Original Article

Effect of targeted temperature method on the ICU length of stay for traumatic severe brain injury patients

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ABSTRACT

Background and aims: Traumatic brain injury (TBI) is a major cause of death and disability worldwide. This study aimed to evaluate the role of targeted temperature method (TTM) on decreasing ICU length of stay in severe TBI patients. Patients and Methods: This study involved 40 patients with severe TBI who were divided into two groups; group A which included twenty patients who were treated according to ICU standard care of brain injury, and group B which included other twenty patients who had the same care along with TTM application, in an open label study. Results: (TTM) group had significant (P= 0.021) shorter ICU stay compared to standard care group. Treatment with hypothermia, also showed non-significant (P= 0.38) improvement in the neurological outcome after 24 hours initiating the (TTM). The initiation of (TTM) showed significant effect ($p<0.05$) regarding metabolic profile including less hypokalaemia, thrombocytopenia, and hyperglycaemia. No difference was reported between the two groups regarding the mortality or the risk of pulmonary infection. Conclusion: The TTM causes significant decrease in length of ICU stay, but regarding neurological outcome in patients with severe TBI, there was no statistically significant amelioration. TTM is proved to be a safe intervention.

Keywords: Severe, targeted temperature method, Traumatic brain injury, length of stay

Introduction

Advances in Knowledge

1. Many researchers have studied the use of TTM post cardiac arrest but it is still an optional choice for TBI patients [1], and its use has not been proven in large Randomised Control Trials yet [2, 3] .
2. In this investigation, the authors tried to maximize the care for these TBI patients, by using TTM to minimise secondary traumatic brain injury. This was proven to give many financial and prognostic advantages.
3. Although, this study was conducted on a small number of patients, the authors think it would refresh old-new issues about the use of TTM in TBI, especially in this area.

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Application to Patient Care

1. The main purpose of this study was to improve the care of patients in order to decrease the sequalae of brain injury.
2. In Critical Care Department, Cairo University, the use of TTM was applicable and welcomed, to see better results
3. The researchers standardized their own protocol according to standard updated guidelines and applied it strictly with a thorough observation.
4. In this study, TTM was a part of the standard care for selected patients, and the researchers believed it was so beneficial.

Introduction

Traumatic brain injury (TBI) is one of the major causes of death and severe disability among patients with this injury worldwide. Management of TBI includes rapid resuscitation, and prevention of secondary insult guided by intracranial pressure (ICP) monitoring. [4-7]

Brain ischemia is a complex process at the level of the brain cells that starts immediately after the injury till 72 hours or longer, through this period, hypothermia can be applied. TTM can slow the metabolism of the brain and decrease the glucose and oxygen consumption. It also inhibits caspase enzyme activation, and decreases the excitatory neuro-transmitters. [8] and reduces

the cerebral metabolism and cerebral blood volume. [9]

(TTM) has adverse effects such as shivering, sepsis, coagulopathy, cardiac arrhythmia, electrolytes and metabolic disturbances, but large trials showed that these drawbacks are infrequent. TTM can be beneficial post cardiac arrest. [10, 11] The aim of this work was to evaluate the role of TTM on the ICU length of stay for these patients. [12] Christos Lazaridis and colleagues in 2015 postulated that, the length of ICU stay is an important and effective measure of health care in TBI, but the researches in this field are not enough yet. [13]

Methodology

Subjects: This study started on 1/1/2016 and continued till 31/10/2016 in Critical Care Department, Faculty of Medicine, Cairo University. The study was approved by the ethical committee of the Critical Care Department and all subjects gave a written consent to participate in the study.

Inclusion criteria: Patient aged >18 years, with severe TBI, admitted within 72 hours of injury with GCS <9 and Computerized Axial Tomography (CAT) scan showing oedema and/or contusions and hematomas were enrolled. Traumatic brain injury with GCS below 9 was considered severe.

Exclusion criteria: Patients were excluded if their age was less than 18 years (n= 3), the presence of any coagulopathy (n= 5), uncontrolled bleeding (n= 3), patients having refractory shock with organ failure (n= 4), patients with severe metabolic acidosis (n= 5), patients with chronic kidney diseases (n= 3) patients with cancers (n= 2) and non-volunteers (n= 1)

Randomization: All the 40 patients with clinical diagnosis of severe TBI were randomized to either standard care (Group A, n=20) or standard care with TTM (Group B, n=20) using double blinded study. Treatment with TTM was administered according to a standard protocol.

Neuromonitoring included GCS, and motor response scores for every patient were included in the study. Richmond agitation sedation scale (RASS) was applied for patients with a target of (-3 to -4 score). [14]

Temperature measurements through oesophageal probe were obtained continuously and in correlation with the reading that was measured from the screen of the cooling machine, which was used to control the patients' body temperature. The patients' temperature monitoring was continued.

Management: In both groups, standard care for TBI included Basic ICU supportive care.

