Insulin does not reverse bupivacaine-induced cardiac systole *in vitro*: the importance of drug elimination to be resuscitated

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INTRODUCTION

➤ In an *in vivo* study using dogs, insulin-glucose-potassium in conjunction with chest compression effectively reversed BPV-induced cardiovascular collapse.

➤ However, the mechanisms for the recovery are poorly defined.

RESULTS

III. Non-recirculation Experiments - BPV washout

1. stable contractions at 1.2 Hz → asystole with 500 μ M BPV → 2×10^{-1} units/ml insulin for 60 min
2. Stable contractions at 1.2 Hz → asystole with 500 μ M BPV → 33 mM glucose and 2×10^{-1} units/ml insulin at 5 min after asystole for 60 min

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CONCLUSIONS

Neither insulin nor insulin/glucose treatment is likely to reverse BPV-induced cardiac conduction block and asystole *in vitro*, but, these treatments are likely to replenish the metabolic energy in the myocardium.

Circulatory support to eliminate BPV from the heart after BPV-induced cardiac arrest appears to be critical when treating with insulin and glucose.

MATERIALS and METHODS

Preparation of Cardiac Muscles

- 400-450 g male guinea pigs
- Excision of a Rt. ventricular papillary muscle under SEVO anesthesia
- Mounted horizontally in a tissue bath superfused at 37°C with normal Tyrode solution which was recirculated through the bath from a reservoir containing 100 ml of Tyrode solution through with 95% O₂ and 5% CO₂ were bubbled maintaining a pH of 7.4 ± 0.05.

- GRASS F03 force transducer
- Field stimulation using a Grass S44 stimulator
- Powerlab® Data analysis system

Experimental Protocols

I. Effects of Insulin

Cumulative concentration-responses to

- Insulin (Humulin insulin R): 10^{-3} , 10^{-2} , 10^{-1} , 2×10^{-1} , 5×10^{-1} units/ml

II. Recirculation Experiments - continuing BPV

1. Stable contractions at 1.2 Hz → 50 μ M BPV → 10^{-3} , 10^{-2} , 10^{-1} , 2×10^{-1} , 5×10^{-1} units/ml insulin
2. Stable contractions at 1.2 Hz → asystole with 500 μ M BPV → 10^{-1} , 2×10^{-1} , 5×10^{-1} units/ml insulin
3. Stable contractions at 1.2 Hz → asystole with 500 μ M BPV → 33 mM glucose at 5 min after asystole for 10 min → 10^{-1} , 2×10^{-1} , 5×10^{-1} units/ml insulin
4. Stable contractions at 1.2 Hz → 200-300 μ M BPV → Intermittent contractile responses (conduction block) → 10^{-1} , 2×10^{-1} , 5×10^{-1} units/ml insulin
5. Stable contractions at 1.2 Hz → 200-300 μ M BPV → conduction block → 33 mM glucose at 5 min after conduction block for 10 min → 10^{-1} , 2×10^{-1} , 5×10^{-1} units/ml insulin

IV. Measurements of BPV Concentrations in Solution

Measured under recirculating conditions at 5 min after asystole, 15, 30, 45, and 60 min in either control solution or the control solution containing 2×10^{-1} units/ml insulin