Changes of myocardial lipid content and left ventricular function in the course of acute hypoglycemia and inhibition of lipolysis.

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Purpose

Tight glycemic control is the most important action to prevent secondary complications in patients with diabetes. This has been repeatedly confirmed for microvascular and neuropathic complications. On the other hand recently published large, randomized prospective clinical trials reported that tight glycemic control, probably due to hypoglycemic episodes, increased cardiovascular mortality in patients with diabetes [1]. At the same time, evidence emerged that heart failure in diabetes is also linked to alterations of myocardial substrate metabolism. It is suggested that hypoglycemia counter-regulation relates to the development of heart failure in patients with diabetes by the action of counter-regulatory hormones as well as free fatty acids (FFA) on myocardial lipid metabolism and cardiac function. Which mechanism mainly contributes to, remains subject of investigation. Myocardial lipid content (MYCL) can be non-invasively measured by magnetic resonance (MR) spectroscopy [2] and it was shown to be elevated in patients with diabetes and associated with left ventricular diastolic dysfunction [3]. Studies on mechanism of MYCL accumulation pointed to the dynamic nature of this compartment and revealed the effects of increased plasma FFA, hyperglycemia and hyperinsulinemia [4,5]. Hence we aimed to study the acute effects of hypoglycemic episode and associated counter-regulation on myocardial function and lipid accumulation. Possible effects of increased lipolysis from adipose tissue caused by hypoglycemia associated counter-regulation were assessed by alternative inhibition of lipolysis. Second aim was the examination of possible changes in hepatocellular lipid content (HCL) which is another co-factor in development of diabetes mellitus.

Methods

Up to now eight healthy young male volunteers (age: 24.7±2.3a, BMI:23.6±3.3kg/m²) underwent 4 study days (SD, summarized in fig 1) each: SD1: placebo, SD2: hypoglycemia plus placebo, SD3: hypoglycemia plus Acipimox® 250 mg (lipolysis inhibitor) at the time point of 0 and 180 minutes, SD4: Acipimox® only. Hypoglycemia was induced by single dose Insulin Aspart® 1 IU/kgbw i.v. at the time point of 60 min. MYCL, HCL and left ventricular ejection fraction (LVEF) were measured by MR (described bellow) at 0, 180 and 420 min and 24 h.

Results

Insulin bolus induced substantial hypoglycaemia in all volunteers (mean minimal plasma glucose concentration: 36.6±4.7mg/dl). In the course of hypoglycemia associated counter-regulation we could observe transient increase of LV EF (SD2: +10.7 % of baseline, p=0.02) and decrease of MYCL (~45% of baseline, p=0.03) and decrease of LVEF (-9.5% of baseline, p=0.01). HCL did not significantly change on any study day. Lipolysis (Acipimox, SD3 and SD4) yielded acute reduction (240 min) of MYCL (~45% of baseline, p=0.03) and decrease of LVEF (-9). Twenty-four hours later decrease of MYCL (SD2: -34% of baseline, p=0.06) could be detected. Suppression of adipose tissue lipolysis (Acipimox, SD3 and SD4) yielded acute reduction (240 min) of MYCL (~45% of baseline, p=0.03) and decrease of LVEF (-9.5% of baseline, p=0.01). HCL did not significantly change on any study day.

Conclusion

Hypoglycemic counter-regulation induced inhibition of lipolysis from adipose tissue can overcome shortage of glucose substrate and supply sufficient energy for myocardium, which uses MYCL stores in course of next 24 hours. Specific inhibition of adipose tissue lipolysis leads to acute decrease of MYCL stores and reduction in left ventricular function. This leads to the conclusion, that MYCL pool plays a major role for the maintenance of myocardial function.

References
