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CONFERENCE REPORT

Respiratory muscle fatigue

The International Meeting on Respiratory Muscle Fatigue was held in Florence (Italy) on March 8th–9th, 1990 with the sponsorship of 3rd Clinica Medica Institute (Florence University), Pro-Juventute Don Carlo Gnocchi Foundation (Florence) and S.E.P.C.R. Rehabilitation Working Group

G. Scano (Italy)

The aims of the meeting were to clarify the conditions and mechanisms involved in respiratory muscle fatigue and to critically assess relevant therapeutic strategies.

A. de Troyer (Belgium) reviewed the action and co-ordination of respiratory muscles. Rib cage and abdominal muscles function in parallel, during quiet breathing, to achieve uniform expansion. The dome of the diaphragm descends during inspiration by contraction of the vertical muscle fibres. This action helps the lower ribs to swing outwards and upwards.

In patients with cervical cord transection at C5, who breathe only with the diaphragm, the abdomen expands during tidal ventilation with the lower part of the rib cage. The upper part of the cage is sucked in. In the normal person, during normal tidal breathing there must be some action on the upper rib cage to prevent it from being drawn inwards. Electromyographic recordings demonstrate activity of the scalene muscles, which are not therefore solely accessory muscle.

Intercostal muscles are also important. There are three groups, the parasternals, the external intercostals and the levator costae. They are all active during tidal inspiration. In a series of dog experiments, involving selective section of the nerve supply to the three groups of muscles, the parasternals were determined to be by far the most important accounting for 80% of the movement of the upper rib cage. The muscles of tidal breathing are, therefore, the diaphragm, the scalenes and the parasternals, a view that many traditional physiologists might find surprising.

The amount of activity varies with body position. Parasternal inspiratory shortening is reduced in the upright standing position compared to the supine posture, but still plays a role in elevating the ribs despite the increased loading. The question of whether expiratory muscles contract during diaphragmatic tidal breathing was answered negatively.

M. Green (UK) reviewed respiratory muscle function and fatigue with an overall view that demonstrated the remarkable difficulty in proving the presence and extent of respiratory muscle fatigue in normal and pathological man. Symptoms and signs such as impaired cough, breathlessness, orthopnoea, repeated infection, weakness and wasting of intercostal muscles, paradoxical and chest wall movement are all highly nonspecific. Equally, vital capacity and other simple respiratory function tests such as lung volumes and carbon monoxide transfer coefficient (Kco) are nonspecific, although in certain circumstances vital capacity may be useful if the clinical situation and previous history are well known. Maximal inspiratory pressures (Pimax and maximal expiratory pressures are more specific but suffer the problem of a very wide range of normal values. Pimax can be as low as 30–50 cmH_2O when values are mostly >100 cmH_2O. Pressures of <80 cmH_2O in males, <60 cmH_2O in females, stand a high chance of being associated with respiratory muscle weakness. Other tests using gastric and oesophageal balloons measure transdiaphragmatic pressure (Pdi) and electrodes measure diaphragmatic electromyography (EMG). M. Green (UK) supported his use of the "Sniff test" for measuring diaphragmatic twitches as one of the best available measures of respiratory muscle function.

To evaluate nerve function, the phrenic nerve is stimulated percutaneously in the neck, and the transdiaphragmatic pressures measured. Conduction time of the phrenic nerve, also measured, is normally <10.5 ms from the stimulus artifact to the muscle action potential (MAP).

Respiratory muscle fatigue is more difficult to evaluate. The following techniques, not available for use in the clinical setting, are being studied: a) frequency-force curve of the diaphragm to measure low frequency fatigue (LFF) and high frequency fatigue (HFF); b) power spectrum electromyogram of the diaphragm or intercostal muscle to calculate the H/L ratio; and c) relaxation rate of a single diaphragmatic sniff or phrenic twitch particularly in Intensive Care Units. Low frequency stimulation is very unpleasant for both normal subjects and patients, and HFF is difficult to interpret in a clinical setting. The relationship between H/L ratio and LFF is still unclear. The tests are not easy to use and thus precise recognition and quantitation of fatigue changes remain elusive.

