Sustainable health improvement through prolonged fasting in people with type 1 diabetes – a multicenter randomized trial (SHIFT1D) – Study procol

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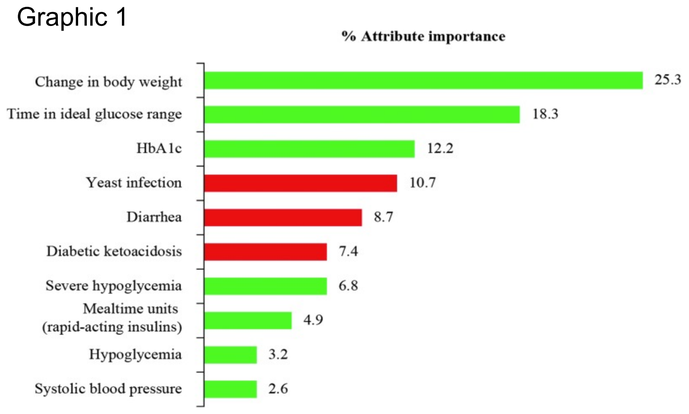
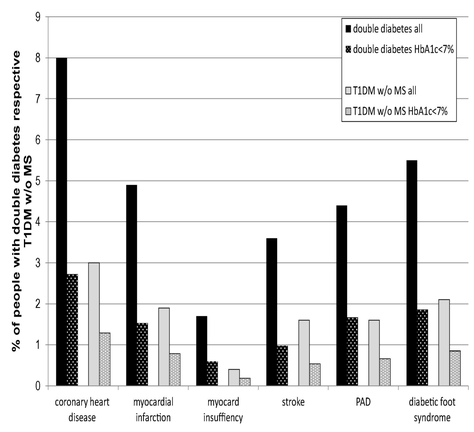
Background

Type 1 diabetes (T1D) appears to be on the rise in Europe, with it burden across a number of outcomes (health status, productivity, activity, healthcare resources). The complex nature of diabetes itself, fluctuations in blood glucose and the fear of long-term complications contribute to a high level of diabetes-specific distress (1). People with T1D are inherently exposed to an elevated risk of developing psychological and neurological long-term consequences such as depression and cognitive decline (2). 25 % percent of all type 1 diabetes patient already suffer from double diabetes (around 94 000 people) (3). Persons with double diabetes showed significantly more macrovascular comorbidities compare to usual T1D (retinopathy 32.4% versus 21.7%, nephropathy 28.3% versus 17.8%) (Graphic 2). Both macrovascular and microvascular comorbidities were increased independent of glucose control, even patients with good metabolic control (HbA1c <7.0%, 53 mmol/mol) showed significantly more macrovascular (coronary heart disease 2.3% versus 1.8%, p < 0.0001) and microvascular problems (retinopathy 8.7% versus 6.6%, p < 0.0001) (3). Reduction of weight turned out to be the most relevant patient relevant outcome (4) (see Graphic 1)but is rarely addressed in interventions for people with T1D. The pilot study showed persuading results, so we decided to repeat this study as an interventional randomized controlled trial. (5)

Graphic 1



Graphic 2



Objective:

Can prolonged multimodal 7 day fasting following the Buchinger protocol enable overweight people with type 1 diabetes to reduce their BMI at least 3 months after intervention and hence other related complications as surrogate for metabolic flexibility

Endpoints:

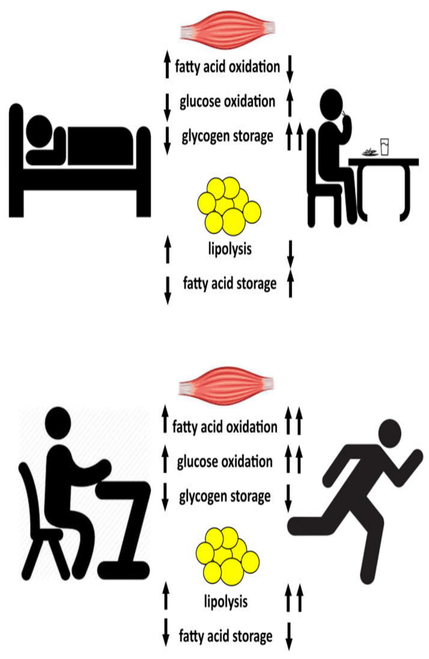
Primary efficacy endpoint: Change in BMI after 3 months
Key secondary endpoint(s): Time in range (TIR), HBA_{1c}, insulin resistance (eGDR), insulin sensitivity in unit per kg, Cardiological Fitness, measured by VO2max, quality of life (WHO 5), depression (HADS), diabetes related measurements (DDS-17, PAID) at 11 days, 3, 6, and without control group 9, 12 months

Intervention:

