2018

The Neuroprotective Effects of Targeted Temperature Management on Post-Cardiac Arrest Patients

Timothy Hovde

University of North Dakota

Follow this and additional works at: https://commons.und.edu/pas-grad-posters

Part of the Cardiology Commons, and the Cardiovascular Diseases Commons

Recommended Citation
https://commons.und.edu/pas-grad-posters/14

This Poster is brought to you for free and open access by the Department of Physician Studies at UND Scholarly Commons. It has been accepted for inclusion in Physician Assistant Scholarly Project Posters by an authorized administrator of UND Scholarly Commons. For more information, please contact zeinebyousif@library.und.edu.
The Neuroprotective Effects of Targeted Temperature Management in Post Cardiac Arrest Patients

Timothy Hovde PA-S
Department of Physician Assistant Studies, University of North Dakota School of Medicine & Health Sciences
Grand Forks, ND

Abstract

- Novel methods of ensuring survival following cardiac arrest and reanimation are of supreme importance to the medical community.
- Targeted temperature management (TTM) has been increasingly utilized pre-hospital, in emergency departments, and when intensive care units are unable to increase the patient's core temperature. TTM has further been used to attempt to improve neurologic functioning. The efficacy and mechanism behind TTM remains poorly understood. In several patient populations it also remains unproven. The purpose of this study is to assess the physiological mechanism, survival, neurologic recovery and methodology behind TTM.

Methods

- To acquire relevant research PubMed, Clinical Key, Cochrane review and Google Scholar databases were referenced.
- Search terms included: targeted temperature management, therapeutic hypothermia, cardiac arrest, return of spontaneous circulation (ROSC) and/or survival. These terms were used in several combinations to obtain appropriate research materials.
- Dynamed and the American Heart Association (AHA) were further assessed and recommendations on patient selection, implementation, and methodology behind TTM.

Literature Review

- Literature review was utilized to assess the physiological mechanism by which TTM elicits its beneficial effects on neurologic outcomes and survival rates were further examined. Finally, the proposed method to safely and efficiently induce and maintain TTM in appropriate patients was also assessed through literature review.
- TTM was found to improve survival and neurologic functioning in adults suffering cardiac arrest both in-hospital and out-of-hospital. No improvement has been shown in studies on pediatric patients, thus TTM is not indicated in pediatric patients. Animal studies demonstrate a decrease in cerebellar edema and mitochondrial apoptosis of neuronal cells with TTM application. Serum biomarkers of brain injury and dysfunction including markers constituting the brain blood barrier (BBB) have also been found to be decreased in patients undergoing TTM. Finally, serum assay of antioxidants demonstrates a decrease in oxidative damage and increase in antioxidant protection following reperfusion.

Clinical Applicability

- TTM is most effectively accomplished by rapidly decreasing core body temperature to 32-36 degrees Celsius, though fevers and shivering are more effectively tolerated at 34-37.5 degrees Celsius.
- Damped recommendations rapid induction to target temperature 32-36 degrees Celsius and maintained by rewarming over 24-24 hours. Then Yuan et al. (2017) study further suggests that earlier implementation is effective in preserving neurological function.
- Per Nurnberger et al. (2017) found that TTM should be induced in patients who remain unresponsive following OHCA with ROSC and a presenting shockable cardiac rhythm. TTM should be started before patient comatose following ROSC with non-shockable rhythms or following IHCA. Core body temperature should be decreased to 32-34 degrees Celsius and maintained for 24 hours.
- The AHA does not currently endorse routine pre-hospital cooling methods as TTM can readily be applied in rural ER practice and maintained for transport to a higher level of care by EMS, decreasing the time to therapeutic effect.

- An endovascular, epidural, brachial or rectal temperature probe should be placed for continuous core temperature monitoring.

Acknowledgements

- I would like to extend my gratitude to the staff of the University of North Dakota’s Physician Assistant Program. Of special note is my advisor Prof. Jay Metzger. I would further like to acknowledge the contributions of Prof Barry Morquio, Joshua Fischer and Attilio Attacino made toward the completion of this project.

References


Copywrite 2015 by the Indian Journal of Anaesthesia

Statement of Problem

- Targeted temperature management is a poorly understood intervention. It is believed to confer benefit to survival and neurologic outcome, though the mechanism is still under research. The magnitude of potential benefit to survival and neurologic functioning also remains unclear. Finally, the method of TTM induction remains poorly standardized. Assessment into the methods and procedures of several studies may yield a more consistent and effective and efficient method to confer the greatest benefit to survival and neurologic functioning.

Methods

- By what proposed mechanisms does targeted temperature management improve survival and neurologic functioning following cardiac arrest and reanimation? Is there clinical applicability to this intervention?

- Do studies evaluating the benefit of targeted temperature management demonstrate statistically significant improvements in survival to hospital discharge as well as improvements in cognitive function following resuscitation?

- While there is currently agreed upon method of inducing targeted temperature management and what is its ease of implementation?

