Inspiratory muscle relaxation rate assessed from sniff nasal pressure

D Kyroussis, G Mills, C H Hamnegard, S Wragg, J Road, M Green, J Moxham

Abstract

Background – Slowing of the maximum relaxation rate (MRR) of inspiratory muscles measured from oesophageal pressure (POES) during sniffs has been used as an index of the onset and recovery of respiratory muscle fatigue. The purpose of this study was to measure MRR at the nose (PNASAL MRR), to investigate its relationship with POES MRR, and to establish whether PNASAL MRR slows with respiratory loading.

Methods – Five normal subjects were studied. Each performed sniffs before and after two minutes of maximal isocapnic ventilation (MIV). In a separate session the subjects performed submaximal sniffs. POES, PNASAL were recorded during sniffs and the MRR (% pressure fall/10 ms) for each sniff was determined.

Results – Before MIV mean POES MRR was 8.9 and PNASAL MRR was 9.3. The mean (SD) difference between PNASAL MRR and POES MRR during a maximal sniff was 0.48 (0.34) (n = 64) and for submaximal sniffs was 0.28 (0.46) (n = 526). The subjects showed a mean decrease in sniff POES MRR of 27.4% (range 22.5–36% ) after MIV and a similar reduction in sniff PNASAL MRR of 28.5% (range 24.1–41.3%). Both returned to control values within 5–10 minutes.

Conclusions – PNASAL MRR reflects POES MRR over a wide range of sniff pressures, PNASAL MRR of maximal sniffs reflects POES MRR in normal subjects at rest and following MIV, so measurement of PNASAL MRR may be a useful non-invasive method for measuring inspiratory muscle MRR, thereby providing an index of respiratory muscle fatigue.

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We measured MRR from pressures sampled at the nose (PNASAL MRR) during sniffs which varied in peak pressure, between 10% and 100% of each subject's maximum sniff POES, to investigate the agreement of the two methods over a wide range of sniff pressures. We also measured PNASAL MRR during maximal sniffs, before and after maximal isocapnic ventilation (MIV), to investigate its relationship with maximum sniff POES MRR and to establish whether PNASAL MRR slows with respiratory muscle loading.

Methods

Five well trained members of our laboratory were recruited. All were non-smokers and without respiratory disease. The study was approved by the ethics committee of the Royal Brompton Hospital and all subjects gave informed consent.

Oesophageal pressure (POES) was measured using commercially available balloon-tipped catheters, 11 cm in length (PK Morgan, Rainham, Kent, UK), positioned in the standard manner. Nasal pressure (PNASAL) was measured using polyethylene catheters without distal balloons passed through a nasal cast (see below). Both catheters were connected to Validyne MP45-1 differential pressure transducers (range ± 200 cm H₂O; Validyne Corporation, Northridge, California, USA) calibrated before each study using a Universal Pressure Meter (Bio-Tek Instruments Inc, USA) which was regularly tested for accuracy with a water manometer. All signals were displayed on a 12-bit NB-M10-16 analogue digital board and a Macintosh Quadra 700 computer (Apple Computer Inc, Cupertino, California, USA) running LabVIEW software (National Instruments, Austin, Texas, USA).

We investigated whether the individual pressure transducer-amplifier systems could introduce errors into our results by linking the pressure inputs of the two catheter-transducer-amplifier systems that were used for measuring pressures sampled in the oesophagus and the nose. We were then able to record simultaneously the same pressure signals during sniffs via the two systems and compare the data. Pressure amplitude, MRR, and non-normalised MRR were measured (see below for definitions). The mean (SD) ratio of the values derived from the two transducer-amplifier systems for pressure amplitude, MRR, and non-normalised MRR were: 1.007 (0.009), 0.992 (0.036), 0.998 (0.030), respectively (n = 26).

Maximal isocapnic ventilation (MIV) was performed with apparatus previously de-
ventilation. Immediately upon stopping the MIV run maximal sniffs were performed from FRC every five seconds for five minutes and a further 10 sniffs were performed at 10 minutes. End expiration POES was marked on the computer screen to help the subjects perform sniffs from FRC.