C. Roussos (Greece) discussed the physiology of respiratory muscle fatigue. Fatigue was described physiologically as a progressive disorder starting with normal 100% muscle performance, leading into phases of weakening muscle, and rapid terminal decline to exhaustion and cessation of function. Respiratory failure may be due to fatigue of central respiratory control mechanisms, or peripheral respiratory muscle fatigue which depends upon a balance between the energy demand for the work of breathing and the energy available through oxygen supply, blood flow and energy substrate. The balance of fatigue is markedly shifted by the lung volume at which the respiratory muscles are expected to function.

Increasing lung volume increases energy demands. Respiratory failure is either acute or chronic in onset. Acute failure passes through a stage of normal breathing to tachypnoea, than bradypnoea and finally output failure. In chronic respiratory failure, the process takes several years, with tachypnoea and low tidal volume being the most extended stages. The concept of respiratory muscle fatigue in chronic obstructive airways disease and chronic muscle disorders has been promoted by various authors. It gave rise to a number of studies which looked at external negative pressure ventilation as a means of achieving respiratory muscle rest. Indicators such as dyspnoea, maximal inspiratory and expiratory pressures, diaphragmatic EMG and Pdi were measured. The results were unconvincing in terms of both physiological and clinical benefit.

A. Grassino (Canada) discussed approaches to therapy involving a number of basic principles. Firstly, to deal with toxicity from such sources as sepsis, acidosis and heart failure. Ensure good nutrition and consider drugs such as theophyllines, β_2-agonsits, oxygen and digitalis to enhance muscle function. Studies by Aubier (France) and J Moxham (UK) using aminophylline produced conflicting results for respiratory muscle fatigue, probably because clinical conditions, patients, and techniques differed. The effect of aminophylline is not dramatic, but β_2-agonists are promising. They may improve respiratory muscle endurance and/or recovery time from fatigue. When the diaphragm is forced into strenuous activity, hypoxia or a combination of hypoxia and hypercapnia may impair contractile force. In his series of 300 chronic obstructive pulmonary disease (COPD) patients, an airways resistance maximal inspiratory pressure (Raw/MIP) ratio of 0.3–0.4 related to CO_2 retention. When chronic CO_2 retaining patients enter a state of acute respiratory failure, a decision has to be taken as to whether the respiratory muscles are overloaded and liable to failure or, whether ventilation/perfusion ($\dot{V}/Q$) mismatching is the major explanation of deteriorating blood gases. Both causes may be present and it is difficult to apportion responsibility. If respiratory muscles do not provide sufficient ventilation and there are strong suspicions of fatigue, they need to be rested. Respiratory muscle rest, although theoretically of value, remains a contentious issue. If a ventilator is used to support respiration suitable operating pressures are selected and the patient must not fight the system. High positive expiratory pressures shorten the diaphragm and reduce transdiaphragmatic pressures. The iron lung is a good means of treating comatose patients. Blood gases are corrected but excessive hyperventilation will create weaning problems. It may be necessary to control the treatment using EMG and Pdi measurements. Improving hypoxia and reducing hypercapnia are generally thought to be worthwhile.

For long-term prevention of respiratory muscle fatigue there are theoretical benefits in training the force and endurance of respiratory muscles and diaphragm but such suggestions are by no means of proven value.

S. Cibella (Italy) discussed the applicability of EMG spectral analysis to respiratory pathophysiology and the detection of respiratory muscle fatigue. Many indices, derived from EMG spectral analysis have been used to detect fatigue, but central frequency (cf) has the lowest coefficient of variability. Unfortunately, some experimental and biological variables time-elapsed from the beginning of the contraction and length of the EMG portion under analysis can determine changes in the EMG power spectrum and central frequency independently of fatigue. Variations in fibre length occur continuously in the diaphragm due to changes in lung inflation and abdominothoracic configuration. The influence of these variables on cf obtained from the diaphragmatic EMG demonstrates that abdominothoracic configuration has an important influence on cf at least at the lowest levels of lung inflation.