- Animal studies performed by Fan et al. (2017) and Chan et al. (2017) demonstrate inhibition of mitochondrial induced cellular apoptosis through alteration of mediators of mitochondrial pore opening such as CVT-C, 

  - Cardiac Arrest Syndrome Through Cyclophilin D Mediated Mitochondrial Permeability Transition. doi: 10.1097/01.dcr.0000620873.29583.3b

  - Pathophysiology of the Neuroprotective Effects of Targeted Temperature Management. doi: 10.1186/s40747-015-0083-0

- Improvement in survival noted in survival, and in neurologic functioning as measured by autonomic reflexes and operantly defined observation for 24-72 hours post-resuscitation in animal studies. Improvement in neurologic outcome is associated with better outcomes in patients with a non-shockable cardiac rhythm. Perman, Gomesrauer, Douglas, Wible, Carr. (2015) found statistical significant improvements in patient survival with TTM vs normothermia when the initial presenting rhythm is non-shockable. (29% vs 15% P < 0.05). Continued assessment found patients are more likely to be discharged neurologically intact if TTM is utilized following resuscitation in patients with non-shockable arrests.

- The studies do not currently support the use of TTM in pediatric patients with endocardial arrest and thus results are inconclusive to the different causes of pediatric cardiac arrest.

- Benefit of TTM is associated with improved likelihood of neurological improvement. TTM application prior to ED arrival however, is controversial. TTM appears to extend its effects during reperfusion. Problems with TTM may be the time altered until TTM application is likely to diminish the potential benefit.

- Literature Review

  - Pathophysiology of the Neuroprotective Effects of Targeted Temperature Management. doi: 10.1186/s40747-015-0083-0

  - Jonckheere et al. (2017) demonstrated mitochondrial apoptosis in all cardiac arrest groups (P < 0.05) suggested decreasing mitochondrial induced neuronal apoptosis (P < 0.05).

  - Hackenherij et al. (2017) performed a study focused on reactive oxygen species (ROS) development. TTM was effective in decreasing reactive oxygen species (P < 0.05).

  - Jahandiez et al. (2017) performed studies using rabbits to model cardiac arrest. A decrease in mitochondrial apoptosis was noted (P < 0.05).

  - Jeben et al. (2016) performed a series of porcine studies assessing the effect of TTM. These studies demonstrated good neurological function is 85% (Buck et al., 2016). Targeted temperature management has become a mainstream within hospital systems to improve neurologic function in patients after cardiac arrest.

  - Proponents further suggest that implementation improves survival to hospital discharge.

  - The inability to perform a reactive-mechanistic, improvements in survival and neurologic functioning, and recommendations for implementation were assessed through literature review.

- Discussion

  - Animal studies performed by Fan et al. (2017) and Chan et al. (2017) demonstrate inhibition of mitochondrial induced cellular apoptosis through alteration of mediators of mitochondrial pore opening such as CVT-C, 

  - Cardiac Arrest Syndrome Through Cyclophilin D Mediated Mitochondrial Permeability Transition. doi: 10.1097/01.dcr.0000620873.29583.3b

  - Pathophysiology of the Neuroprotective Effects of Targeted Temperature Management. doi: 10.1186/s40747-015-0083-0

- Improvement in survival noted in survival, and in neurologic functioning as measured by autonomic reflexes and operantly defined observation for 24-72 hours post-resuscitation in animal studies. Improvement in neurologic outcome is associated with better outcomes in patients with a non-shockable cardiac rhythm. Perman, Gomesrauer, Douglas, Wible, Carr. (2015) found statistical significant improvements in patient survival with TTM vs normothermia when the initial presenting rhythm is non-shockable. (29% vs 15% P < 0.05). Continued assessment found patients are more likely to be discharged neurologically intact if TTM is utilized following resuscitation in patients with non-shockable arrests.

- The studies do not currently support the use of TTM in pediatric patients with endocardial arrest and thus results are inconclusive to the different causes of pediatric cardiac arrest.

- Benefit of TTM is associated with improved likelihood of neurological improvement. TTM application prior to ED arrival however, is controversial. TTM appears to extend its effects during reperfusion. Problems with TTM may be the time altered until TTM application is likely to diminish the potential benefit.

- Theory of targeted temperature management is a poorly understood intervention. It is believed to confer benefit to survival and neurologic outcome, though the mechanism is still under research. The magnitude of potential benefit to survival and neurologic functioning also remains unclear. Finally, the method of TTM induction remains poorly standardized. Assessment into the methods and procedures of several studies may yield a more consistent and effective and efficient method to confer the greatest benefit to survival and neurologic functioning.

- Methodology

  - Fan et al. (2017) performed an experiment performing TTM on lab rats. Improvements were noted in the TTM group in survival and neurological function. (P < 0.05).

  - Maserger et al. (2017) utilized data obtained from the Circulation Improving Resuscitation Card Care Trial (CIRCRT). The results suggest that survival to discharge is superior in patients who receive prehospital TTM in hospital TTM (P < 0.006).

  - Moler et al. (2017) performed a study to determine the efficacy of TTM for pediatric patients who experience IHCA. No significant difference was found in survival, nor was there difference in cognitive function (P < 0.5).

  - Perman et al. (2015) used retrospective analysis to determine the effectiveness of TTM who present with a non-shockable rhythm (asystole/PEA). Both cohorts enjoyed improved neurologic functioning and survival to discharge regardless of the location of arrest (P < 0.001).

  - Method of implementation

  - Casamento et al. (2016) utilized review of patient records to assess varying survival rates of TTM at 32-36 degrees Celsius in patients undergoing TTM at 32-36 degrees Celsius compared to 36 degrees Celsius. Greater likelihood of complications was found in the 32-36 degree group (P < 0.01). They also note an increased discharge to home rate in the 36-degree group (P = 0.02).

  - Yuan et al. (2017) performed a porcine study on the effects of early versus delayed administration of TTM. CPC scores demonstrated improved neurologic function in the early TTM group (P < 0.012).