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ORIGINAL ARTICLE

Efficacy of Early Therapeutic Hypothermia after Cardiac Arrest on Neurological Outcome in ICU Patients

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ABSTRACT

Objective: To learn about efficacy of early therapeutic hypothermia affects neurological outcomes in post cardiac arrest patients.
Study design: Quasi Experimental study.
Place and duration of study: Study was conducted from May 2021 to Feb 2022 at Department of critical care management services hospital Lahore.
Methodology: Patients having age 18 to 70 years were included in the study. The daily neurological assessment was carried out when sedation was off till patient was discharged by critical care physician. The results were expressed in cerebral performance categories On the basis of neurological outcome patients were divided in two groups. Group A (good outcome) consists of patients of cerebral performance category 1 and 2, while group B (poor outcome) consists of patients of cerebral performance category 3 and 4.
Results: Total 60patients were included in study. 10 patients of group A and 22 patients of group B have died during hospital stay. Mean age of patients in Group A (good prognosis) was 56.72 ± 9.11 years and in Group B (poor prognosis) it was 53.85 +7.95 years. The starting temp which was taken before inducing hypothermia was 35.28 ^{0}C (mean) in group A and 35.75 ^{0}C in group B which was statistically significant (p= 0.04). Coldest temp achieved in group A was 33.07 ^{0}C and in group B it was 33.25 ^{0}C which was statistically significant (p= 0.01).
Conclusion: Among patients of in hospital cardiac arrest the overall survival rate and better neurological outcome was seen in patients in whom therapeutic hypothermia was induced as soon as possible after successful resuscitation as compare to those in which usual treatment was given.
Keywords: cardiac arrest, therapeutic hypothermia

INTRODUCTION

The importance of temperature regulation in neurological outcomes was known to humans since long as stated by Aristotle in his writings "Man's superior intelligence depends on the fact that his larger brain is capable of keeping the heart cool enough for optimal mental activity"[1]. Cardiac arrest and its related mortality and morbidity is one the common events seen in hospitals frequently. An estimated nearly 400,000 cardiac arrest events occurs annually in USA[2] and 375,000 in Europe each year[3]. In USA in hospital cardiac arrest (IHCA) mortality rate has reduced markedly in last few years i-e from 69.6 to 59.8%[2]. A study by Khan NU et al which was conducted in Pakistan states that out of 72% patients of IHCA who were successfully resuscitated only 19% could be discharged and 12% were alive at 6 months follow up[4]. Recovery from sudden cardiac event without any neurological deficit is seldom seen. According to American heart Association (AHA) the most important objective of cardiopulmonary cerebral resuscitation is to prevent cerebral anoxia[5]. One of the most important measures to prevent cerebral damage is mild therapeutic hypothermia (MTH) in patients of cardiac arrest who have returned to spontaneous circulation (ROSC). Since 2010 AHA announced that MTH to be carried out in every patient of cardiac arrest[5]. A study by Busto Et al in rats showed that a temperature of 2 ^{0} C temperature difference during a period of global ischemia decreases neuronal death and vice versa[6]. The best outcomes of hypothermia are seen in term neonates of birth asphyxia with limited major disability, better long term outcomes and brain structural preservation[7]. As brain has a very low tolerance of ischemia cardiac arrest leads to brain anoxia with release of free radical and proteases cascades which leads to brain death in about 2-5 minutes[8]. Those who survive of cardiac arrest generally sustain serious neurological insults with disability and brain injury[9]. Raised body temperature post cardiac arrest also enhances brain insult by promoting inflammatory cascade, release of free radicals and increasing excitotoxic injury to neurons[10]. With every 1^0 C rise in temperature after cardiac arrest worsens neurological outcome and leads to high mortality[9]. Mild therapeutic hypothermia is decreasing temperature from 32 ^{0} C to 34 ^{0} C which is reported as the best method to improve neurological outcomes in post cardiac arrest patients[9].

Only few hospitals in Pakistan are using this hypothermia technique insudden cardiac arrest patients despite evidencebased recommendations widely established since 2010[5]. This study was done to assess the neurological outcomes and see the effects of early MTH and efficacyof therapeutic hypothermia in adult post-CA patients in intensive care unit of services hospital Lahore, Pakistan.

METHODOLOGY

This quasi experimental study was conducted from May 2021 to Feb 2022 at Department of critical care management services hospital Lahore. Study was started when the committee of the Institutional Review Board has approved the manuscript. The WHO sample size calculator was used to estimate the sample size of 60 patients. Any patient with age of 18 to 70 years having cardiac arrest, successful CPR with return of palpable arterial pulse, restoration of circulation within 60 mins of CPR and comatose state after revival (GCS< 8) will be included in the study. Exclusion criteria was any malignancy or any other terminal illness, patients with known brain injury already documented like stroke, Parkinson disease, epilepsy or dementia. All patients were given standard intensive care. Sedation was achieved by propofol (200mg/hr) and fentanyl (0.5mg/hr) intravenously. Paralysis was achieved by intravenous atracurium. As soon as possible cooling was initiated after stabilizing and necessary investigations by use of endovascular device. Femoral catheter was passed and external cooing system was used to maintain body core temperature between 32.5 ^{0}C to 33.5 ^{0}C using normal saline for a period of 24 hours. This stage was followed by rewarming phase during which body core temp was raised to 36.5 ^{0}C. The daily neurological assessment was carried out when sedation was off till patient was discharged by critical care physician. The results were expressed

in cerebral performance categories as mentioned in literature[11]. The following are the 5 performance categories: Those who are extremely conscious with healthy cerebral function or a little handicap, those who are conscious but have a moderate or severe disability, those who are comatose or in a permanent vegetative state, and those who have suffered brain death[11]. Category 1 and 2 are labeled as good outcome and category 3 and 4 are labeled as poor outcome. On the basis of neurological outcome patients were divided in two groups. Group A(good outcome) consists of patients of cerebral performance category 1 and 2, while group B (poor outcome) consists of patients of cerebral performance category 3 and 4.

