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Studying the Influence of Epinephrine Mixed With Prednisolone on The Neurologic Side Effects After Recovery in Patients Suffering From Cardiopulmonary Arrest

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ABSTRACT

Early neuro-cognitive disorders usually take place after cardiopulmonary arrest. As the previous studies indicate, this disorder is observed among 30 to 60 percent of the patients which can damage the memory or the psychomotor performance, impair post-cardiopulmonary arrest recovery, reduce life quality and delay return to work. The present study seeks to propose a method to reduce the neurologic side effects after CPR. In this research, we studied the clinical trials of 50 patients past 18 years who required cardiopulmonary resuscitation. The patients were divided into 2 groups. Intervention group was given an IV injection of 125 mg Methylprednisolone beside epinephrine. The placebo group was injected with saline as placebo. During the first 24 hours after resuscitation, the neurologic side effects of the patients was measured and analyzed using CPC score. The average age of the patients participating in this study was 68.92 years old. 33 patients (66 percent) were male, while 17 (34 percent) were female. The initial rhythm of resuscitation was VT in 14 patients, while this rhythm was Asystole in 36 patients. The CPR was successful for 9 patients in E+M group and for 6 patients in E group. Among the 9 patients in E+M group, 4 survived up to 24 hours. One patient had a CPC score of 1, two had a CPC score of 4, and one had a CPC score of 5. Of the six patients in group E, just 3 of them survived for 24 hours among whom one had a CPC score of 4 and two had a CPC score of 5. The comparisons made between the two groups in terms of percentage of successful CPR (P=0.269) and CPC score of the patients (P=0.329) revealed no significant difference. Utilizing Methylprednisolone had no significant influence on raising the level of ROSC or on attenuation of neurologic side effects in resuscitated patients suffering from cardiac arrest.

Key words: cardiac arrest, neurologic side effects, epinephrine, prednisone, return of spontaneous circulation (ROSC) .

INTRODUCTION

Cardio-pulmonary resuscitation or CPR includes a series of organized actions conducted on patients suffering from cardio-pulmonary arrest. It is an attempt to artificially preserve the respiratory and circulatory systems so that enough oxygen can be provided to the vital organs of the body until the spontaneous physiological activity of the circulatory system is restored. Not undertaking such actions would result in permanent brain death in 4 to 6 minutes (the golden period) due to the lack of oxygen. As proposed by Peter Sefer (father of resuscitation science), the term cardio-pulmonary resuscitation was changed to cardio-pulmonary cerebral resuscitation (CPCR) to emphasize the

importance of cerebral resuscitation and preserving her performance. These actions comprise of two stages: basic life support (BLS) and advanced cardiac life support (ACLS)[1-2].

In developed countries, the survival rate of cardiac arrests which take place inside and outside the hospital are less than 10 and 30 percent respectively[3]. Most of the patients who survive also suffer from its side effects such as neurological side effects.

Early neuro-cognitive disorders usually take place after cardiopulmonary arrest. As the previous studies indicate, this disorder is observed among 30 to 60 percent of the patients which can damage the memory or the psychomotor performance, impair post-cardiopulmonary arrest recovery, reduce life quality and delay return to work[4].

As various studies have shown, Adrenal insufficiency and high levels of ACTH and ADH in plasma cause shock and increase the mortality level in patients. Thus, adrenal insufficiency after cardiac arrest in patients with ROSC results in poor outcome of the patients. Treating adrenal insufficiency with Corticosteroid (even when there are normal to high levels of Cortisol) reduces the mortality level of functional disorders of the vital organs and improves neurologic side effects[5].

Cerebral damages due to coronary arrest present themselves in a vast spectrum including stroke, encephalopathy, and cognitive disorders. The commonest sign of cerebral damage is stroke which is observed in 1 to 3 percent of the patients after cardio-pulmonary arrest[6-7]. However, the cognitive disorders are the commonest neurological disorder observed in 30 to 65 percent of the patients in the first month and observed after the fifth month among 20 to 45 percent of the patients. The clinical variables associated with the risks of neurologic side effects include old age, systematic hypertensions, previous strokes, female gender and ascending aorta atherosclerosis. Seemingly, cerebral embolism and Ischemia due to hypoperfusion are the main causes of cerebral damages caused during the cardio-pulmonary arrest[9 & 10].

From both ethical and economic points of view, it is necessary to study all the factors which influence the success or failure of a cardio-pulmonary resuscitation and propose appropriate and scientific strategies to remove the obstacles to a successful resuscitation. Thus, the present research seeks to propose a method to prevent or attenuate these side effects so that the levels of mortality and the functional disorders of the vital organs can be reduced and the neurological side effects can be improved.

