Does Blood Ammonia Level at Time of Initial Treatment Predict the Outcome of Patients in Cardiopulmonary Arrest on Arrival?

Kiichi Nagamine

ABSTRACT Recently, comprehensive medical care is being promoted for when resuscitation is performed on patients in cardiopulmonary arrest on arrival (CPAOA), with an emphasis on not only cardiac resuscitation but also on brain resuscitation. When a patient in CPAOA is transported to hospital, how the arrest occurred and how much time has elapsed from the onset of arrest are frequently unknown. Even in witnessed CPA cases, the time elapsed since CPA is often incorrect, and this information is especially important. In this study, we examined an objective index to enable estimation of the time elapsed from the onset of CPA to the arrival at hospital where emergency management was performed. We studied 225 patients with witnessed intrinsic cardiogenic out-of-hospital CPA (128 male and 97 female) who were transported to our hospital during the period from April 1996 to March 2003. We statistically analyzed the correlation between the blood ammonia level at the time of the initial management and the time elapsed from confirmation of CPA to arrival at the hospital (CPA-arrival time). There was a positive correlation between the blood ammonia level at the time of initial management and the CPA-arrival time. Patients who made a full recovery showed a significantly lower blood ammonia level at the time of initial management than those who did not make a full recovery. Also, many patients whose blood ammonia level was less than 180 μg/dl at the time of initial management were able to make a full recovery. Based on these results, we conclude that the blood ammonia level can potentially be used as a useful index for estimating the time elapsed since CPA and the neurological prognosis including brain resuscitation.

Key words: cardiopulmonary arrest, blood ammonia level, brain resuscitation

Accepted for publication on December 7, 2004 (04-076)

Introduction

In performing emergency management, information on how the illness or injury occurred is important and useful in deciding what treatment should be performed. Especially for resuscitation of patients in cardiopulmonary arrest on arrival (CPAOA), detailed information on the occurrence of the event and time elapsed since CPA is crucial. Because the time when initial basic life support is provided and the time elapsed since CPA greatly affect the prognosis of patients\(^1\), this information must be fully

Correspondence author: Kiichi Nagamine, MD
Division of Critical Care and Emergency Medicine,
Chiyuukai Komonji Hospital
Obatake 1-7-25 Kokurakita-ku, Kitakyushu-shi,
Fukuoka 802-0026, Japan

JJAAM 2005; 16: 283-8
correlation among the time elapsed from confirmation of CPA to the patient’s arrival at hospital (CPA-arrival time), the blood ammonia level and the neurological outcome, in order to determine whether blood ammonia level can be used for prediction of a patient’s outcome.

Patients and methods

1) Patients

Among patients in intrinsic cardiogenic out-of-hospital CPA who were transported to our hospital from April 1996 to March 2003 (465 patients), we included patients in this study if their CPA was witnessed CPA and the time elapsed between CPA and hospital arrival was able to be estimated. We excluded patients if they were obviously addicted to drugs, had experienced unusual circumstances (e.g. hyperpyrexia, hypothermia or submersion in water), had a previous history of diseases such as liver disease that would affect blood ammonia level, or had hemolysis. In addition, we also excluded patients whose measured values exceeded the upper limit of the measurement range of the equipment (1,000 µg/dl) or CPA-arrival time exceeded 120 minutes. Patients who experienced a return of spontaneous circulation during transportation to hospital and were found in CPAOA were also excluded from our study. In the end, 225 patients were enrolled in the study. The definition of the terminology used for the patient cohort and the events followed Utstein-style reporting system. The patients’ background is shown in Table 1.

2) Measurement of blood ammonia level

Immediately after patients with CPAOA were transported to the emergency room, femoral arterial puncture was performed to collect blood from all patients, and blood ammonia level was measured using FUJI DRI CHEM 100 (NH3) (FUJI PHOTO FILM CO., LTD.; Japan) and DRI-CHEM SLIDE NH3-WII (FUJIFILM CO., LTD.; Japan).

The measurement is done within 120 sec with the sample volume of 10 µg.

3) Correlation between blood ammonia level and outcome

We examined the correlation among the ammonia level in arterial blood measured immediately after arrival at hospital, the CPA-arrival time and the outcome. We obtained the CPA-arrival time by measuring the time elapsed since CPA was confirmed until the patient was transported to the emergency room, based on the information provided by witnesses and ambulance attendants. We used the Glasgow-Pittsburgh Cerebral Performance Category (CPC) and Overall Performance Category (OPC) to estimate the prognosis of patients. Patients who were categorized as OPC 1 or 2 and CPC 1 or 2 at the time of hospital discharge were classified as the group who made a full recovery (22 patients), and other patients were classified as the group who did not make a full recovery (203 patients).

