Use of a combined oxygen and carbon dioxide transcutaneous electrode in the estimation of gas exchange during exercise

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Abstract

Background—Accurate and reliable measurement of gas exchange during exercise has traditionally involved arterial cannulation. Non-invasive devices to estimate arterial oxygen (O_2) and carbon dioxide (CO_2) tensions are now available. A method has been devised and evaluated for measuring gas exchange during exercise with a combined transcutaneous O_2 and CO_2 electrode.

Methods—Symptom limited exercise tests were carried out in 24 patients reporting effort intolerance and breathlessness. Exercise testing was performed by bicycle ergometry with a specifically designed protocol involving gradual two minute workload increments. Arterial O_2 and CO_2 tensions were measured at rest and during exercise by direct blood sampling from an indwelling arterial cannula and a combined transcutaneous electrode heated to 45°C . The transcutaneous system was calibrated against values obtained by direct arterial sampling before each test.

Results—In all tests the trend of gas exchange measured by the transcutaneous system was true to the trend measured from direct arterial sampling. In the 140 measurements the mean difference between the O_2 tensions estimated by direct sampling and the transcutaneous method was 0.08 kPa (0.62 mm Hg , limits of agreement 4.42 and -3.38 mm Hg). The mean difference between the methods for CO_2 was 0.02 kPa (0.22 mm Hg , limits of agreement 2.20 and -1.70 mm Hg). There was no morbidity associated with the use of the transcutaneous electrode heated to 45°C .

Conclusions—A combined transcutaneous O_2 and CO_2 electrode heated to 45°C can be used to provide a reliable estimate of gas exchange during gradual incremental exercise in adults.

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carbon dioxide (CO_2) tensions,³ and monitoring of airway CO_2 tensions⁴ are the techniques that are in use to provide a non-invasive estimate of gas exchange. This study evaluates the use of a combined O_2 and CO_2 monitor in the field of exercise testing.

The combined transcutaneous electrode consists of a Clark polarographic electrode that measures O_2 and a modified Severinghaus glass pH electrode integrated into a single unit that can be applied directly to the skin.⁵ The unit also incorporates a thermostatically controlled heater which promotes local hyperaemia, enabling O_2 and CO_2 levels in cutaneous capillaries to approach arterial levels. While studies have shown that the combined electrode provides a reliable estimate of gas exchange in haemodynamically stable adult patients in the critical care setting,⁶ there has so far been no evaluation of the technique in exercise testing. We have attempted to develop this combined transcutaneous electrode for use in the measurement of gas exchange during exercise in adults.

Methods

Twenty four patients (15 men, nine women; age range 27-67 years) referred from respiratory or general medical clinics for a symptom limited progressive exercise test were studied. The group comprised patients with a range of cardiopulmonary disorders of varying degrees of severity, and also included patients with unexplained breathlessness (table). Referring clinicians cited various reasons for requesting exercise tests including: (1) an attempt to elucidate poor response to therapy (chronic obstructive pulmonary disease); (2) to define more precisely the cardiac *v* respiratory component of exercise intolerance; or (3) further assessment of unexplained breathlessness in those patients with both normal electrocardiograms and standard lung function.

EXERCISE TESTING

Exercise testing was carried out by an electrically braked bicycle ergometer (Siemens Ltd) with the patient breathing through a low dead space, low resistance valve box. The valve box incorporated a turbine ventilometer on the inspired limb for the measurement of ventilation. Expired gas was analysed for O_2 and CO_2 content by an infrared spectrometer and

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Non-invasive devices that estimate arterial blood gas tensions are now widely available and have been the subject of a recent comprehensive review.¹ Pulse oximetry,² transcutaneous monitoring of arterial oxygen (O_2) and

Characteristics of the study population

Diagnosis	n	Age range (y) Sex	Summary of cardiorespiratory function
Chronic obstructive pulmonary disease (COPD)	8	57–67 5M, 3F	Mean FEV ₁ 42% predicted (range 34–67%)
Ischaemic heart disease (IHD)	5	52–65 3M, 2F	ECG evidence of IHD; on active treatment
COPD and IHD	2	57 and 66 2M	Reduced FEV ₁ and ECG evidence of IHD
Pulmonary thromboembolic disease	2	31 and 45 2F	Angiographically proven pulmonary thromboembolism
Respiratory failure due to scoliosis	1	46 M	FEV ₁ 0.7 l; VC 1.1 l
Hyperventilation syndrome	1	27 M	Normal FEV ₁ , TLCO
Unexplained breathlessness	5	32–54 3M, 2F	Normal ECG
			Normal cardiorespiratory function

FEV₁—forced expiratory volume in one second; VC—vital capacity; TLCO—carbon monoxide transfer factor; ECG—electrocardiographic.

paramagnetic analyser respectively (PK Morgan, Rainham, Kent). The electrocardiogram was monitored throughout exercise. After a two minute rest while seated on the bicycle the patients were instructed to cycle with no additional load for two minutes. Thereafter the load was increased by 15–25 W every two minutes until symptoms limited further exercise (chest pain, breathlessness, leg fatigue).

