Adrenaline in cardiac arrest
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ABSTRACT
The use of adrenaline during a cardiac arrest is well-established and supported by international guidelines. However, recent studies\(^1\)\(^–\)\(^2\) have questioned the appropriateness of adrenaline administration whereas other papers indicate that any benefit from adrenaline may be time-sensitive.\(^3\)\(^–\)\(^4\)

Two recently published studies have both challenged the use of adrenaline during resuscitation and whilst both papers used different methodologies they demonstrated similar results. The Paramedic 2 study\(^1\) was a placebo-based randomised control trial whereas the paper by Loomba et al.,\(^2\) used a meta-analysis of 14 peer-reviewed publications recruiting 655,853 patients, 7.4% of whom received adrenaline. Neither study was able to demonstrate any meaningful survival benefit associated with adrenaline administration (Table 1 and 2). However, both studies noted poor neurological outcome in post-cardiac survivors. It is noteworthy that both of these studies used different, but validated,\(^5\) neurological scoring systems (either the Modified Rankin Scale or the Cerebral Performance Category).

Whilst there is an acceptable correlation between the Modified Rankin Scale or the Cerebral Performance Category (Table 3) there is a degree of variation.\(^5\) This variation is partly due to what the two scales accept as being a good neurological outcome as well as
an inbuilt degree of subjectiveness of any assessment of neurological status.\(^5\)

Whilst The Paramedic 2 study\(^1\) and Loomba et al.,\(^2\) meta-analysis demonstrated no benefit of adrenaline, studies by Goto et al.,\(^3\) and Donnino et al., (adults)\(^4\) have published contradictory findings. Importantly Donnino et al.,\(^4\) reported improved neurological status in non-shockable cardiac arrest when adrenaline was administered.\(^2\) However, to date no study has demonstrated a benefit of adrenaline when used to treat shockable cardiac arrest.

Interestingly both Goto et al.,\(^3\) and Donnino et al.,\(^4\) indicated that any benefit from adrenaline administration was time-sensitive. Goto et al.,\(^3\) noted that the optimal time for adrenaline administration was <9 minutes. Whereas, Donnino et al.,\(^4\) reported on the impact of increasing time delay to the first dose noting that when adrenaline was administered <1 minute of confirmation of cardiac arrest, 12% of patients survived, but that this dropped to 9% after the fourth minute and was down to 7% after seven minutes (\(p < 0.001\)). The findings of Goto et al.,\(^3\) and Donnino et al.,\(^4\) represent a clinical challenge. Notably, during the Paramedic 2 study the average time of administration of adrenaline was approaching 20 minutes (6.6 minutes response time and 13.8 minutes) raising the question would the results of Paramedic 2 have been different if adrenaline was administered faster and whether adrenaline should only be administered in witnessed cardiac arrest?

The routine use of adrenaline as the mainstay of resuscitation is being challenged, especially with regards to long-term patient survival and its role in the management of shockable cardiac arrest. However, in specific patients, when given early, adrenaline may still have a role to play in resuscitation. The 2020 International Resuscitation Guidelines are eagerly awaited.

Keywords: adrenaline, epinephrine, cardiac arrest, ROSC, resuscitation

Table 1. Survival data Paramedic 2 study

| Adrenaline | Initial ROSC | Favourable neurological outcome at discharge | Favourable neurological outcome at 3 months |
|------------|--------------|---------------------------------------------|---------------------------------------------|
| Paramedic 2 | Yes (n = 4015) | 36.3% | 2.2% of survivors | 2.1% of survivors |
| Perkins et al.\(^1\) | No (n = 3999) | 11.7% | 1.9% of survivors | 1.6% of survivors |

ROSC: Return of spontaneous circulation

Table 2. Survival data Loomba et al., meta-analysis

| Adrenaline | Initial ROSC | Survival at one month | Favourable neurological outcome |
|------------|--------------|-----------------------|--------------------------------|
| Loomba et al.\(^2\) | Yes (n = 48,755) | 19.7% | 5.4% | 1% of survivors |
|               | No (n = 607,098) | 5.5% | 4.5% | 2.2% of survivors |

ROSC: Return of spontaneous circulation
Table 3. Neurological scoring systems

| Modified Rankin Scale | Cerebral Performance Category |
|-----------------------|------------------------------|
| 0 – No symptoms.      | 1 – Good cerebral performance might have mild neurological or psychological deficit |
| 1 – No significant disability. Able to carry out all usual activities, despite some symptoms. | 2 – Moderate cerebral performance able to work in a sheltered environment |
| 2 – Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities. | 3 – Severe disability |
| 3 – Moderate disability. Requires some help, but able to walk unassisted. | 4 – Coma |
| 4 – Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted. | 5 – Brain death |
| 5 – Severe disability. Requires constant nursing care and attention, bedridden, incontinent. | |

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