VER
Vascular & Endovascular Review

Effect of Hydrocortisone on Outcome of Post-Cardiac Arrest Between Road Traffic Accident Poly-Trauma Patients

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ABSTRACT

Background: Post-cardiac arrest carrying a very poor outcome especially after road traffic accident (RTA) between polytrauma patients. Corticosteroid used recently by many authors to improve outcome.

Objective: This study aimed to assess the effect of hydrocortisone on outcomes of cardiac arrest between RTA polytrauma patients.

Methods: This prospective, double-blinded, randomized controlled study enrolled 200 patients admitted to our ICU as post-cardiac arrest following RTA poly trauma. Patients were randomly allocated to either group A(n=100), received resuscitation according to advanced cardio-vascular life support (ACLS) protocol, group B (n=100) received same protocol with administration of hydrocortisone 200 mg intravenous (IV) state and 50 mg IV every 6 hours for 3 days. Number of patients died, re-arrested and revived, showed stunning heart on echocardiogram (echo), return of spontaneous circulation (ROSC) with vasopressor support, ROSC without vasopressor, had improvement in their Glasgow coma scale (GCS), showed normal tissue perfusion, developed coagulopathy were collected and compared.

Results: Patients in Groups B showed a significant improvement in all outcome parameters measured after cardiac arrest between RTA poly-trauma patients at the end of the studied period. As there was significant lower number of patients died, lower number of patients who developed re-arrest, lower number of patients who need high dose of inotropes to support ROSC and developed coagulopathy. And significant higher number of patients who showed improvement in their GCS and restored normal tissue perfusion.

Conclusion: This study high light and clarify the effect of hydrocortisone in improving all outcome parameters measured after cardiac arrest between RTA poly-trauma patients as regard lowering number of patients died, re-arrest, showed post-arrest stunning myocardium, developed post-arrest coagulopathy and increasing number of patients who showed improved conscious level and restores normal tissue perfusion.

KEYWORDS: Hydrocortisone, Outcome, Cardiac Arrest, Road Traffic Accident, Poly-Trauma Patients.

How to Cite: Mohamed Gaber Ibrahim Mostafa Allam, Ahmed Gamal Salah Elsawy, Ahmed Maher Abouelnasr Khalifa, Mohamed A. Elbadawy, Mohamed Mohamed Hegab, Ayman Salah Emara Abouelnour, Mahmoud Elsayed Abdelmawla Elsayed, Abdelkarem Hussiny Ismail Elsayed, Mohamed Alshahat Elsayed Ali, Tarek Abualkasem Abualwafa Mohammed, Mohamed Hassan Mohamed Arafa, Emad Abd Elhaliem Abd Elsalam Mahmoud, Hazem Abdallah Ali, Alaa Abdelraouf Taha Hassan, Ahmed R.I. Ali, Walid Mohamed Kamel Ahmed, Mahmoud Gaballah Montaser, Ayman Saleh Mohamed Ragab, Kamal SH Ibraheem, Reda Ramadan Hussein Yousef , Eman Gabr S. Hemaidah, Shaimaa Ramadan Barakat, Yasser M.S Eita, Hatem Attia Mostafa Ismail, Atef A. Alfeky, (2025) Effect of Hydrocortisone on Outcome of Post-Cardiac Arrest Between Road Traffic Accident Poly-Trauma Patients, Vascular and Endovascular Review, Vol.8, No.3, 98-104.

INTRODUCTION

Cardiac arrest is a catastrophic event, with poor outcome [1,2]. It is associated with high mortality, and even among survivors, hypoxic-ischemic brain injury and resultant functional disability are common [3,4]. Post cardiac arrest anoxic encephalopathy is more common between RTA poly-trauma patients who developed cardiac arrest, as sudden severe anemia from bleeding, together with hypotension and hypovolemia which are very common in poly trauma patients, lead to a stat of global brain hypoxemia which aggravated by cardiac arrest. Especially in those who had other causes of traumatic global hypoxemia as severe chest trauma with lung contusion or aspirated due to loss of conscious in accident. Even after resuscitation and ROSC hemodynamic instability occurs in at least 40% of those patients in the peri and post-resuscitative period, and patients often require vasopressor in high doses therapy to maintain adequate mean arterial pressures and maintain tissue perfusion [5-6]. There are many causes lead to cardia arrest in RTA poly-trauma patients. Direct cardiac trauma either blunt or penetrating, hemorrhage, tension pneumothorax and cardiac tamponade are the most common cause. There is some evidence supporting the administration of corticosteroids during acute resuscitation in cardiac arrest. Although the mechanism of action for corticosteroids in cardiac arrest remains uncertain. It may reduce the systemic inflammatory response of the body to this catastrophic event and improve neurological outcome. [7-10]