P. Howard (UK) discussed the use of external negative pressure ventilation (ENPV) particulary in patients with obstructive airways disease and respiratory failure. It is not clear from the literature what is to be expected of external negative pressure ventilation. There are two views, firstly to relieve respiratory muscle fatigue and secondly to improve blood gases. The two features were not necessarily associated. A review of the literature pointed to the remarkable difficulties of measuring respiratory muscle fatigue in COPD patients. Highly inconsistant results are obtained but probably the most widely used test is diaphragmatic EMG.

It is important to capture the ventilatory rhythm of patients whatever system of external negative pressure ventilation is selected, Poncho, pneumowrap or cuirass. In COPD, the pressures need to be negative of the order of 20–25 cmH_2O at a ventilatory rate one or two breaths per minute above the patient's resting frequency. No clear benefit to respiratory muscle fatigue or improvement of the sensation of dyspnoea has been observed. The large Montreal study, which attempted to relieve dyspnoea in severe bronchitics using ENPV, apparently produced negative results. The machines were found to be uncomfortable and intolerable beyond one or two hours of use.

As a means of improvement of blood gases, more consistant results are obtained. Short periods of daytime or nocturnal ventilation in bronchitics might be useful, but consistant improvement is more often seen in neuromuscular respiratory failure. Care has to be taken when using external negative pressure ventilation

in hypoxic bronchitics to avoid exacerbation of obstructive sleep apnoea.

D. Rodenstein (Belgium) reviewed the use of the new technique of ventilatory support, *i.e.* nasal intermittent positive pressure ventilation. He stressed that a detailed evaluation of individual patients, whether they suffer from COPD or neuromuscular ventilatory failure, is essential. This necessitates not only respiratory function measurements and blood gases but also measures of maximal inspiratory and expiratory pressures and tests of diaphragmatic function. The use of the various types of assisted ventilation should be judged against the results of these indicators. In the sleep apnoea syndromes, continuous positive airway pressure (CPAP) is undoubtedly the best form of therapy. In restrictive lung disease with neuromuscular failure, assisted ventilation with cuirass might give the best results. In COPD, the situation is much more difficult. Patients do not easily accept cuirass ventilation. Intermittent nasal pressure ventilation has been applied with benefit in acute exacerbations and in one or two patients over a longer-term but the major difficulty is still to get patients to accept assisted ventilation. Long-term domicilliary oxygen therapy should always be tried first and may well be the only option for many patients.

A. Rossi (Italy) summarized the treatment of ventilatory pump failure stressing the need to optimize drug therapy and relieve, as far as possible, systemic disease and reversible respiratory disorder. In chronic obstructive airways disease, the importance of PEEP during ventilatory support in acute ventilatory failure was stressed for flow-limited patients. External PEEP must be less than intrinsic PEEP. The management of carbon dioxide retention, the use of mechanical ventilation and the problems of weaning, reduction of ventilatory load by relief of bronchoconstriction, treatment of infection and thick mucus and the addition of extrinsic PEEP to flow-limited patients were all reviewed. In his view, the use of both aminophylline and adrenergic agonists were associated with a significant increase in maximum transdiaphragmatic pressure in COPD patients. The improvement was not fully explained by changes in lung volume. Other mechanisms, such as a direct action on the muscle fibre or a local increased blood flow to the diaphragm, need consideration. Selective approaches titrating therapeutic options to the patient particularly in COPD were stressed.

It is clear from the last three papers that no easy therapeutic solution to the problem of respiratory failure in COPD yet exists.