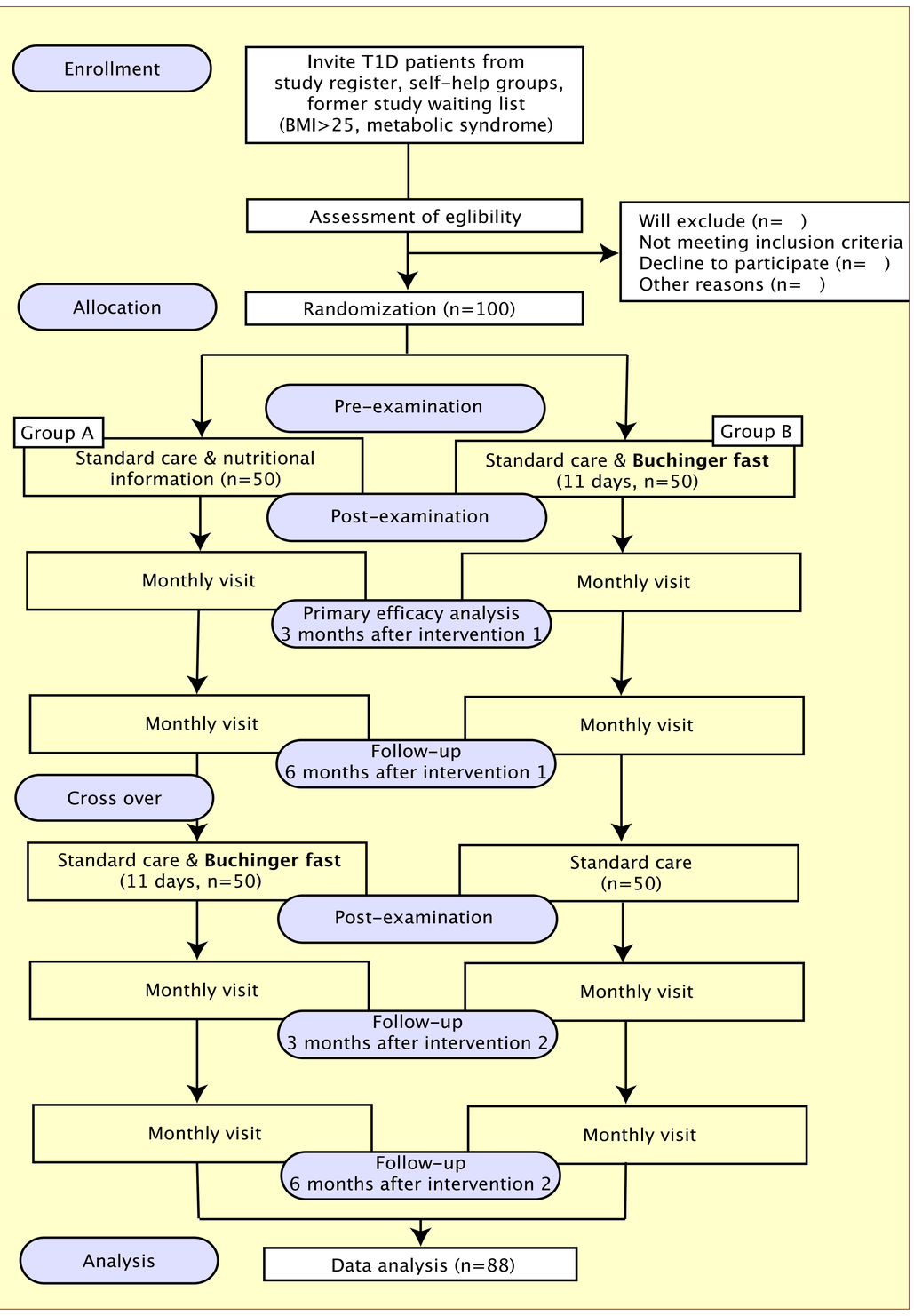
Randomized Controlled Experimental intervention, comparing prolonged multimodal 7 day fasting following Buchinger protocol (6) with waiting group following standard care with monthly follow up for one year (Flow chart)

Description of the complementary intervention:

Fasting leads to metabolic changes: The shift from carbohydrates and glucose to fatty acids and ketones as the major cellular fuel source for body and brain seems to play a key role. The ability to change between ketone and glucose related nutrition is currently discussed in relation to it's therapeutic and preventive potential, called metabolic flexibility. Prolonged fasting as a multimodal intervention usually is not available as a treatment option for people with type 1 diabetes. The trial challenges existing para-digms: Ketone bodies in diabetology were regarded only as indicator for diabetic keto-acidosis (DKA), but the ability to change between glucose based and ketone-based fuel until now could not be used by patients with T1D as preventive option. (7)



Flow Chart



Biometrics:

Efficacy: Analysis of covariance model comparing 3 months BMI change, with therapy as fixed factor, center as random factor and baseline-BMI as continuous covariate
Description of the primary efficacy analysis and population: To show a change of BMI with an effect size of 0.7 after intervention for at least three months in overweight people with insulin dependent T1D in comparison to educational standard care, with 90% power and 5% alpha error. Safety: Descriptive statistics of daily blood gas analysis values (ph, bicarbonates, anion gap) during intervention and any serious adverse events, diabetic ketoacidosis (DKA), serious hypoglycemia up to 6-12 months follow-up. Secondary endpoints: Repeated measurement variance analyses and descriptive and graphical presentations with 95% confidence interval

Discussion:

We intend to enable patients with t1d to improve metabolic flexibility, defined as the ability to change between glucose based and ketone-based fuel supply. Patients can gain self-efficacy by the experience to be able to stay without food and to change between different fuel sources to become more active in preventing complications following T1D. Until now, we could not succeed in gaining research grant and would like to discuss this protocol with readers of this paper to improve this concept.

Literatur:
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