



The Apnea Test for Brain Death Determination An Alternative Approach

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Abstract

Introduction: Problems associated with the standard apnea test relate to overshooting or undershooting the target PaCO₂, potentially compromising the viability of organs for transplantation or invalidating the test.

Materials and Methods: In 60 adult patients, the authors used an alternative method using exogenously administered CO₂ and measurement of end-tidal CO₂.

Results: All patients achieved an adequate respiratory stimulus (mean increase in PaCO₂ was 28 ± 3 mmHg, postapnea test pH was 7.20 ± .02). There was a clinically insignificant reduction in arterial blood pressure during testing, but no other complications occurred. Multiple regression analysis demonstrated a correlation between the predicted PaCO₂ (predicted from the end-tidal CO₂) and measured PaCO₂ (64 ± 9 versus 67 ± 9; $r = .75169$, $p < 0.0001$).

Conclusion: Exogenously administered CO₂ as an alternative method for the standard apnea test was a reliable and safe method, with minimal complications that offers several advantages over the standard method.

Key Words: Brain death; apnea testing; capnometry.

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Introduction

The apnea test is a key component in the clinical declaration of brain death (1,2). The premise is that a rise of PaCO₂ to >60 mmHg or a >20 mmHg rise above baseline maximally stimulates the medullary respiratory centre (3). The standard apnea test involves normalization of PaCO₂ (PaCO₂ approximately 40 mmHg) before initiating the apnea test, and the patient is then disconnected from the ventilator. Oxygen is administered at 6 L/minute via a cannula inserted into the endotracheal tube (4). It is assumed that PaCO₂ will rise during a period of apnea at a rate of 2–3 mmHg/minute, and the period of apnea required to achieve an adequate rise

of PaCO₂ (i.e., 20 mmHg) is therefore estimated to be approximately 7–10 minutes. In our experience using this procedure, the target PaCO₂ was sometimes not achieved, because the rate of PaCO₂ rise is highly variable from patient to patient and is not uniform over time within a given patient. On occasion, this resulted in having to repeat the apnea test, posing additional hazards and stress to the patient. Other complications experienced included hypoxemia, hypotension, respiratory acidosis, and arrhythmias, all of which potentially threaten the viability of organs, which may lead to posttransplanted organ dysfunction. Cardiac arrest has also been described as a complication occurring during the apnea test (5,6).



Table 1
Respiratory Therapy Apnea Test Data Collection Form

Apnea Test - Data Collection
Respiratory Therapy Services

Date: _____

Diagnosis (Cause of brain death): head trauma Intracerebral bleed other: _____

Desaturation during test? Yes No History of Smoking? Yes No

Hemodynamic instability during test? Yes No History of COPD? Yes No

Time	Arterial Blood Gases						PE TC O ₂	PaCO ₂ PetCO ₂ difference	HR	Blood Pressure s/d/m	Ventilator Settings		
	PaO ₂	PcO ₂	Ph	HcO ₃	BE	SpO ₂					rate	mode	other
Initial													

Therefore, we elected to revise their apnea testing procedure by administering exogenous carbon dioxide (CO₂) to reduce the complications mentioned. End-tidal capnometry was used as a means to monitor the rise of PaCO₂ (7).

Materials and Methods

The project was reviewed by the deputy chair of the Health Sciences Research Ethics Board. The charts of 60 patients who underwent an apnea test for brain death declaration in the intensive care unit (ICU) at London Health Sciences Centre–University Campus from February 1995 to August 2002 were reviewed, along with data from an Apnea Test-Data Collection form (see Table 1). The latter is completed by the respiratory therapist performing the test and includes measurements of blood pressure, heart rate, arterial oxygen saturation, end-tidal CO₂ concentration (PetCO₂), and ventilator settings during the apnea test. Data are also collected on whether the patients were hemodynamically unstable (requiring discontinuation of apnea test or use of fluid resuscitation and/or inotropic agents) or demonstrated arterial oxygen desaturation (<90%) during the apnea test.

To determine if the increase in PetCO₂ measured during the apnea test accurately reflected the increases in arterial carbon dioxide concentration (PaCO₂) during CO₂ administration, the arterial PaCO₂-PetCO₂ gradient was determined by calculating the difference in PaCO₂ and PetCO₂ measurements recorded before and at the end of the apnea test. The authors

also compared the measured end apnea test PaCO₂ to the predicted PaCO₂, as determined by the measured PetCO₂.