ARTERIAL BLOOD GAS MEASUREMENT

Arterial tensions of O₂ and CO₂ were monitored during exercise both by direct sampling and by the transcutaneous method described below. Arterial blood was sampled from an indwelling arterial cannula sited in the radial or brachial artery of the non-dominant forearm before the test. Blood was sampled over a 30 second period with the patient at rest, half way through each level of workload, and the instant the patient stopped exercise. All

samples were stored in ice and analysed immediately thereafter (Corning Blood Gas Analyser 178).

TRANSCUTANEOUS MEASUREMENT

The transcutaneous O₂ tensions were measured by a single PO₂/PCO₂ electrode (TINA electrode, Radiometer Ltd, Copenhagen) and its monitoring system (T_CM3). Based on the manufacturer's data the typical 90% response time is 30 seconds for the O₂ electrode and 60 seconds for the CO₂ electrode. Accordingly the transcutaneous O₂ and CO₂ values noted at the end of each stage of exercise were taken to correspond to the O₂ and CO₂ tensions obtained by direct sampling at the mid point of each stage of exercise. All gas tensions were expressed in mm Hg as the output of the transcutaneous system was in these units. All subjects gave informed consent and local hospital ethical committee approval was obtained to use a transcutaneous electrode heated to 45°C on the volar aspect of the forearm.

The arterial cannula was inserted as the first manoeuvre and thereafter the transcutaneous electrode was sited on the volar aspect of the same forearm and allowed to "settle", heating to 45°C. When a stable reading was apparent (five minutes) the values for transcutaneous O₂ and CO₂ were noted and an arterial sample was drawn for comparison. The gain controls of the transcutaneous monitoring system were then adjusted so that the transcutaneous values corresponded to the directly measured arterial sample. After resting for a further two minutes the baseline transcutaneous readings were noted.

DATA ANALYSIS

The transcutaneous method of estimating O₂ and CO₂ tensions was compared with the direct sampling method by the procedure suggested by Bland and Altman for assessing agreement between two methods of clinical measurement.⁷ The mean difference between the methods for the various measurements and the limits of agreement (mean difference plus two standard deviations of the difference) were calculated.

Results

Figure 1 shows a plot of the difference between O₂ and CO₂ tensions for the two methods in the 24 initial readings before the in vivo calibration. There was close agreement for the arterial CO₂ tension but a wider scatter for O₂ with a consistent tendency for the transcutaneous method to underestimate arterial O₂ tension.

A total of 140 data points were obtained from the 24 tests after in vivo calibration of the transcutaneous electrode. The range of arterial PO₂ and PCO₂ measured was 6.1–14.2 kPa and 3.6–7.6 kPa respectively. Figures 2 and 3 show plots comparing the differences between transcutaneous and direct arterial blood gas estimation for O₂ and CO₂ respectively at each data point. The mean differ-

Figure 1 Scatterplot of difference between transcutaneous O₂ and PaO₂ (open squares) and between transcutaneous CO₂ and PaCO₂ (closed squares) without an in vivo calibration of transcutaneous system. Mean difference between methods: O₂, 0.64 kPa (4.89 mm Hg); CO₂, 0.02 kPa (0.19 mm Hg).

Figure 2 Scatterplot of difference between transcutaneous O_2 and PaO_2 with in vivo calibration of the transcutaneous system. Mean difference between methods: 0.08 kPa (0.62 mm Hg, limits of agreement 4.42 and -3.38 mm Hg).

ences in the O_2 and CO_2 tensions measured by the two methods were 0.08 kPa (0.62 mm Hg, limits of agreement 4.42 and -3.38 mm Hg) and 0.02 kPa (0.22 mm Hg, limits of agreement 2.20 and -1.70 mm Hg). In all the tests changes in the transcutaneous O_2 and CO_2 tensions were true to the real trend of arterial O_2 and CO_2 tension changes as estimated by direct sampling. The data for those five patients with apparently normal resting cardiorespiratory physiology (table) were also analysed separately (fig 4) and the mean difference between methods for PaO_2 was 0.05 kPa (0.34 mm Hg, limits of agreement 1.89 and -1.2 mm Hg). These results compare favourably with the results over the wider range of PaO_2 (fig 2) which show the applica-

Figure 3 Scatterplot of difference between transcutaneous CO_2 and $PaCO_2$ with in vivo calibration of the transcutaneous system. Mean difference between methods: 0.02 kPa (0.22 mm Hg, limits of agreement 2.20 and -1.70 mm Hg).

