EFFECT OF EVENING FOOD COMPOSITION ON PRE-BREAKFAST FASTING AND

OVERALL GLUCOSE CONTROL IN TYPE 1 AND TYPE 2 DIABETES: A REVIEW

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The Supervisory Committee certifies that this *disquisition* complies with North
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ABSTRACT

This paper reviews current data on medical nutrition therapy (MNT) strategies related to evening food composition and the effect on pre-breakfast fasting and overall blood glucose control in people with type 1 and type 2 diabetes. A comprehensive literature search was conducted to locate pertinent articles, and a review of literature was completed. Eight studies related to type 1 diabetes and nine studies related to type 2 diabetes were identified and reviewed.

The available evidence shows that people living with type 1 diabetes should consume a daily bedtime snack composed of carbohydrate and protein, but not high in fat. People with type 2 diabetes may not benefit from a bedtime snack, since eliminating the snack does not result in hypoglycemia and studies have not definitively shown that a snack reduces pre-breakfast fasting glucose compared to placebo. People with type 2 diabetes should also avoid a supper meal high in kilocalories.

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CHAPTER 1. INTRODUCTION

Overview of Topic

Diabetes is a chronic disease that affects 8.3% of the United States population. An

estimated 18.8 million people have been diagnosed with diabetes, including 1.9 million people

aged 20 years or older who were newly diagnosed just in 2010. In addition, an estimated 7.0

million people are thought to be undiagnosed. Type 2 diabetes accounts for approximately 90-

95% of all diagnosed cases of diabetes, while type 1 diabetes accounts for 5-10% of all cases.

Type 1 diabetes develops when the body's immune system destroys pancreatic beta cells that

make insulin. Type 2 diabetes usually begins as insulin resistance in which the cells do not use

insulin properly. This type of diabetes gradually progresses to the pancreas losing its ability to

produce insulin (American Diabetes Association [ADA], 2010). Diabetes as a whole contributed

to an estimated cost of $174 billion in the United States in 2007 (Centers for Disease Control and

Prevention [CDC], 2011).

Medical Nutrition Therapy (MNT) provided by Registered Dietitians is a vital element of

diabetes management and self-management education for people with all types of diabetes.

There is strong evidence to show that MNT is an effective and essential therapy in diabetes

(Franz, Boucher, Green-Pastors, & Powers, 2008). MNT for diabetes is important in the

prevention and management of diabetes, as well as for the prevention or slowing of the rate of

diabetes complications (ADA, 2008). It calls for the use of scientific evidence while considering

strategies to attain treatment goals and changes that people with diabetes are able and willing to

make. People with both type 1 and type 2 diabetes are encouraged to make lifestyle

modifications to prevent obesity, dyslipidemia, cardiovascular disease, hypertension, and

nephropathy. In addition, people with diabetes are encouraged to make healthy food choices to

improve health (ADA, 2004). The ADA (2008) has set goals of MNT for treatment of diabetes, which includes achieving and maintaining plasma blood glucose concentrations in the normal or as close to normal range as is safely possible.

The goal of achieving normal plasma blood glucose concentrations in people with diabetes is often difficult due to hyperglycemia after an overnight fast. Many factors have been identified as possible causes of early morning hyperglycemia: increased postabsorptive hepatic glucose production rates from glycogenolysis and gluconeogenesis, dawn phenomenon, bedtime hyperglycemia, and impaired glucose disappearance (Basu, Schwenk, & Rizza, 2004; Boden, Chen, & Stein, 2001; Consoli, Nurjhan, Reilly, Bier, & Gerich, 1990; Hundal, et al., 2000; Wajngot, et al., 2001). Since even brief periods of hyperglycemia increase the risk of complications related to diabetes, it is important that we explore different MNT strategies to improve glucose control.

