The roles of transcutaneous carbon dioxide measurement in a respiratory support center

December 1997

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Transcutaneous monitoring of carbon dioxide plays an important role during short-term and long-term treatments for ventilatory failure.

Progress during short-term treatments can be judged through tc$p$CO$_2$ recordings - especially to avoid crash reintubation of patients who have been weaned off invasive ventilation. Transcutaneous carbon dioxide measurements can detect the presence of an excess of hypercapnia, a common side effect of long-term oxygen therapy.

VENTILATORY FAILURE

Definitions

If an individual has an arterial oxygen tension (pO$_2$(a)) which is less than 8 kPa (60 mmHg), he/she is said to be in respiratory failure.

In **Type I** respiratory failure the arterial carbon dioxide tension (pCO$_2$(a)) is normal or low. In **Type II** respiratory failure (or ventilatory failure) the pCO$_2$(a) is abnormally elevated, that is, it is greater than 6.5 kPa (48.8 mmHg).

The level of pCO$_2$(a) is inversely proportional to the level of ventilation. Thus, for example, if ventilation is halved the pCO$_2$(a) doubles. The causes of ventilatory failure include an inadequate ventilatory drive, weak respiratory muscles or an excessive respiratory impedance due to, for example, a stiff chest wall in scoliosis or a high resistance to air flow in chronic bronchitis.

Effects of hypercapnia

In normal healthy subjects an elevated pCO$_2$(a) is a powerful stimulus to increase ventilation. Respiratory drive can be tested using protocols where the subject rebreathes from a bag. The pCO$_2$(a) rises approximately linearly and so does ventilatory effort.

In clinical situations, as hypercapnia develops the patient fails to increase the level of ventilation appropriately and the stimulus is therefore ineffective. The excess of CO$_2$ leads to a build-up of hydrogen ions, that is, a

respiratory acidosis develops which may adversely affect cardiac function.

Other effects of the elevated $pCO_2(a)$ include a flapping tremor and vasodilatation which causes headaches and may contribute to ankle swelling. If the $pCO_2(a)$ rises high enough the patient will lapse into coma.

If $pCO_2(a)$ is chronically elevated (for > 24 hours) the acidosis becomes compensated as the kidneys generate extra bicarbonate to buffer the hydrogen ions. The increase in buffering capacity especially in the cerebrospinal fluid reduces the sensitivity to further changes in $pCO_2(a)$. A chronically elevated $pCO_2(a)$ therefore leads to a reduction in ventilatory drive.

Limitations of pulse oximetry in the assessment of ventilation

Pulse oximetry is a simple method for the measurement of arterial oxygen levels, expressed as the saturation $sO_2(p)$. It is widely used as a surrogate measure of ventilation.

However while the level of oxygen in arterial blood is related to ventilation, the relationship between ventilation and $sO_2(p)$ is not linear. This is because of the sigmoidal shape of the oxyhemoglobin dissociation curve.

In the higher ranges of $pO_2(a)$ large changes in value are accompanied by relatively small changes in $sO_2(p)$. Once the $pO_2(a)$ falls below 8 kPa (60 mmHg), the $sO_2(p)$ falls much more quickly and is a more sensitive index of change in $pO_2(a)$.

If a patient with normal lungs and gas transfer develops hypoventilation, then large changes can occur in $pO_2(a)$ and $pCO_2(a)$ with little change in $sO_2(p)$, as shown in the example below:

Example

Starting gas tensions:
$pCO_2(a)$ 5 kPa (37.5 mmHg), $pO_2(a)$ 14 kPa (105 mmHg), $sO_2(p)$ approx. 98 %

Ventilation halved:
$pCO_2(a)$ 10 kPa (75 mmHg), $pO_2(a)$ 9kPa (67.5 mmHg), $sO_2(p)$ approx. 92 %

A $pO_2(a)$ of 10 kPa (75 mmHg) may be sufficient to cause coma (CO_2 narcosis), but the $sO_2(p)$ is misleadingly normal. If additional oxygen is given to a patient, then the $sO_2(p)$ no longer gives any useful information about the level of ventilation.