Methodology

Patients

Among the patients who had had cardio-pulmonary arrests in the emergency service department of Imam Reza (PBUH) hospital in 2015 who required cardio-pulmonary resuscitation, 50 patients past the age of 18 who had no neurological problems and their relatives had no problem with them being studied took part in this research.

Design of the study

In this clinical trial study, the patients were divided randomly into two groups (intervention and placebo) based on the table of random numbers. There were 25 patients in each group. There were 25 patients in each group. The resuscitation operation was conducted for each of these groups according to AHA protocol (consisting of chest compressions, shock and application of epinephrine and anti-arrhythmic).

Intervention

Patients in both group received 1 milligram of epinephrine in each CPR cycle which lasted about three minutes. Methylprednisolone IV injection was prescribed for the intervention group during the first cycle of resuscitation or the second time for injection of epinephrine (3 to 5 minutes). In the placebo group, saline was used as placebo. Methylprednisolone and saline were prepared in separate syringes and the person in charge of the injections did all the injections based on particular codes.

Information and analysis

Demographic information, records of past diseases, heart rhythm of the patient, need for shock and the vital signs after resuscitation were

recorded. Then, the neurologic side effects of the patients during the first 24 hours after resuscitation were recorded based on the patient records and doctor's examination according to CPC.

CPC score is defined in the following ways:

1. Good cerebral performance (he is conscious and capable of working and normal life)
2. Average performance disorder (he is conscious and independent for his daily chores, however, he has cognitive disorders, paresis, seizure)
3. Severe performance disorder
4. Coma or vegetative life
5. Death

SPSS version 16 was used for statistical analysis and P-values less than 0.05 were deemed significant from the statistical point.

RESULTS

We studied the clinical trials conducted on 50 patients requiring cardio-pulmonary resuscitation in 2015 in the emergency service department of Imam Reza (PBUH) hospital. The patients were divided randomly into two groups (intervention and placebo) based on the table of random numbers. There were 25 patients in each group.

The average age of the patients participating in this study was 68.92±15.96 years. The average age of the participants in Epinephrine (E) group and Epinephrine+ Methylprednisolone (E+M) was 67.64 and 70.2 respectively.

33 patients (66%) were male and 17 (34 %) were female. There were 15 men (60%) and 10 women (40 %) in group E. In E+M group, 18 patients (72%) were male and the rest were female. The difference between these 2 groups was not significant in terms of gender distribution (P=0.136).

Concerning the record of previous diseases, high blood pressure observed among 22 patients (44%, 14 in E+M group and 8 in E group),

Table 1: Records of past diseases among patients participating in the study

disease	Total		group E+M		group E		P.value *
	Number	Percent	Number	Percent	Number	Percent	
IHD	11	22	7	28	4	16	0.248
CHF	12	24	10	40	2	8	0.009
kidney failure	4	8	3	12	1	4	0.305
DM	9	18	5	20	4	16	0.5
HTN	22	44	14	56	8	32	0.077
cancer	5	10	1	4	4	16	0.174

* Fisher's exact test

Table 2: A comparison between groups E+M and E in terms of CPR success level and CPC score of patients

		E+M group	E group	P. value
CPR	successful	9	6	0.269*
	unsuccessful	16	19	
CPC score	1	1	0	0.329**
	2	0	0	
	3	0	0	

* Fisher's exact test ** Chi-square

was the commonest problem. The records associated with 6 diseases were recorded. The total frequency of these diseases in group E+M was 40 and this total frequency in group E was 23, thus no significant different was observed (P=0.081). The prevalence and the separate comparison of each disease among the patients in both groups are presented in table 1.

Concerning the cardiac arrest panel, 7 had MI panel, 9 had chronic pulmonary failure panel, 3 had metabolic disorder panel, 3 had Sepsis panel, 18 had septic shock panel and one had suffered cardiac arrest due to food poisoning.

The initial rhythm of resuscitation in 14 patients was VT, while this rhythm was Asystole in 36 patients. The number of cases of VT and Asystole rhythms in E+M were 5 and 20 respectively, while these numbers were 9 and 16 respectively for group E and no significant difference was observed (P=0.173).

The CPR was successful in 15 patients and failed in 35. Of the 15 patients who had a successful CPR, only 7 survived up to 24 hours. Of these 7 people, only one could attain CPC score 1 and two got the CPC score 4 (vegetative life or coma), while 4 attained a CPC score of 5 (death).