Figure 4 Scatterplot of difference between transcutaneous O_2 and PaO_2 in five patients with normal resting cardiorespiratory physiology. Mean difference between methods: 0.05 kPa (0.34 mm Hg, limits of agreement 1.89 and -1.21 mm Hg).

bility of this transcutaneous system in measuring gas tensions in the normal range during exercise.

The close agreement between these two methods in following the trend of gas exchange is illustrated in fig 5 which gives the results for a patient with inappropriate hyperventilation. Figure 6 shows the data from the patient with the widest discrepancy between arterial and transcutaneous values in our

Figure 5 Blood gas changes during exercise in a 27 year old man presenting with breathlessness. Onset of symptoms at low workloads with rising O_2 tensions and falling CO_2 tensions suggest inappropriate hyperventilation. PaO_2 , $PaCO_2$ —arterial oxygen and carbon dioxide tensions; $TcPO_2$, $TcPCO_2$ —transcutaneous oxygen and carbon dioxide tensions.

Figure 6 Exercise induced changes in blood gas tensions in a 60 year old man with severe emphysema. PaO_2 , PaCO_2 —arterial oxygen and carbon dioxide tensions; TcPO_2 , TcPCO_2 —transcutaneous oxygen and carbon dioxide tensions.

study. In this patient with emphysema the minute ventilation rapidly approached the predicted maximum and PaO_2 fell sharply even at very low workloads. The trend of gas exchange as monitored from the transcutaneous system was true to the actual PaO_2 values but showed a difference of 1.0 kPa from the arterial level even though an in vivo calibration had been performed.

No test was associated with any local problem at the transcutaneous electrode site.

Discussion

The measurement of gas exchange during exercise usually involves arterial cannulation.⁸ Although this procedure is safe in experienced hands, it may be associated with significant complications.⁹ It would be advantageous, therefore, to have available a system which could monitor gas exchange in exercise without the potential morbidity associated with arterial cannulation. Our study suggests that a combined transcutaneous O_2 and CO_2 monitoring system could fulfil such a role.

Although transcutaneous O_2 monitors have been shown to provide a reliable estimate of arterial oxygen trend during exercise,¹⁰ it has been pointed out that the slow response renders them unsuitable for use in exercise testing. It has been proposed that an acceptable 90% response time for a blood gas monitor should be < 20 seconds if it is to be recommended for use in exercise testing.¹ Transcutaneous systems, especially the CO_2 electrodes, have response times of the order of 45–60 seconds and clearly do not fulfil such stringent criteria. We have adapted our exercise protocol, however, to enable the system to provide reliable information on the state of gas exchange during exercise.

Firstly, the electrode was heated to the highest recommended temperature (45°C) as the higher temperature is associated with a decrease in response time. Secondly, to pre-

vent abrupt and large changes in blood gas tensions a protocol of gradual workload increments was employed with a two minute exercise interval for each workload. Although some protocols employ workload increments at one minute intervals, the two minute stepup has been well tolerated in our experience across a range of cardiorespiratory problems.

The results also draw attention to the advantages of using a combined O_2 and CO_2 monitor. In addition to enabling the calculation of the alveolar-arterial O_2 difference and dead space/tidal volume ratio which are more specific indicators of the function of the pulmonary gas exchange mechanism, measuring transcutaneous CO_2 during exercise aids the detection of inappropriate hyperventilation as illustrated in fig 5.

The data from the initial transcutaneous readings and arterial blood sample indicate the advantage of an in vivo calibration to improve the accuracy of the transcutaneous system. While the need for an arterial puncture necessarily detracts from the non-invasive nature of the technique, we would suggest that a considerable advantage over traditional cannulation is retained. Our study suggests that this system is robust and reliable for monitoring a trend in gas exchange alterations during exercise over the range from apparently "normal" persons (fig 4) to those with advanced cardiorespiratory diseases. We have not, however, undertaken studies in healthy volunteers, believing that insertion of arterial cannula might prove difficult to justify.