MRR was calculated as the maximal rate of decay of pressure/peak pressure, and had units of % pressure loss/10 ms. This normalisation of MRR for changes in pressure amplitude allows the comparison of MRR values of different peak pressure. In this study we were particularly interested in the comparison of PNASAL and POES MRR calculated from traces obtained from the same sniff. We therefore also looked at MRR values which had not been normalised for sniff amplitude (MRR nC). MRR nC was defined as the maximal rate of pressure decay/10 ms (dP/dt) and had units of cm H2O/10 ms. MRR was obtained from POES and PNASAL sniffs that satisfied the following criteria: (1) sniff performed from FRC as judged by baseline POES before the sniff; (2) peak pressure maintained for less than 50 ms; (3) total sniff duration less than 500 ms; and (4) pressure waveform of sniff displaying smooth upstroke and decay curves. By these criteria 86-5% of sniffs were suitable for analysis from the MIV study and 89-2% of sniffs were suitable for analysis from the study of sniffs of increasing pressure amplitude. Within-day reproducibility was assessed by three subjects repeating 10 maximal sniffs three times. Each session was separated by an interval of 30 minutes. Day-to-day reproducibility was assessed by repeating 10 maximal sniffs in three subjects on three separate days.

**STATISTICAL ANALYSIS**

In order to assess the agreement between PNASAL and POES MRR we calculated their differences for each sniff. The mean of these differences (d) is a measure of accuracy or bias whilst the standard deviation (SD) is a measure of precision. Both bias and precision are necessary to assess agreement. The limits between which 95% of differences will lie (“limits of agreement”, d ± 2SD) were calculated, and the ratio of PNASAL to POES MRR was also calculated to compare the values of the two methods over the range of MRR observed. Data were presented by plotting the results of one method against those of the other (line of equality graph) and by plotting the differences between the methods against their mean. The day-to-day and within-day coefficients of variation of the ratio PNASAL/POES MRR were calculated to establish whether variations of Pots MRR values are followed by a similar variation of PNASAL MRR.

**Results**

**SNIFFS OF INCREASING EFFORT**

MRR differences (nasal MRR—POES MRR), normalised and non-normalised, for each 10%
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Table 1

<table>
<thead>
<tr>
<th>% max P</th>
<th>PNASAL MRR - POES MRR</th>
<th>PNASAL MRR/POES MRR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MRR</td>
<td>MRR nC</td>
</tr>
<tr>
<td>10-20</td>
<td>0.30(0.82)</td>
<td>-0.04(0.12)</td>
</tr>
<tr>
<td>21-30</td>
<td>0.14(0.61)</td>
<td>0.00(0.15)</td>
</tr>
<tr>
<td>31-40</td>
<td>0.27(0.54)</td>
<td>0.02(0.19)</td>
</tr>
<tr>
<td>41-50</td>
<td>0.25(0.47)</td>
<td>0.03(0.26)</td>
</tr>
<tr>
<td>51-60</td>
<td>0.21(0.33)</td>
<td>-0.05(0.32)</td>
</tr>
<tr>
<td>61-70</td>
<td>0.29(0.40)</td>
<td>-0.08(0.63)</td>
</tr>
<tr>
<td>71-80</td>
<td>0.30(0.37)</td>
<td>-0.10(0.61)</td>
</tr>
<tr>
<td>81-90</td>
<td>0.37(0.27)</td>
<td>0.03(0.45)</td>
</tr>
<tr>
<td>91-100</td>
<td>0.40(0.28)</td>
<td>0.21(0.42)</td>
</tr>
<tr>
<td>All data</td>
<td>0.29(0.46)</td>
<td>0.00(0.42)</td>
</tr>
</tbody>
</table>

MRR = maximum relaxation rate (% pressure drop/10 ms); MRR nC = non-normalised MRR (cm H₂O/10 ms); % max P = percentage of peak pressure of maximum sniffs; PNASAL = nasal pressure; POES = oesophageal pressure (cm H₂O); n/C = PNASAL/POES.

Figure 2

PNASAL MRR plotted against POES MRR. Data from the study of sniffs of increasing effort. The line of identity is also shown.

The ratios of PNASAL MRR/POES MRR for each 10% increment are also shown. Figure 2 shows PNASAL MRR plotted against POES MRR and fig 3 shows the same parameters non-normalised for pressure amplitude.

BASELINE SNIFFS

Table 2 shows the mean (SD) data before the MIV run: PNASAL and POES MRR, their mean (SD) differences, the 95% limits of agreement, and the ratio PNASAL/POES MRR. The same calculations were also performed for non-normalised (nC) nasal and oesophageal MRR and for sniff peak pressure amplitudes (PNASAL, POES). Sniff PNASAL MRR and POES MRR were closely related. A close relationship was also shown between nasal and oesophageal peak pressures. Within-day coefficient of variation for the ratio PNASAL/POES MRR assessed in three subjects for three study sessions was 2.9%. The day-to-day coefficient of variation assessed in three subjects on three different days was 3.3%.

