Hypothermia in the treatment of refractory intracranial hypertension in patients with severe SAH, cases associated with secondary vasospasms

Hipotermia no tratamento de hipertensão intracraniana refratária em pacientes com HSA grave, casos associados a vasoespasmo secundário

Bernardo Lembo Conde de Paiva, MD
Raphael Simões, MD
Thiago Coelho, MD
Renata Simm MD
Paulo Henrique Pires de Aguiar MD, PhD

ABSTRACT

Subarachnoid hemorrhage (SAH) is a severe disease in which 10% of patients may present sudden death before arriving at the hospital. Patients are exposed to a high risk of secondary complications including vasospasm. For refractory vasospasm and essentially for ICP control, hypothermia may be employed for the treatment.

We aimed to evaluate the influence of therapeutic hypothermia in mortality rates of patients with severe SAH with high intracranial pressure despite best clinical treatment. Temperatures were reduced using mattress for a target temperature of 33-35o C.

Five patients were included. Two patients were admitted with a Hunt-Hess scale grade of 2, two of 3 and one of 4. The mean length of therapeutic hypothermia was 7.2 days. Two patients survived with a Rankin scale of 0, and three died.

In our observational study we observed a 180 days mortality rate of 40% that increased to 60% in six month analysis. Recent trials describe a mortality rate of 90% in patients with SAH and refractory ICH11. We believe hypothermia may be the best method to be employed in this clinical situation.

Keywords: Coma, Modified Rankin Scale, Humans, Induced Hypothermia, Intracranial Aneurysm, Intracranial Hypertension, Subarachnoid Hemorrhage, Treatment Outcome, Intracranial Vasospasm.

RESUMO

A hemorragia subaracnóide (HAS) é uma doença grave na qual 10% dos pacientes podem apresentar morte súbita antes mesmo de chegar ao hospital. Os pacientes apresentam um risco elevado de complicações secundárias, incluindo o vasoespasmo. Para vasoespasmo o refatário e, essencialmente, para o controle de PIC, a hipotermia pode ser utilizada de forma terapêutica.

Nosso objetivo foi avaliar a influência da hipotermia terapêutica nas taxas de mortalidade de pacientes com HSA grave e com pressão intracraniana elevada, apesar de melhor tratamento clínico implementado previamente. As temperaturas foram reduzidas utilizando colchão térmico para uma temperatura alvo de 33-35o C.

Cinco pacientes foram incluídos. Dois pacientes foram admitidos com um Hunt- Hess de 2, dois com Hunt Hess de 3 e um com Hunt Hess de 4. O tempo médio de hipotermia terapêutica foi de 7,2 dias. Dois pacientes sobreviveram com uma escala de Rankin de 0, e três faleceram.

Em nosso estudo observacional foi observada uma taxa de mortalidade de 180 dias de 40% , que aumentou para 60% em análise de seis meses. Estudos recentes descrevem uma taxa de mortalidade de 90% em pacientes com HAS com Hipertensão intracraniana refratária. Acreditamos que a hipotermia pode seja o melhor método para ser utilizado na presente situação clínica.

Palavras Chave: Coma, Escala de Rankin Modificada, humanos, hipotermia Induzida, Aneurisma intracraniano, Hipertensão Intracraniana, Hemorragia Subaracnóide, Resultado de Tratamento, Vasoespasmo intracraniano

Neurointensive Care Unit, Department of Neurology, Santa Paula Hospital, São Paulo, Brazil.
Subarachnoid hemorrhage (SAH) is a disease characterized by the sudden onset of a headache and signs of meningeal irritation. Common causes are; the rupture of aneurysms and arteriovenous malformations (AVM). There are some cases in which no aneurysms or AVM are identified by cerebral angiography, this may occur due to perimesencephalic bleeding. 10% of patients who suffer SAH present sudden death before arriving at the hospital due to ventricular bleeding and pulmonary edema. Amongst the survivors; around 20-40% of large volumes SAH, present comatose (Hunt-Hess grade IV and V) on arrival in the emergency room, with a mortality rate of 50% in the first three months, and 20% remain dependent for their daily activities.

The main factors related to outcome are age, level of consciousness at admission and volume of bleeding. 60 year old patients and older, with comatose state at hospital admission and high volume bleeding, have a higher mortality rates. Patients under 60 years old have a more favorable outcome in comparison to patients over 60 years old, which have only a 15.4% mortality. An Italian study among 350 patients showed that age above 60 is an independent predictor of poor prognosis in a logistic regression analysis.

Patients who survive the first bleeding are exposed to a high risk of secondary complications that may appear at an early stage, including hydrocephalus, reactional brain edema, vasospasm and recurrence of bleeding with intra-cerebral and ventricular haemorrhage which may lead to an increase in intracranial pressure (ICP). The recurrence of bleeding occurs in 30-40% of cases in the first month and is most likely to occur in the first 24-48hrs if the aneurysm is not occluded.

Vasospasm is a common complication which may occur in 30-70% of cases from the 4th to 12th day. Nevertheless it is only symptomatic in 20-30% of the cases. Symptomatic severe vasospasm may lead to additional worsening due to secondary neurological lesions leading to ischemic damage and increased intracranial pressure (ICP).

