



Background

ATP reduction plays an important role in neurological injury after asphyxia cardiac arrest (ACA). Dichloroacetate acid (DCA) is a pyruvate dehydrogenase kinase inhibitor, which activates pyruvate dehydrogenase, and increases cell ATP production by promoting influx of pyruvate into the Krebs cycle. In this study, we investigated the effects of DCA on post-resuscitation neurological injury in an ACA rat model. We hypothesized that DCA increases the level of ATP in the brain and therefore improves neurological outcome after ACA.

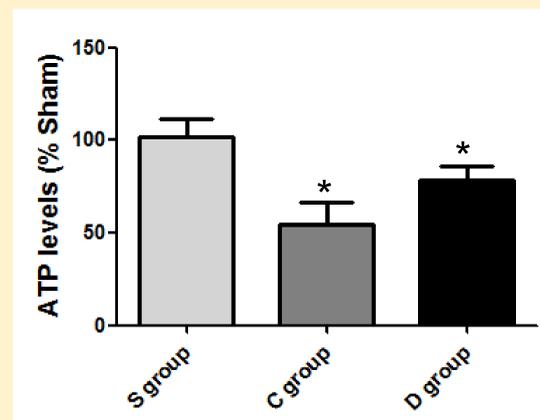
Methods

Animals were randomized into 3 groups after restoration of spontaneous circulation (ROSC): Control group (C, N = 12), DCA intervention group (D, N = 12), Sham group (S, N = 6). Animals in both C and D groups were randomly divided into 2 subgroups: ROSC 6 h (n = 6) and ROSC 72 h (n = 6). DCA (80 mg/kg) or placebo was administered by intraperitoneal injection at 30 min after ROSC. The neurologic deficit scores (NDS) were measured at 24 h, 48 h and 72 h. Brain ATP levels in the S group and ROSC 6 h subgroups were measured at 6 h.

Results

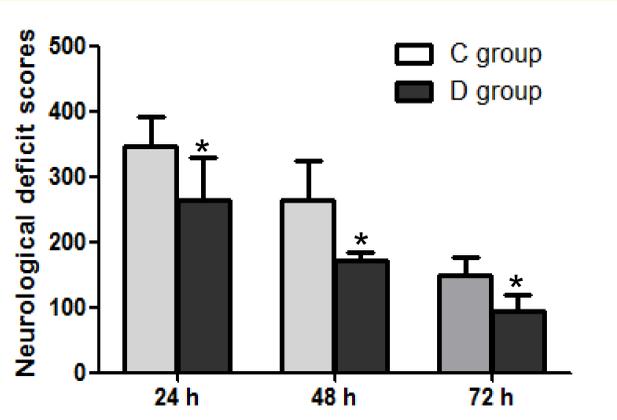
No difference in the duration of asphyxia before mean aortic pressure < 30 mm Hg was observed in either group [(4.7 ± 0.3) min vs. (4.7 ± 0.4) min, P = 1.0]. The brain ATP level in group C was lower than group D (Figure 1). Lower NDS at 24 h, 48 h and 72 h was achieved by treatment with DCA compared to control (Figure 2).

Figure 1 ATP levels after restoration of spontaneous circulation.



S group, Sham group; C group, control group; D group, DCA intervention group. * $p < .05$ vs. the Sham group.

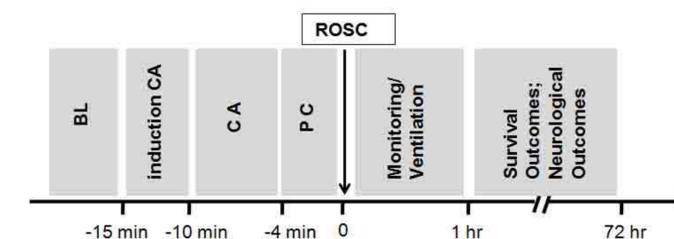
Figure 2 Neurologic deficit score after restoration of spontaneous circulation.



C group, control group; D group, DCA intervention group. * $p < .05$ vs. the C group.

Methods

Experimental Protocol



ACA was induced by endotracheal tube (ETT) clamping. After 11 min of clamping (include cardiac arrest time 6 min, defined mean aortic pressure ≤ 25 mmHg), CPR was initiated with the ETT opening. BL, baseline; CA, cardiac arrest; PC, precordial compression.

Conclusions

DCA improves neurological outcome after ACA via an increase of ATP levels in the brain.

References

- Bersin R, Stacpoole P, Kamimura N, Cbarlotte N, et al. American Heart Journal. 1997; 134: 842-855.
- Marangos P, Turkel C, Dziewanowska Z, et al. Exp Opin Invest Drugs. 1999; 8(4): 373-382.