



Review Article

Systematic review exploring the effect of therapeutic hypothermia on patients with intracranial hypertension

Kamlesh Thakur^{1,2}, Haneet Kaur^{1,3}, Manju Dhandapani⁴, Teenu Xavier⁵, Ganesan Srinivasan⁶, Laskmanan Gopichandran⁷, Sivashanmugam Dhandapani⁸

¹Master neurosciences, National Institute of Nursing Education, PGIMER, Chandigarh, ²Department of Nursing, Chitkara School of Health Sciences, Chitkara University Punjab, Rajpura, Punjab, India, ³Nursing officer, AIIMS, Patna, Bihar, ⁴Lecturer, National Institute of Nursing Education, PGIMER, Chandigarh, India, ⁵PhD candidate, University of Cincinnati, Cincinnati, Ohio, United States, ⁶Clinical Instructor, KGMU College of Nursing, Lucknow, Uttar Pradesh, ⁷Associate Professor, College of Nursing, AIIMS, New Delhi, ⁸Professor, Department of Neurosurgery, PGIMER, Chandigarh, India.

E-mail: Kamlesh Thakur - kamleshthakur870@gmail.com; Haneet Kaur - haneetkaur1602@gmail.com; *Manju Dhandapani - manjuseban@gmail.com; Teenu Xavier - teenu12xavier@gmail.com; Ganesan Srinivasan - sriniaims@gmail.com; Laskmanan Gopichandran - pravigopi@gmail.com; Sivashanmugam Dhandapani - ssdhandu@gmail.com



*Corresponding author:

Manju Dhandapani,
Lecturer, National Institute of
Nursing Education, PGIMER,
Chandigarh, India.

manjuseban@gmail.com

Received : 21 February 2022

Accepted : 13 April 2022

Published : 03 June 2022

DOI

10.25259/SNI_194_2022

Quick Response Code:



ABSTRACT

Background: Intracranial hypertension is found in patients with various neurological and neurosurgical conditions such as subarachnoid hemorrhage (more than 50% of the patients have intracranial pressure > 20 mmHg at some point during their hospital stay), traumatic brain injury, and stroke. Various modalities are used to control intracranial hypertension, therapeutic hypothermia is one of them. This systematic review aims to assess the efficacy of therapeutic hypothermia in controlling intracranial hypertension in an adult patient.

Methods: A systematic review of the literature published between one patient 1990 and 2020 was conducted. Four databases were searched including CINAHL, PubMed, the Cochrane Library, and EMBASE using keywords traumatic brain injury, intracranial pressure, randomized and controlled trials, and the effect of therapeutic hypothermia on intracranial hypertension.

Results: All of the studies included in this review were randomized controlled trials. Most of the studies provided their sample demographics. Sample sizes ranged from 14 to 501. Of the 12 studies, five of them were from the United Kingdom, three of them were from China, two from North America, one from India, and one from Japan.

Conclusion: Treating intracranial hypertension with therapeutic hypothermia may be beneficial according to a few studies but it is also associated with many adverse effects. Both the groups suffered from adverse events which were higher in the hypothermic group. However, these adverse events can be managed in any health-care setting. To treat the patients with therapeutic hypothermia, one (the managing team) should be competent enough to manage the adverse effects.

Keywords: Therapeutic hypothermia, Intracranial hypertension, Raised intracranial pressure

INTRODUCTION

Controlling intracranial hypertension (IHT) has gotten the attention of everyone working in neurosciences.^[32] The normal intracranial pressure (ICP) is the pressure in the cranial vault which is created by three components; brain, cerebrospinal fluid, and blood. Normally, the pressure within the cranium is <20 mmHg. The Monro-Kellie Doctrine states that the contents of the cranium are in a state of constant volume, that is, the volume of brain tissue, cerebrospinal fluid, and blood are fixed, and to compensate for any increase in one component,

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

©2022 Published by Scientific Scholar on behalf of Surgical Neurology International

the other components have to decrease its volume. An increase in these components will lead to decreased blood supply to the brain and herniation of the brain tissues in later stages.^[22] IHT is found in patients with various neurological and neurosurgical conditions such as subarachnoid hemorrhage (more than 50% of the patients have ICP > 20 mmHg at some point during their hospital stay), Traumatic Brain Injury, stroke, etc.^[18] The mechanism of IHT is different in various conditions, for example, in brain tumor, it is due to an increase in neoplastic tissue,^[14] in subarachnoid hemorrhage, it is due to pooled blood inside the brain due to ruptured blood vessels,^[1,11,19] in traumatic brain injury, it is because of brain tissue injury and inflammatory process,^[12,13] and in ischemic stroke, it is due to cerebral edema after the inflammatory process. ICP within the normal range in neurosciences patients is considered a major factor toward better recovery and with the increase in the ICP more than 20 mmHg mortality rate increases.^[24] Among various methods used for controlling IHT, the effectiveness of therapeutic hypothermia has been investigated by various researchers^[15,16] and has been empirically used to treat IHT.^[24]

