

Chapter 14. The role of temperature control following severe pediatric traumatic brain injury

I. RECOMMENDATIONS

A. Standards. There are insufficient data to support a treatment standard for this topic.

B. Guidelines. There are insufficient data to support a treatment guideline for this topic.

C. Options. Extrapolated from the adult data, hyperthermia should be avoided in children with severe traumatic brain injury (TBI).

Despite the lack of clinical data in children, hypothermia may be considered in the setting of refractory intracranial hypertension.

II. OVERVIEW

Posttraumatic hyperthermia is classified as a core body temperature $>38.5^{\circ}\text{C}$, whereas hypothermia is classified as temperature $<35^{\circ}\text{C}$. At present, the data in the basic science literature on adult animal models indicate that hyperthermia contributes to greater posttraumatic damage by increasing the acute pathophysiologic response following injury, through a multitude of mechanisms. The rationale for avoidance of hyperthermia and for use of therapeutic hypothermia is to lessen the effect that temperature may have on these mechanisms of secondary injury by decreasing cerebral metabolism, inflammation, lipid peroxidation, excitotoxicity, cell death, and acute seizures. Based on experimental studies in animal models and clinical studies in adults (1) in which hyperthermia was correlated with poor outcome, it has been recommended that hyperthermia following TBI in children should be avoided. There also may be a role for therapeutic hypothermia in reducing intracranial hypertension in severe pediatric TBI. Evidence in both the pediatric and adult literature is evaluated.

III. PROCESS

We searched Medline and Healthstar from 1966 to 2001 by using the search strategy for this question (see Appendix A) and supplemented the results with literature recommended by peers or identified from reference lists. Of 28 potentially relevant studies, two were used as evidence for this question (Table 1).

IV. SCIENTIFIC FOUNDATION

There was one retrospective study from the 1950s by Hendrick (2) indicating that moderate hypothermia ($32\text{--}33^{\circ}\text{C}$) was effective in the treatment of children following severe TBI. This initial investigation was of 18 children with severe TBI (Glasgow Coma Scale score = 4) who presented with decerebrate posturing. There were ten long-term survivors with only one severely impaired. Hendrick concluded that systemic cooling following injury was a "useful adjunct" and could improve outcome in children after TBI. Since that time, there has been a lack of subsequent randomized or other trials to further evaluate this preliminary finding.

In 1973, Gruszhiwicz et al. (3) conducted a prospective, randomized study of 20 children <16 yrs of age who suffered a severe TBI, presenting with a clinical exam of decerebrate rigidity (Glasgow Coma Scale = 4). The children were randomized to one of two groups: hypothermia vs. hypothermia combined with dexamethasone (2 mg twice daily). There was no normothermic group. Nineteen of these 20 patients were hyperthermic at presentation and suffered various mechanisms of injury. Outcome was determined by duration of coma and time until "recovery," although the length of follow-up was <7 months in all instances. Although no statistical analysis was performed, the authors described similar duration of coma and neurologic recovery for the two groups. Surprisingly, 19 patients survived.

Since 1973, no further studies have evaluated the specific efficacy of hypothermia following head injury from which results could be gleaned for pediatric patients. No other studies compared temperature control (e.g., hypothermia with normothermia or hyperthermia) as it relates to outcome. In all other studies, either only adults were studied, or results for children and adults were so confounded that no conclusions can be drawn specifically for pediatric cases. Thus, only two studies met the criteria for inclusion in this chapter.

Key Elements from the Adult Guidelines Relevant to Pediatric TBI

There was no section on temperature regulation in the adult guidelines (4) and there has not been an evidence report on this topic in adults. However, a number of studies have assessed the efficacy of therapeutic hypothermia following severe TBI in adults.

The induction of hypothermia clinically to treat patients with TBI was originally reported >50 yrs ago (2), but use of therapeutic hypothermia did not become established because early studies lacked modern scientific methods and adequate outcome measures. Renewed interest in moderate hypothermia after severe TBI did not occur until the early 1990s, when preliminary data from single-center clinical trials were published in adults. Shiozaki et al. (5) used therapeutic moderate hypothermia to 34°C for ≥ 2 days in a group of severe TBI patients who had intracranial hypertension and were refractory to barbiturate therapy. They found an improvement in cerebral perfusion pressure, compared with normothermic patients, which was sustained during and after rewarming. Marion et al. (6) reported that moderate hypothermia in adult patients with severe TBI reduced intracranial pressure and showed a trend

Table 1. Evidence table

Reference	Description of Study	Data Class	Conclusion
Gruszhiewicz et al. (3), 1973	Uncontrolled case series of 20 patients treated with hypothermia vs. hypothermia plus glucocorticoids/steroids (dexamethasone, 2 mg twice daily). Outcome was determined by duration of coma and time to recovery. No long-term outcome cited.	III	No difference in outcome with the addition of steroids to hypothermia. No comparisons or analysis with relation to controlled or normothermic patients.
Hendrick (2), 1959	Uncontrolled retrospective case series of 18 children with a severe TBI who presented with decerebrate posturing and were cooled to 32–33°C.	III	Hypothermia is a useful adjunct with the potential for improved outcome in children with severe TBI.

