Hemodynamic effects of insulin and dextrose in healthy volunteers

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INTRODUCTION
The combination of high dose insulin and glucose has been repeatedly used in various cardiac conditions (chronic heart failure (1), acute myocardial infarction (AMI) (2), post-ischemic reperfusion (3), cardiac surgery (4)). It also has become part of the antidotal treatment of overdose with calcium channel and beta-adrenergic blocking agents (5).

Insulin/glucose effects on distressed myocardium have been studied. Whereas hyperglycemia has shown increased mortality in patients with cardiac ischemia, some evidence suggests cardioprotective effects of insulin at the myocyte level given a strict normoglycemic metabolic state can be maintained (6).

Little, however, is understood about the impact of insulin/glucose on healthy myocardium. With this study we tried to assess the effects of insulin-euglycemia treatment on hemodynamics of healthy hearts in vivo.

METHODS
Ten (10) healthy, non-diabetic, females were enrolled in a prospective double blind cross-over trial. Each volunteer received 10 units regular insulin with 25 gm dextrose IV vs. placebo (0.9% saline IV). After each infusion cardiac parameters (heart rate, blood pressure, fractional shortening of the left ventricle) were measured every 15 min for one hour. ANOVA for repeated measures was calculated using insulin/glucose or placebo treatment as subject factors. Post-hoc paired t-tests were done when ANOVA analysis suggested a significant effect at an alpha = 0.05 level.

Measurements for fractional shortening were obtained by cardiac ultrasound. M modes images across the left ventricle (LV) in parasternal short axis probe position (see Image1) were recorded at the various time points. Fractional shortening was found to represent the best approximation of LV function given the type of images obtained. In order to calculate the percentage of fractional shortening, end systolic diameter (ESD) and end diastolic diameter (EDD) were measured and computed in the following formula: 

\[
\text{Fractional Shortening} = \left( \frac{\text{ESD} - \text{EDD}}{\text{EDD}} \right) \times 100
\]

RESULTS
For heart rate (HR), systolic blood pressure (SBP), and fractional ventricular shortening (FVS) no significant differences in group means could be detected.

There was an insignificant difference towards lower diastolic blood pressures (DBP) in the insulin/glucose treatment arm (ANOVA p = 0.004). Paired t-test analysis calculated significant differences for DBP between the treatment arms at 15, 30, and 60 min (p = 0.02, 0.04, and 0.01 respectively). However, the treatment effect was measured as a decrease in DBP of only 3.9-6.4 mmHg.

DISCUSSION
Best possible homogeneity of the study participants was achieved by selecting young, healthy, same sex individuals. Due to practical constraints, population size was kept small in this pilot study, which may impact the ability to detect a significant difference in means of the measured hemodynamic parameters.

We used a low-dose insulin one time bolus regimen in this study. Our study participants received 0.13 IU/kg regular insulin bolus in average. Cardioprotective effects reported in the literature were observed with higher or different insulin regimens. The DIGAMI study insulin protocol used 5 IU/hr bolus initially with rate adjustments over time according to patients blood glucose levels. Recommended treatment doses used in calcium channel and beta-adrenergic blocking agent overdoses are 1 IU/kg insulin bolus followed by a 0.5 IU/kg/hr rate. Therefore, the lack of significant hemodynamic effects in this study might be in part contributed to the low dose insulin regimen used.

Finally, significant effects of insulin on hemodynamics might just be subtle in healthy myocardium, whereas significant improvements of cardiac function occurs only in distressed or pathologic cardiac conditions.

CONCLUSION
In this study, low-dose insulin-euglycemia treatment seems to have little or no effect on the hemodynamic parameters of healthy, non-stressed hearts. Therefore, cardioprotective effects from insulin/glucose might be more evident with use of high-dose insulin regimens or under conditions with maximal cardiac distress.

REFERENCES
(4) Svedjeholm R, Huljebrant I, Hakanson E, Vanhanen I. Glutamate and high-dose insulin-potassium (GIK) in the treatment of severe cardiac failure after cardiac surgery (4)). It also has become part of the antidotal treatment of overdose with calcium channel and beta-adrenergic blocking agents (5).