Therapeutic hypothermia is defined as controlled induced hypothermia in which the potentially deleterious effects such as shivering are being controlled or suppressed.^[32] A systematic review by Andrew *et al.* in 2018 on the effectiveness of hypothermia in reducing IHT or improving ICP in TBI patients found that low-quality studies reported a reduction in mortality rate.^[4] Hence, there is a need for high-quality evidence in its favor. Yet, considering it reported previous benefits, it has been randomly used in neurological and neurosurgical patients. Although its beneficial effects are reported by various studies, many of them^[25-29,31,34] have also reported a variety of adverse effects of therapeutic hypothermia, which are not given much emphasis. Researchers have also enlisted the side effects of rewarming such as abrupt elevation in the level of ICP and delayed extubation of the patient.^[21] Hence, the purpose of this systematic review was to describe and synthesize the existing literature on adverse effects of the therapeutic hypothermia on patients with IHT.

MATERIALS AND METHODS

This systematic review is conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) declaration.

Search strategy

We searched PubMed, CINAHL, the Cochrane Library, and EMBASE using the following keywords: traumatic brain injury, ICP, randomized and controlled trials, and the effect

of therapeutic hypothermia on IHT. We included articles published from January 1990 to July 2020. The search terms were derived from a preliminary review. The search was modified and tailored for searches conducted across the databases to account for differences in syntax. We tracked the search process with PRISMA flow diagram [Figure 1]. In [Table 1], we have provided summaries of the articles meeting our inclusion criteria.

Inclusion and exclusion criteria for selection of randomized and controlled trial

Studies had to meet the following inclusion criteria to be included in the review: (1) randomized and controlled trials on patients with increased ICP, (2) use of therapeutic hypothermia as an intervention to control or reduce increased ICP versus the standardized patient care. Therapeutic hypothermia is defined as any intervention to reduce core body temperature to below 36°C.^[3] (3) Three studies that enrolled adult patients as participants, (4) participants must have sustained increased ICP >20 mmHg, and (5) articles written in and accessible in English. We excluded from our review dissertations, books, abstracts, ongoing unpublished studies, systematic and integrative reviews, and conference proceedings.

Bias

The risk of bias was assessed through the Cochrane Collaboration's tool during the data extraction process. The areas assessed include selection, performance, detection, attrition, reporting, other biases such as small sample size, ethical considerations, funding included, or not [Table 2]. The academic bias was also present because we had included RCTs done by the same author. The selected RCTs were arranged into the domain-based assessment of the risk of bias [Figure 2].

Data management and extraction

For each study, two team members (H.K. and K.T.) completed the data screening and data extraction (H.K., K.T., and M.D.) using a predeveloped form and were exported into Microsoft Word, and the consensus was taken by M.D. and T.X. [Table 1] summarizes the information extracted from each study. The assessment of the risk of bias and quality was done by M.D. and L.G., and the consensus was taken by S.G. The review was done based on PRISMA guidelines in all three stages. First, the duplicates were removed from the databases; then, the abstract and titles were screened against the predetermined inclusion and exclusion criteria. Second, the abstracts were read against the set criteria. Third, all the articles were thoroughly studied and the final decision based on inclusion and exclusion criteria was taken. Other team

members verified all extracted data, and disagreements were resolved through discussion with other team members when consensus could not be reached.

RESULTS

All of the studies included in this review were randomized controlled trials. The most of the studies provided their sample demographics. Sample sizes ranged from 14 to 501. Of the 12 studies, five of them were from the United Kingdom, three of them were from China, two from North America, one from India, and one from Japan.