Statement of Purpose

People with diabetes may seek other options besides prescription medications to decrease their pre-breakfast fasting blood glucose. Although evidence-based position statements describing MNT strategies for diabetes have been created, none have described the evidence regarding evening food intake and the effect on pre-breakfast fasting plasma blood glucose and overall glucose control (ADA, 2004; ADA, 2008; Franz, et al., 2010). However, to address pre-breakfast hyperglycemia, a number of MNT recommendations are commonly given to patients. These recommendations include instructions to consume a small snack with carbohydrate at bedtime, to consume supper earlier in the evening, or to consume an evening meal lower in kilocalories. Since it is a goal of MNT for people with diabetes to achieve plasma blood glucose concentrations in the normal or close to normal range, the relationship between evening food

intake and pre-breakfast fasting blood glucose should be examined. The purpose of this review is to describe the effects of variations in evening food composition on pre-breakfast fasting and overall glucose control in people with both type 1 and type 2 diabetes mellitus.

Brief Review of Literature

Eight studies involving evening food composition and people with type 1 diabetes have been identified for the purpose of this review (Axelsen, Wesslau, Lonnroth, Lenner, & Smith, 1999; Delahanty & Halford, 1993; Diabetes Research in Children Network [DirecNet] Study Group, 2008; Kalergis, Schiffrin, Gougeon, Jones, & Yale, 2003; Kaufman, Halvorson, & Kaufman, 1995; Kaufman, Halvorson, & Kaufman, 1997; Raju, Arbelaex, Breckenridge, & Cryer, 2006; Schiffrin & Suissa, 1987). The research related to evening food composition in type 1 diabetes has mainly focused on plasma blood glucose outcomes related to bedtime snacks. Studies have examined the frequency of the snack: daily consumption compared to no consumption compared to consumption of extra snacks. Results regarding frequency of bedtime snacks have not been conclusive. Schiffrin & Suissa's study (1987) showed that hemoglobin A1C was unchanged and overnight hypoglycemia was eliminated with an extra snack; however, results from the Diabetes Control and Complications Trial (DCCT) showed that extra snacks on three or more days per week produced a higher hemoglobin A1C when comparing extra snacks consumed less than one time per week (Delahanty & Halford, 1993).

Studies have also described the most desirable nutrient composition of a bedtime snack in type 1 diabetes, specifically related to carbohydrate, protein, fat, and uncooked cornstarch. Kaufman, et al. (1995) and Kaufman, et al. (1997) both demonstrated that a bedtime snack containing uncooked cornstarch could reduce overnight hypoglycemia in people with type 1 diabetes when comparing to a snack with equal carbohydrate, but without uncooked cornstarch.

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However, these two studies produced different results regarding overnight and pre-breakfast fasting hyperglycemia. Kaufman, et al. (1995) resulted in no difference in overnight or pre-breakfast fasting hyperglycemia, while Kaufman, et al. (1997) reported a reduction of overnight and pre-breakfast fasting hyperglycemia.

Axelsen, et al. (1999) also showed that an uncooked cornstarch-containing snack with carbohydrate could reduce both overnight and next day pre-breakfast fasting hypoglycemia when compared to a placebo snack with very little carbohydrate. The uncooked cornstarch-containing snack, however, resulted in higher glucose concentrations at both overnight and pre-breakfast fasting the next day when compared to placebo. Kalergis, et al. (2003) also studied an uncooked cornstarch-containing bedtime snack. This was compared to a standard snack, a placebo snack, and a protein-rich snack. The standard snack consisted of two slices of bread with cheese and a placebo drink. The placebo snack consisted of an aspartame-containing drink, and the protein-rich snack was similar to the standard snack but one slice of bread was replaced with 15 grams of protein in a drink form. The study found that the protein-rich snack, although prevented overnight hypoglycemia, produced the highest pre-breakfast fasting glucose concentrations the next day. The placebo resulted in the lowest pre-breakfast fasting glucose at 0700, but had the highest incidence of overnight hypoglycemia. It was concluded that only the standard snack prevented overnight hypoglycemia without significantly increasing overnight and pre-breakfast fasting glucose (Kalergis, et al., 2003).