Artificial CO₂ Administration Protocol

The FIO₂ setting on the ventilator was adjusted to 100% for a minimal period of 10 minutes. An end-tidal CO₂ monitor was placed inline with the ventilator circuit at the end of the endotracheal tube, and the ventilator was set on IMV to provide a minute ventilation necessary to maintain a PaCO₂ of 35–40 mmHg. The apnea test was not performed until all the other clinical criteria for brain death were met and the patient’s hemodynamics and ventilation were considered stable and in a steady state, respectively. Before the initiation of the apnea test, an arterial blood gas was taken to measure the PaCO₂. The oxygen bayonet from the wall O₂ outlet was then disconnected and reconnected to the Carbogen (97% O₂/3%CO₂) cylinder. The IMV was set at 4 breaths/minute and was gradually decreased by 1 breath/minute until the predetermined PetCO₂ was achieved. The physician who monitored the apnea test observed the patient for evidence of spontaneous respiratory efforts for the test duration. The pressure-volume loops display on the ventilator is also capable of demonstrating any spontaneous ventilatory efforts by the patient, and these were also visualized during the apnea test. The apnea test was discontinued if there was evidence of spontaneous respirations or when the target PetCO₂ was reached.

Table 2
Preapnea and Postapnea Test Hemodynamics and Arterial Blood Gases

Parameter	Preapnea	Postapnea	p
Heart rate (bpm)	99 ± 29	100 ± 27	0.692
Mean blood pressure (mmHg)	86 ± 20	82 ± 21	0.024
PaO ₂ (mmHg)	247 ± 148	347 ± 110	<0.0001
PaCO ₂ (mmHg)	40 ± 6	67 ± 9	<0.0001
pH	7.38 ± .04	7.20 ± .02	<0.0001
Arterial saturation (%)	99 ± 2	97 ± 1	0.223
PaCO ₂ -PetCO ₂ gradient (mmHg)	7 ± 4	9 ± 6	0.001

Our goal of Carbogen therapy was to raise the PaCO₂ to decrease the arterial pH to 7.20, using the relationship that for every increase in PaCO₂ by 1 mmHg the pH will decrease by 0.006. Using the formula:

$$\text{final pH} = (\text{initial pH} - 7.20) / 0.006$$

will determine the required increase in PaCO₂ to reach a pH of 7.20 (8). Adding this number to the baseline PetCO₂ determined the final PetCO₂ to be achieved. Once the target PetCO₂ was reached, an arterial blood gas was drawn to confirm that an adequate increase in PaCO₂ was achieved. After the apnea test, the patient was placed on full ventilation, with 100% O₂ (with initial hyperventilation for up to 5 minutes) to return the PaCO₂ to preapnea test levels.

Statistical Analysis

Data were collected and entered into an Excel 97 spreadsheet. Statistical analysis was performed using SPSS (Version 8.0). Paired student's *t*-test was used to compare preapnea and postapnea test variables. Multiple linear regression analysis was used to compare predicted PaCO₂ and measured PaCO₂ at the end of the apnea test. Values are presented as mean ± SD. *p* < 0.05 was considered significant.

Results

There were 29 women and 31 men with a mean age of 46 ± 16 years (range 16–78). All patients had confirmation of brain death (i.e., no spontaneous respiratory efforts were detected clinically or by the flow-volume loops on the ventilator display). The prehemodynamic and posthemodynamic and arterial blood gas data are listed in Table 2. During the apnea test, there was a significant decrease in mean blood pressure; however, this was considered clinically insignificant. The mean core temperature recorded at the time of the apnea test was 37 ± 1°C (range 34–40.2). The IMV setting required to achieve the predetermined PetCO₂ was 3 ± 1 (range 1–5) breaths/minute. The total time to perform the apnea test was approximately 15–20 minutes, which was comparable to our previous experience when performing the standard apnea test. All patients achieved an adequate respiratory stimulus (the mean increase in PaCO₂ was 28 ± 3 mmHg, and the post apnea test pH was 7.20 ± 0.02). No patient showed arterial oxygen desaturation (<90%) during the apnea test. Although there was no significant difference between the predicted PetCO₂ and measured PetCO₂ at the end of the apnea test

(58 ± 10 versus 59 ± 11, *p* = 0.170), there was a significant difference between the predicted PaCO₂ and the measured PaCO₂ (64 ± 9 versus 67 ± 9, *p* = .0001), as well as an increase in the PaCO₂-PetCO₂ gradient (7 ± 4 versus 9 ± 6, *p* = 0.001). Multiple regression analysis indicated a correlation between the predicted PaCO₂ and actual PaCO₂ (*r* = .75169, *p* < .0001) measured at the end of the apnea test (see Fig. 1).