RESPIRATORY SUPPORT TECNIQUES

Central to each of the respiratory support techniques described below is the optimisation of the arterial blood gases in patients who have compromised ventilatory function and/or gas exchange. In each, it is important to remember that hypoxia and hypercapnia are to be avoided. Below is a brief history of the techniques and a discussion of the evidence of their benefits.

Long-term domiciliary noninvasive ventilation

Mechanical devices to assist ventilation were described as long as 150 years ago [1]. The first devices were external negative pressure ventilators (ENPV) such as the 'iron lung' or 'tank' ventilator.

Development of the technique was closely linked to the poliomyelitis epidemics which affected large numbers in Europe and the USA in the early part of this century [2]. However, positive pressure ventilation using a tracheostomy tube improved survival in acute poliomyelitis and soon replaced ENPV as the ventilation method of choice [3, 4].

Some patients with poliomyelitis did not recover to full ventilatory independence and domiciliary ventilation services were developed for their care.

Tracheostomy ventilation can be effective for long-term home care [5], but it has important disadvantages, including the risk of occlusion by secretions as well as impaired coughing, swallowing and speech [6, 7]. ENPV also has disadvantages for home ventilation [8,

9] Noninvasive intermittent positive pressure ventilation (NiIPPV) has been shown to have advantages over ENPV and tracheostomy ventilation for domiciliary treatment and is now the method of choice.

NiIPPV was described as early as 1912 in conjunction with anesthesia but the equipment required the constant presence of an attendant to hold the mask, and a pressurized gas source, making it unsuitable for home use [10] Despite improved ventilator pumps the mask seal remained a major difficulty until the development of modern silicon-based rubber (**Fig. 1**).

The first use of home NiIPPV was described only as recently as 1984 [11]. A detailed study of the physiological effects of the technique was published in 1987 [12]. This showed improvements in overnight gas exchange and in daytime blood gas tensions even though the ventilator was only used at night.

FIG. 1: A patient using nasal intermittent positive pressure ventilation. The inner edge of the mask is made of silicone rubber and seals against the face. It is held in place during sleep by the cap.

NiIPPV is most commonly used for the long-term domiciliary support of patients with chronic ventilatory failure. The mask is usually only worn during sleep when self-ventilation is least effective (**Fig. 2**).

There is evidence of a benefit in a number of conditions leading to chronic ventilatory failure. These include neuromuscular disorders such as the muscular dystrophies and myopathies [12], chest wall deformities including scoliosis and kyphosis [13, 14], and previous tuberculosis [15].

Chronic obstructive pulmonary disease (COPD) may also lead to chronic ventilatory failure, and some patients have been treated with long term NiIPPV, but it is not as effective as in those disorders where the pulmonary deficit is restrictive [16].
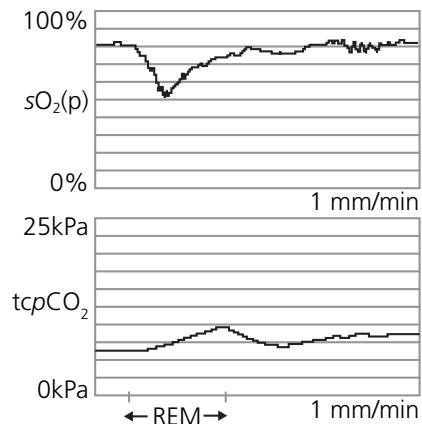

FIG. 2: Ventilatory failure is usually more pronounced during sleep. This patient with a scolioisis demonstrates a marked deterioration in ventilatory failure, particularly during rapid eye movement (dream) sleep.

The benefits of long-term home NiIPPV include an improvement in the symptoms of ventilatory failure, such as breathlessness, fatigue and poor quality sleep. The number of days spent hospitalized can be reduced [17] and patients previously confined at home may return to work or school.