N. Pride (UK) discussed respiratory muscles in neurological disorders such as traumatic quadriplegia, motor neurone disease, old poliomyelitis and disseminated sclerosis, neuromuscular disorders such as myasthenia gravis and muscle disease such as dystrophia myotonica and the dystrophies. When the only abnormality of the respiratory system is known to be respiratory muscle or neurological disease then vital capacity is a reasonable indicator of prognosis. Total lung capacity and functional residual capacity (FRC) are diminished and the pattern of breathing is one of rapid shallow breaths. In all muscle disorders there is marked inspiratory muscle weakness with MIP generally less than -40 cmH_2O. There is a dispute as to whether one should measure the pressure during a cough or a sniff. In these disorders supportive ventilation has generally given good results on blood gas improvement, the non-invasive method of nasal positive pressure ventilation and cuirass negative pressure ventilation being far more successful than in COPD. There was less certainty about improvement of respiratory muscle weakness. In early stages of the disease, disproportionate muscle weakness associated with respiratory failure, given a period of daily ventilation may lead to a successful prolongation of life.

C. Donner (Italy) discussed respiratory muscle management in rehabilitation. In obstructive airways disease, hypoxia and mechanical distortion of the thoracic cage give rise to increased ventilatory need which may be associated with dyspnoea and possible muscle fatigue. Any method of increasing ventilation by the patient involves more energy expenditure. A number of options are available for rehabilitation to try to bring the balance between energy need and supply closer. Measures of improving hypoxaemia by treatment of bronchoconstriction and infection and supplemental oxygen should be undertaken. Diaphragmatic training, whole-body exercise and specific inspiratory muscle training are available. Whole-body training had little effect on respiratory muscles. Specific inspiratory muscle training has more potential but care has to be taken to ensure that the necessary inspiratory muscle pressures are achieved during the training programme. Studies are still proceeding. Thus, for the treatment of respiratory failure external negative pressure and nasal ventilation are options. It was still not clear whether in the longer-term these are any better than tracheostomy and intermittent positive pressure ventilation. In all cases blood gases improve. Long-term domiciliary oxygen therapy (LTOT) is the first method of treatment and when this fails the other options are available. Tracheostomy and IPPV should not necessarily be rejected at this stage.

Problems of nutrition lead to negative energy balance and muscle wasting in COPD. It may be necessary to increase calorific intake to 30% above baseline levels. This is difficult due to loss of appetite and intolerance of normal food intake. There is clearly a need for further research in this area.

R. Sergysels (Belgium) reviewed the application of physiotherapy to rehabilitation, questioning whether alteration of breathing pattern could usefully improve energy conservation, relieve muscle fatigue and achieve less dyspnoea. Several techniques of breath training had been suggested to include low frequency breathing, abdomino-diaphragmatic breathing and body positional change. There was no evidence, despite many claims in the literature, that any of the directed breathing techniques could lead to a permanent change of breathing pattern. Many of the low frequency types of breathing and abdomino-diaphragmatic breathing which change

breathing pattern by increasing inspiratory time as a fraction of total breath duration (Ti/Ttot) may induce fatigue in patients with severe airflow obstruction.

The only body position that significantly decreases FRC in normal subjects and COPD patients is the supine position. Few patients describe a decrease of breathlessness when so positioned and prefer to adopt a forward sitting position. In the latter position, an increase in FRC occurs in normal subject and in some COPD patients making it difficult to explain the relief of dyspnoea. The effect of body position on dyspnoea remains unexplained. These techniques should not be included in rehabilitation programmes until further information is available.

In the free papers, maximum transdiaphragmatic pressures were studied in normal persons. It was felt possible to produce diaphragmatic fatigue after vigorous exercise but recovery was quick and certainly within 30 min during resting conditions. Maximum Pdi fell due to changes of gastric pressure. It was not clear why this should be so. Diaphragmatic EMG measured in relation to respiratory fatigue and neurorespiratory drive was found to indicate respiratory drive more accurately than mouth occlusion pressure ($P_{0.1}$) in COPD. Two papers reviewed the treatment of acute and chronic ventilatory failure in COPD with nasal intermittent positive pressure ventilation; benefit was claimed.