Table 1. Patient’s background and exclusion criteria.

<table>
<thead>
<tr>
<th>Patients’ background</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients registered: 465</td>
<td></td>
</tr>
<tr>
<td>Number of patients excluded: 240</td>
<td></td>
</tr>
<tr>
<td>Number of patients entered: 225</td>
<td></td>
</tr>
<tr>
<td>Male: 128</td>
<td></td>
</tr>
<tr>
<td>Female: 97</td>
<td></td>
</tr>
<tr>
<td>Mean age: 65.6 ± 12.0 years (24-96 years)</td>
<td></td>
</tr>
<tr>
<td>Number of patients who received bystander CPR: 12 (5.3%)</td>
<td></td>
</tr>
<tr>
<td>Number of patients who received specified medical treatment by emergency paramedics: 155 (68.9%)</td>
<td></td>
</tr>
</tbody>
</table>

Exclusion criteria (240 patients)

- Drug-addicted patients
- Patients who experienced unusual circumstances (e.g. hyperpyrexia, hypothermia or submersion in water)
- Patients with a previous history of diseases such as liver disease that would affect blood ammonia level
- Patients with hemolysis, which would make effective measurement impossible
- Patients whose measured values exceeded the upper limit of the measurement range of the equipment (1,000 µg/dl)
- Patients whose CPA-arrival time exceeded 120 minutes
- Patients who experienced return of spontaneous circulation during transportation to hospital and were found in CPAOA
Blood ammonia level

*Table 2. Breakdown of patients.*

<table>
<thead>
<tr>
<th></th>
<th>Patients with full recovery</th>
<th>Patients without full recovery</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 22</td>
<td>n = 203</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
<td>116</td>
<td>NS</td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td>87</td>
<td>NS</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>65.5 ± 9.2 (48-88)</td>
<td>65.6 ± 12.3 (24-96)</td>
<td>NS</td>
</tr>
<tr>
<td>Number of patients who received bystander CPR</td>
<td>1 (4.5%)</td>
<td>10 (4.9%)</td>
<td>NS</td>
</tr>
<tr>
<td>Number of patients who received specified medical treatment by emergency paramedics*</td>
<td>15 (68.2%)</td>
<td>140 (69.0%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

* 1. airway management with advanced airway devices, 2. peripheral IV line with Lactated Ringer's, and 3. electrical defibrillation

**Fig. 1.** Correlation between CPA-arrival time and blood ammonia level.

\[ y = 249.66 \ln(x) - 670.23 \quad r^2 = 0.8887 \]

X-axis: CPA-arrival time; the time elapsed from the onset of cardiopulmonary arrest to arrival at hospital

Y-axis: Blood ammonia level measured immediately after arrival at hospital

patients) (Table 2). In the treatment process, standard advanced cardiovascular life support (ACLS) was performed to start resuscitation. None of the patients received special treatment such as brain hypothermia.

4) Statistical analysis

To determine the correlation between blood ammonia level and CPA-arrival time, simple linear regression analysis was used to obtain the regression coefficient (r). To determine the correlation between prognosis and blood ammonia level, t-test was used and probability values < 0.05 were considered statistically significant. Data are expressed as mean ± SD.

Results

1) Correlation between CPA-arrival time and blood ammonia level

The blood ammonia level at the time of initial management in patients with CPAOA was 270 ± 140.6 μg/dl. There was a significant positive correlation between CPA-arrival time and blood ammonia level (r = 0.95, p<0.05, Fig. 1).
Kiichi Nagamine

Fig. 2. Comparison of blood ammonia level at time of initial treatment between patients with and without full recovery. Blood ammonia levels of patients who made a full recovery did not exceed 180 µg/dl at the initial management.

2) Correlation between blood ammonia level and outcome

The mean blood ammonia level of patients who made a full recovery was 88.7 ± 49.9 µg/dl (33-180 µg/dl), while that of patients who did not make a full recovery was 289.5 ± 133.6 µg/dl (37-678 µg/dl). The mean blood ammonia level of patients who made a full recovery was significantly lower than that of those who did not.

Discussion

1) Correlation between CPA-arrival time and blood ammonia level

Ishida et al. reported the lactic acid level and time elapsed since CPA as factors that increase the blood ammonia level in patients with CPA, and speculated that the oxygen debt in cells was responsible for the increase in blood ammonia level. Oxygen deprivation induces various types of cell injury including suppression of aerobic respiration involving oxidative phosphorylation with resultant ATP depletion. This triggers activation of anaerobic glycolysis producing ATP and AMP from ADP. AMP is, in turn, metabolized by AMP deaminase releasing ammonia.