Conclusion

Although apnea test protocols vary, most suggest raising the PaCO₂ from a baseline of approximately 40 to 50–60 mmHg. Under normal physiological conditions, this translates into an arterial pH of 7.28 using the formula described in the Methods section (8). The production of CO₂ relates to body metabolism, and body temperature is considered to be the major factor in determining the actual rise in CO₂ during the apnea period (9). The range of PaCO₂ rise at the end of the apnea test is not surprising, because any core temperature greater than 32.2°C is sufficient to proceed with brain death determination. Dobb et al. reviewed six studies that demonstrated the unpredictability of rise of CO₂ during apnea testing (4). An additional study reported the widest range of PaCO₂ rise (0.5 to 10.5 mmHg/minute) during an apnea test, which was not predictable from other patient variables measured (10). Thus, the usually recommended apnea period of 10 minutes is often either insufficient, requiring repetition of the apnea test, or too long, causing both hypoxemia and/or respiratory acidosis leading to hemodynamic instability.

There is still a debate whether the acute rise in CO₂ or decrease in pH is the actual respiratory stimulus in the brainstem respiratory center. In either case, the end points of the apnea test for the purposes of brain death declaration are similar, and whether to increase PaCO₂ either endogenously (apnea) or by administering exogenous CO₂ should have no bearing on achieved end points to stimulate respiration.

One concern is that of "CO₂ retainers" (patients with chronically elevated PaCO₂ concentrations usually from a chronic respiratory problem or secondary to metabolic derangements) in whom a rise in PaCO₂ to 60 mmHg may not represent a sufficient respiratory stimulus. It is uncertain whether using hypoxemia to stimulate the respiratory center in CO₂ retainers would serve as a safe or an adequate stimulus. However, an acute decrease in cerebral spinal fluid (CSF) pH, should serve as an adequate respiratory stimulus (11). Therefore, we chose to use arterial pH as the final end point and calculated

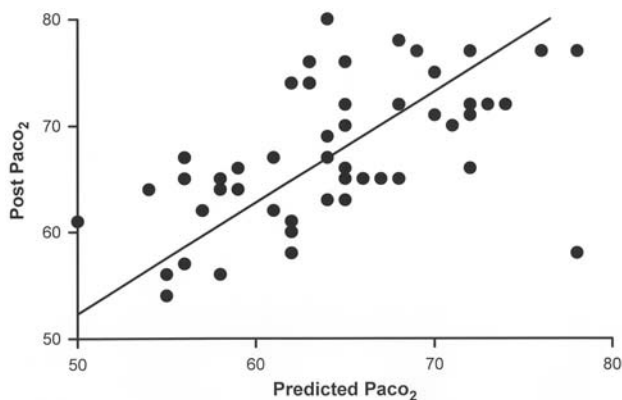


Fig. 1. Plot of data of postapnea test PaCO₂ versus predicted postapnea test PaCO₂.

the end apnea test PaCO₂ required to achieve this final pH. One could then be assured that the CSF pH would be acidic, because of the acute rise in arterial pH.

We predicted the PaCO₂ with reasonable accuracy, despite the PaCO₂-PetCO₂ gradient. The mean increase in PaCO₂ in the patients was 28 ± 8 mmHg, which resulted in a significant decrease in arterial pH ($7.38 \pm .04$ to $7.20 \pm .02$, $p < 0.0001$). Monitoring the rise in PetCO₂, which corresponded to a rise in PaCO₂, allowed us to predict the level of PetCO₂ that corresponded to an adequate rise in PaCO₂, allowing for termination of the apnea test. In addition, application of end-tidal capnometry allowed us to prevent overshooting the target PaCO₂, thus avoiding complications associated with a profound respiratory acidosis, including hypotension, arrhythmias, and hypoxemia.

The ability to ventilate patients with 97% oxygen during the apnea test prevented them from becoming hypoxemic. In the classical apnea test, patients receive adequate oxygen via bulk diffusion during apneic oxygenation. However, this method does not prevent hypoxemia in some patients (i.e.,

those with lung disease) (12). Furthermore, cases of barotrauma have been reported as a result of instillation of oxygen at 6 L/minute through the endotracheal tube. These two complications are unlikely to occur using this method.

In summary, administering exogenous CO₂ with low IMV ventilation and monitoring PetCO₂ as a means of predicting increases in PaCO₂ is a reliable, safe, and convenient alternative method of apnea testing for brain death determination.

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