Complications associated with the apnea test in the determination of the brain death

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Keywords: apnea test; brain death; complications

Background An apnea test is essential in the clinical determination of brain death. This study was conducted to analyse complications associated with the apnea test in the determination of the brain death.

Methods On 93 adult patients in coma in Zhejiang Province of China from January 2003 to December 2006, 179 apnea tests were performed as a part of the determination of brain death. Potential risk conditions and complications were analysed during apnea tests.

Results During apnea, serious cardiac arrhythmia did not occur in all patients. Complications occurred in 37 of 179 (21%) apnea tests. Hypotension occurred in 30 patients (17%) and it was observed in 8/94 (9%) tests with baseline value of systolic arterial blood pressure not less than 120 mmHg, and 22/85 (26%) less than 120 mmHg ($P<0.05$). Severe hypoxaemia occurred in 10 patients (6%) of which 3/138 (2%) tests with baseline value of arterial oxygen pressure not less than 200 mmHg, and 7/41 (17%) less than 200 mmHg ($P<0.05$).

Conclusions This study demonstrated that complications occurred mostly in patients with inadequate baseline systolic arterial blood pressure and preoxygenation. Adequate precautions during the apnea tests may reduce the risk of cardiovascular and oxygenation complication.

Death was classically described as the cessation of circulation and respiration. The advent of mechanical ventilation and of methods for cardiovascular support presented new challenges for determining the end of life for patients with catastrophic cerebral injuries whose lives could be preserved by using these complex technological devices. So brain death, a new concept of death, as defined by neurological criteria emerged and evolved as a necessary measure for determining death.1

The ad hoc Committee of the Harvard University Medical School defined irreversible coma, with no discernible central nervous system activity, as a criterion for brain death in 1968.2

The diagnosis of brain death is based on the clinical diagnosis of deep coma, loss of all brainstem reflexes, the demonstration of apnea, and using technical confirmatory tests to corroborate the clinical signs in accordance with the Drafting Committee for Diagnostic Criteria of Brain Death of the Ministry of Health.3,4

Loss of brain stem function definitely results in loss of centrally controlled breathing, with resultant apnea. Apnea test is an effective method to detect apnea. Therefore, it is an essential component in clinical determination of brain death.

The main problem in apnea testing is that the testing procedure has to be rigorous enough to demonstrate apnea reliably, but must not bear the risk of further organ damage. Possible life threatening complications of apnea testing include severe hypoxia, hypotension, complex cardiac arrhythmias or even cardiac arrest.5,6

As data on the complications under this testing procedure in China are scarce, we monitored complications during apnea testing.

METHODS

Study sample On 93 adult patients with a clinical diagnosis of brain death in 25 cities in Zhejiang Province of China from January 2003 to December 2006, 179 apnea tests were performed. Relevant pulmonary dysfunctions (severe chronic obstructive pulmonary disease or adult respiratory distress syndrome) were not present in any of our patients. Prior to apnea testing, the patients fulfilled all other clinical criteria for the diagnosis of brain death. One of three confirming tests including electroencephalography (no electrical activity during 30 minutes of recording), transcranial Doppler sonography (showed a typical pattern of cerebral circulatory arrest), short latency somatotensory evoked potentials (showed the interruption of conduction within the cervical spinal...
oxygen saturation (SPO2) via a sensor placed over the pressure sensor placed in the radial artery and pulse electrocardiogram and arterial blood pressure (BP) via a Cardiovascular functions were monitored using a bedside Data collection initial and repeat observations for brain death in adults. The 93 brain dead patients had an age range of 18–82 years and 61 were male and 32 female. The median time from the fatal trauma to the onset of brain death was 2 days (range 0–6). Table 1 shows the causes of coma.

Apnea tests The apnea testing procedure was as follows: patients with the clinical diagnosis of brain death were ventilated with 100% oxygen for at least 10 minutes and the respiratory volume adjusted to get basal normocapnia. During the apnea test, patients were disconnected from the ventilator, a cannula introduced into the endotracheal tube to the level of the carina through which 100% oxygen at 6 L per minute was administered. The disconnection was maintained long enough to reach an arterial carbon dioxide pressure (PaCO2) level of 60 mmHg or an increase of >20 mmHg above normocapnia. If the patient did not respond with any respiratory movements, the trial was considered positive in terms of diagnosis for brain death.