Interventions

Hypothermia was applied immediately after injury in TBI patients; right after decompressive craniotomy in a few and just before applying the first clip in patients with an aneurysm. The treatment with hypothermia was given for 48 h in maximum in the experimental group and for 72 h in one of the groups. The methods used for cooling were water circulating cooling blankets,^[15] infusion of I.V refrigerated NaCl 20–30 ml/kg of body weight,^[16] cooling catheter inserted in the femoral vein to the inferior vena cava.^[16] In the studies which used hypothermia intraoperatively: OT temperature was reduced to 18–20°C; polar air machine was set at 10°C, and cold NS and RL were infused.^[21,33] In one of the studies, internal and external techniques were used for cooling, but it is not mentioned which techniques were used.^[23] In the majority of the studies, the temperature was brought down to 32–35°C except in one study^[33] in which the body temperature was kept at 33°C. Then, the rewarming was introduced after 48 h with 0.25°C/h (until ICP was 20 mmHg or less). In the control group, the standard care or

usual care was given to the patients but without therapeutic hypothermia. In one of the studies, 45 patients were randomized into Group A, Group B, and Group C. Group A patients received ICP and cerebral perfusion pressure (CPP)-guided management only. Group B patients received mild hypothermia along with ICP and CPP-guided management. Group C patients received mild hypothermia and PO2 management ICP and CPP-guided management.^[20]

Comparators

We included comparator interventions which are defined as the usual or the standard care. Routine care is the standard medical care received in the hospitals or ICU by patients to reduce the ICP and maintain the CPP with other supportive measures such as monitoring the vital signs and ICP/ CPP, maintaining normal body temperature by either ice bags if the temperature was <38.5°C, and administering the antipyretics if temperature >38.5°C, administering prophylactic antibiotics, sedatives, etc. Studies in patients with TBI, the routine care consisted of “guidelines for the management of severe TBI” given by the American Brain Injury Association which included measures to manage ICP and CPP.

Outcome

We have included 12 studies in our review, out of which six studies concluded positive outcomes for patients with raised ICP,^[20,21,26,27,29,31] two reported negative outcomes for patients,^[3,5,23] and four were showing no difference.^[2,6,33] Between both groups, one of which showed more complications in the experimental group.^[23] In one study, there was a decrease in ICP and raised CPP assessed^[31] 1–7 days after randomization, there was no significant difference between both the groups in neurological outcomes in 6–48 months assessment. One study showed improvement in the neurological outcomes in 6 months assessment; on the other hand, one study reported no difference in the outcomes and one concluded serious complication in the experimental group. In five studies, the time of follow-up is not mentioned. In one of the RCTs, the mortality and the rate of complications were higher in the experimental group.

Along with the beneficial effects, there are side effects of hypothermia mentioned in the nine studies in the present review. The most common adverse event was an infection, particularly pneumonia reported in three and bacteremia and other infection in two studies. Other reported adverse effects were delayed extubation, shivering, nausea/vomiting, electrolyte disorders such as hyperkalemia and hyponatremia, GI complications such as bleeding, gastric retention, and stress hyperglycemia in one study (once in different studies). Cardiovascular events such as bradycardia and arrhythmias

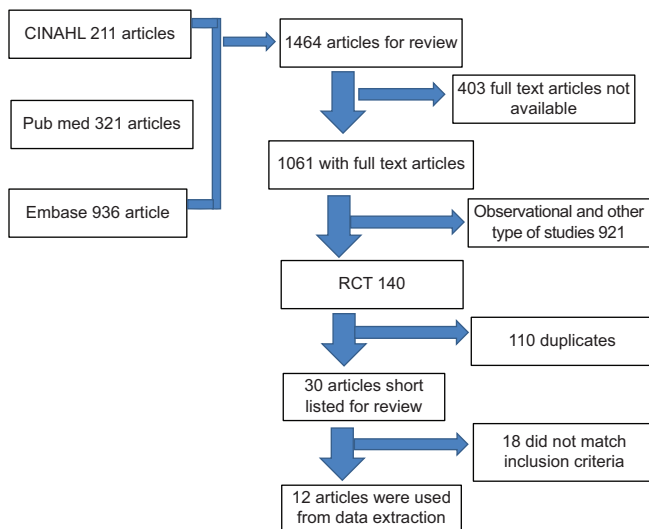


Figure 1: PRISMA flow diagram for study selection.

