Appetite 110 (2017) 15–24

Contents lists available at ScienceDirect

Appetite

journal homepage: www.elsevier.com/locate/appet

Effects of polydextrose with breakfast or with a midmorning preload on food intake and other appetite-related parameters in healthy normal-weight and overweight females: An acute, randomized, double-blind, placebo-controlled, and crossover study

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ARTICLE INFO

Article history:
Received 29 August 2016
Received in revised form
9 November 2016
Accepted 1 December 2016
Available online 2 December 2016

Keywords:
Appetite
Energy intake
GLP-1
Insulin
Overweight
Satiation

ABSTRACT

Polydextrose (PDX) reduces subsequent energy intake (EI) when administered at midmorning in single-blind trials of primarily normal-weight men. However, it is unclear if this effect also occurs when PDX is given at breakfast time. Furthermore, for ecological validity, it is desirable to study a female population, including those at risk for obesity. We studied the effects of PDX, served as part of a breakfast or midmorning preload, on subsequent EI and other appetite-related parameters in healthy normal-weight and overweight females. Per earlier studies, the primary outcome was defined as the difference in subsequent EI when PDX was consumed at midmorning versus placebo. Thirty-two volunteers were enrolled in this acute, double-blind, placebo-controlled, randomized, and crossover trial to examine the effects of 12.5 g of PDX, administered as part of a breakfast or midmorning preload, on subsequent EI, subjective feelings of appetite, well-being, and mood. Gastric emptying rates and the blood concentrations of glucose, insulin, cholecystokinin, ghrelin, glucagon-like peptide 1 (GLP-1), and peptide tyrosine-tyrosine were measured in the group that received PDX as part of their breakfast. There were no differences in EI between volunteers who were fed PDX and placebo. PDX intake with breakfast tended to elevate blood glucose ($P = 0.06$) during the postabsorptive phase, significantly lowered insulin by 15.7% ($P = 0.04$), and increased GLP-1 by 39.9% ($P = 0.02$); no other effects on blood parameters or gastric emptying rates were observed. PDX intake at midmorning reduced hunger by 31.4% during the satiation period ($P = 0.02$); all other subjective feelings of appetite were unaffected. Volunteers had a uniform mood profile during the study. PDX was well tolerated, causing one mild adverse event throughout the trial.

1. Introduction

The prevalence of obesity and type 2 diabetes (T2D) continues to rise worldwide (Chen, Magliano, & Zimmet, 2012; NCD-RisC, 2016). It is estimated that by 2025, the global incidence of obesity (BMI $\geq$ 30 kg/m^2) in women will reach 21% and 9% of all women will have severe obesity (BMI $\geq$ 35 kg/m^2) (NCD-RisC, 2016). Epidemiological evidence indicates that dietary fibers can prevent the development of obesity and T2D (Clark & Slavin, 2013; Liu et al.,

Abbreviations: CCK, cholecystokinin; CON-B, placebo at breakfast; CON-M, placebo at midmorning; EI, energy intake; GLP-1, glucagon-like peptide 1; PDX, polydextrose; PDX-B, verum (12.5 g of PDX) at breakfast; PDX-M, verum (12.5 g of PDX) at midmorning; PYY, peptide tyrosine-tyrosine; T2D, type 2 diabetes; VAS, visual analogue scale.

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http://dx.doi.org/10.1016/j.appet.2016.12.002

2003). Several types of dietary fiber control appetite and subsequent energy intake; however, the effects tend to be small, and the dose-response relationships are not always apparent (Clark & Slavin, 2013; Wanders et al., 2011). The capacity of dietary fibers to affect appetite is linked to their physicochemical properties (Wanders et al., 2011). In general, fibers that are more viscous reduce appetite and control energy intake more extensively than those with less viscosity (Wanders et al., 2011). However, this generalization does not apply universally (Clark & Slavin, 2013).

Polydextrose (PDX) is a soluble fiber with low viscosity that provides one-fourth of the energy that is supplied by glucose (Auerbach, Craig, Howlett, & Hayes, 2007), thus lowering glycemic and insulinemic responses (Canfora & Blaak, 2015; Shimomura et al., 2004). Recent studies suggest that its consumption governs appetite. In a meta-analysis, we found that PDX reduces subsequent energy intake (EI) dose-dependently (Ibarra, Astbury, Olli, Alhoniemi, & Tiihonen, 2015) and alters subjective feelings of appetite (Ibarra, Astbury, Olli, Alhoniemi, & Tiihonen, 2016). Most studies have measured the effects of administering PDX as a midmorning preload, with which its reduction of subsequent EI is better observed (Astbury, Taylor, & Macdonald, 2013; Astbury, Taylor, French, & Macdonald, 2014; Hull, Re, Tiihonen, Viscione, & Wickham, 2012; Ranawana, Muller, & Henry, 2013). However, these studies are considered to be susceptible to a high risk of bias, based on their single-blinded design—primarily due to the complexity of the setup of acute appetite studies (Ibarra et al., 2015); thus, double-blind designs are needed to strengthen the existing scientific evidence in this regard.