Many studies have shown that daytime blood gas tensions are improved by nocturnal ventilation [12-20]. Three large series have reported the long-term survival with NiIPPV [17, 21, 22].

Overall, these show that survival is longest in patients with a stable chest wall or neuromuscular condition and less certain in those with a progressive neuromuscular disorder, COPD or bronchiectasis. In one series, the mean survival for patients with a scoliosis was eight years compared with three years for those with COPD [22].

Noninvasive ventilation for acute ventilatory failure

NiIPPV is being increasingly used for the treatment of acute on chronic ventilatory failure with the aim of avoiding intubation or supporting patients for whom invasive ventilation is not thought to be appropriate.

Most of the published data describing the use of NiIPPV for acute ventilatory failure are from patients with COPD. This treatment is not only used in Respiratory Support Centers, but also in intensive care units (ICUs) and general medical wards though most reports of its use have been published by specialist centers.

Although there are several series describing the use of NiIPPV for acute ventilatory failure in patients with COPD, there is still controversy over its effectiveness. It appears that only a sub-group of patients, which is difficult to identify, benefit.

In uncontrolled series it has been shown that NiIPPV may rapidly improve arterial blood gas tensions (ABGs) [23, 24] especially if the initial $pCO_2(a)$ is elevated, but this has not been a consistent finding [25, 26].

The effect of NiIPPV on the frequency of intubation has been examined in comparison to historical controls [27, 28] and in randomized controlled trials [29, 30]. NiIPPV can, it seems, reduce the frequency of intubation, though in none of the studies has a statistically significant survival benefit been demonstrated [31].

Weaning from invasive ventilation

One motivation for the use of NiIPPV in acute ventilatory failure is to avoid intubating patients who may subsequently prove difficult to wean from invasive ventilation.

Most patients who are intubated and ventilated have this done electively to facilitate a surgical procedure. They have good respiratory function and after a short time most can be extubated without difficulty.

Patients with long-term ventilatory disability who are intubated during an acute deterioration may prove more difficult to wean and can remain ventilator-dependent for months or even years.

When this occurs NiIPPV may be a useful tool in reestablishing ventilator independence, and where this is not completely achieved, in supporting patients in the long term, allowing discharge to home.

The survival of patients to discharge from hospital after nonelective invasive ventilation in the ICU is only around 40 to 50 % [32-34]. Many patients fail to wean from invasive ventilation and between 6 and 16 % die on a general ward after discharge from the ICU [35].

One cause of these deaths is probably recurrent ventilatory failure. There is evidence to suggest that the outcome of patients invasively ventilated in the ICU can be improved if they are referred to a Respiratory Support Center.

Descriptive studies have shown that NiIPPV can be useful in patients with long-term ventilator dependence in ICU [36, 37]. There have been no controlled trials of the use of NiIPPV for weaning, but when it is used as part of a comprehensive care program survival may be improved compared to historical controls [38].

In our experience, survival to discharge from hospital for patients with long-term ventilator dependence is around 90 %. Although 60 % of patients require some form of ventilatory support at discharge, this is usually only used at night.

Factors other than noninvasive ventilation are important in improving the likelihood of survival and weaning from ventilation. Diagnostic review may reveal a treatable cause for ventilatory failure or allow inappropriate treatment to be stopped.

Asthma appears to be overdiagnosed and the corticosteroids used to treat it can cause a loss of muscle strength, immunosupression, sleep disruption and sometimes psychosis. Resetting the day/night cycle,

which is difficult to maintain in the ICU allows sedative medication to be withdrawn and improves respiratory drive.

Patients on long-term ventilation are often allowed to retain CO_2, and as described above this reduces respiratory drive. The ABGs should therefore be normalized before weaning is attempted.

Long-term oxygen therapy

Chronic obstructive pulmonary disease such as bronchitis and emphysema is most commonly caused by cigarette smoking. Cessation of smoking is to be strongly encouraged if the progression of the disease is to be slowed.