Title	Author Year Country	Intervention	Time of starting hypothermia	Duration of intervention	Outcome variables	Results	Adverse effects	Rewarming
Therapeutic hypothermia to reduce intracranial pressure after traumatic brain injury. The Eurotherm3235 RTC ^[3]	Andrews et al., 2018, UK	EXPERIMENTAL-195 Hypothermia CONTROL-192 Standard care	Immediately after TBI	48 h	Mortality rate and functional recovery	Reduced ICP, high mortality, and poor functional recovery in the experimental group	Not mentioned	Effects of rewarming not mentioned
Mild induced hypothermia for patients with severe TBI after decompressive craniectomy ^[31]	Tang et al., 2016, China	EXPERIMENTAL-30 Hypothermia (32–35°C + standard care) CONTROL-30 Standard care	Not specified	48 h	ICP, CPP, GOS-E	Lower ICP and high CPP and low mortality in the experimental group. No significant difference between both groups in neurological outcomes	Higher incidence of pulmonary infections, hyperkalemia, and hypernatremia in the experimental group	Effects of rewarming not mentioned
Hypothermia for intracranial hypertension after traumatic brain injury ^[5]	Andrews, 2015, UK	Hypothermia-195 Standard care-192	Not specified	48 h	GOS-E	Serious adverse events were reported more in the experimental group	Pneumonia (3–7 days), unfavorable outcomes 6 months	Effects of rewarming not mentioned
Early hypothermia induction in patients with severe brain injury. ^[9]	Clifton, 2011, North America	EXPERIMENTAL-52 hypothermia CONTROL-45 standard care	Not specified	48 h	GOS-E, complication	No significant difference, the experimental group had more complications.	Neurological complications, infectious, cardiovascular, bleeding, miscellaneous complications	Not mentioned
Applying cerebral hypothermia and brain oxygen monitoring in treating severe traumatic brain injury ^[20]	Lee et al., 2010, China	Group A-16 guided management Group B-15 hypothermia Group C-14 hypothermia + CPP monitoring	Immediately after surgery	Not mentioned	Length of ICU stay, ICP, Po2, GOS-E, mortality, and complications	Low ICP, raise in P _a O ₂ longer hospital stays higher hospital cost, 60% favorable outcomes, and low mortality in the hypothermic group.	High, Cpk higher in Group C group. Pulmonary infection peptic ulcer and leukocytopenia was higher in the hypothermic group (not severe)	Pulmonary infection peptic ulcer and leukocytopenia was higher in the hypothermic group (not severe)

(Contd...)

Table 1: (Continued).

Title	Author Year Country	Intervention	Time of starting hypothermia	Duration of intervention	Outcome variables	Results	Adverse effects	Rewarming
Mortality risk stratification after traumatic brain injury and hazard of death with titrated hypothermia ^[2]	Andrews et al., 2017, U.K.	Experimental group-257 hypothermia Control group-129 standard care	Not clear	48 h	GOS-E, 6 months GOSE mortality	No significant difference found	Not mentioned	Not mentioned
Intraoperative hypothermia for brain protection during intracranial aneurysm surgery ^[10]	Chouhan, 2016, India	Experimental-24 mild hypothermia Control group-23	Soon after aneurysm clipping	Not clear	Neurological complications and recovery	Better neurological recovery in the experimental group	Late extubation, shivering, nausea, and vomiting	Late extubation due to difficult rewarming
A multi-centered randomized control trial of moderate hypothermia to prevent intracranial hypertension in acute liver failure. ^[6]	Bernal et al., 2016, U.K.	Experimental-17 mild hypothermia Control-26 standard care	Not specified	72 h	ICP, adverse effect, mortality	No significant difference was found between both groups.	35% of the patients in the experimental group showed an adverse event	Rewarming was done in both the groups but effects were not mentioned
Improved neurological outcomes with mild hypothermia in surviving patients with a massive cerebral hemispheric infarction ^[29]	Su et al., 2016, China	Experimental-16 mild hypothermia Control-17 standard care	Immediately after admission	24-72 h	Mortality and neurological	Improved neurological outcome, and no improvement in mortality in (decrease) experimental group	Higher incidence of bradycardia, electrolyte disorder, GI bleeding, gastric retention, and stress hyperglycemia in the experimental group. (no-severe).	ICP at initiation- 18.8±17.4 mmHg ICP at the end 39.4±9.6 mmHg.
Mild intraoperative hypothermia during surgery for intracranial aneurysm ^[33]	Michel M Todd, 2005, England	Experimental-499 mild hypothermia (intraoperative) Control-501 normothermia	Before the application of the first clip	Till the end of the last application of the clip	Duration of ICU stay, length of hospitalization, mortality, and destination at discharge, GOSE.	No significant difference found	Longer intubation period, a higher rate of bacteremia in the experimental group	Not mentioned

(Contd...)

Table 1: (Continued).