MAXIMUM ISOCAPNIC VENTILATION (MIV) STUDY

Figure 4 shows pressure traces obtained in the oesophagus and at the nose before, immediately after, and 10 minutes after MIV. The slopes of oesophageal and nasal pressure decay curves are similar. Immediately after muscle loading the slope changed in both traces and recovered 10 minutes after the MIV run. The subjects showed a mean decrease in sniff POES MRR of 27.4% (range 22.5–36%) the first minute after MIV, which returned to control values within 5–10 minutes. A similar reduction and time course of recovery was observed for sniff PNASAL MRR, with a mean fall of 28.6% (range 24.1–41.3%) (fig 5). PNASAL MRR and POES MRR expressed as % of baseline values during each minute after MIV, and PNASAL and POES expressed as % of baseline values over the same time period are shown in table 3. Table 4 shows

Table 2

<table>
<thead>
<tr>
<th>% P</th>
<th>MRR (cm H₂O/10 ms)</th>
<th>n/C MRR (cm H₂O/10 ms)</th>
<th>Limits of agreement</th>
<th>Limits of agreement</th>
<th>Limits of agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.30(0.131)</td>
<td>8.50(0.21)</td>
<td>0.48(0.34)</td>
<td>1.15 to −0.19</td>
<td>0.95(0.136)</td>
<td>0.60(0.24)</td>
</tr>
<tr>
<td>1.05(0.03)</td>
<td>0.05(0.05)</td>
<td>0.96(0.16)</td>
<td>9.80(0.148)</td>
<td>0.97(0.05)</td>
<td>−1.88(3.64)</td>
</tr>
</tbody>
</table>

MRR = maximum relaxation rate (% pressure drop/10 ms); MRR nC = non-normalised MRR (cm H₂O/10 ms); PNASAL = nasal pressure; POES = oesophageal pressure (cm H₂O).
MRR differences (PNASAL – POES MRR), normalised and non-normalised for pressure amplitude, for the control values, for each minute after MIV, and for all the data. The ratio of normalised MRR to non-normalised MRR is also shown. Figure 6 shows PNASAL MRR plotted against POES MRR. Figure 7 shows the mean MRR values of the two methods plotted against their differences. Values for figs 6 and 7 correspond to measurements before and after the MIV run.

Discussion

This study indicates good agreement between POES MRR and PNASAL MRR in normal subjects over the whole range of pressure amplitudes for sniffs performed with increasing effort. After inspiratory muscle loading POES MRR slowed and returned to control values within 5–10 minutes and a similar slowing and time course of recovery was found for PNASAL MRR.

In this study we assumed that inspiratory muscle relaxation rate could be detected from the decay curve of pressure generated by voluntary inspiratory manoeuvres and that the peak pressure of sniff coincides with the beginning of the muscle relaxation phase. Earlier studies using simultaneous inspiratory muscle EMG and pressure recordings during occluded and unoccluded sniffs showed that inspiratory muscle activity ceased at the peak pressure point and that the inspiratory muscles remained electrically silent during the decay portion of the pressure curve.

The similarity of pressures sampled in the upper airways and oesophagus during occluded inspiratory manoeuvres has been described in previous studies. When an inspiratory effort is performed against an occlusion there is no airflow and therefore no pressure gradient between lower and upper airways. Although the unoccluded sniff is a dynamic manoeuvre, bulk flow is relatively small. During a sniff a large transnasal pressure gradient is created. The nostrils behave as a starling resistor, collapsing as a result of negative nasal pressure. It is estimated that 10–12 cm H₂O transnasal pressure leads to nostril collapse in the region between the junction of the pyriform aperture and the upper and lower lateral cartilages, 2.5 cm from the external orifice. Flow therefore reaches a plateau very early during sniff and stays unchanged until almost the end of the pressure decay curve, despite inspiratory muscle activity ceasing at the peak pressure point. The flow limitation during a sniff manoeuvre explains the similarity of pressure traces obtained from the oesophagus and the occluded nostril and the high pleural pressures developed during a sniff.
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Table 4. Mean (SD) differences of MRR values, normalised and non-normalised (nC), derived from nasal and oesophageal sniff pressure traces before and after the MIV run. The ratios of the two methods for all data are also shown. Differences and ratios of the two methods for all data are shown at the bottom of the table.

