Review Article

Is cardiac arrest an inflammatory state? Adding steroid into ACLS guidelines will save more lives?

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Abstract:

Cardiac arrest is a life-threatening condition with low survival rate. Over the years ACLS guidelines have been developed to reduce cardiac arrest specific mortality rate. In this review article, the authors researched steroid use during and after CPR for determining its effect on survival rate and post cardiac arrest disabilities. Scholarly articles from well-known reputed journals relevant to both cardiac arrest and steroid use since 1960 have been reviewed. This article first examines the question whether cardiac arrest can be considered an inflammatory state. Afterwards, evidence of the beneficial role of steroid use in cardiac arrest and in other cardiac conditions have been outlined. In conclusion, this review paper summarizes any benefits of steroid use in cardiac arrest.

Introduction:

According to American Heart Association, in 2016 In-Hospital Cardiac Arrest (IHCA) and Out-Hospital Cardiac Arrest (OHCA) incidences among adults in USA were around 209,000 and 350,000 respectively, with in-hospital survival rate of 24.8% and out-hospital survival rate of 12%[1]. With an increase in various cardiac diseases, the incidence of cardiac arrest is also climbing. Cardiac arrest is defined by the abrupt cessation of working capability of heart, resulting in blood circulatory failure. A cardiac arrest (either in-hospital or out-hospital) is an emergency condition where early cardiopulmonary resuscitation (CPR), epinephrine and defibrillation can increase the survival rate significantly. In this article, the use of steroid during and after CPR has been reviewed, with an emphasis to determine its effect on survival and post cardiac arrest disabilities.

Methods:

The authors searched Google Scholar (1960 - June 2018) using the keywords and medical subject heading such as cardiac arrest, congestive heart failure, myocarditis, post cardiac surgery, acute coronary syndrome, steroid. We only reviewed the papers published in English. The following criteria were applied while selecting studies: studies on patients with related medical conditions, randomized or non-randomized studies, studies published in prominent journals with significant number of citations.

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Is cardiac arrest an inflammatory state?

There is evidence of dysregulation of the hypothalamic–pituitary–adrenal axis and concurrent adrenal insufficiency along with increase systemic inflammation as assessed by serum interleukin (IL)-6 levels in comatose survivors of out-of-hospital cardiac arrest (OHCA) in the early post-resuscitation phase[2,3] Furthermore, cytokines (i.e. IL-1, IL-6, IL-8 and tumor necrosis factor-alpha), synergistically depress myocardial contractile function and may thus contribute to post-resuscitation myocardial dysfunction[4,5]. Lower levels of steroids and higher levels of IL-6 following return of spontaneous circulation (ROSC) have been associated with worse outcomes[2,3,5]. Vaahersalo et al. reported that high IL-6 levels on hospital admission following OHCA are associated with post-resuscitation organ dysfunction and independently predict poor neurologic outcome at 12 months [6] Usually a stressful physiological event causes blood cortisol level to increase. However, in case of a cardiac arrest, researchers have found that although this event is extremely stressful for the body, it actually decreases the blood cortisol level[7,8]. Moreover, in vasodilatory shock states, stress dose steroids potentiate the action of vasopressors and accelerate shock reversal[9].

Effect of steroid in cardiac arrest:

Due to potential benefits of steroid use, there has been a recent trend in the medical community across the globe to perform clinical research on the effects of administering steroids to patients in cardiac arrest during CPR[10,11,12,13]. Tsai et al. conducted a retrospective cohort study with the data from the Taiwan National Health Insurance Research Database to determine the effect of steroids in OHCA outcomes[11]. The researchers found significant improvement in both survival to hospital discharge rate and 1-year post cardiac arrest survival rate, due to administration of steroids during CPR[11]. Patients with Chronic Obstructive Pulmonary Disease (COPD) and Asthma also benefited from steroid use during CPR administration[11]. They hypothesized that when a steroid is administered alongside CPR, it (steroid) counteracts the adrenal gland insufficiency and maintains adequate level of

circulating corticosteroid[11]. In another retrospective study conducted in Japan by Nimura et al. with both IHCA and OHCA patient data, they also found an improvement in survival rate to hospital discharge and decrease in the length of hospital stay from cardiac arrest to discharge due to hydrocortisone administration during CPR[13]. Both of these studies were performed with a large number of subjects to ensure higher statistical power[11,13]. However, due to the retrospective nature of these studies, they have some limitations, such as: (a) the subjects could not be randomized, and (b) effect of different steroid dosage could not be measured appropriately. In a separate randomized, double-blinded, prospective study conducted in a tertiary care center in Greece, an improvement in the survival rate of cardiac arrest patients with use of steroid (40 mg) during CPR, was reported[12]. There also has been at least one randomized clinical study that reported to the contrary[10]. It stated that the use of steroid did not significantly improve the clinical outcome in patients with cardiac arrest due to pulseless idioventricular rhythm. The lack of improvement in survival rate might be due to the severity of this etiology[10].