OBJECTIVE

Study Design and Setting: This prospective, double-blinded, randomized controlled study was conducted in the Anesthesia, Intensive Care, and Pain Management Department at Al-Azhar University Hospitals. Ethical approval was obtained from the Institutional Review Board (IRB), and the study was registered at ClinicalTrials.gov (468/2025)

Study Population: A total of 200 patients admitted to our surgical ICU with cardiac arrest following RTA poly-trauma traumatic were enrolled. Inclusion criteria were: Patient 1st degree relative acceptance**,** adult Age: ($\geq$21- 65$\leq$ years), without any previous co-morbidities (DM, HTN, IHD, on regular corticosteroid therapy before), RTA poly-trauma patients and both sexes (males or females).

Exclusion criteria included:

Patient had traumatic injure incompatible with life e.g. decapitation, brain matter herniation from nose or mouth, evisceration from severe abdominal trauma, multiple penetrating cardiac injury, history of comorbidities (DM, HTN, IHD), and/or on regular corticosteroid therapy before.

Randomization and blinding: Patients were randomized into three groups (n=100 each). Neither the medical team, injector team nor the data collection team was aware of the treatment allocation. Only the researcher team was aware about the drugs given to group B.

Intervention:

•Group A (Control): Standard CPR according to ACLS protocol, with aggressive resuscitation in the form of fluid, blood, blood product.

•Group B (hydrocortisone Group): same as before with administration of hydrocortisone 200 mg stat slowly intravenous during resuscitation and 50 mg iv slowly intravenous every 6 hours for 3 days (duration of the study).

Outcome Measures:

- **Primary Outcome:** Number of patients died, re-arrest, showed post-arrest stunning myocardium, had ROSC with or without inotropic support, developed post-arrest coagulopathy and number of patients who showed improved conscious level and restores normal tissue perfusion.

MATERIAL AND METHODS

Sample size:

Depending of the previous study and on the annual statistics given to the authors by the community department of our hospital about the annual incidence of post cardiac arrest between RTA poly-trauma patients,100 patients were sufficient to produce significant statistical data.

All Cases Underwent:

patient Examination and investigation:

All patients admitted to surgical ICU, Cardiopulmonary resuscitation (CPR) was done according ACLS protocol and full circulatory resuscitation was done by blood, blood product and fluid. Our end point of resuscitation was [Mean arterial blood pressure $\geq$90 mmHg, Hemoglobin (Hb) 10 gm %, urine output (UOP) was 0.5 ml /kg /hour, platelets $\geq$ 100.000 cm^3, INR $\leq$ 1.5, PT $\leq$14 second and PTT $\leq$ 45 second and arterial blood gases shows PH $\geq$7.35, hypoxic index $\geq$ 400, PCO2 $\leq$ 45 and HCO3 $\geq$ 20 mmol/L]. ETT intubation and inotropes used if needed. Then full history from the 1st degree relative to exclude any comorbidities as diabetes mellitus, hypertension and ischemic heart disease (DM, HTN, IHD), and/or on regular corticosteroid therapy before. Physical examination done including Glasgow coma scale (GCS) and routine investigations (complete blood count (CBC), Coagulation profile, sepsis screen, liver and kidney function testes) and Vital data monitoring were done daily. All radiological study (X-ray, CT) and all consultations needed (as surgical, neurosurgical, orthopedic, comprehensive geriatric assessment or cardiothoracic consultations) were done. Only improvement of GCS $\geq$ 2 from the previous patient's GCS assessment was considered improvement in GCS in our study.

