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COMPARISON OF AMIODARONE AND LIDOCAINE IN A PROLONGED VENTRICULAR FIBRILLATION CANINE MODEL

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Liu Donglin, Zheng Zhaotong, Zeng Qixian, Wang Yuanlong, Meng Xianglin, Liu Hongzhen, Li Jingsha, Zhang Yun, Zhong jingquan. *Department of Cardiology, Qi Lu Hospital, Shandong University*

Objectives Ventricular fibrillation (VF) is one of the most common reasons for sudden cardiac death. Many events may prevent paramedics from timely arrival to treat cardiac events. In the USA, more than 400 000 adult deaths each year are due to

sudden cardiac death, and 80% of all the sudden cardiac arrest cases are associated with VF. In China, more than 540 000 adult deaths are due to sudden cardiac death each year. Most patients experiencing cardiac events have structural heart diseases such as coronary heart disease, myocardiopathy and pericardial disease. The others have congenital cardiac arrhythmia such as Brugada syndrome and long QT syndrome. Implantable cardio verter defibrillator (ICD) is the best treatment for patients at risk, but many people in China cannot afford this treatment. So antiarrhythmic drugs have become the first choice for preventing cardiac arrhythmia, especially VF, and may be the first emergency drug used in cardiopulmonary resuscitation in China. Lidocaine is a traditional class IB antiarrhythmic drug for VF and pulseless ventricular tachycardia (VT). Amiodarone, a class III antiarrhythmic agent, has been widely used for cardiac arrhythmia. Many clinical trials have demonstrated that amiodarone may be used to replace lidocaine. The Amiodarone versus Lidocaine in Prehospital Ventricular Fibrillation Evaluation (ALIVE) trial and the Amiodarone in Out-of-Hospital Resuscitation of Refractory Sustained Ventricular Tachyarrhythmia (ARREST) study are two large, randomised trials finding the benefit of amiodarone to treat refractory VF during cardiopulmonary resuscitation (CPR). However, in these trials, the mean time to receive first aid was about 8 min. In the ALIVE trial, the time that patients received the first shock was 8 ± 3 min in the amiodarone group and 9 ± 4 min in the lidocaine group. In the ARREST study, the first responder arrived within 4 min, and paramedics arrived and gave patients the first shock within 9 min, though the accurate time from sudden death to receive first aid is difficult determined during prehospital or outof-hospital investigations. In a Japanese clinical study comparing nifekalant and lidocaine to treat refractory VF, the time to start CPR was about 7 min. In developed countries, the emergency medical system is better and the CPR technique and devices for first aid such as AED are more widespread than in developing countries. So, especially in less-developed countries, if patients experiencing sudden cardiac events cannot receive rescue measures in time, antiarrhythmic agents may have a positive effect on refractory VF. However, which agent is better, amiodarone or lidocaine? Few studies have compared the two drugs.

The purpose of this randomised, experimental canine study was to compare the effect of amiodarone and lidocaine on CPR when given simultaneously with adrenaline in a canine model of prolonged VF.

Methods Twenty-one mongrel dogs of both sexes (13.5–19 kg) were used. The dogs were anesthetised with pentobarbital (25 mg/kg intravenous, bolus). Animals were restrained in the supine position at the four extremities on the experimental table. A 5.0 cuffed tracheal tube was inserted into the trachea for intubation. The tube was attached to a ventilator. Ventilation began at a tidal volume of 10-15 ml/kg, a ventilator rate of 16-20 breaths/min, and an inspiration: expiration ratio of 1:1.5–2.0. Three electrocardiographic leads were placed to correspond to standard lead II electrocardiography (ECG). The right femoral artery was cannulated, and the tip of a fluid-filled polyurethane catheter was positioned in the proximal descending aorta for measuring aortic systolic pressure (AOSP) and diastolic pressure (AODP). A second fluid-filled polyurethane catheter was introduced through the right femoral vein into the right atrium (RA) to measure systolic pressure (RASP) and diastolic pressure (RADP). The remaining cannulated femoral vein was used for drug infusion. Heparin, 100 U/kg, was administered for anticoagulation. A continuous infusion of 0.9% NaCl, 3 ml/kg/h, was given throughout the experiment. Heart rate (HR) and QT