One of the concerns after cardiac arrest is vegetative state or cerebral dysfunction, which includes seizures, myoclonus, and neurocognitive dysfunction. Steroid administration during and after CPR helps in alleviating cerebral complications by correcting adrenal dysfunction[14]. There is also evidence that utilizing therapeutic mild hypothermia after cardiac arrest can produce better neurological outcome[15]. However, recent studies have concluded that instead of therapeutic mild hypothermia, steroid use can be an effective alternative to prevent neurological impairment significantly[14]. Mentzelopoulos et al. reported the benefit of administering steroids during (40 mg) and after (300 mg per day) CPR, over epinephrine and saline only [14]. In that clinical study, it was found that patients who have been administered steroid after cardiac arrest, fell into two best possible neurological outcomes CPC 1 & 2, according to Cerebral Performance Category (CPC) scale[16,17]. They also reported other benefits of such steroid use, namely improved mean arterial pressure, central venous oxygen saturation, and decreased lactate.

Other than reported better survival rate, and neurological outcomes, steroid is also known to provide anti-inflammatory benefits[4,18]. Patients who survive after 24 hours of cardiac arrest, a cytokine IL-6 increases significantly[2]. A study by Donnino et al. showed that the steroid use decreased IL-6 level post cardiac arrest[19]. However, the reduction in IL-6 did not result in better clinical outcome[19]. This contradictory result may be explained by the relative small sample size used in that study.

Although, theoretically a steroid can interfere with cardiac healing, in patients with acute myocardial infarction, but there is evidence of it not causing any harm; on the contrary, it has mortality benefit[20].

Effect of steroids in other cardiac conditions:

According to several clinical studies, administering steroid to treat various cardiac conditions has been promising. In a clinical trial conducted by Chao et al. it was concluded that steroid co-administration with standard therapy results in reversibility of refractory volume overload in CHF stage IV through improvement in renal functions[21]. Steroid plays an important role in reducing the volume overload there, by synthesizing and releasing an endogenous diuretic Atrial Natriuretic Peptide[21]. In case of an inflammatory cardiac condition such as acute myocarditis, studies reveal that steroid use can reduce myocardial inflammation, resulting in better prognosis by improving myocardial functionality[22,23]. Therefore, steroid is an integral part of immunosuppression therapy in myocarditis.

Post cardiopulmonary bypass surgery, SIRS (induced by cytokines IL-6 and IL-8 among others) can be apparent, which increases postoperative complications. Early steroid administration reduces these inflammatory cytokines[24]. Another most common complication of cardiac bypass surgery is Atrial Fibrillation (AF). In general, patients exhibiting sinus rhythm after bypass surgery, spend less time being hospitalized[25]. Steroid use decreases the risk of AF but slightly increases the risk of other complications. However, those complications can be managed by steroid dosage adjustment with respect to patient's age, and comorbidities[25]. Furthermore, low pulsed steroid dose before and during cardiac surgery decreases morbidity, including better hemodynamic and respiratory outcomes, and lower hospitalization time, but not mortality[26,27]. Prophylactic steroid use before warm cardiac surgery reduces post-surgical complications by reduced release of inflammatory mediators during surgery[28]. Through reactive oxygen radical formation and inflammation within atherosclerotic plaques of coronary arteries, polymorphonuclear leukocytes (PMN) inflame them, causing Acute Coronary Syndrome (ACS)[29]. Although, steroid use exhibits mortality benefits in ACS, but there is a risk of infarcted tissue remodeling due to such use [30].

Key Advantages of Steroid use:

After reviewing a significant number of available scholarly articles, we can summarize the benefits of steroid use during and after CPR in the following way. Steroid use is beneficial in treating cardiac arrests during and after CPR due to:

(1) early establishment of ROSC,

(2) increased hospital survival rate,

(3) increased 1-year post cardiac arrest survival rate,

(4) decreased post cardiac arrest organ failure, and neurological impairment; and

(5) indifference in incidence of adverse effects when compared to standard therapy.

Conclusion:

Although there are few studies about the benefits of steroid in cardiac arrest, but many studies showed increased systemic inflammatory response after CPR. Furthermore, administration of steroids post CPR, presents with favorable neurological outcomes. However, more randomized clinical studies, with larger sample size, and variable parameters to

account for various etiologies, and dosage are necessary to better understand the effect of steroid use on post cardiac arrest complications.

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