The CPR for 9 patients in E+M group and 6 in E group was successful. Of the 9 patients in E+M group, 4 survived for 24 hours with 1 patients having the CPC score of 1 (good cerebral performance, conscious, normal life), 2 had a CPC score of 4 and 1 had the CPC score of 5. Of 6 patients in group E, only 3 survived for 24 hours among whom 1 had a CPC score of 4 and 2 had a CPC score of 5. The comparison made between the 2 groups in terms of successful CPR (P=0.269) and CPC score of patients (P=0.329) revealed no significant difference.

DISCUSSION

In this research, we studied the effects of IV injection of 12 mg of Methylprednisolone in improving the post-resuscitation neurologic side effects in patients suffering from cardiac arrest as it is possible that adding and using Steroids (30) during CPR might be useful for patients.

As old age and being female are among the clinical variables associated with neurologic side effects risk[9-10], due to absence of a significant difference between the 2 groups (P>0.05) they can not be considered as factors that distort the results.

Concerning the records of previous diseases, systematic hypertension, previous cerebral stroke and diabetes are among the factors that raise the risk of neurological side effects[9-10]. The prevalence of all these diseases in group E+M was more than what was observed in group E, however this difference was not significant.

CPR was successful in 15 patients and failed among 35 (30% success in return of ROSC). Of 15 patients who had successful CPR, only 7 survived for 24 hours. Of these 7, only one could attain a CPC score of 1 to 3 and gets discharged from hospital (2%).

As stated in previous studies, the post-resuscitation death rate in Iran is 90 and the patients' discharge rate from hospitals is less than 7 % (11 and 12). However, the statistics in other parts of the world are completely different. For example, a study conducted in Croatia showed that of 96 patients who received cardio-pulmonary resuscitation services, 22.5% left the hospital alive[13]. Of 14720 adult patients in 207 hospitals in U.S who were reported to have cardiac arrest, the blood circulation and pulse were restored among 44% of them and 17% left the hospital alive[14].

CPR conducted in groups E+M and E was conducted in 36 and 24 percent of the cases respectively. In E+M group, 4 patients survived for 24 hours among whom 1 had a CPC score of 1, 2 had a CPC score of 4 and 1 had a CPC score of 5. In group E, 3 patients survived for 24 hours among whom 1 had a CPC score of 4, and 2 had a CPC score of 5.

Comparisons between 2 groups in terms of percentage of successful CPR and CPC score of the patients showed no significant difference. However, these results are not reliable due to the small sample of the patients who took part in the research.

Our results were not in line with the 2 studies conducted by Mentzelopooulos et al.[15]. The studied the effects of using a compound of vasopressin-epinephrine and corticosteroid supplement on improving the survival rate and being discharged from hospital with CPC scores 1 and 2 in patients afflicted with cardiac arrest. They observed that the probability of ROSC return (at least for 20 minutes) in VSE group was significantly more (83.9% versus 65.9%). Survival till being discharged from hospital with CPC scores 1 and 2 was significantly more in VSE group (13.9% versus 5.1%). Their other study also showed the possibility of ROSC formation in the first 20 minutes of CPR and the survival rate in VSE group to be more than what was obseved in the control group[5]. The level of neurologic side effects after resuscitation in our study was much less in the group receiving methylprednisolone, however, the small sample rendered the difference between the two groups insignificant.

Comparing the patients who had received hydrocortisone and saline, Tsai et al. reported the frequency of ROSC in hydrocortisone group to be significantly more than what was observed in other groups (61% versus 39%). No difference was observed between the two groups in terms of prevalence, and in terms of survival rate 1 and 7 days after being discharged from hospital[16].

On the other hand, Paris et al. studied the influence of injecting 100 mg dexamethasone on patients afflicted with cardiac arrest before resorting to hospital with pulseless idioventricular rhythm (PIVR) was studied and the results showed no benefits associated with using dexamethasone[17].

We encountered many restrictions in this research including various factors influencing the result of resuscitation. It was also impossible to measure and unify the demographic information of patients, their hemodynamic status, the period before they get to the emergency service department of a hospital, the factors contributing to cardiac arrest and many other factors affecting the result of resuscitation.

On the other hand, the number of patients who could participate in research was so limited. The success level of the CPR's was so little, thus the sample never reached the favorite level and the result would not be much reliable.

The small number of ICU beds results in patients staying in the emergency center of Edalatian for a longer time. This factor contributes a lot to low levels of CPR success in this center.

CONCLUSION

Generally, utilizing methylprednisolone in this study didn't have much influence on increasing the production rate of ROSC or on reduction of neurologic side effects in patients afflicted with cardiac arrest who have undergone resuscitation.

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