We found a significant positive correlation between CPA-arrival time and blood ammonia level. In CPA cases, we must consider whether any pre-hospital care was performed, and if so, to what extent. Currently there is no appropriate index to evaluate the pre-hospital care precisely. Accordingly, it will be impossible to simply estimate the time elapsed since CPA only by the blood ammonia level. However, because there are no other parameters available to predict the time elapsed since CPA, the blood ammonia level can possibly be used as a reference to estimate the time elapsed since CPA and as an index of oxygen debt in cells.

2) Correlation between blood ammonia level and neurological outcome

We examined the correlation between blood ammonia level and outcome. According to Lowenstein’s report on the existence of the purine nucleotide cycle, and in vitro experiments and the study by Ishida et al. on the correlation between CPA and blood ammonia level, the blood ammonia level increases in proportion to the time elapsed since CPA. It has also been reported that prolonged hemorrhagic shock and hypoxemia are associated with an increase in blood ammonia level. Based on these reports, if patients in shock or CPA have a low blood ammonia level at the time of hospital arrival, it can be predicted that...
the time since CPA is relatively short and the degree of organ ischemia caused by cardiac arrest is comparatively slight. The blood ammonia level at the time of hospital arrival is a potential index to predict the degree of organ ischemia. Considering that a significantly lower blood ammonia level was observed in patients who made a full recovery, the blood ammonia level may be used as an index to estimate the degree of ischemia in not only organs, but also in the brain. In fact, regarding the outcome in CPAOA cases, there were extremely few patients who made a full recovery if the blood ammonia level exceeded 180 µg/dl (Fig. 2). We thus consider that a blood ammonia level of 180 µg/dl at the time of initial management can possibly be used as an index in considering brain resuscitation. This does not mean that we should be more reluctant to resuscitate people whose blood ammonia level at the time of initial management is higher than 180 µg/dl, but we propose a low blood ammonia level as one of the criteria to decide whether to perform more aggressive resuscitation and subsequent treatment. This study is limited to witnessed, out-of hospital CPA with presumed cardiac etiology according to the Utstein nomenclature and definition. Accordingly, the result obtained in this study is only applicable to this cohort. Through an accumulation of experience in various causes of CPAOA cases, we need to analyze in detail the correlation between the blood ammonia level at the time of initial management and the outcome, and also study other parameters.

Conclusions

1. In witnessed caidiogenic CPAOA cases, a positive correlation was observed between the time elapsed since CPA and blood ammonia level at the time of initial management.

2. When patients in witnessed caidiogenic CPAOA had a low blood ammonia level at the time of initial management, we could predict that the time elapsed since CPA was comparatively short and the degree of organ ischemia was slight, and a high percentage of the patients made a full recovery.

3. A high percentage of patients in witnessed caidiogenic CPAOA made a full recovery if the blood ammonia level at the time of initial management was lower than 180 µg/dl, which suggested that the blood ammonia level at the time of initial management could possibly be used as an index to predict the outcome of CPAOA cases.

References


原著論文

初療時の血中アンモニア値で来院時心肺停止例の予後推定は可能か？

長嶋 貴一

要旨 近年、来院時心肺停止例（CPAOA）の検出においては心蘇生の成功はもちろんのこと、脳蘇生に重点をおく包括的医療が推進されている。CPAOAでは患者搬入時に十分な発症状況や時間経過が不明なことも多く、ときに心肺機能停止持続時間の把握は重要であるにも関わらず、目指しがあるCPAにおいてできさえも時間経過が曖昧であることが多い。今回、筆者は救急初期において心肺機能停止持続時間が推測可能となりうる客観的指標について検討を行った。対象は1996年4月から2003年3月まで当院に搬入された目撃者のある内因性心原性院外心肺停止例225例（男性128例、女性97例）であり、初療時のアンモニア値と心肺停止確認から、来院時までの時間（CPA-arrival time）の相関について統計学的に検討した。初療時のアンモニア値とCPA-arrival timeとは正の相関を認めた。さらに社会復帰となった群においては非社会復帰群と比較し初療時のアンモニア値が有意に低値であった。また初療時アンモニア値が180 μg/dl以下の症例で多くの社会復帰例を認めた。以上よりアンモニア値が心肺機能停止持続時間や、脳蘇生を含む神経学的予後を推測するうえでの一助となる可能性があることが考えられた。

（日救急医会誌 2005; 16: 283-8）

キーワード：心肺停止、血中アンモニア値、脳蘇生

池友会小文字病院救急救命部
著者連絡先：〒802-0026　北九州市小倉北区大昌1-7-25
原稿受理日：2004年12月7日（04-076）