In our study a satisfactory term given to UOP daily if rate of UOP is 0.5 ml /kg /hour, given to coagulation profile daily if platelets $\geq$ 100.000 cm^3, INR $\leq$ 1.5, PT $\leq$14 second and PTT $\leq$ 45 and given to arterial blood gases daily if PH $\geq$7.35, hypoxic index $\geq$

400, PCO2 ≤ 45 and HCO3 ≥ 20 mmol/L done every 8 hours/day. If any result from the 3 ABG done daily for all patients not fulfilling the previous mentioned parameters before, so it was excluded and not recorded as satisfactory ABG in that day. A satisfactory tissue perfusion term given in our study if both UOP and ABG were satisfactory according to the criteria mentioned before.

All the former data recorded and presented daily during the studied period.

Method of sample collection:
patients were randomly allocated by a computer - generated table into two groups, each group of (100 patients). For all patients in all groups a daily routine investigation done according to protocol of our hospital including complete blood picture, hemoglobin concentration, coagulation profile and platelets count, arterial blood gases, daily evaluation for weaning from inotropes and weaning from the ventilator according to our hospital protocols.

Withdrawal Criteria: patient's relative given the right to withdraw from the study at any time without any negative consequence on their medical treatment plan.

Operational design:
Patients selected from Al-Azhar University Hospitals who admitted to surgical ICU with cardiac arrest following RTA poly-trauma. Outcome assessor (physician not sharing in the study) monitored the patients for all parameters mentioned above. All Patients followed for 3 days.

Clinical Data monitored and methods of its presentation:
Clinical data include, Number of patients died, re-arrest, showed post-arrest stunning myocardium, had ROSC with or without inotropic support, developed post-arrest coagulopathy and number of patients who showed improved conscious level and restores normal tissue perfusion in both groups on daily basis and presented in tables numerically and by percent.

RESULTS

A total of 200 patients admitted to our surgical ICU with cardiac arrest following RTA poly-trauma.

Patient Characteristics: There were no significant differences between patients of both groups as regard their baseline demographic and clinical characteristics.

Primary Outcome:
A significantly lower percentage of patients in Group B who died, re-arrest, showed post-arrest stunning myocardium, developed post-arrest coagulopathy and significantly high number of patients who showed ROSC without inotropic support, improving conscious level and restores normal tissue perfusion in both groups

Table (1) shows the demographic data of patients

	Group A (n=100)		Group B (n=100)		P value
Age Group	No	%	NO	%	
≥21 - <45 years	65	65%	66	66%	1.000
45 - ≤65 years	35	35%	34	34%	
Sex					
Male	71	71%	73	73%	0.875
Female	29	29%	27	27%	

Table (2) shows outcome data of patients in both groups recorded at the end of first day post arrest

	Group A (n=100)		Group B (n=100)		P value
	No	%	No	%	
Died within 1st day	35	35%	17	17%	0.006
Re-arrest in 1st but revived	15	15%	8	8%	0.184
Picture of stunning heart	65	65%	29	29%	0.0007
ROSC with Nor-epi ≥1mq/kg/min	93	93%	47	47%	0.0003
ROSC with Nor-epi <1mq/kg/min	5	5%	25	25%	0.00017
ROSC without vasopressor	2	2%	28	28%	0.00007
GCS improvement	23	23%	60	60%	0.0002
Satisfactory ABG	25	25%	61	61%	0.0005
Satisfactory UOP	24	24%	61	61%	0.0002
Satisfactory Coag.profile	30	30%	62	62%	0.001

Table (3) shows outcome data of patients in both groups recorded at the end of second day post arrest

	Group A (n=65)		Group B (n=83)		P value
	No	%	No	%	
Died within 2nd day	18	27.7%	8	9.6%	0.0081
Re-arrest in 2nd but revived	12	18.5%	4	4.8%	0.017
Picture of stunning heart	38	58.5%	12	14.5%	0.0005
ROSC with Nor-epi ≥1mq/kg/min	54	83.076%	2	2.409%	0.0008
ROSC with Nor-epi <1mq/kg/min	7	10.769%	42	50.602%	0.0006
ROSC without vasopressor	4	6.154%	39	46.987%	0.0001
GCS improvement	18	27.692%	61	73.494%	0.0007
Satisfactory ABG	19	29.231%	60	72.289%	0.0004
Satisfactory UOP	19	29.231%	60	72.289%	0.0004
Satisfactory Coag.profile	20	30.769%	62	74.699%	0.0002

Table (4) shows outcome data of patients in both groups recorded at the end of third day post arrest