In patients who become hypoxic due to lung damage survival is poor. The adverse effects of chronic hypoxia include confusion and poor concentration, pulmonary hypertension, right heart strain, arrhythmias and peripheral oedema. Long-term oxygen therapy (LTOT) to correct the hypoxia has been shown to improve survival.

The first controlled study to demonstrate this was the NOTT study in 1980, which showed that continuous oxygen gave a greater survival benefit than oxygen therapy used only at night [39].

Patients were given a fixed rate of oxygen, 1 L/min in the day and 2 L/min at night. Subsequently, the MRC study in 1981 compared treatment with oxygen for 15 hours a day with no treatment, and showed a survival benefit intermediate between that of nocturnal and continuous oxygen in the NOTT study [40].

In the MRC study the oxygen flow rate was a minimum of 2 L/min and increased when necessary to keep the $sO_2(p) > 90$ %. In this and subsequent studies an elevated pCO2(a) was a predictor of a poor outcome.

It is well known that patients with COPD may develop hypercapnia if given additional oxygen for hypoxia (**Fig. 3**), although there is debate about the mechanism [41].

It seems likely that in the NOTT, MRC and subsequent studies, the prescription of LTOT at fixed rather than individualized flow rates led in to an elevated $pCO_2(a)$, which may have adversely affected the outcome.
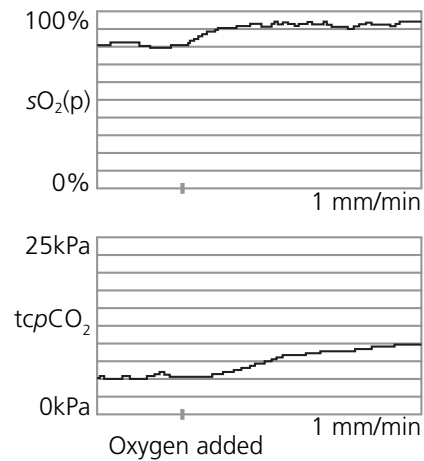

FIG. 3: Oxygen therapy may produce hypercapnia
In this patient with chronic bronchitis additional oxygen lead to dangerous levels of hypercapnia. The dose of oxygen should be carefully titrated. Noninvasive ventilatory support at night should be borne in mind as an alternative or adjunctive treatment.
At 21 min: Additional oxygen supply.

THE METHOD OF tc$p$CO$_2$ MEASUREMENT

Principles of the electrode system

The transcutaneous electrode comprises a heating element, temperature sensor, silver/silver chloride reference electrode, and an H^+ measuring electrode. Heating the skin leads to local vasodilatation and increased skin permeability to CO_2.

The released CO_2 from the skin diffuses through the selectively permeable membrane of the electrode, reacting with the electrolyte between the membrane and electrode. This reaction forms carbonic acid which dissociates into H^+ and HCO_3^-. The potential difference is proportional to $[H^+]$ and thus CO_2 concentration.

Factors affecting measured tc$p$CO$_2$

Electrode site and electrode temperature are the main determinants of quality in transcutaneous

measurements. The electrode site should allow optimal coupling of the electrode to well perfused skin with minimal movement.

A site over a joint or a large muscle is likely to result in shifting of the electrode and should be avoided. Although the electrode is small, flat skin contours are preferable. For long measuring periods, the electrode and its lead should be secured to the skin to avoid distortion caused by the weight of the lead pulling the electrode from the skin.

These factors and the need to select a capillary bed under lean tissue - free of obvious veins, tattoos, excessive hair or regular exposure to the aging affects of the sun - make the inside of the forearm nearest to the monitor the optimal site in most patients. Compression of the capillary bed underneath the measuring electrode caused by taping or bandaging over the electrode, should be avoided.

The site temperature must be high enough to promote gas diffusion through the skin without causing tissue damage. The increase in temperature increases metabolism in the skin and CO_2 production. $tcpCO_2$ is therefore higher than $pCO_2(a)$.

The difference is generally small, being on the order of 1 kPa (7.5 mmHg), but the higher the temperature selected the greater the disparity. A site temperature of 42.5 Celcius is suitable for overnight measurements on a single site in adults.