In clinical determination of brain death, persisting observation further confirms the irreversibility of the patient’s condition. A repeat clinical evaluation of cardinal findings in brain death is recommended. Our study adopted an interval of 12 hours to 24 hours between initial and repeat observations for brain death in adults.

Data collection Cardiovascular functions were monitored using a bedside monitor registering heart rate (HR) via an electrocardiogram and arterial blood pressure (BP) via a pressure sensor placed in the radial artery and pulse oxygen saturation (SpO2) via a sensor placed over the forehead. Values were read directly from the monitor screen. Registration started during previous ventilation with fraction of inspired oxygen of 1 and was continued until the patient was reconnected to the respirator after a 5 minutes observation.

Hypoxaemia, arterial hypotension and acidemia were among the most common complications encountered during the apnea test. Two criteria mandated immediate discontinuation of the apnea test: any arrhythmia associated with haemodynamic instability or the presence of respiratory movement. In case of premature termination of a test, arterial blood was immediately drawn before connecting the patient to the ventilator.

Statistical analysis Values were presented as percentages or mean ± standard deviation (SD). Nonparametric tests were used to analyse variables that did not follow a Gaussian distribution. Statistical analysis was done by paired samples t test for the same subject measured before and after apnea testing or chi-squared test for comparisons. The Wilcoxon’s signed rank test was used to determine statistical significance of skew distribution for PaO2 before and after apnea testing. All tests were two sided, and P < 0.05 was considered significant. Statistical calculation was performed using the SPSS 10.0.

RESULTS

General characteristics There were no respiratory movements during any of the apnea tests. Brain death was confirmed in each case. All apnea tests were uneventful (neither cardiac arrest, nor severe arrhythmia). Among 93 patients, 7 patients died before clinical and confirming tests could be repeated. The test time was 4 minutes in 14 tests, 8 minutes in 154 tests, more than 8 minutes in 8 tests and the other 3 tests were ended because of severe hypoxaemia, but arterial blood was immediately drawn before connecting the patient to the ventilator.

The groups were compared regarding their demographic features and pretest state and no statistically significant differences were found when analyzing the following variables: cause of death, the duration of comatose state, gender or age.

There was a significant increase in arterial PaCO2, and decrease in arterial pH, BP and arterial oxygen pressure (PaO2) following completion of the apnea tests. HR did not significantly change following apnea testing. The average rate of rise in arterial PaCO2 was (4.2±1.4) mmHg/min (Table 2).

Complications of apnea tests Complications of severe hypoxaemia (PaO2 <60 mmHg) and hypotension (ABPs <90 mmHg), were present in 37 tests (21% of 179 apnea tests). Hypotension developed in 30 tests (17%), severe hypoxaemia developed in 10 tests (6%) and both hypotension and severe hypoxaemia developed in 3 tests (2%) (Figure 1). Hypotension (ABPs <90 mmHg) as compared with the ABPs at the onset of apnea testing occurred in 8/94 (9%) tests with baseline value of ABPs not less than 120 mmHg and 22/85 (26%) less than 120 mmHg (χ2=9.656, df=1, P=0.002, Figure 2).

Severe hypoxaemia (PaO2 <60 mmHg) was noted in 3/138
Table 2. Blood gas and cardiovascular parameters at baseline and after apnea testing

<table>
<thead>
<tr>
<th>Groups</th>
<th>No. of cases</th>
<th>pH</th>
<th>( \text{PaCO}_2 ) (mmHg)</th>
<th>( \text{PaO}_2 ) (mmHg)</th>
<th>ABPs (mmHg)</th>
<th>ABPd (mmHg)</th>
<th>HR (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>179</td>
<td>7.34±0.08</td>
<td>41.8±3.0</td>
<td>343 (50–631)</td>
<td>125.6±24.8</td>
<td>75.8±17.3</td>
<td>98.9±25.4</td>
</tr>
<tr>
<td>After apnea testing</td>
<td>179</td>
<td>7.16±0.08*</td>
<td>73.3±9.3*</td>
<td>223 (43–659)*</td>
<td>109.2±21.1*</td>
<td>62.0±15.9*</td>
<td>99.5±27.0</td>
</tr>
</tbody>
</table>

ABPs: systolic arterial blood pressure; ABPd: dilated arterial blood pressure; HR: heart rate. *P <0.05 vs baseline.

