



# Clinical Factors Influencing the Increment of Blood Carbon Dioxide During the Apnea Test for the Diagnosis of Brain Death

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**T**HE ABSENCE of ventilatory response is one of the most accepted elements included in the protocol of the diagnosis of brain death. Though several protocols have been described for performing the apnea test, most of them accept that a carbon dioxide ( $\text{pCO}_2$ ) blood level of 60 mm Hg or higher must be reached to establish the absence of activity of the brainstem respiratory centre. However, there are not enough surveys about the elements that influence the increase of  $\text{pCO}_2$  during the apnea test in brain-dead patients.<sup>1-3</sup>

The objective of the present study has been to show the influence of several clinical factors on the rate increase of  $\text{pCO}_2$  during apnea test in suspected brain-dead patients. We have also tested the value of a fixed rate increase of  $\text{pCO}_2$  in the prediction of calculation of apnea test time when this began in values less than 40 mm Hg. We also analysed the influence of the apnea test over the cardiocirculatory system in this type of patients.

## METHODS

Twenty-six patients admitted to a neurologic intensive care unit formed the population of this study. In all of them, the diagnosis of brain death was suspected at the time of the study. The mechanisms of brain damage were head trauma in 10 patients and cerebrovascular attacks in 16 patients (10 cases of spontaneous intracerebral hematoma, 5 cases of subarachnoid haemorrhage, and 1 case of ischemic stroke). The mean age of the patients was of 53.3 years. None of the patients have clinical antecedents of chronic pulmonary illness nor myocardial dysfunction. Seven patients had antecedents of arterial hypertension, and two patients had suffered previous episodes of atrial tachyarrhythmias, although both were in sinoatrial pace during the performance of the apnea test. At the time of the diagnosis in dopamine (at a mean dose of 6  $\mu\text{g}/\text{kg}/\text{min}$ ) had been administered in 10 patients. Four patients had presented clinical signs of diabetes insipidus, but polyuria was controlled after administration of desmopresine. Before apnea tests, it had been confirmed in every patient the following clinical signs: absence of photomotor reflex, absence of corneal reflex, absence of pharyngeal reflexes, absence of motor movements with origin in brain, absence of cough reflex, absence of nausea reflex, absence of oculocephalic reflex, and the absence of oculomotor reflex. In all cases, before the apnea test, the cerebral circulatory arrest was confirmed by transcranial Doppler sonography following criteria previously published.<sup>4</sup> The apnea test was performed using the following schedule: ventilation for at least 20 minutes with an

**Table 1. Mean Values (in mm Hg) of Arterial  $\text{pCO}_2$ ,  $\text{pO}_2$  and Mean Arterial Pressure Before the Apnea Test and Before Reconnection to Ventilator**

	Before Apnea Test	At the End of Apnea Test
$\text{pCO}_2$	34.7	68.73
$\text{pO}_2$	453	226
TAM	87.4	79.4

inspiratory fraction of oxygen of 100%; arterial blood sample for knowing the basal  $\text{pCO}_2$ ; calculation of the apnea test time (according an estimation increase of  $\text{pCO}_2$  during apnea of 2.8 mm Hg) to reach an end  $\text{pCO}_2$  equal or higher than 60 mm Hg; and disconnection of the ventilator. After that, the patient was disconnected from the ventilator and an intratracheal cannula was inserted with oxygen flow of 6 L/min. Once the estimated time of apnea elapsed, the patient was reconnected to the ventilator before extraction of a blood sample to determine the final values of  $\text{pCO}_2$ .

In all patients the  $\text{pO}_2$ , the arterial pressure (before the test and before reconnection to the ventilator), and the axillary temperature were also measured. During the apnea test, the arterial pressure, the capillary saturation of oxygen, and the cardiac rhythm were monitored.

We compared the values of  $\text{pCO}_2$ ,  $\text{pO}_2$ , and mean arterial pressure before and after the test. According to the temperature we also performed a comparison of the mean of these parameters. The rate increment of  $\text{pCO}_2$  with the temperature was correlated.