Adults will not normally develop skin burns at this setting. If the skin at the optimal site appears particularly translucent or sensitive (for example in elderly patients or those on long-term steroid treatment), the electrode temperature should be reduced to 42.0 Celcius and the site changed every 4 hours.

ELECTRODE AND SITE PREPARATION

In regular daily use the electrode and electrode membranes remain moist between measurements. However, storage of the electrode in electrolyte or re-membraning prior to measurement will improve the quality of measurements.

Conditioning of the electrode can be achieved by removing the electrode membrane and soaking the electrode for hours in electrolyte solution. Gentle cleaning of the electrode with the disk papers is necessary prior to remembraning the electrode. Single point gas calibration is necessary before use or if the measurement site is changed.

Measurement site selection is detailed above. Excess hair should be removed and the site cleaned thoroughly with an alcohol wipe. The site is dried with tissue paper and a fixation ring applied. Additional tape can be used to secure the adhesive ring but this should not cause compression to the underlying capillary bed.

After filling the electrode cup within the fixation ring with three drops of contact solution the electrode should be twisted into the cup, ensuring that the electrode lead lies towards the monitor, or if the forearm is selected, downwards towards the wrist.

The electrode lead can be looped and then taped to the skin before a gauze bandage is wrapped lightly over the electrode and secured over the electrode lead. Once stable values are measured, a quick check for patient movement distortion should be made.

The electrode should be relocated if the CO_2 measurement changes with 0.3 kPa (2.25 mmHg).

CLINICAL PROTOCOLS INCLUDING $tcpCO_2$ MEASUREMENTS

Initiation of noninvasive ventilation

The initial symptoms of ventilatory failure include lethargy, breathlessness on exertion, early morning headache and poor sleep quality. Examination may reveal a cause for ventilatory failure such as diaphragmatic weakness, and signs of end organ dysfunction, such as right ventricular heave and ankle oedema.

Laboratory investigations can show polycythaemia and right heart strain on the electrocardiogram. In most cases the daytime ABGs will be abnormal with an elevated $pCO_2(a)$ and a low $pO_2(a)$, but in some symptomatic patients the daytime ABGs may be normal.

Overnight studies will most often reveal far greater abnormality as respiratory impedance rises and ventilatory drive falls during sleep [43].

Overnight studies should include a minimum of pulse oximetry and $tcpCO_2$ measurement. $tcpCO_2$ measurement is particularly important in patients with no lung disease (e.g. those with a chest wall or neuromuscular disorder), since in these patients the $sO_2(p)$ may be relatively normal despite a greatly raised $pCO_2(a)$ (see **chapter 1** above and **Fig. 4**).
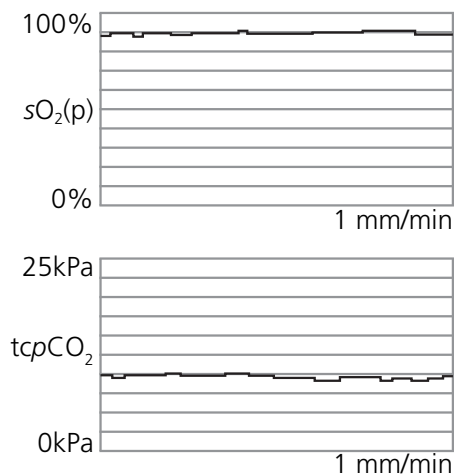
FIG. 4: An elevated $tcpCO_2$ with a misleadingly normal $sO_2(p)$
This patient has a muscular dystrophy and complained of morning headaches despite normal daytime ABGs. Some patients with normal lungs but hypoventilation may have a dangerously elevated $tcpCO_2$ during sleep with a misleadingly normal $sO_2(p)$.

In patients using additional oxygen the $sO_2(p)$ is of no value as a surrogate measure of ventilation. In this circumstance it is best if the overnight study can be performed without added oxygen, but it is mandatory to measure $tcpCO_2$ if it cannot.