Many studies on EI have enrolled normal-weight populations of males only (Astbury, Taylor, & Macdonald, 2008; Ranawana et al., 2013; Soong et al., 2016) or mixed-sex cohorts (Astbury et al., 2014; Astbury et al., 2013; Hull et al., 2012; King, Craig, Pepper, & Blundell, 2005), and although our meta-analysis concluded that the effects of PDX on appetite are similar in both sexes (Ibarra et al., 2015, 2016), no study has been conducted solely in females. This sex category is of ecological interest as they represent the majority of consumers of weight-loss dietary supplements (Pillitteri et al., 2008). Thus, we are particularly interested in assessing the appetite suppression effect of PDX in a female population, including those at risk for obesity, to confirm the results for this sex category.

Observational studies in children and adults suggest an inverse (protective) association between the frequency of eating breakfast and the risk of obesity and chronic diseases, such as T2D (Pereira et al., 2011). Thus, the administration of dietary supplements at breakfast is usually preferred to the consumption of snacks between meals. When consumed with breakfast, PDX regulates glucagon-like peptide 1 (GLP-1), a potential biomarker for appetite control, in obese persons (Olli et al., 2015). However, previous studies that aimed to determine whether PDX reduces subsequent EI when given with breakfast failed to show such an effect (Monsivais, Carter, Christiansen, Perrigue, & Drewnowski, 2011; Timm, 2012). Also, little is known about the influence of PDX on other mechanisms of appetite control, such as gastric emptying and mood. Thus, the effects of PDX when administered with breakfast or with a midmorning preload should be compared in the same trial, which should include other appetite-related parameters.

We conducted a double-blind intervention to study the effects of 12.5 g of PDX—an effective and safe dose that reduces subsequent EI (Ibarra et al., 2015)—served as part of a breakfast or midmorning preload. Per earlier studies (Astbury et al., 2014; Astbury et al., 2013; Hull et al., 2012; Ibarra et al., 2015; King et al., 2005; Ranawana et al., 2013), the primary outcome was defined as the difference in subsequent EI when PDX was consumed midmorning versus a placebo. Further, other appetite-related parameters that are associated with food intake, such as subjective feelings of appetite (Blundell et al., 2010; Flint, Raben, Blundell, & Astrup, 2000), glycemia and insulinemia (Benelam, 2009), gastrointestinal peptides (Benelam, 2009; Blundell et al., 2010), and gastric emptying (Jackson et al., 2004), were assessed as secondary outcomes. Well-being and mood (Hetherington et al., 2013) were also evaluated, because they may influence appetite.

2. Methods

2.1. Ethics and good clinical practices

The study was performed per the Declaration of Helsinki (WMA., 2001), following Good Clinical Practice (GCP) standards (ICH., 1996), and registered at ClinicalTrials.gov (NCT02064205). The protocol and informed consent forms were approved by the IEC "Stichting Beoordeling Ethiek Bio-Medisch Onderzoek" on March 17, 2014. The trial was conducted at QPS Netherlands B.V. (Groningen, NL) and TNO (Zeist, NL) and sponsored by DuPont Nutrition and Health (Kantvik, FI). The screening started on May 27, 2014 and the intervention took place between June 6 and October 31, 2014. The site and labs were audited by TFS A.B. (Lund, SE). The study is reported following the CONSORT statement (Schulz, Altman, & Moher, 2010).

2.2. Investigational products

The verum was 400 g of nonfat yogurt (Friesland Campina, NL) that contained 17.86 g of Litesse® Ultra™ (DuPont, Terre Haute, IN, US) in solution (70% solids), equivalent to 12.5 g of PDX, with a caloric content of 800 kJ. The placebo control (CON) was 400 g of yogurt that was supplemented with glucose syrup to match the energy content in the verum. The yogurt was selected as a vehicle, based on previous studies of PDX (Hull et al., 2012; King et al., 2005), which used similar nutritional compositions in their formulations. The formulations and nutritional compositions are shown in Supplementary Table S1 and S2. The off-flavor from the ^{13}C-octanoate sodium salt that was added to the formulations was masked with flavorings that were developed *ad hoc* in collaboration with Firmenich Denmark ApS (Brabrand, DK). A ranking test (Watts et al., 1992) of experimental products that was conducted at DuPont Nutrition and Health (Kantvik, FI) showed no differences in overall quality, appearance, flavor, or off-flavor. There was a significant difference in texture between yogurts with or without PDX that was deemed to be irrelevant due to the 1-week washout between test days.

2.3. Study design

The trial was an acute, randomized, double-blind (during the entire study), placebo-controlled, and four-arm crossover (allocation ratio 1:1:1:1) study that was designed to measure the effects of 12.5 g of PDX, consumed as part of a breakfast (t = 0 min) or midmorning preload (t = 150 min) before an *ad libitum* lunch meal (t = 240 min).

The study consisted of a screening visit, followed by four test days that were separated by a washout of at least four days. Table S3 describes the assessment schedule for each visit, and Table S4 and S5 show the schedules on the test days. The four treatments that we evaluated were:

- PDX-B: Verum (12.5 g of PDX) at breakfast (t = 0 min)
- CON-B: Placebo at breakfast (t = 0 min)
- PDX-M: Verum (12.5 g of PDX) at midmorning (t = 150 min)
- CON-M: Placebo at midmorning (t = 150 min)