<table>
<thead>
<tr>
<th>PNASAL MRR – POES MRR</th>
<th>PNASAL MRR/POES MRR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MRR</td>
</tr>
<tr>
<td>Baseline</td>
<td>0-48(0-34)</td>
</tr>
<tr>
<td>1 min</td>
<td>0-20(0-45)</td>
</tr>
<tr>
<td>2 min</td>
<td>0-23(0-31)</td>
</tr>
<tr>
<td>3 min</td>
<td>0-27(0-32)</td>
</tr>
<tr>
<td>4 min</td>
<td>0-29(0-41)</td>
</tr>
<tr>
<td>5 min</td>
<td>0-40(0-35)</td>
</tr>
<tr>
<td>10 min</td>
<td>0-65(0-33)</td>
</tr>
<tr>
<td>All data</td>
<td>0-38(0-38)</td>
</tr>
</tbody>
</table>

PNASAL = maximum inspiratory ventilation; MRR = maximum relaxation rate; (%) pressure drop/10 ms; MRR nC = non-normalised MRR (cm H2O/10 ms); PNASAL = nasal pressure; POES = oesophageal pressure (cm H2O).

Agreement between PNASAL and POES MRR depends on two factors: the peak pressure achieved by the two methods and the peak rate of pressure decay (dP/dt, non-normalised MRR) derived from PNASAL and POES traces. Although peak pressures were very similar in our study, the small differences of 2–3 cm H2O could explain some of the small differences in MRR. The agreement between non-normalised MRR for the two methods was therefore better than the agreement between normalised MRR, especially when pressure agreement was less than usual. A small difference was observed, usually due to the faster dP/dt of the nasal trace. This constant difference could not be explained by differences in the measurement apparatus. During a brief inspiratory manoeuvre pharyngeal muscles contract to preserve the patency of the upper airways.2021 The rate at which PNASAL declines could be influenced by upper airway muscle relaxation as well as relaxation of the inspiratory muscles. There are data to suggest that upper airway muscles have a higher percentage of fast twitch fibres than the diaphragm and other inspiratory muscles.2223 As a consequence they are likely to have different fatigue, potentiation, and relaxation characteristics.24 It is possible that the fast relaxation rate of the upper airway muscles explains the slightly faster rate of decline in PNASAL traces although other factors, including asynchronous muscle activity, may also play a part.25 Furthermore, the better agreement between PNASAL and POES MRR found after MIV could reflect the greater fatigability of the upper airway muscles,24 although we have no direct evidence to support this hypothesis.

Following MIV, in parallel with MRR slowing, a pressure decline was also observed. This pressure drop was relatively less than the fall in MRR, varied substantially between subjects, and tended to recover faster. These findings are in agreement with a previous study.26 Sniff pressure amplitude has an effect on MRR values.26 However, when sniff pressure exceeds 60% of maximum the effect of peak pressure on relaxation rate is minor.26 In the present study sniff peak pressures always exceeded 60% of maximum after MIV and the influence of sniff amplitude on the MRR was therefore negligible.

The change in lung volume, and consequently in muscle fibre length, observed during an unoccluded sniff could possibly influence MRR. In a recent study27 it was postulated that the small differences in MRR between occluded and unoccluded sniffs could be the result of differences in the degree of muscle shortening. However, other factors such as different patterns of muscle activation may play a part.27 We are confident that differences of lung volume change that occur during a sniff before and after MIV are of such small magnitude that they cannot explain the changes in relaxation rate after muscle loading. Flow during a sniff is not dependent on the peak pressure amplitude because of the flow limiting.
mechanism in the nose, and the difference in gas expansion before and after MIV is likely to be trivial. Indeed, the increased duration of the sniff after the MIV might have contributed to an increased volume change and possibly a small underestimation of the fall in MRR.

We measured PNASAL and POES MRR over a wide range of pressure amplitudes to investigate the agreement of the two measurements. Even in sniffs of very low effort when pressure amplitudes of 10 or 20 cm H₂O were created, MRR and pressure values were very closely related and showed a similar agreement to those found during maximal sniffs. This suggests that the starting resistor mechanism can function adequately at low pressures. Nasal collapse probably occurs at a lower transnasal gradient when only one nostril is open during an inspiratory manoeuvre.²⁶

MRR measurements from pressures sampled within the mouth and nasopharynx using balloon-tipped catheters have recently been reported.¹ However, measurements derived from a balloon-tipped catheter in the mouth may be affected by suction and the positioning of a balloon in the nasopharynx is relatively uncomfortable.