TBI, traumatic brain injury.

toward improved outcome at both 3 and 6 months after injury. Clifton et al. (7) cooled patients to 32–33°C after severe TBI for 48 hrs and similarly reported a trend toward improved outcome. Marion et al. (8) later demonstrated that moderate hypothermia for 24 hrs specifically hastened neurologic recovery in patients who presented with a Glasgow Coma Scale score of 5–7 and that the treated patients tended to have improved overall outcome. Although these single-center studies provided evidence of efficacy, Clifton et al. (9) more recently reported lack of effectiveness in adults in a multiple-center clinical trial of moderate hypothermia following severe TBI. Despite failure to replicate the earlier single-center findings in the larger multiple-center trial, there was a suggestion of improved outcome in those patients who presented as hypothermic and were then kept cool and in the younger age groups within the study (<40 yrs of age). Children (≤16 yrs) were not included in the Clifton et al. (9) study.

V. SUMMARY

There is presently no published support for temperature control or therapeutic

hypothermia in pediatric TBI. Based on studies in adults, therapeutic options include the avoidance of hyperthermia and the consideration of hypothermia for refractory intracranial hypertension.

VI. KEY ISSUES FOR FUTURE INVESTIGATION

- The effect of temperature control on outcome following pediatric TBI needs to be studied.
- The role of therapeutic hypothermia, both as a neuroprotective measure and for refractory intracranial hypertension, deserves investigation in pediatric TBI. Direct comparisons to other therapies should be conducted.
- Evaluations of therapeutic hypothermia should be age stratified. Additional documentation of the effect of hypothermia and temperature regulation in studies restricted to infants and children is needed.
- In addition, studies will be needed to better understand the effect of temperature regulation on other physiologic variables (e.g., intracranial pressure, cerebral perfusion pressure, cardiac

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output, and immune status) and how this might affect long-term outcome.

REFERENCES

1. Jones PA, Andrews PJ, Midgley S, et al: Measuring the burden of secondary insults in head injured patients during intensive care. *J Neurosurg Anesthesiol* 1994; 6:4–14
2. Hendrick EB: The use of hypothermia in severe head injuries in childhood. *AMA Arch Surg* 1959; 17–20
3. Gruszhiewicz J, Doron Y, Peyser E: Recovery from severe craniocerebral injury with brain stem lesions in childhood. *Surg Neurol* 1973; 1:197–201
4. Bullock R, Chesnut RM, Clifton G, et al: Guidelines for the management of severe traumatic brain injury. *J Neurotrauma* 2000; 17: 451–553
5. Shiozaki T, Hisashi S, Taneda M, et al: Effect of mild hypothermia on uncontrollable intracranial hypertension after severe head injury. *J Neurosurg* 1993; 79:363–368
6. Marion DW, Obrist WD, Carlier PM, et al: The use of moderate therapeutic hypothermia for patients with severe head injuries: A preliminary report. *J Neurosurg* 1993; 79:354–362
7. Clifton GL, Allen S, Barrodale P, et al: A phase II study of moderate hypothermia in severe brain injury. *J Neurotrauma* 1993; 10: 263–271
8. Marion DW, Penrod LE, Kelsey SF, et al: Treatment of traumatic brain injury with moderate hypothermia. *New Engl J Med* 1997; 336:540–546
9. Clifton GL, Miller ER, Choi SC, et al: Lack of effect of induction of hypothermia after acute brain injury. *New Engl J Med* 2001; 344: 556–563

See APPENDIX on Next Page

APPENDIX: LITERATURE SEARCH STRATEGIES

SEARCHED MEDLINE AND HEALTHSTAR FROM 1966 TO 2001

Chapter 14. Temperature Control

1. exp craniocerebral trauma/
2. head injur\$.tw.
3. brain injur\$.tw.
4. 1 or 2 or 3
5. hypothermia, induced/
6. 4 and 5
7. limit 6 to (newborn infant <birth to 1 month> or infant <1 to 23 months> or preschool child <2 to 5 years> or child <6 to 12 years> or adolescence <13 to 18 years>)