing spondylitis and could not flex her neck, preventing satisfactory contact of the magnetic coil. The second patient had systemic lupus erythematosus and had received high doses of steroids causing marked adiposity around the neck. In cushingoid patients we have previously observed that a "buffalo hump" can lead to submaximal phrenic nerve stimulation.[18] However, it should be noted that electrical stimulation is also technically difficult if the neck is obese; indeed, the phrenic nerves may be impossible to locate.

In normal subjects supramaximal stimulation has been demonstrated[7 8] but the plateau of the PDI response as the magnetic output increases occurs close to maximum stimulator output.

Thus, in most normal subjects and patients supramaximal stimulation is only just achieved. Great care should therefore be taken to find the optimal position for the magnetic coil on the neck, and to flex the neck to obtain maximal contact. Failure to achieve this may result in stimulation that is significantly submaximal with consequently low TwPDI values. For these reasons we do not routinely measure diaphragm electromyographic changes. Instead we prefer simply to use the stimulator at 100% of maximum output and take care to optimise the position. This problem may be overcome in the future by the use of simultaneous bilateral/unilateral phrenic nerve stimulation[19] or a single cervical magnet with more power.

Our evaluation of cervical magnetic stimulation in clinical practice suggests that TwPDI invoked by this method is a valid measure of diaphragm strength which is acceptable to patients. The major advantage of magnetic stimulation is that the test is independent of patient aptitude and motivation. Because patients find it so acceptable it may be a useful technique for evaluating strategies aimed at altering muscle strength – for example, inspiratory muscle training.

In conclusion, magnetic stimulation of the phrenic nerves appears to be a clinically useful method for the detection of diaphragm weakness. It is a non-volitional and relatively easy test which has the potential to become a widely adopted method for the assessment of diaphragm strength.

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