In some instances PNASAL was slightly greater than POES. In one subject the nasal trace was sometimes distorted during maximal sniffs showing prolonged peak pressures and fast MRR. Both observations are likely to be the result of vigorous upper airway and neck muscle recruitment and were not observed in sub-maximal sniffs.

Activation of the inspiratory muscles during the relaxation phase might falsely increase MRR in cases in which the rise of tension of inspiratory muscles exceeds the rate of decline in inspiratory muscles. However, activation of the expiratory muscles can be easily identified and the sniff rejected when POES becomes more positive than that at end expiratory pressure.²⁵ The inability to exclude the above phenomenon is a limitation of measuring MRR from nasal pressure traces. In normal subjects this rarely causes a problem but in patients with chronic obstructive pulmonary disease (COPD) recruitment of the abdominal muscles is common during expiration and activation of this muscle group during the sniff relaxation phase occurs more frequently.²⁵ Falsey high PNASAL MRR values might therefore be difficult to identify.

Previous studies have shown that the equilibrium of pressures measured in the oesophagus and the upper airways is a function of airway resistance and extrathoracic airway compliance (time constant for pressure equilibrium).²⁹⁻³¹ In patients with COPD pressures measured in the oesophagus and the upper airways show a poor level of agreement²⁵ and, as a consequence, upper airway pressure MRR will be falsely high. To avoid the error introduced by the pressure discrepancy non-normalised MRR (dp/dt) of the upper airway and the oesophagus could be compared. In this case a good agreement would be expected unless there is vigorous recruitment of upper airway and neck muscles as during maximum sniffs.²⁵ Our results show a good agreement between non-normalised PNASAL MRR and POES MRR in very low sniff efforts. It therefore seems reasonable to hypothesise that inspiratory manoeuvres that require little effort will minimally recruit these muscle groups, thus enhancing the agreement of the two parameters. Studies designed to confirm this hypothesis would be of clinical importance.

We conclude that PNASAL MRR obtained from a maximal sniff accurately reflects POES MRR. PNASAL MRR can be used as an index of the onset and recovery of respiratory muscle fatigue in normal subjects. The fact that an oesophageal balloon is not necessary makes the studies easy to perform. We also conclude that PNASAL MRR accurately reflects POES MRR over a wide range of sniff pressures created by graded effort. The similarity between nasal and oesophageal peak pressure decay (dp/dt) recorded during sniffs of low effort could make this a useful method for non-invasively measuring MRR in patients with COPD.

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23. Van Lunteren E, Salome RJ, Manubay P, Supinski GS,
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Adventitia

The case of the Queen’s head: a confession

As befits a building erected in the last century, the old Brompton Hospital was graced by a bust of Queen Victoria which stood on a plinth in an alcove in the main corridor. One night, three decades ago, the bust disappeared!

In the autumn of 1963 two young Brompton housemen were returning unsteadily to their rooms after enjoying a game of rugby and a convivial evening with their bibulous colleagues. The oriental combat sport of “kung fu” was in fashion at that time and, fired by an exuberance of spirit, one of the young friends jokingly aimed a blow at the Queen’s bust as he passed along the corridor. To his amazement, his glancing blow decapitated the Queen and her head fell to the ground!

The night porter in his office at the hospital door was sleeping, and no one seemed to have heard the commotion. The malefactors were faced with the evidence of their wrongdoing and the prospect of chastisement on the following day. The abrupt termination of promising careers was a sobering thought and, following a hurried consultation, they decided to hide the fruits of their folly. Acting with urgent common purpose, they carried the bust and the head past the sleeping porter and buried them in the flower bed at the side of the driveway to the main hospital entrance.

On the following day the Queen’s plinth stood glaringly empty in its alcove, but the absence of the bust went unnoticed and attracted no comment whatsoever. Five months later, with their crime undetected, the young men went their separate ways and both eventually achieved full professorial status in their chosen fields.

A decade after the heinous crime one of the perpetrators was passing through London on his way back to his new home on the other side of the world. In a fit of nostalgia and acting on impulse, he took a taxi to the Brompton Hospital, secretively exhumed the Queen’s head, and carried it away. For the past 20 years the Queen has reposed in a quiet garden in a faraway part of her former Empire. She seems happy in this environment and it is the repentant but necessarily anonymous author’s earnest hope that the Brompton Hospital governors will neither seek retribution nor insist upon her return. (The Statute of Limitations and the precedent of the Elgin marbles may be relevant.)
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