Title	Author Year Country	Intervention	Time of starting hypothermia	Duration of intervention	Outcome variables	Results	Adverse effects	Rewarming
Effect of therapeutic hypothermia on the incidence and treatment of intracranial hypertension ^[27]	Slade <i>et al.</i> , 1999, Pits burgh	Experimental-18 hypothermia Control-22 normothermia	With 10 h of injury	24 h	ICP and its interventions (secondary analysis, discussion not clear)	(First 12 h) ICP in the hypothermic group-9.1±6.4 mmHg Normothermia ICP 19.9±19.1 Higher no. of CSF drainage in normothermia before rewarming	Not clear	Started 12–26 h following injury and there was an increase in ICP and higher incidence of CSF drainage
Effect of mild hypothermia on uncontrollable intracranial hypertension after severe head injury ^[26]	Shiozaki <i>et al.</i> , 1993, Japan	Experimental-16 mild hypothermia Control-17 normothermia	Not cleared	48 h or it was not considered effective	GOSE	A decrease in ICP and rise in CPP. A decrease in CBF, arterio-jugular venous difference of oxygen 2 cerebral rate of oxygen 2 in the experimental group	Arrhythmias and pneumonia were higher in the hypothermia group, though not statistically significant	Hypovolemic shock (rewarming shock) and abrupt ICP elevation

ICP: Intracranial pressure, CPP: Cerebral perfusion pressure, Cpk: Creatinine phosphokinase

Table 2: Risk of bias assessment.

Article	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias	Total
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Anything else, ideally prespecified	Low one risk of bias
Andrews <i>et al.</i> , 2018	✓	?	X	✓	X	X	?	2/7
Tang <i>et al.</i> , 2017	✓	✓	✓	?	✓	✓	X	5/7
Andrews, 2015	✓	?	?	?	✓	✓	✓	4/7
Clifton, 2011	X	?	?	?	X	✓	X	1/7
Lee <i>et al.</i> , 2010	X	?	?	?	✓	?	X	1/7
Andrews <i>et al.</i> , 2017	X	?	?	✓	✓	X	✓	3/7
Chouhan, 2006	X	?	✓	?	✓	✓	X	3/7
Bernal <i>et al.</i> , 2016	✓	✓	✓	?	✓	✓	X	5/7
Su <i>et al.</i> , 2016	✓	✓	✓	?	✓	✓	X	5/7
Todd <i>et al.</i> , 2005	✓	✓	✓	?	✓	✓	✓	5/7
Slade <i>et al.</i> , 1999	X	?	?	?	X	✓	X	1/7
Shiozaki <i>et al.</i> , 1993	?	?	?	?	?	✓	X	1/7

were documented in three studies. Neurological complications, unfavorable outcomes, and higher mortality were reported in one study. In one three-armed study; the group with hypothermia showed high creatinine phosphokinase (CpK). The steps of rewarming after treatment with hypothermia were mentioned in three studies, and in four studies, rewarming was mentioned without its side effects or its effects. The most common effect of rewarming was an abrupt increase in ICP three studies and late extubation in two studies, hypovolemic shock (also named as a rewarming shock) in one study, and pulmonary infections, peptic ulcer, and leukocytopenia in one study in the hypothermic group.

DISCUSSION

Overall; this systematic review concluded that therapeutic hypothermia is beneficial for patients with IHT but it can lead to delay in recovery in many patients. Hence, there is a need for high-quality evidence on this aspect to bring it into practice or to excise it from practice. Some studies reported benefits to the patients with hypothermia;^[20,21,26,27,29,31] the temperature of the control group was maintained between 36°C and 37°C and analgesics were used to lower down

the temperature if it was > 38.5°C. In all of the studies, the temperature was kept to the lower side for 48 h except for the patients with aneurysms. The beneficial effect of hypothermia for patients is considered due to low metabolic demands in lower temperature and does not lead to increases cerebral blood flow and ultimately high ICP as is the care of high CMR (cerebral metabolic rate).^[30]

Talking about the adverse effects of therapeutic hypothermia: Infections; including pulmonary infections, pneumonia, bacteremia, electrolyte imbalances; hyperkalemia and hyponatremia, cardiovascular events; bradycardia and arrhythmias, gastric complications; peptic ulcers, gastric retention, GI bleeding, stress hyperglycemia, longer incubation period, high CPK, shivering, neurological complications at 6-month follow-up, an abrupt surge in the ICP and hypovolemic (rewarming shock), and leukocytopenia as effects of rewarming, were reported in the majority of the studies included in this review.

Although the reported adverse effects were not severe and were manageable, they were seen in the hypothermic group; furthermore, some complications were present in both groups and the incidence was higher in the hypothermic