The transcutaneous system compares favourably with other non-invasive systems of estimating gas exchange during exercise. Arterial O_2 saturation (SaO_2) by pulse oximetry has been widely used. The main limitation of the system is the shape of the oxygen dissociation curve; significant changes in arterial O_2 tension can occur without major changes in SaO_2 when arterial O_2 is > 8 kPa. The other non-invasive technique for indicating the state of gas exchange is end tidal CO_2 monitoring (PETCO_2). The PETCO_2 is an approximation of PaCO_2 only under circumstances of ventilation/perfusion homogeneity and uniform emptying of alveolar units.¹¹ Neither of these conditions can be assumed in patients with cardiopulmonary disorders.

The findings of our study suggest that a combined transcutaneous O_2 and CO_2 electrode can be used to provide a reliable non-invasive estimate of gas exchange in exercise provided a maximal permissible temperature is selected (45°C), together with gradual stepups in workload at two minute intervals. The technique circumvents the need for arterial cannulation, but is enhanced by an initial in vivo calibration. The system may be particularly valuable in following gas exchange trends in patients undergoing repeated exercise tests.

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Adventitia

Origin of the word “asthma”

Most of our old medical words come originally from Greek since Roman medicine is essentially Greek medicine at Rome. When there is a choice we more frequently use the Greek alternative—for example *hepar* for liver, not the Latin *jecur*.

In modern medical texts the word “asthma” is rightly said to be derived from the identical Greek word, but meaning “wheezing”, which I don’t think it does. (Greek words here will be transliterated into approximately equivalent English letters.) Asthma is a very old word. Homer uses it twice in a famous passage. In the *Iliad* Book 14 Hector has come up against the greater (Telamonian) Ajax, cast his spear with no effect, and is trying to withdraw. Ajax, the giant, throws a huge boulder and strikes Hector on the chest just below the neck (sternomanubrial junction?), spinning him round like a top. Hector collapses and the narrative moves on until Book 15 where it states: “*ho d’ argaleoi echet’ asthmatihaim’ emeon*”. He was “gripped by (*echeto*) difficult (*argaleoi*) asthma, vomiting up (*emeon*) blood (*haima*).”

To distinguish between haematemeses and haemoptysis from the history was apparently as difficult for Homer as it can be for us now. The second passage in the same book refers to his recovery, when the “*asthma kai hidros*”—“asthma and sweating”—ceased.

The verb that is cognate with *asthma* is *asthmaino* which appears, for example, in Book 10. Odysseus and Diomedes are chasing the Trojan, Dolon, on foot at speed over a long distance. Diomedes throws a spear over Dolon’s shoulder. It sticks in the ground in front of him and stops him in his tracks. The two pursuers come up “*asthmainonte*”. What follows is horrid. I refuse to believe that this is the first description of exercise-induced asthma.

We must go on to Hippocrates (whoever he was—probably several people) to find *asthma* in one of his or their Aphorisms. The first (1,1) is the one about art being long, life short, usually quoted in Latin translation and just visible in the arms of the London Royal

College of Physicians. In 3,22 he includes asthma, in the plural, in a list of diseases which occur in summer, which is interesting, but it is sandwiched between angina and ileus which spoils the impact. In the Hippocratic corpus the word is used to mean accelerated difficult breathing or shortness of breath, definitely a clinical symptom. (I am grateful to Dr Peter Jones of the Department of Classics, Newcastle, for advice on this and other points.)

We have to go a long way on to find *asthmatikos*, asthmatic, probably to Herodotus Medicus (1st century AD) quoted by Oribasius (4th century AD). Oribasius was physician to Julian the Apostate who tried to reintroduce to Rome the worship of the Olympian gods and sent him off to sound out the long silent Oracle at Delphi which (who?) replied, in still passable hexameters, that unfortunately the old firm was no longer in practice at the address stated.

Perhaps it would be better to go backwards and see if we can find the *ur-word* from which *asthma* derives. I would like it to be *ao*—“blow”—for which one could make a case. It is composed of alpha and omega, the beginning and the end, and would briefly symbolise the supreme importance of our specialty of thoracic medicine, a badly needed gesture. I think I shall have to settle for *awo*, however, where “w” is the Greek digamma, a letter which disappeared from the alphabet about the time Homer’s text was being written down, equivalent to Latin “v” and pronounced as English “w”. Better perhaps is *awemi*, also “blow”. From that comes eventually the Latin *ventus* and our English “wind”. You may feel that the linguistic connection between “asthma” and “wind” is not immediately apparent, but there it is.

In short, *asthma* did not originally mean “wheeze” but rather “noisy breathing”, “making a blowing noise”, “panting”, or even “groaning”.

KB SAUNDERS