DISCUSSION

Acidaemia and hypercapnia inevitably developed during apnea test. The former has cardiac depressant effects by decreasing cardiac contractility, restraining the myocardial response to catecholamines and decreasing conduction velocity. However, not every patient showed a marked fall in BP. HR did not change significantly. Oxygenation could be maintained in most patients without respiratory movement.

Twenty-one percent of all the tests had complications of hypotension or severe hypoxaemia. During these tests, patients underwent all processes of determining of brain death in spite of hypotension or severe hypoxaemia.

Severe hypoxaemia occurred in 6% of all tests. It was developed in 2% of tests with adequate preoxygenation and 17% of inadequate preoxygenation. Three tests, all under poor preoxygenation, were terminated prematurely for rapidly decreasing SPO2, but arterial blood was drawn before connecting the patient to the ventilator. This study indicated that adequate preoxygenation might be associated with increased hypoxaemia. Goudreau et al6 found that complications occurred most frequently in patients with inadequate preoxygenation (14/26). Mards’ study11 demonstrated that performance of apnea testing in poorly preoxygenated patients could lead to significant hypoxaemia, despite delivery of 100% oxygen to the patient. All these studies suggested that adequate preoxygenation is needed, because adequate
preoxygenation could remove alveolar nitrogen stores and facilitates oxygen transport.

Heart rate did not significantly change in our study. Lang et al reported that in most patients (55%) the HR changes did not exceed the ±10% range. A decrease in HR was significantly less frequent than a decrease in BP. Heart rate might lose its susceptibility to parasympathetic modulation in brain death. However, Belsh et al described the possibility of an increase in HR.

The risk of hypotension during apnea testing was recently discussed as a significant threat to patients undergoing examination for brain death. In our study, 17% of all tests were under hypotension. Baseline value of ABPs not less than 120 mmHg was considered adequate precaution in BP. Hypotension occurred in 9% of tests with adequate ABPs and 26% inadequate ABPs. Inadequate baseline BP might be associated with increased hypotension. Therefore, fluid infusion or vasopressor treatment will be taken to improve blood pressure before disconnecting respirator in apnea test. An appropriate baseline to avoid hypotension may be 120 mmHg.

Corresponding to the increasing PaCO2 during the observation period, a decline of arterial pH was observed. The low baseline pH was associated with severe acidosis and the high baseline CO2 value was associated with acute hypercarbia. The phenomenon can be affected not only by lengthening time of apnea testing, but also body temperature, inflammatory reaction and basic metabolic rate. Hypercapnic narcosis happened if PaCO2 value went above 100 mmHg, so it should be avoided.

In the present study, hypotension did not always occur with high baseline CO2 value or posttest hypercarbia. In addition, it was reported that a marked fall in BP was not directly related to severe acidosis although the reason for this is still unclear. But in Ebata study, haemodynamic disturbance was avoided during apnea testing when respiratory acidosis was limited to a pH of 7.17±0.02 and the PaCO2 to 60 to 80 mmHg.

In conclusion, when pretest baseline oxygenation was not less than 200 mmHg, apnea testing had reduced risk of cardiovascular complications. Acidosis was less likely when baseline pH was more than 7.35. These baseline values were important in apnea testing.

In addition, this study demonstrated that complications occurring in apnea testing were related to inadequate baseline systolic blood pressure and preoxygenation. Adequate precautions during the apnea tests may reduce the risk of cardiovascular and oxygenation complication.

REFERENCES

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