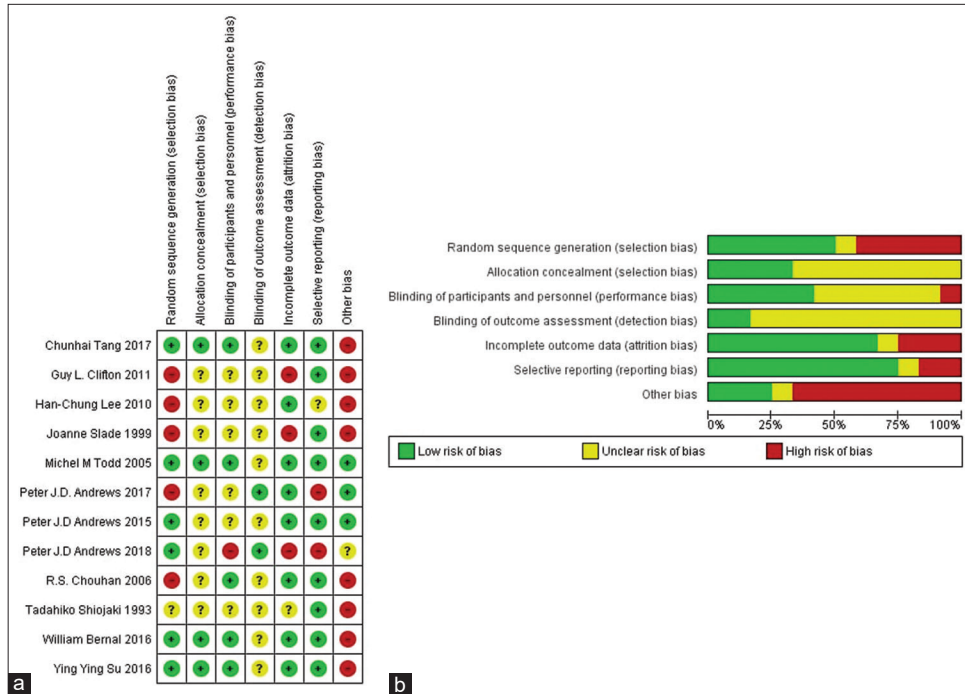


Figure 2: (a and b) Risk of bias assessment.

group. The patients in the hypothermic group suffered from more pulmonary infections such as pneumonia and bacteremia. In a study by Broessner *et al.*, infection is shown as a complication of hypothermia secondary to impairment in the secretion of pro-inflammatory cytokines and suppresses leukocyte migration and phagocytosis.^[8]

The patients who received therapeutic hypothermia were intubated for a longer period or extubated late than the normothermic group, it is reported in one of the studies that in low temperature, the lung functions were altered; low respiratory rate and VT and hypothermia-induced acidosis which lungs cannot compensate without external support.^[7] In another study, lung edema is reported as an effect of hypothermia.^[15] All these factors can be the cause of delayed extubation in the hypothermic group.

Cardiovascular events such as bradycardia and cardiac arrhythmias were found in the rewarming phase, hypothermia causes significant changes in the hemodynamic parameters leading to loss of cardiac contractility and decreased heart rate. In hypothermia, there is blood volume shifting from the periphery to the central vascular system which leads to sinus bradycardia.^[28] Shivering is also reported in one of the articles and is documented as a normal physiological response to hypothermia, it is used to generate heat when the body temperature is low.^[28]

In one study, gastric retention, N/V, GI bleeding, and stress hyperglycemia were reported in hypothermia patients, which are also mentioned in an article that hypothermia induces

insulin resistance leads to hyperglycemia.^[28] Hypothermia causes Wischnewsky spots on gastric mucosa which are dark brown colored, ranging 1–5 mm in diameter, which leads to gastric mucosa erosion and GI bleeding.^[9]

Leukocytopenia is also reported in one of the studies in the rewarming phase in patients with therapeutic hypothermia which is comparable to the result of a previous study that reported that in hypothermia, there is a risk of intravascular thrombosis and cytopenia from splenic sequestration and thrombocytopenia, especially during rewarming.^[10] Hypothermia leads to disruption in the platelet functions, slowing down of coagulation enzymes,^[35] which explain the occurrence of bleeding in the hypothermic group.

Rewarming is associated with hypovolemic shock/rewarming shock which is due to fatal circulatory derangement and posts hypothermic circulatory instability which is caused by cardiac insufficiency and alteration of the peripheral vascular bed, cellular calcium overload leads to change in the myocardial responsiveness to cellular calcium. All these factors contribute to the maintenance of low cardiac output, hence, hypovolemic shock.^[34] In the rewarming phase, an abrupt increase in the ICP was seen, probably due to cerebral vasospasm. In one study, the rate of CSF drainage was higher which was a consequence of elevated ICP. In one of the studies, the neurological complications were higher in the hypothermic group which is contrary to the findings of the study where the neurological outcomes were better in the hypothermic group.^[17]

CONCLUSION

Treating IHT with therapeutic hypothermia may be beneficial according to a few studies but it is also associated with many adverse effects. The patients in the control group also suffered from a few adverse events but the incidence was toward the higher end in the hypothermic group. The present review provides information about the adverse effects of therapeutic hypothermia in neurosciences patients which has not got much emphasis so far. Although, the adverse effects were not of much severity and can be easily managed in any health-care setting. The comprehensive knowledge of the adverse effects of hypothermia to neurosciences team working with neurosciences patients can minimize the side effect of hypothermia and will enhance the quality of care of patients treated with hypothermia.