	Group A(n=47)		Group B (n=75)		P value
	No	%	No	%	
Died within 3rd day	14	29.8%	3	4%	0.00019
Re-arrest in 3rd but revived	10	21.3%	2	2.66%	0.0023
Picture of stunning heart	30	63.83%	5	6.66%	0.0004
ROSC with Nor-epi ≥1mq/kg/min	28	59.6%	1	1.33%	0.0009
ROSC with Nor-epi <1mq/kg/min	12	25.5%	6	8%	0.0166
ROSC without vasopressor	7	14.9%	68	90.66%	0.00002
GCS improvement	15	31.9%	63	84%	0.0001
Satisfactory ABG	16	34.04%	65	86.66%	0.0006
Satisfactory UOP	14	29.8%	66	88%	0.001
Satisfactory Coag.profile	14	29.8%	66	88%	0.001

	Group A (n=100)		Group B (n=100)		P value
	No	%	No	%	
Total number of mortalities	67	67%	28	28%	0.0007

DISCUSSION

In this study we demonstrate the effect of hydrocortisone on the outcome of post-arrest between RTA poly-trauma patients. There was no any significant difference between the demographic data of the patients allocated in both groups. Male was more common than females in both group this could be explained by our community social rules as still males are more vulnerable to motor car accident than females. RTA poly trauma patients who had no any history of co-morbidities (DM, HTN, IHD and not on regular corticosteroid therapy before) was chosen as this type of patients are always heathy and young so the effect of post cardiac arrest can be monitored without being biased with co- morbidities, corticosteroid therapy before or/and old age. the biases effect of trauma reduced to its minimal by fixed inclusion criteria which guarantee a full resuscitation of all patients in both groups, by this full resuscitation the only effect lift on all patients is the effect of post cardiac arrest which followed by the previous mentioned parameters. The parameters used in our study to follow the outcome of post cardiac arrest were chosen from the previous study and were chosen to cover the neurological outcome (conscious level by GCS), hemodynamic parameters (ROSC with or without inotropes and ECHO for evaluation of post cardiac arrest myocardial stunning), global tissue perfusion parameters (ABG/ 8hous and urine output/ day), number of patients had re-arrest and mortality rate. Unlike previous study we could not follow neither the incidence of chest infection nor the incidence of renal impairment as important outcomes post cardiac arrest as our study focused on RTA poly-trauma patients and in those patient lung contusion and traumatic kidney injuries are very common and this will lead to biases of the result.

The duration of the study was only three consecutive days; this duration was chosen by our research and community department of our hospital. As we reviewed our annual medical records about mortality rates for those patients admitted to our hospital with post-cardiac arrest following RTA poly-trauma and we found that peak time for mortality was three days after cardiac arrest in those patients. There was no any specific duration was recommended by any clinical trial or published meta-analysis in this issue. [7-10]

Our study found significant difference in both mortality rate and all outcome parameters measured in corticosteroid group as there was significant lower number of patients died, lower number of patients who developed re-arrest, lower number of patients who need high dose of inotropes to support ROSC and developed coagulopathy. And significant higher number of patients who showed improvement in their GCS and restored normal tissue perfusion.