TTM: The target was body core temperature of (32-34 °C) within 4 hours and maintain it for 48 hours from time of cooling initiation, through applying cooling pads connected to the cooling machine. Moreover, ventilatory settings, the electrolytes, coagulation profile, glucose level and platelets count were monitored, and the needed intervention was applied. The three phases included *first*, **Induction phase** where Patients were kept sedated and paralyzed. Required temperature was achieved through applying the cooling pads. *Second*, **Maintenance phase (after reaching 33°C)** where Patients were kept sedated paralyzed for 48 hours. Adjustment for temperature was done through cooling blanket guided by the display screen of the cooling machine as shown in figure 1. *Third*, **Re-warming phase** as during this time, the re-warming with rate of 1 °C per 4 hours was initiated, and the fluid resuscitation had to be used if needed to compensate for hypotension that might happen during re-warming.

The two groups were compared according to the following measurements: *first*, the neurological outcome assessment as it was guided by the clinical improvement, and the patients were classified into these categories: (a) Complete recovery, (b) Disability with different grades, (c)Vegetative state, and (d) Death; *Second,* the length of ICU stays; and *Third,* mortality rate.

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Figure 1: Diagram showing the screen display of the temperature management system.

End points of the study:

It included the discharge from the ICU, death and the ventilator dependent state.

Statistical analysis

The researchers used standard statistical analysis including the SPSS version 23 in the current study. The data were coded using the statistical package SPSS version 23. [15, 16]

Results

There was no statistical difference between the two groups regarding the age and sex as shown in table (1). In patients treated with TTM, there was a clinical improvement in the Glasgow coma scale (GCS) and motor response after 24 hours from starting the TTM, but without statistical difference between two groups. Initiation of TTM showed a significant effect on lowering the level of potassium (K) and platelets count, increasing the blood glucose level and insignificant effect on mean blood pressure. Regarding the risk of pulmonary

infection table (1), the two groups didn't differ statistically regarding the incidence of VAP. TTM had a significant effect on decreasing the length of ICU stay compared to those on the control group (see Table 2).

Complications during initiation of hypothermia and rewarming

During the initiation of TTM, seven patients (35%) reported complications like (hyperglycaemia, hypokalaemia, bradycardia, hypotension, thrombocytopenia and increased INR) and thirteen patients (65%) didn't experience any complications (Figure 2).

In the study group, during rewarming phase, five patients (25%) experienced complications including (hyperkalaemia, bradycardia, hypoglycaemia, thrombocytopenia and hypotension), and fifteen patients (75%) didn't show any complications (Figure 3).

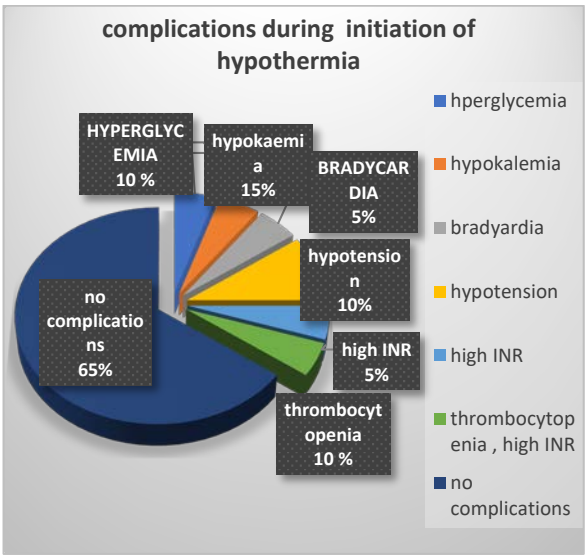

Figure 2: Pie chart showing complications during the initiation phase of hypothermia in the study group.

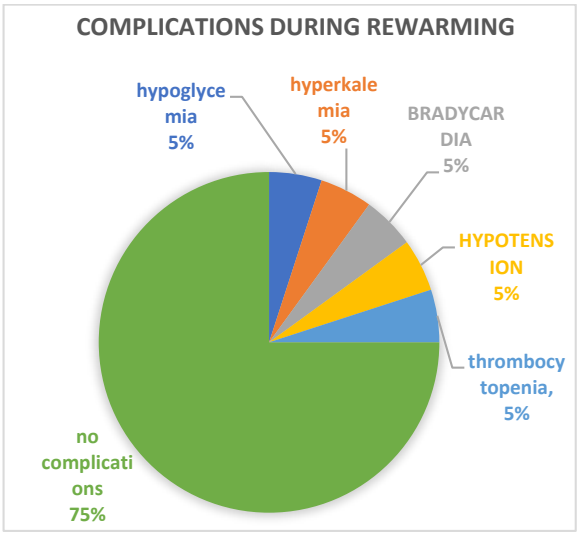

Figure 3 : Pie chart complications during rewarming.

Table 1: Demographic, clinical data at baseline and complications in the intervention and control group.