Limitations

- Meta-analyses were not done.
- The primary authors were not contacted.
- The factors causing adverse effects were not studied.

Recommendations

Although therapeutic hypothermia is practiced in various settings for reducing IHT, there is no high-quality evidence available for its beneficial effects. Hence, it can be used cautiously.

Acknowledgment

I wish to acknowledge Mrs. Lalita Dheer, Assistant Library and Information Officer, Dr. Tu lsi Da s Li brary, Po stgraduate Institute of Medical Education & Research, Chandigarh, India for helping in retrieving the full manuscript of included studies.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

Financial support and sponsorship

Publication of this article was made possible by the James I. and Carolyn R. Ausman Educational Foundation.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Alotaibi NM, Wang JZ, Pasarikovski CR, Guha D, Al-Mufti F, Mamdani M, *et al.* Management of raised intracranial pressure in aneurysmal subarachnoid hemorrhage: Time for a consensus? *Neurosurg Focus* 2017;43:E13.
2. Andrews PJ, Rodriguez A, Suter P, Battison CG, Rhodes JK, Puddu I, *et al.* Mortality risk stratification after traumatic brain injury and hazard of death with titrated Hypothermia in the eurotherm3235trial. *Crit Care Med* 2017;45:883-90.
3. Andrews PJ, Sinclair HL, Rodriguez A, Harris B, Rhodes J, Watson H, *et al.* Therapeutic hypothermia to reduce intracranial pressure after traumatic brain injury: The Eurotherm3235 RCT. *Health Technol Assess Winch Engl* 2018;22:1-134.
4. Andrews PJ, Sinclair HL, Rodriguez A, Harris B, Rhodes J, Watson H, *et al.* Updated systematic review of therapeutic hypothermia for adult patients following traumatic brain injury. In: *Therapeutic Hypothermia to Reduce Intracranial Pressure after Traumatic Brain Injury: The Eurotherm3235 RCT.* NIH Journals Library; 2018.
5. Andrews PJ, Sinclair HL, Rodriguez A, Harris BA, Battison CG, Rhodes JK, *et al.* Hypothermia for intracranial hypertension after traumatic brain injury. *N Engl J Med* 2015;373:2403-12.
6. Bernal W, Murphy N, Brown S, Whitehouse T, Bjerring PN, Hauerberg J, *et al.* A multicentre randomized controlled trial of moderate hypothermia to prevent intracranial hypertension in acute liver failure. *J Hepatol* 2016;65:273-9.
7. Blair E, Esmond WG, Attar S, Cowley RA. The effect of hypothermia on lung function. *Ann Surg* 1964;160:814-23.
8. Broessner G, Fischer M, Lackner P, Pfausler B, Schmutzhard E. Complications of hypothermia: infections. *Crit Care* 2012;16:A19.
9. Clifton GL, Valadka A, Zygun D, Coffey CS, Drever P, Fourwinds S, *et al.* Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): A randomised trial. *Lancet Neurol* 2011;10:131-9.
10. Chouhan RS, Dash HH, Bithal PK, Chaturvedi A, Pandia, MP, Radhakrishnan M, *et al.* Intraoperative mild hypothermia for brain protection during intracranial aneurysm surgery. *J Anaesthesiol Clin Pharmacol* 2006;22:21-8.
11. Dhandapani S, Aggarwal A, Srinivasan A, Meena R, Gaudihalli S, Singh H, *et al.* Serum lipid profile spectrum and delayed cerebral ischemia following subarachnoid hemorrhage: Is there a relation? *Surg Neurol Int* 2015;6 Suppl 21:S543.
12. Dhandapani S, Bajaj A, Gendle C, Saini I, Kaur I, Chaudhary I, *et al.* Independent impact of plasma homocysteine levels on neurological outcome following head injury. *Neurosurg Rev* 2018;41:513-7.
13. Dhandapani S, Sarda AC, Kapoor A, Salunke P, Mathuriya SN, Mukherjee KK. Validation of a new clinico-radiological grading for compound head injury: implications on the prognosis and the need for surgical intervention. *World Neurosurg* 2015;84:1244-50.
14. Dhandapani S, Sharma K. Is "en-bloc" excision, an option for select large vascular meningiomas? *Surg Neurol Int* 2013;4:102.
15. Dundee JW, King R. Clinical aspects of induced hypothermia. *Br J Anaesth* 1959;31:106-33.
16. Harris B, Andrews PJ, Murray GD, Forbes J, Moseley O. Non-invasive head-cooling methods and devices. In: *Systematic Review of Head Cooling in Adults After Traumatic Brain Injury and Stroke.* NIH Journals Library; 2012.
17. Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome

- after cardiac arrest. *N Engl J Med* 2002;346:549-56.
18. Idris Z, Yee AS, Kandasamy R, Manaf AA, Hassan MH, Hassan WN. Direct brain cooling in treating severe traumatic head injury. In: *Traumatic Brain Injury Neurobiology, Diagnosis and Treatment*. London: IntechOpen; 2019.
 19. Kapoor A, Dhandapani S, Gaudihalli S, Dhandapani M, Singh H, Mukherjee KK. Serum albumin level in spontaneous subarachnoid haemorrhage: more than a mere nutritional marker! *Br J Neurosurg* 2018;32:47-52.
 20. Lee HC, Chuang HC, Cho DY, Cheng KF, Lin PH, Chen CC. Applying cerebral hypothermia and brain oxygen monitoring in treating severe traumatic brain injury. *World Neurosurg* 2010;74:654-60.
 21. Li LR, You C, Chaudhary B. Intraoperative mild hypothermia for postoperative neurological deficits in people with intracranial aneurysm. *Cochrane Database Syst Rev* 2016;3:CD008445.
 22. Nuccio A, Amadio J, Fountain A, Karakis I. The Monro-Kellie doctrine in action: posterior reversible leukoencephalopathy syndrome (PRES) due to intracranial hypotension from lumboperitoneal shunt placement. *Neurology* 2016;86 Suppl 16:207.
 23. Pierson R, Torlinski T. Early hypothermia induction in patients with severe brain injury. *J Intensive Care Soc* 2011;12:335-7.
 24. Rangel-Castillo L, Gopinath S, Robertson CS. Management of intracranial hypertension. *Neurol Clin* 2008;26:521-41.
 25. Rim HT, Ahn JH, Kim JH, Oh JK, Song JH, Chang IB. Therapeutic hypothermia for increased intracranial pressure after decompressive craniectomy: A single-center experience. *Korean J Neurotrauma* 2016;12:55-60.
 26. Shiozaki T, Sugimoto H, Taneda M, Yoshida H, Iwai A, Yoshioka T, *et al.* Effect of mild hypothermia on uncontrollable intracranial hypertension after severe head injury. *J Neurosurg* 1993;79:363-8.
 27. Slade J, Kerr ME, Marion D. Effect of therapeutic hypothermia on the incidence and treatment of intracranial hypertension. *J Neurosci Nurs* 1999;31:264-9.
 28. Soleimanpour H, Rahmani F, Golzari SE, Safari S. Main complications of mild induced hypothermia after cardiac arrest: A review article. *J Cardiovasc Thorac Res* 2014;6:1-8.
 29. Su Y, Fan L, Zhang Y, Zhang Y, Ye H, Gao D, *et al.* Improved neurological outcome with mild hypothermia in surviving patients with massive cerebral hemispheric infarction. *Stroke* 2016;47:457-63.
 30. Tameem A, Krovvidi H. Cerebral physiology. *Contin Educ Anaesth Crit Care Pain* 2013;13:113-8.
 31. Tang C, Bao Y, Qi M, Zhou L, Liu F, Mao J, *et al.* Mild induced hypothermia for patients with severe traumatic brain injury after decompressive craniectomy. *J Crit Care* 2017;39:267-70.
 32. *Therapeutic Hypothermia: Adverse Events, Recognition, Prevention and Treatment Strategies*. London: IntechOpen; 2020.
 33. Todd MM, Hindman BJ, Clarke WR, Torner JC, Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST) Investigators. Mild intraoperative hypothermia during surgery for intracranial aneurysm. *N Engl J Med* 2005;352:135-45.
 34. Tveita T. Rewarming from hypothermia. Newer aspects on the pathophysiology of rewarming shock. *Int J Circumpolar Health* 2000;59:260-6.
 35. Van Poucke S, Stevens K, Marcus AE, Lancé M. Hypothermia: Effects on platelet function and hemostasis. *Thromb J* 2014;12:31.

How to cite this article: Thakur K, Kaur H, Dhandapani M, Xavier T, Srinivasan G, Gopichandran L, *et al.* Systematic review exploring the effect of therapeutic hypothermia on patients with intracranial hypertension. *Surg Neurol Int* 2022;13:237.