It is well known that in cardiac arrest there are two main mechanisms responsible for direct cell injury especially nerve cell injury. First one is the severe hypotension which can be explained by massive inflammatory response secondary to cardiac arrest which start a cascade exactly similar to systemic inflammatory response occurs in sepsis with release of pro-inflammatory cytokines (TNF-a, IL-1, IL-6), together with prolonged tissue ischemia and myocardial stunning. The second mechanism is the Stress imposed by cardiac arrest results in an acute stress response which is mediated by the activation of the Hypothalamus Pituitary Adrenal axis (HPA). Although an intact HPA axis will increase levels of circulating cortisol, the response of the adrenal gland is inadequate related to the degree of hypoxic stress associated with cardiac arrest [11]. The stat of global hypoxia and no- flow of cardiac arrest followed by the low flow of CPR results in inadequate perfusion of the adrenal cortex and impairs the integrity of the HPA axis [12]. The ischemic injury of the adrenal gland leads to adrenal insufficiency, which may be manifested as an inability to increase cortisol secretion during and after CPR. [13]. Hydrocortisone given in such life-threatening condition considered as a replacement therapy that support the inadequate synthesis of cortisone due to the ischemic injury of the adrenal gland. Moreover, Corticosteroid can increase the sensitivity of beta- and alpha-adrenergic receptors to the released catecholamine during the stress of cardiac arrest and CPR and also improve the response to any inotropic support given to the patients during this stress condition. [11-13]. These previous mentioned pharmacological actions could explain the significant higher number of patients had ROSC without inotropes or with minimal inotropes, had satisfactory ABG, satisfactory urine output and satisfactory tissue perfusion. Also, it could explain the significant lower number of patients had re-arrest, post-cardiac arrest myocardial stunning due to better response of corticosteroid group to catecholamine released from their body or from inotropes given to support the hemodynamics. While improvement in coagulopathy could be explained by cessation or at least reducing the systemic inflammatory response which occur due to cardiac arrest, hypoxemia and stress. This systemic inflammatory response activates the extrinsic coagulation pathway and lead to coagulopathy. The improvement in conscious level monitored in our study by improvement of patient's GCS by $\geq$ 2 from the previous last GCS recorded and this could be explained by anti-inflammatory action of corticosteroid and anti-edematous effect which led to complete resolve of the cytotoxic brain edema which may be due to prolonged period of hypotension and hypoxemia. Also, improvement of tissue perfusion and of course brain perfusion between corticosteroid group could also explain this neurological improvement.

The results of our study support the results published in this field as [14-20] all those studies clarify the effect of corticosteroid either methylprednisolone [14-19] or dexamethasone [20] on restoring ROSC with no or minimal inotropic support and prove its effect on restoring myocardial function followed post-cardiac arrest stunning but they conclude that no effect of corticosteroid on the mortality rate. On the other hand, a meta-analysis done in 2023 [21] and clarify that hospital in patients during or after cardiac arrest, corticosteroids have an uncertain effect on mortality but probably increase ROSC and may increase the likelihood of survival with good functional outcome at hospital discharge. Corticosteroids may decrease ventilator associated pneumonia, may increase renal failure, and have an uncertain effect on patients with post cardiac arrest

Unlike previous mentioned studies our study found that hydrocortisone during resuscitation and as a maintenance dose for three consecutive days markedly improve the overall mortality rate.

LIMITATIONS AND FUTURE DIRECTIONS

Despite its strengths, this study has several limitations. First, the sample size was relatively small, which may limit the generalizability of our findings. Second, our sample was restricted to RTA poly trauma patients only not including medical cases. Third, was the short duration of our study which limit our results. In spite of decreasing the biases of trauma effect on our results by good resuscitation as mentioned before still could be effect of trauma especially those who had cardiac contusion and not diagnosed.

Future research should focus on randomized controlled trials with larger cohorts to better define the risk-benefit profile of corticosteroids in this life-threatening condition. Additionally, a fixed dose, duration and protocol should be emphasized to be followed by all physician.

In conclusion, hydrocortisone is an effective and efficient option for hemodynamic support and improving neurological outcome and decreasing mortality rates offering advantages over the conventional way of resuscitation by ACLS in terms of speed and safety. While our study supports its clinical utility, careful patient selection and further research into individualized dosing and long-term outcomes are warranted to optimize its use.

CONCLUSION

Hydrocortisone is an effective and efficient option in improving cardiac arrest outcomes and decreasing mortality rate, decreasing percent of re-arrest, restoring normal tissue perfusion and coagulation profile between post- arrest RTA poly trauma patients. While our study supports its clinical utility, careful patient selection and further research into individualized dosing and long-term outcomes are warranted to optimize its use.

Acknowledgment

The authors would like to express their sincere gratitude to ALLAH SWT and all team working on manuscript.

Author Contributions
Concept and design.
Acquisition, analysis, and interpretation of data.
Drafting of the manuscript, Critical review of the manuscript for important intellectual content,
Supervision, and approval of publication.

Conflicts of Interest
The authors declare that they have no conflicts of interest to disclose related to this work.

Confidentiality of Data
The authors affirm that all data collected were handled in accordance with confidentiality protocols approved by their institution. No identifying patient data has been published.

Financing Support
The authors declare that no financial support was received from any public or private institution, commercial entity, or nonprofit organization for the submitted work.

Financial Relationships
The authors have no financial relationships to disclose with any organizations that could have an interest in the submitted work, either now or within the past three years.

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