## RESULTS

In no patient was a positive ventilatory response observed during the apnea period. The values of  $\text{pCO}_2$ ,  $\text{pO}_2$ , and mean arterial pressure before and after the test are shown in Table 1. In five patients the final  $\text{pCO}_2$  was less than 60 mm Hg. One of the patients (who suffered a neurogenic pulmonary oedema) was reconnected to the ventilator before the estimated time of apnea elapsed because of the presence of serious ventricular arrhythmias. The mean body temperature (axillary) during the apnea test was of 36.1°C. The average increment of  $\text{pCO}_2$  in the total of the patients was of  $3.39 \pm 0.88$  mm Hg/min. That average increase of  $\text{pCO}_2$  was

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significantly higher ( $P < .05$ ) in the group of patients with temperature equal or higher than to  $36^{\circ}\text{C}$  (increase of  $\text{pCO}_2 = 3.68 \pm 0.7$  mm Hg/min) compared with the increment observed in the group of patients with a body temperature less than  $36^{\circ}\text{C}$  (increase of  $\text{pCO}_2 = 3.0 \pm 0.86$  mm Hg/min). Similarly, the increase of  $\text{pCO}_2/\text{min}$  was significantly higher ( $P < .05$ ) in the group of patients with a  $\text{pCO}_2$  at the beginning of the test higher than 35 mm Hg ( $\text{pCO}_2 = 3.88$  mm Hg/min) compared with the increment detected in the group with a basal  $\text{pCO}_2$  inferior to 35 mm Hg (average increase of  $\text{pCO}_2$  per minute of 2.96 mm Hg/min). There was a significant correlation between the body temperature and the rate of  $\text{pCO}_2$  increase per minute of apnea ( $r = 0.512$ ). There was not a significant correlation between the basal  $\text{pCO}_2$  and the average increase of  $\text{pCO}_2$  during apnea ( $r = 0.2911$ ). There were no significant changes of the mean arterial pressure during the apnea test.

## DISCUSSION

Apnea is one representative clinical sign of the absence of function of the brain stem, and it is included in most of protocols for diagnosis of brain death. However, there is no general agreement about the necessary apnea time to reach a blood level  $\text{pCO}_2$  of 60 mm Hg (the most accepted value as sufficient for stimulation the brain stem respiratory centre). This is probably because of the different clinical (hemodynamic, metabolic, etc.) situations that we can find in suspected brain-dead patients. Most protocols accept a period of apnea time of 10 minutes if the  $\text{pCO}_2$  at the beginning of the test is 40 mm Hg. However, in some patients 10 minutes of apnea is insufficient for reaching a  $\text{pCO}_2$  of 60 mm Hg; inversely, in other patients with the same apnea time the  $\text{pCO}_2$  blood level increases to very high values. In patients with a hemodynamic instability, an unnecessary prolonged apnea time could generate severe cardiac arrhythmias or even cardiac arrest.

Our study confirms the difficulty of calculating the adequate apnea test time,<sup>5,6</sup> and provides evidence that there is

no homogeneous increment of  $\text{pCO}_2$  during the apnea test (five patients did not reach the levels of  $\text{pCO}_2$  predicted). Our results show the importance of two clinical factors in this calculation: the body temperature and the basal  $\text{pCO}_2$ . Some previous surveys have related the body temperature and the  $\text{pCO}_2$  increase during the apnea test. Our investigation confirms this data, showing how patients with a normal or high temperature have higher production of  $\text{pCO}_2$  than hypothermic patients. The well-known correlation between metabolic activity, body temperature, and  $\text{pCO}_2$  production could explain our results. More studies are necessary to confirm the relationship between basal  $\text{pCO}_2$  and the increase of  $\text{pCO}_2$  during apnea.

To assure levels of  $\text{pCO}_2$  higher than 60 mm Hg at the end of the apnea test during the clinical confirmation of brain death the suppression of the therapeutic hyperventilation is advisable, situating the blood  $\text{pCO}_2$  near 40 mm Hg. In hypothermic patients a more prolonged apnea time could be necessary to reach the blood  $\text{pCO}_2$  of 60 mm Hg; therefore, a body temperature higher than  $36^{\circ}\text{C}$  is advisable. However, the hypothesis that if the physical rewarming (termic blankets, etc.) of the suspected brain-dead patient could increase the production of  $\text{pCO}_2$  demands further studies. On the other hand, a confirmatory blood sample at the end of the test is always necessary to confirm the final blood  $\text{pCO}_2$  value.

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