Data	Control group A (n= 20)	Intervention group B (n= 20)
Male gender, n (%)	19 (95%)	18(90)
Mean age, years	31.9 (2.16)	33.85 (3.67)
Mean body weight, Kg	67.5 (1.9)	68.2 (1.86)
Mean Body mass index, Kg/M2	23.2 (1.1)	23.5 (0.9)
Coma, Glasgow coma scale	7.2 (0.22)	6.45 (0.44)
Injuries and fractures, n (%)	4 (20%)	6 (30%)
Intracranial HTN, n (%)	10 (50%)	11 (55%)
Chest compressions with rib fractures, n (%)	2 (10%)	3 (15%)
Persistent fever, n (%)	3 (15%)	4 (20%)
Hypotension, n (%)	3 (15%)	2 (10%)
CPIS	8.8 (0.37)	9 (0.41)

Mean (standard error of mean), CPIS: Modified Clinical Pulmonary Infection Score

Table 2: Stay (in days) in the intensive care unit in both groups.

	Control group	Intervention group	P value
Length of ICU stay (in days)	13.90 (1.96)	8.25 (1.28)	0.021

Mean (standard error of mean), ICU=Intensive care unit.

Discussion

TTM is a method for controlling, monitoring, and lowering the body temperature with the aim of preserving the cerebral blood flow that might be disturbed due to the brain injury. Some clinical studies showed the benefit of TTM in patients with traumatic brain injuries. [17-19] On the other hand, other studies didn't recommend this method as a standard care. [20]

In the current study, TTM proved to improve the neurological outcomes, nevertheless, no statistical significance was found for this improvement without statistical significance. Similarly, Jiang et al, in 2000, reported an improved neurological outcome rate in brain injury patients [21], and this was partially in agreement with the results of this study, so both studies denoted that; the use of hypothermia as a rescue therapy can improve neurological outcomes in these patients. Conversely, Clifton and others in 2011 reported that neurological outcome did not improve on using TTM in these patients which was not in agreement with the results of this study. [22]. The variation in the effect of TTM on neurological outcome between the current study and the mentioned studies could be due to the variations in timing of initiation of hypothermia, the duration of treatment, and the duration of follow up. Sydenham et al., in 2009, in a study postulated that the longer the duration of treatment and the longer the follow up period, the better would be the outcome. [23]

In this study, the mortality rate was less in patients treated with

TTM compared with the others who did not, but this was statistically insignificant. In agreement with the current study, Jiang and colleagues obtained almost the same results in 2000 [21]. Surprisingly, Harris and others in 2009 had different results where they concluded that, TTM increased mortality in the same category of patients [24] . In a systematic review by Georgio and Manara in 2013 [25], it was reported that there was a delineated effect of TTM on mortality in patients with TBI with safety profile of TTM. From the previous studies, it can be summarized that neurological outcome and mortality rate are not the main targets of treatment methods using targeted temperature.

The main concern of this study was to try to shorten the ICU length of stay which was evident in TTM treated patients. A similar study done by Storm et al., in 2008 proved the same results regarding the survivors of cardiac arrest patients with neurological sequalae who received TTM, that had shorter ICU stay. [26]

Excessive hypothermia induced diuresis and excess potassium loss which led to hypokalaemia in some cases. In agreement with the current study, TTM has been shown to be associated with significant hypokalaemia, like in the study by Kirkegaard et al, in 2012 who reported that serum potassium levels decreased significantly during cooling, and 76% of patients reached values of <3.5mEql/L (mild hypokalaemia). [27]

TTM did not increase the risk of coagulopathy or thrombocytopenia (though the mean platelets count significantly dropped) during this study with the resultant low incidence of haemorrhage either intra-cranial or systemic, and this agreed with a large systemic review done by Fox and others in 2010. [28]

Regarding the incidence of VAP, the two groups did not differ statistically even though it happened in some cases. Sydenham et al., in 2009 had almost similar results [23]. On the other hand, Fox and others in 2010 revealed the significant incidence of VAP in patients treated with TTM [28]. In this study, the researchers assumed that these differences may be explained by the versatility in using treatment protocols between different ICUs. The authors recommend involving larger number of patients in future studies to add more information and values to using TTM in severe TBI, and also establish local TTM protocol for ICU for management of TBI in its severe forms.

Limitations of this study

Limitations of the current study were mostly related to the shortage of cost and resources availability, specially limited number of studied patients combined with other co morbidities.

Conclusion

From the current study, it can be concluded that, TTM significantly shortened the length of stay in those patients who have been exposed to TBI especially those classified as suffering from a severe form of injury, compared with those who did not have the TTM protocol. TTM has been proved to be a safe intervention. These all would encourage different ICU care facilities to emphasize the earlier use of TBI.

Financial Support Issues

There was no organization body offering special funds or sponsorship to the present study.

Conflicts of Interest

None of the sharing authors claimed any conflict of interest.

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