interval were measured at baseline and after resuscitation, during stable sinus rate. The corrected QT interval (QTc) was calculated by Bazett's formula. The catheters were connected to pressure transducers connected directly to a computer for on-line recording of data (Acknowledge, Biopic Systems, Inc, CA, USA). Aortic and right atrial pressures were monitored throughout the study. Coronary perfusion pressure (CPP) was calculated on-line at middiastole by subtracting RADP from AODP. After baseline measurements. VF was induced by delivering a 5-s alternating current at 50 Hz externally across the thorax through two needles. Assisted ventilation was discontinued immediately on establishment of 12 min VF, dogs were allowed to breathe spontaneously, to simulate the delay that often occurs after out-ofhospital cardiac arrest. After 12 min, external chest compression and ventilation with 100% oxygen was started. The rate of compression was 100/min, and a synchronised ventilation: compression ratio of 2:30 was delivered by a manual bag-valve ventilator (Ambu bag Glostrup Denmark) at a constant tidal volume of approximately 20 ml/kg body weight. Ventilations were delivered during the decompression phase of CPR. After 2 min of compression, defibrillation with 150 J biphase was attempted immediately. Animals that were still in VF or pulseless VT after only once defibrillation were randomised to three groups (n=7) for each) for treatment: amiodarone plus adrenaline, lidocaine plus adrenaline or placebo and adrenaline. Adrenaline was given in intravenous boluses of 0.02 mg/kg; amiodarone (Cordarone, amiodarone hydrochloride injection, polysorbate-80, a diluent which on its own is a potent vasodilator and may be also negatively inotropic, was not included), 5 mg/kg; lidocaine, 1.5 mg/ kg; and placebo (normal saline) 5 ml. Amiodarone was injected in 2 min. All drugs were followed by a 10-ml saline intravenous bolus to decrease the time for medication to reach the central circulation. Researchers were blinded to the treatment. CPR was not interrupted during drug administration. After the first administration of drugs, canines were given 6 min external thoracic compression (2 min per turn) and one shock with the same energy of defibrillation in every 2 min CPR as necessary. If animals were still VF, we gave drugs once more. Animals with successful return of spontaneous circulation (ROSC) (defined as arterial-systolic pressure >50 mm Hg sustained for >1 min continuously within 30 min of CPR were treated with advanced life support and observed for 2 h. Animals without successful ROSC after 30 min of CPR were allowed to die. The study endpoints were ROSC, survival for 2 h under advanced life support, and

Results The three groups did not differ in survival rate, hemodynamic measurements after drug administration, or heart rate, PR interval or QRS complex (p=0.074, 0.077 and 0.415, respectively). ROSC did not significantly differ among the groups (p=0.807), with 4, 5, and 3 dogs achieving ROSC in the amiodarone, lidocaine and placebo groups, respectively. Three, 5, and 3 dogs in the amiodarone, lidocaine and placebo groups, respectively, survived for more than 2 h. The survival rate for the three groups was 42.9%, 71.4% and 42.9% respectively, with no significant difference between groups. ECG measurements did not differ between the amiodarone and lidocaine groups, except for QT interval (420.0 \pm 192.2 vs 234.0 \pm 19.5 ms, p=0.036). One case of atypical torsades de pointes was found in the amiodarone group. Three, 5, and 3 dogs in the amiodarone, lidocaine and placebo groups, respectively, survived for more than 2 h.

Conclusions In the prolonged VF model, amiodarone and lidocaine had a similar effect on terminating VF, hemodynamics and survival rate. Lidocaine may be safer than amiodarone in terminating refractory VF.

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