The essential treatment for SAH consists in the occlusion of the aneurysm as early as possible by surgical clipping or embolization. This stops the bleeding and enables a more aggressive management of complications. Although, there is no evidence, from clinical trials, that this improves patients' survival rates (AHA Guideline 2009). For the vasospasm treatment, the 3 H therapy (Hyperhydration, Hypertension, and Hemodilution) may be employed, but essentially the ICP control is the major goal of this treatment. In critically ill patients, deep sedation, orotracheal intubation and hypothermia may be recommended aiming to reduce brain's metabolism. Multimodal monitoring in these patients may detect, in advance, secondary lesions in order to avoid a worsening of the primary injury.

Fever may occur in more than a half of SAH patients and is mostly associated with infections, such as pneumonia and meningitis, but may not be associated in 20% of cases being caused by higher volumes of bleeding. Fever is an independent predictor of unfavorable outcome and its control should be strongly recommended.

Hypothermia has become a promising therapeutic option for SAH due to its neuroprotective effects. It was employed for the management of refractory vasospasm, secondary ischemic lesions and intracranial hypertension (ICH) not responsive to standard treatment, in which mortality rates and disability are 95 and 100% respectively. Hypothermia to SAH was studied using systemic techniques with the use of cooling blankets, ice packs or with an intravascular device as well.

**Methods**

We aimed to evaluate the influence of therapeutic hypothermia in mortality rates of patients with severe SAH, associated with secondary vasospasm which had become comatose. Hypothermia was induced in patients with refractory high intracranial pressure (over 20 mmHg) despite best clinical treatment to control intracranial pressure (deep sedation, normocarbia and the use of manitol or hypertonic saline). The criteria chosen to withdraw therapeutic hypothermia were the stabilization of Intracranial Pressure (ICP) values, as well as, head Computed Tomography (hCT) images improvement. Temperatures were reduced using a systemic method with the use of cold water circulating mattress for a target temperature...
reduction of 33-35°C. All patients were closely monitored for the early detection of infectious, electrolytes and coagulation disorders during the ICU hospitalization. The method we used for early detection of infectious states was Reactive C Protein (RCP), hence fever and leucocytes count are difficult to interpret when patients are hypothermic.

RESULTS

At Santa Paula Hospital’s Neurocritical care unit, in a period of 18 months, 5 patients, 4 females and only one male, with a median age of 34 years old and a length of stay of 74.4 days. Patient number 5 had serious infectious complications which lead to a 230 days of hospitalization. All patients had SAH with secondary vasoconstriction and refractory ICH in which therapeutic hypothermia was necessary to be employed due to its severity. Three were admitted with a Fischer scale of IV (F IV), one with III (F III) and the last of I (F I). Hunt-Hess scale was more heterogeneous; two with a grade of 2 (HH 2), two of 3 (HH 3) and one of 4 (HH 4).

All aneurysmatic arteries were occluded by embolization or clipping. The mean length of therapeutic hypothermia was 7.2 days, being effective to control refractory ICH in 3 out of 5 patients. Two patients survived after 180 days with a Rankin scale of 0. One (patient number 5) was discharged from NICU with a Rankin scale of 3 and came back to NICU and thereafter died of an infectious disease after 230 days of hospitalization. No serious (grade III or IV) complications directly related to this method were observed in this study. The two patients in which ICP was not controlled with hypothermia died due to brain death.

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
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<td>Fisher (F) And Hunt-Hess (Hh) Scales On Admission</td>
<td>F IV/HH 3</td>
<td>F III/HH 4</td>
<td>F IV/HH 3</td>
<td>F IV/HH 2</td>
<td>F I/HH 2</td>
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<td>22</td>
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<td>230</td>
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<td>LICA*</td>
<td>Blister An. Of P2-P3</td>
<td>LICA*</td>
<td>Basilar Artery</td>
<td>ACOA*</td>
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<td>endovascular coiling</td>
<td>neurosurgical clipping</td>
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<td>Brain Death (Due To Refractory Intracranial Hypertension)</td>
<td>Not Applicable</td>
<td>Late Sepsis</td>
</tr>
</tbody>
</table>

* LICA - left internal carotid artery, ¥ACOA - anterior communicating artery.

DISCUSSION

In our observational study we observed a 180 days mortality rate of 40% that increased to 60% in six month analysis. Recent trials describe a mortality rate of 90% in patients with SAH and refractory ICH11. Standard treatments, such as deep sedation, normocapnia and hypertonic saline or mannitol, may not be enough to control the ICH. Hypothermia is currently the method of choice for ICH control, when these methods are no longer effective.
The complications did not differ from literature, with the presence of infection, ileus, gastroparesis, vomiting, hemodynamic instability, and platelet dysfunction.

The reduced number of patients is a limitation of our study, as well as the allocation method. There was no randomization or control group, which did not allow us to come to conclusions with statistical validation.

We believe hypothermia may be the best method to be employed in this clinical situation and further clinical trials with a larger number of patients and appropriate methods for statistical evaluation could determine the actual benefits of this method to be employed for those so severe patients.

**CONCLUSION**

In conclusion, hypothermia is a very good method of neuroprotection and remaining doubts need to be answered in order to let it be widely used on neurocritical patients.

**DISCLOSURE**

The authors have no personal, financial or institutional interest in any of the drugs, materials, or devices described in this article.

**REFERENCES**


CORRESPONDING AUTHOR

Bernardo Lembo Conde de Paiva, MD
Neurointensive Care Unit, Department of Neurology,
Santa Paula Hospital, São Paulo, Brazil.
neuro@drbernardolembo.com.br

CORRIGENDA

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“1Department of Neurology and Neurosurgery – UNIFESP. São Paulo, Brazil.
2Neuropathologist – Department of Pathology – UNIFESP. São Paulo, Brazil.”

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