Effects of morphine or ketamine in rats with asphyxial cardiac arrest: a pilot study

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Abstract

Acute hypoxia results in uncontrolled release of glutamate and the consequent excitation of N-methyl-D-aspartic acid (NMDA) receptors, which affects the whole homeostasis and finally activates apoptosis of neurons. A potential therapeutic approach to prevent this sequence of events is a blockade of NMDA receptors. Meanwhile, in different models of acute hypoxia, activation of delta-opioid receptors demonstrates significant cardio- and neuroprotective effects with a consequent increase in animal survival. Thus, we aimed to test the effects of Morphine or Ketamine on hemodynamics, acid-base status and early survival in rats after asphyxia cardiac arrest (ACA).

Methods: After instrumentation under anesthesia with Thiopental sodium (60 mg/kg, i.p.), Wistar rats (n=21) weighing between 350-400 g were randomly assigned to three groups where: 1. Morphine 3 mg/kg iv (n=7) was given 10 min before ACA. 2. Ketamine 40 mg/kg iv (n=7) given 10 min before ACA. 3. Control (n=7), the same amount of NaCl 0.9% iv was given 10 min before ACA. The rats were asphyxiated by corking the trachea at the end of expiration for 3 min. Resuscitation was initiated by an injection of epinephrine (0.02 mg/kg, iv), followed by manual thoracic compressions (180 compressions/min) and mechanical ventilation (21% O₂, 80 breaths/min). Lactate, mean arterial pressure (MAP), heart rate, and cGMP levels were measured at baseline (BL), 10 min after ACA (As), and every 5 min in post-resuscitation (PR) period. Blood gas samples were taken at the BL, and 10 min at the PR period. Early survival was determined at the 20 min after ACA.

Methods and Materials

Evaluations: the experimental study with rats was approved by the Animal Care and Use Committee of the Astana Medical University, Astana, Kazakhstan. Animal Anesthetization: under anesthesia with Thiopental sodium (60 mg/kg, i.p.), each rat was immobilized with lidocaine-epinephrine solution in a custom-made acrylic chaise. The rats were mechanically ventilated with room air and a tidal volume of 8 ml/kg using small animal ventilator (TOPS Dual mode ventilator, Kent Scientific Corp., USA). A 24G central venous catheter (Arrow) was inserted into the right femoral vein for drug administration and taking of blood sampling. A 23G catheter (201 venflon, BD, Sweden) was inserted into the right femoral artery for continuous blood pressure monitoring.

Results

Pre-treatment of rats with Ketamine resulted in significantly better hemodynamic stability after asphyxial cardiac arrest as compared with two other study groups (Fig.1). The rats in Ketamine group demonstrated significantly low accumulation of lactate and hydrogen ion in blood as compared to the rats in Control group (Fig. 2 and 3). As we did not apply oxygen in our experiments, a very high mortality in the Control group was observed (Fig. 4). However, some trends for increased survival in both Ketamine and Morphine groups and those with Ketamine and Morphine groups were also observed (Fig. 4). Finally, we did not find any differences in plasma concentration of NSE and s100 calcium binding protein B between the study groups (data not shown).

Conclusions

In terms of mortality, our experimental model of asphyxial cardiac arrest in rats without application of oxygen mimics closely cardiac arrest situation in humans. After 5 min period of anoxia condition, most of the rats in Control group died during the first 20 min after cardiac arrest. In turn, we did not observe severe mortality increase in rats from both Ketamine and Morphine group. Influence of Ketamine on hemodynamic status in our study is very consistent with findings from previous experimental and clinical works. Further investigations are needed to elucidate whether Ketamine or Morphine play any role in prevention of neuronal injury in experimental animals and humans after cardiac arrest.

Financial support

1. National fund of Department of Anesthesiology and Intensive Care, Astana Medical University, Astana, The Republic of Kazakhstan.
2. International fund of Department of Anesthesiology and Intensive Care, Astana Medical University Hospital, Lørenskog, Norway.
3. Private money of Dr. Vladimir Kuklin.

References

1. Boden HE: Pharmacologic and neuroprotective effects with a consequent increase in animal survival. Thus, we aimed to test the effects of Morphine or Ketamine on hemodynamics, acid-base status and early survival in rats after asphyxia cardiac arrest (ACA).

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