Clinical Investigation

Disassociation Between Intracranial and Systemic Temperatures as an Early Sign of Brain Death


Departments of *Neurosurgery and †Radiology, The Medical Center of Central Georgia, Mercer University School of Medicine, Macon, Georgia

Summary: Intracranial temperature and its normal variation, as well as its response to various pathologic conditions, has become a critical component of monitoring in neurosurgical intensive care. In a prospective clinical study of 54 neurosurgical patients, intracranial pressure, cerebral perfusion pressure, and intraventricular and systemic temperatures were monitored in a neurosurgical intensive care unit. All of our patients’ intraventricular temperatures were initially higher than their systemic temperatures. In 11 patients, the intraventricular temperature became lower than the systemic temperature, in a median time of 4.43 hours (range, 4.21–5.18 hours), prior to any changes in intracranial and cerebral perfusion pressures. Reversal of the disassociation between intraventricular and systemic temperatures may be an early marker of patients with a poor prognosis.

Key Words: Brain death—Cerebral perfusion pressure—Intracranial pressure—Intraventricular temperature—Systemic temperature.

The relationship between intracranial temperature and cerebral metabolism is well known (1,2). Widespread employment of contemporary neurophysiologic monitoring has provided important information on intracranial temperature, its circadian variation, and its relationship to systemic temperature. Intracranial temperature is slightly elevated in comparison with systemic temperature, and a predictable association exists between these two parameters (3–7). A marked change in the association between these two parameters could be a marker of major neuronal dysfunction.

The purpose of this prospective clinical trial was to study the relationship between intracranial and systemic temperatures and cerebral perfusion pressure (CPP = MAP − ICP, where MAP is mean arterial pressure and ICP is intracranial pressure) in critically ill neurosurgical patients and possibly identify the prognostic value of such a relationship in the patient’s outcome.

MATERIALS AND METHODS

In our institution, the use of fiber-optic ICP monitoring devices coupled with intracranial temperature probes is the standard technique for managing patients with increased ICP. The American Association of Neurological Surgeons and Brain Trauma Foundation criteria for using an ICP monitoring device were used, and 54 patients (38 males and 16 females) were treated at the Neurointensive Care Unit, The Medical Center of Central Georgia (Macon, GA, U.S.A.), over a period of 14 months (January

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All patients were candidates for ICP monitoring, and their underlying pathologic conditions are shown in Table 1. The patients’ ages ranged between 19 and 66 years (mean age, 39.6 years). The mean Glasgow Coma Scale score at arrival to the neurointensive care unit was 5.83 (range, 4–8). A temperature probe coupled with an intraventricular ICP monitor (Camino Laboratories, CA, U.S.A.) was used in all patients. All of these monitors were inserted by the standard sterile technique in the lateral ventricle of the most compromised hemisphere; in circumstances in which diffuse pathologic lesions existed, the monitor was inserted into the lateral ventricle of the nondominant hemisphere. A rectal temperature thermistor probe was used for monitoring rectal temperature (Debusk, Deroyal, IN, U.S.A.). Even though the rectal temperature is not considered as accurate as the tympanic membrane temperature for monitoring the body core temperature, severe head injuries and otorrhea did not allow us to use such methodology. None of the patients received treatment with barbiturates at any point. Arterial blood pressure, heart rate, mechanical ventilator parameters and arterial blood gas levels, intracranial and rectal temperatures, ICP, and CPP were monitored and recorded.

Our prospective clinical trial was designed to examine the relationship between intracranial and systemic temperatures and CPPs in critically ill neurosurgical patients. The inclusion criteria were as follows: age of older than 16 years, admitting Glasgow Coma Scale score after resuscitation of <8, radiographically documented intracranial pathologic lesion (by computed tomography and/or magnetic resonance imaging), hemodynamic stability, and no barbiturate use or hypothermia. The Institutional Review Board approved the study, and a specially designed consent form was obtained from the patients’ relatives or legal representatives for inclusion in the study.

The patients were sedated with an intravenous propofol drip as necessary, and a fentanyl and morphine drip or bolus doses were used for analgesia. None of the patients received treatment with barbiturates at any point. The protocol for ICP management included mild temporary hyperventilation ($P_{CO_2} = 30–32$ mm Hg), bolus doses of corticosteroids with the exception of patients with closed head injuries, bolus intravenous administration of 3% NaCl and/or mannitol and diuretics, and head elevation (15°–30°). No antiinflammatory medications were used at any point during the patients’ stays in the neurointensive care unit. All patients received prophylaxis with intravenous ceftriaxone (1 g every 24 hours), and no changes in their intracranial and rectal temperatures were documented after administration of any of the above-mentioned medications.

