



**VERAPAMIL PROTECTS AGAINST SEVERE HYPOGLYCEMIA-INDUCED FATAL
CARDIAC ARRHYTHMIAS**

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More than 30 million Americans have diabetes. Diabetes is a disease of high blood sugar and is treated with drugs, such as insulin, to lower blood sugar. For people with insulin-treated diabetes, extremely low levels of blood sugar (severe hypoglycemia) can occur and can be fatal. Our laboratory has demonstrated in animal models that hypoglycemia-induced sudden death is mediated via fatal cardiac arrhythmias. A contributing factor to cardiac arrhythmias is calcium overload in the heart. To investigate the role of cardiac calcium overload in mediating severe hypoglycemia-induced cardiac arrhythmias, calcium channels were blocked with verapamil. Verapamil is an FDA approved antiarrhythmic drug that is used to treat cardiac arrhythmias, hypertension, and angina pectoris in clinical settings. It was hypothesized that blocking calcium channels with verapamil would decrease fatal cardiac arrhythmias during severe hypoglycemia. To test this hypothesis, calcium channels were blocked with continuous intravenous infusion of verapamil (1.0 mg/kg, n = 25) or saline as a control (n = 24) in Sprague Dawley rats during insulin-induced (0.2mU/kg/min) severe hypoglycemia (10-15 mg/dl) for 3 hours with continuous heart rhythm (electrocardiogram) recording. In both saline and verapamil treated rats, hormones levels for glucagon, epinephrine, and norepinephrine were similar, suggesting no unintended effect on the body's counter-regulatory response during severe hypoglycemia. Heart block, a type of fatal cardiac arrhythmia, occurred at 0.99 ± 0.32 /min in the control rats, which was associated with a 21% mortality during severe hypoglycemia. Interestingly, verapamil treatment completely prevented fatal heart blocks and mortality during severe hypoglycemia ($p < 0.05$). In conclusion, blocking calcium channels prevents cardiac arrhythmias and mortality due to severely low blood sugar. Clinically, reduction of calcium overload in the heart could be a logical approach to prevent sudden death in people with insulin-treated diabetes at risk for hypoglycemia.