SPSS 24.0 was used to analyse the gathered data. For both qualitative and quantitative variables, descriptive statistics were produced. The frequency and proportion of certain qualitative characteristics, such as gender, were computed. Mean and standard deviation were used to quantify quantitative variables such as age. An independent sample test was used to compare the mean values of two groups. a significance level of 0.05 was considered to be acceptable.

RESULTS

There were 60 patients total in the research. During their hospital stays, 22 patients in group B and 10 patients in group A both passed away. 60 patients were involved; 25 were assigned to group A and 35 to group B. In Group A mean age of patients (good prognosis) was 56.72 ± 9.11 years and (poor prognosis) it was 53.85 +7.95 years in Group B. In group A, there were 16 (64%) males and 9 (36%) females and in group B, 23 males (65.7%) and 12 (34.3%) females.

Table 1: Demographics of patients included in the study

	Study Group	
	Group A (Good prognosis)	Group B (Poor Prognosis)
No of patients	25	35
Age (years)	56.72 ± 9.11	53.85 +7.95
Gender		
Male	16 (64%)	23 (65.7%)
Female	9 (36%)	12 (34.3%)
BMI	29.4 ± 3.01	31.65 + 4.83
Mean CPR time (mins)	27.76 + 8.68	28.02 + 11.08

The starting temp which was taken before inducing hypothermia was 35.28 ^{0}C (mean) in group A and 35.75 ^{0}C in group B which was statistically significant (p= 0.04). Coldest temp achieved in group A was 33.07 ^{0}C and in group B it was 33.25 ^{0}C which was statistically significant (p= 0.01). Subsequently 24 h of hypothermia rewarming was started and temperature achieved after rewarming in group A was 36.86 ^{0}C and in group B it was 36.58 ^{0}C which was statistically significant (p= 0.001). Time to achieve target temp in group A was 344.36+71.75mins and group B time taken was 392.29+91.84 mins. (p = 0.03).

Table 2: variables comparison of both groups

Variable	Study Group		P value
	Group A (good prognosis)	Group B (poor prognosis)	
Starting temp (^{0}C)	35.28	35.75	0.04
Temp after 1 hour (^{0}C)	34.11	34.48	0.02
Coldest temp (^{0}C)	33.07	33.25	0.01
Temp after Rewarming (^{0}C)	36.86	36.58	0.001
Time to target Temp (mins)	344.36+71.75	392.29+91.84	0.03

DISCUSSION

All patients in coma following successful cardiac arrest resuscitation are advised to maintain a temperature of 32°C to 36°C, under 2015 International Liaison Committee on Resuscitation (ILCOR) guidelines12. There are three stages to mild therapeutic hypothermia: induction, maintenance, and rewarming. Following successful cardiac arrest resuscitation, MTH should be initiated as soon as feasible and maintained for at least 24 hours before slow rewarming (0.25-C to 0.5-C per hour).[9]

It has been advocated in some studies that body temp has prognostic effects on neurological outcomes in patients after cardiac arrest. It has been observed that patients who presented with hyperthermia and fever after cardiac arrest had worst neurological outcome[13]. Two clinical trials have clearly shown that mild therapeutic hypothermia has neuro protective effects and hypothermia protects brain from anoxic brain injury with better neurological outcomes[3,13].

In present study patients who had lower starting temp and had lower temp after 1 hour of hypothermia induction and achieved target temp sooner after resuscitation shows better neurological outcome as compare to others. These results are similar to results shown by Billaird G et al that therapeutic hypothermia is well associated with good neurological outcome. Also in our study survival rate was60% in hypothermic group and 36% in other which were comparable to results shared by Billaird G who stated that survival rate was better in hypothermic group when compared with others i-e (56%vs 36%)[14]. Similarly a study by Kongpolprom N et al showed that out of 17 survivors of cardiac arrest patients in which hypothermia was induced 15 patients show minimal disability with better long term survivor and functional ability was better seen in patients who had therapeutic hypothermia after cardiac arrest as compared to patients in which hypothermia was not induced[15]. A study by Permann SMand Soleimanpour H et al showed a better neurological outcome in post cardiac arrest patients in which therapeutic hypothermia was induced[16,17]. A study by Chan PS et al stated that therapeutic hypothermia decrease mortality in first 24 hours after therapeutic hypothermia but it doesn'taffect overall survival rate in cardiac arrest patients[18]. Similarly Lascarrou JB et al showed a better neurological outcome and 90 days survival in patients of therapeutic hypothermia when compared with usual treatment[19].

The median time in our study to achieve target temp in group A was 344.36+71.75 mins and group B time taken was 392.29+91.84 mins. (p = 0.03). a study by Haugk M et al showed that faster decline in body temp after cardiac arrest leads to good neurological outcome. In their study the median time to reach a temp of 34°C was 209 minutes in patients with favorable neurological outcomes[20](10.2% survival as compared to 5.7%).

Limitation of the study was cardiac arrest without sorting the cause/ rhythm seen during resuscitation which may affect over all survivor and neurological disability as reported in some studies. Secondly out hospital cardiac arrest patients were not included which may also be included in upcoming studies.

CONCLUSION

Among patients of in hospital cardiac arrest the overall survival rate and better neurological outcome was seen in patients in whom therapeutic hypothermia was induced as soon as possible after successful resuscitation as compare to those in which usual treatment was given.

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