Vasopressin and its analogues in treatment of cardiac arrest

Introduction: Recent guidelines for cardiopulmonary resuscitation (CPR) recommend use of drugs as an integral part of treatment. Vasoactive drugs have been used in resuscitation to increase myocardial and cerebral perfusion during chest compressions. Resuscitation research is trying to find alternative vasopressors to adrenaline, for which the long-term survival benefit has not been proven. Successful use of terlipressin in cardiac arrest (CA) was documented in small studies in children and some rare case reports. Terlipressin has never been tested in CA of cardiac aetiology in any clinical or experimental study.
Objectives: We aimed to evaluate the role of catecholamines and non-adrenergic vasopressors, vasopressin and terlipressin, during CPR based on review of selected trials. Introduction of a standardized experimental porcine model of ventricular fibrillation (VF) was done for research of therapeutic interventions during CPR. We aimed to evaluate the effects of terlipressin with adrenaline on perfusion of vital organs during prolonged CPR compared to placebo with adrenaline. We tested our hypothesis that terlipressin, if given simultaneously with the first dose of epinephrine during CPR for VF, increases CorPP (coronary perfusion pressure) or CPP (cerebral perfusion pressure).
Material and methods: Fourteen domestic pigs were randomly assigned into group ADR (placebo + adrenaline; n = 7) and TER (terlipressin + adrenaline; n = 7). VF was induced using an intra-cardiac pacing lead. After 5 min of untreated CA, compression-only resuscitation was applied for 10 min, followed by advanced life support. Terlipressin in a single-dose of 30 μg kg^{-1} was added to the first dose of adrenaline (30 μg kg^{-1}) in group TER, while placebo was given in group ADR. Coronary (CorPP) and cerebral (CPP) perfusion pressures were calculated from right atrial, aortic and intracerebral pressures. Data were analyzed using repeated ANOVA and Fisher´s protected LSD post hoc test.
Results: Administration of terlipressin with adrenaline was effective to maintain CorPP higher than 10 mmHg for 17.7 min longer than adrenaline alone (P = 0.003). CorPP (mean ± SD) measured at 35, 45, and 55 min after the onset of VF was 12.2 ± 4.0, 11.0 ± 6.2, and 9.6 ± 4.5 mmHg in group TER; and 5.8 ± 3.8, 0.6 ± 4.9, and -1.0 ± 4.5 mmHg in group ADR (P = 0.03, < 0.001, and < 0.001). CPP measured at the same times was 23.0 ± 7.2, 20.4 ±6.9, and 23.1 ± 6.7 mmHg in group TER; and 13.3 ± 6.5, 6.2 ± 5.3, and 5.6 ± 6.5 mmHg in group ADR (P = 0.01, < 0.001, and < 0.001). A trend towards extended duration of VF was observed after administration of terlipressin with adrenaline.
Conclusion: The porcine model of CA has been successfully introduced. A consecutive study performed on this model of VF confirmed our hypothesis that terlipressin, when given with the first dose of adrenaline during CPR, increases CorPP and CPP compared to adrenaline with placebo. However, based on the conclusions of clinical and experimental studies, routine use of vasopressin or terlipressin in humans still cannot be recommended.

Key words: cardiopulmonary resuscitation, cardiac arrest, ventricular fibrillation, therapy, terlipressin, cerebral perfusion pressure, coronary perfusion pressure