Once ventilatory failure has been diagnosed and the decision made to commence noninvasive ventilation, the treatment must be titrated to correct for hypoventilation.

The ventilators used for NiIPPV are either volume or pressure preset. The tidal volume delivered to the lungs of an intubated patient can be guaranteed (with a volume preset ventilator) but during NiIPPV the volume varies since leaks from the mask vary considerably [17].

The only way to be sure that the patient is adequately ventilated at night is to monitor $tcpCO_2$. Pulse oximetry may be helpful, especially if it is markedly abnormal before treatment, but as explained above, it is not a good surrogate measure of ventilation in patients with normal lungs, and is of no use in patients who are receiving additional oxygen.

In our practice the ventilator is initially set up with the patient awake, and according to his or her comfort. The preset volume or pressure is subsequently titrated against continuous overnight $tcpCO_2$ measurements (**Fig. 5**).

We would consider a range of 4 to 7 kPa (30 - 52.5 mmHg) to be acceptable values of $tcpCO_2$. It is important not to reduce the $pCO_2(a)$ too far as this may lead to problems with upper airway occlusion [43] and dangerous, prolonged apneas if the patient is disconnected from the ventilator.

If the nocturnal $tcpCO_2$ is acceptable but the $sO_2(p)$ remains < 90 % additional oxygen may be prescribed. When the daytime ABGs are normalized and the patients are confident using the equipment, they are allowed home.
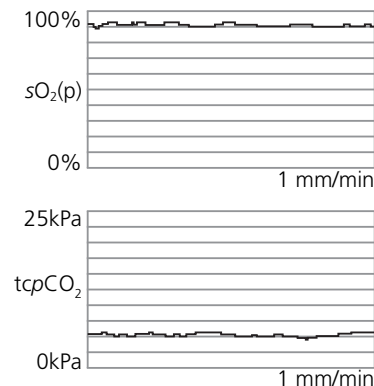
FIG. 5: Normalized overnight monitoring when using NiIPPV
The pretreatment nocturnal monitoring of this patient is shown in Fig. 2. After a few days on NiIPPV at night both nocturnal monitoring and the daytime gases were normalized.

On subsequent visits the overnight studies are repeated to ensure that the prescription of ventilation remains optimal. Long term surveillance is important, as in many patients ventilatory failure is due to a progressive disorder and the requirement for ventilatory support may change over time [44].

Noninvasive ventilatory support in acute ventilatory failure

If NiIPPV is introduced during an acute episode of ventilatory failure, a similar approach is used but continuous monitoring to allow timely decisions is even more important. To determine whether the treatment is working it is necessary to chart the CO_2.

Arterial measurements cannot be made continuously, and if additional oxygen is used this will invalidate $sO_2(p)$ as a surrogate measure of ventilation. If the $tcpCO_2$ does not fall with NiIPPV, the patient may require intubation and ventilation.

Weaning from invasive ventilation

Whenever changes are made to ventilatory support it is important to check the effect on the ABGs. This is especially important during weaning, when ventilatory support is being reduced.

Sleep deprivation impairs respiratory drive, and sedative medication to maintain sleep at night will also affect this. Re-establishing day/night cycles is important in the optimization of respiratory function before weaning is attempted in patients who are chronically ventilator-dependent.

Using noninvasive measurements rather than repeated arterial stabs or in-dwelling lines will contribute to improved sleep at night.

At the time of extubation changes in blood chemistry may occur quickly, and continuous monitoring with $sO_2(p)$ and $tcpCO_2$ will give an early indication if the patient's own ventilatory effort is inadequate. As in other circumstances, the $sO_2(p)$ will be falsely reassuring if additional oxygen is being used.

If the $tcpCO_2$ rises by more than 1.5 to 2 kPa (11.3 - 15 mmHg) after extubation, the initiation of NiIPPV may be considered. Patients with a tracheostomy tube may practice with NiIPPV before extubation, with the tube capped and the cuff deflated.