We define temperature disassociation as the point at which rectal temperature exceeds intraventricular temperature. Our results are presented as means ± SD or medians (range) as appropriate. Statistical analysis of our results was performed by a two-sided Fisher exact test for comparing the incidence of brain death among patients with (11 patients with 11 deaths) and without (43 patients with no deaths) disassociation between systemic and intraventricular temperatures. A two-sided $P$ value of <.0001 was considered significant.

### RESULTS

In this series, the mean intraventricular temperature was 37.96 ± 1.04°C and the mean rectal temperature was 37.75 ± 0.89°C. The mean monitoring period was 46.22 ± 2.37 hours (range, 8–96 hours). In 43 of our patients, there was a strong association between the intraventricular temperature and the systemic temperature. None of these patients died during their hospitalization in the neurointensive care unit. In 11 patients (8 with closed head injury, 2 with subarachnoid hemorrhage, and 1 with intraparenchymal hemorrhage), there was disassociation between these two parameters. All of these patients died in the neurointensive care unit. In this later cohort, the intraventricular temperature was decreased, while the rectal temperature remained elevated. This disassociation occurred ~265 minutes before any major change in ICP or CPP. The time between the disassociation of intraventricular and systemic temperatures and some major alteration in ICP and CPP measurements, which had been prospectively defined at 40 mm Hg for CPP, is shown in Figure 1. The mean time from the disassociation between rectal and intraventricular temperatures to CPP of <40 mm Hg was 265.64 ± 3.14 minutes. Within 24 hours after the initial temperature disassociation, all patients were judged to be clinically brain dead on the basis of results of a radionuclide cerebral perfusion study and clinical examination by two different physicians who were not involved in the patient’s treatment.

### TABLE 1. Admitting diagnoses in our study

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Closed head injury</td>
<td>32</td>
</tr>
<tr>
<td>Spontaneous subarachnoid hemorrhage</td>
<td>9</td>
</tr>
<tr>
<td>Intraparenchymal hemorrhage</td>
<td>11</td>
</tr>
<tr>
<td>Ischemic infarction</td>
<td>2</td>
</tr>
</tbody>
</table>

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DISASSOCIATION BETWEEN INTRACRANIAL AND SYSTEMIC TEMPERATURES

The present extensive use of hypothermia protocols in treating patients with closed head injuries has emphasized the importance of understanding the nuances of the relationship between intracranial and systemic temperatures (2–6,8–11). Several studies have reported a well-established circadian variation as well as a relatively higher intracranial temperature in comparison with systemic temperature (2,5,8). This temperature difference appears constant even in the presence of significant head injury, subarachnoid hemorrhage, or ischemic infarction (3,4,10–12).

If, however, the normal physiologic relationship is reversed, it may be evidence of a major, life-terminating event (8,11). Confirming findings of earlier reports (7,9), all 11 patients in our study population in whom such a disassociation occurred died. In this study, the observation regarding the time in which this temperature disassociation occurred is our contribution to this growing body of information. We found that this disjunction occurs several hours before any other change of routinely monitored neurophysiologic parameters. The clinical utility of such an early marker may well be substantial. Such early information may provide clinicians with an opportunity for early intervention or help in establishing a poor prognosis.

The physiologic mechanism by which this temperature disassociation occurs is unclear. One possible theory explaining this observation involves the early depletion of stored interleukin-1β (3). Such depletion might cause the brain parenchyma to be noncompliant to any metabolic rate changes in contrast to the rest of the body. Unfortunately, relatively little experimental evidence exists to support this theory. Likewise, the theory of the hypothalamic–pituitary paralysis syndrome could be the underlying explanatory mechanism of this temperature disassociation (13). However, the relatively long time before the systemic temperature fell in our patient cohort militates against this theory. A third theory argues that the decreased metabolism of the brain parenchyma, especially diminished glycolysis, in combination with the well-known susceptibility of neuronal tissue to disturbances in the supply of energy might be the underlying pathophysiologic mechanism of the observed temperature disjunction (4). Cerebral temperature is diminished not only by diminished cerebral metabolism but also by a concomitant decrease in the regional cerebral blood flow.

Further clinical studies are needed to test the replicability of our observations. Multiparameter neurophysiologic monitoring and modern functional imaging techniques (functional magnetic resonance imaging and proton magnetic resonance spectroscopy) (14) might lend to themselves to explaining our observations.

REFERENCES