Endurance-type exercise combined with acipimox administration provides superior benefits for glycaemic control compared with endurance-type exercise alone in male patients with type 2 diabetes

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Introduction

- Despite implementation of exercise intervention, excessive postprandial blood glucose excursions remain a major concern in type 2 diabetes mellitus (T2DM) patients.
- Therefore, adjuvant strategies during exercise intervention to attenuate blood glucose excursions during the day and improve glycaemic control are warranted.
- Disturbances in fatty acid metabolism and excess free fatty acid (FFA) availability results in ectopic lipid deposition in insulin sensitive metabolic tissues, leading to insulin resistance (Figure 1).
- Reducing systemic FFA availability during exercise leads to targeted oxidation of intramyocellular triacylglycerols in T2DM patients, and hence greater improvements in insulin sensitivity up to 2h after exercise.

Objective

To investigate the impact of *in vivo* adipose tissue lipolysis inhibition (by acipimox intake) during endurance-type exercise on postprandial blood glucose and insulin excursions during the first 24h after exercise in male T2DM patients

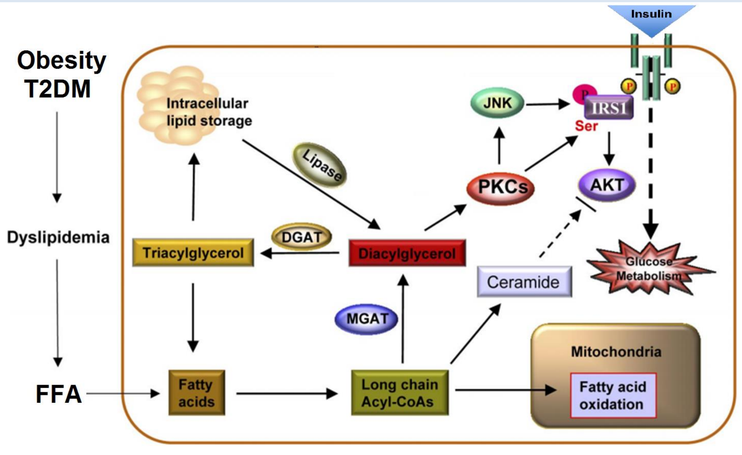

Figure 1. Model for the regulation of insulin sensitivity in skeletal muscle

Excess systemic FFA availability results in ectopic lipid deposition skeletal muscle. The insulin resistant state is further accompanied by major disturbances in skeletal muscle substrate metabolism and a reduced skeletal muscle oxidative capacity, resulting in a state of metabolic inflexibility which stimulates storage of intramyocellular triacylglycerols. Adapted from Shi Y, et al. Am J Physiol Endocrinol Metab 2009;297:E10-8.

Declaration of interest

The authors declare that there is no conflict of interest associated with this publication
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Methods

- 14 male T2DM patients (65±2 yrs, HbA_{1c} 6.7±0.1%) participated in a randomised double-blind, placebo-controlled, cross-over trial, and were exposed to
- Three conditions (interspersed by 1 week between conditions):
  - A 60-min endurance-type exercise bout (at 45% W_{peak}) after acipimox (250mg) intake (*black boxes*)
  - A similar exercise bout after placebo intake (*blue boxes*)
  - A visit without exercise and placebo intake (*light blue circles*)
- Blood glucose, insulin, FFA, triglyceride and lactate concentrations were measured before, during and 24h after exercise and expressed as total area under the curve (tAUC)
- 2 standardised meals were consumed after exercise
- An oral glucose tolerance test (OGTT) was executed 22h after each condition

Results

As result of the intake of acipimox, blood FFA concentrations were significantly lowered during and after exercise (p<0.001, Figure 2)

Such *in vivo* adipose tissue lipolysis inhibition during exercise led to:

- Significantly lower plasma glucose concentrations after exercise (Figure 3, tAUC 3500±124 mmol/L/450min)
  - by -11±3% vs. exercise after placebo intake (tAUC 3946±183 mmol/L/450min) (p<0.05)
- Significantly lower plasma insulin concentrations after exercise (Figure 4, tAUC 76±7 nmol/L/450min)
  - by -25±4% vs. exercise after placebo intake (tAUC 103±13 nmol/L/450min) (p<0.001)

During OGTT no differences in blood glucose and insulin concentrations were observed between trials (p>0.10)

Conclusion

Inhibition of adipose tissue lipolysis during exercise lowers subsequent postprandial blood glucose and insulin excursions throughout the remainder of the day in male T2DM patients. These findings introduce the combined use of exercise with adipose tissue lipolytic inhibition as an effective interventional strategy to augment exercise-induced improvements in glycaemic control in T2DM patients.

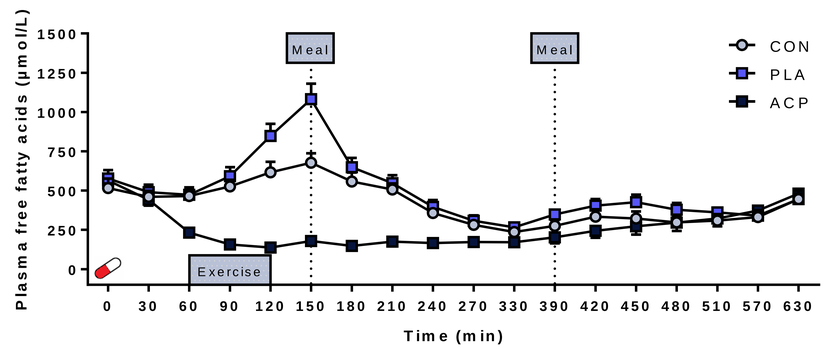

Figure 2. Blood FFA concentrations

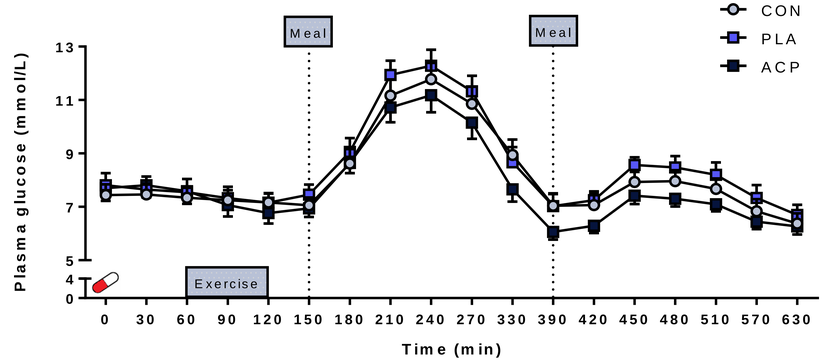

Figure 3. Blood glucose concentrations

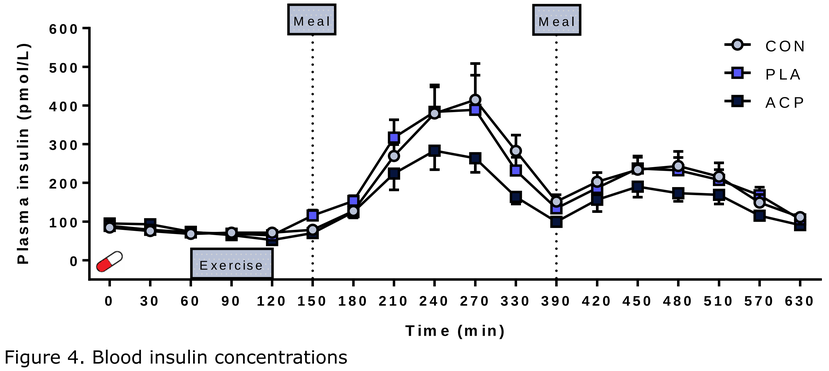

Figure 4. Blood insulin concentrations