In our experience, around 60 % of patients who are difficult to wean from invasive ventilation require some form of noninvasive support after extubation.

Titrating long-term oxygen therapy

LTOT is most frequently prescribed for patients with COPD. The precise recommendations for the use of LTOT vary among countries but they are governed by the same general principles. It is important to ensure that the prescription is appropriate since it is an expensive treatment, and while it may prolong life it does not necessarily improve the quality of life.

It may indeed reduce the quality of life since it restricts the patient's mobility. The patient should have hypoxia of a sufficient severity to warrant treatment. It must be stable and not secondary to an infective or other exacerbation of airways disease.

In the UK, this level of hypoxia is taken as a $pO_2(a) < 7.3$ kPa (54.8 mmHg) alone or a $pO_2(a) < 8$ kPa (60 mmHg) in the presence of evidence of end organ dysfunction, including right heart strain on electrocardiogram, peripheral oedema or polycythaemia.

Once the patient has been identified as likely to benefit from LTOT, the oxygen level should be titrated up to the minimum flow rate which corrects the hypoxia. In our unit we perform a titration study during daytime wakefulness, recording $sO_2(p)$ and $tcpCO_2$ continuously.

The oxygen flow rate is increased in 0.25 to 0.5 L/min increments at hourly intervals. When it seems that the optimal oxygen flow rate has been found ($sO_2(p) > 90$ %, $tcpCO_2 < 8$ kPa (60 mmHg)), ABGs are checked again to ensure that hypoxia is corrected and that hypercapnia has not been induced.

Different flow rates of oxygen may be required by day and by night, so the study is repeated overnight. Using this method, around 90 % of patients are prescribed oxygen flow rates of < 1 L/min.

In our experience, despite the careful titration of LTOT prescription around 10 % of patients develop hypercapnia which is symptomatic or which we consider puts them at risk of rapid deterioration when they are given additional oxygen. We have started these patients on NiIPPV. In 50 %, nocturnal ventilation improves the daytime gases sufficiently to make LTOT unnecessary.

In the other half, most use NiIPPV at night and LTOT during the day only. In previous studies looking at LTOT an elevated $pCO_2(a)$ has been associated with a worse outcome.

We have shown that in patients unable to tolerate LTOT who are started on NiIPPV the level of $pCO_2(a)$ is no longer a predictor of outcome suggesting that adequate treatment of ventilatory failure improves survival [45].

Summary

The range of techniques available to support patients with respiratory impairment has grown considerably in the last two decades and among the most important have been NiIPPV and LTOT.

In order to establish which patients are likely to benefit from NiIPPV as a long-term treatment in the home overnight, CO_2 estimations are required and the best available method to obtain these is using $tcpCO_2$ measurements.

Matching the patient's requirements with the ventilator's output also requires the measurement of $tcpCO_2$ during undisturbed sleep.

When short-term treatment for ventilatory failure with NiIPPV is introduced, progress can be most usefully judged by calibrated $tcpCO_2$ recording. This allows limits to treatment to be set, dictating when it may be safely withdrawn or when it can be judged to have failed and more invasive methods of support considered.

When weaning patients from invasive ventilation, the effects of changes in ventilation can be best appreciated by continuous monitoring. This can avoid crash reintubation and will indicate when NiIPPV may be needed in order to bridge the gap between full ventilator dependence and full self-ventilation.

Long-term oxygen therapy may induce hypercapnia. This should be excluded at the initiation of treatment, not only on daytime arterial blood gas tensions but also during sleep when ventilation is most vulnerable.

This is again best achieved using $tcpCO_2$. The tendency to use $sO_2(p)$ as a surrogate measure of ventilation should be resisted where possible, as it may lead to dangerous hypercapnia being overlooked.

In particular where additional oxygen is prescribed, repeated ABGs should be taken and ideally $tcpCO_2$ will be recorded continuously by day and night. If the $tcpCO_2$ is elevated, then NiIPPV may be a more appropriate treatment.

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