A final study compared no bedtime snack to a conventional snack, a conventional snack plus an alpha-glucosidase inhibitor (acarbose), an uncooked cornstarch bar, and a $beta_2$-adrenergic agonist (terbutaline) (Raju, et al., 2006). This study showed that only the conventional snack, which contained 200 kilocalories, 26 grams of carbohydrate, six grams of

fat, and 11 grams of protein, combined with an alpha-glucosidase inhibitor resulted in no increase in overnight glucose concentrations compared to not consuming a bedtime snack. However, neither the uncooked cornstarch-containing snack nor the conventional snack with or without the diabetes medication acarbose could prevent overnight hypoglycemia. Only the beta$_2$-adrenergic agonist reduced hypoglycemia, but also resulted in increased blood glucose concentrations between 0245 and 0700. Since none of the treatments could prevent hypoglycemia, they were considered not clinically acceptable (Raju, et al., 2006).

Finally, fat content in a bedtime snack has been studied in people with type 1 diabetes using continuous glucose monitoring (CGM) (DirecNet, 2008). This study provided evidence that increasing the fat content in a bedtime snack was not beneficial for reducing overnight hypoglycemia, even though the glucose concentrations measured by CGM overnight were higher after consumption of the snack than when consuming a lower fat snack.

Research related to type 2 diabetes and bedtime snack consumption is lacking when compared to research in type 1 diabetes; however, there are many studies related to evening meal composition and glucose control in type 2 diabetes. Nine studies regarding type 2 diabetes and evening food composition have been identified for the purpose of this review (Arauz-Pacheco, Clements, Cercone, Brinkley, and Raskin, 1998; Axelsen, et al., 1999; Axelsen, Lonnroth, Lenner, Taskinen, & Smith, 2000; Beebe, et al., 1990; Dyer-Parziale, 2001; Gannon, Nuttall, Westphal, Fang, & Ercan-Fang, 1998; Gannon, Nuttall, Saeed, Jordan, & Hoover, 2003; Navas-Carretero, Abete, Zulet, & Martinez, 2011; Pearce, Noakes, Keogh, & Clifton, 2008). Similar to studies involving people with type 1 diabetes, uncooked cornstarch has been a common component of the bedtime snacks studied in people with type 2 diabetes. Varying amounts of uncooked cornstarch and carbohydrate have been compared. Axelsen, et al. (1999) showed that

an uncooked cornstarch-containing bedtime snack resulted in less rapid glucose peak elevations compared to a conventional snack that consisted of bread with butter and meat. Both snacks contained a similar amount of carbohydrate; however, there was no difference in pre-breakfast fasting glucose the next day between the snacks. A follow-up study examined blood glucose results when comparing a lower versus higher intake of uncooked cornstarch (0.30 gram per kilogram body weight compared to 0.55 gram per kilogram body weight (Axelsen, et al., 2000). This study showed that a lower dose of uncooked cornstarch in a bedtime snack could reduce pre-breakfast fasting glucose compared to the higher dose of uncooked cornstarch; however, no difference in hemoglobin A1C was seen. A final study involving uncooked cornstarch showed that a snack bar containing uncooked cornstarch reduced midnight and pre-breakfast fasting glucose without causing hypoglycemia at the same time points when comparing to a snack bar without uncooked cornstarch but the same amount of carbohydrate (Dyer-Parziale, 2001). Arauz-Pacheco, et al. (1998) showed that a small supper containing 14 kilocalories per kilogram of ideal body weight resulted in no significant difference in pre-breakfast fasting finger stick blood glucose when compared to no supper, which included no caloric intake after lunch. A large supper of 28 kilocalories per kilogram of ideal body weight produced a significant, but modest elevation in pre-breakfast fasting plasma blood glucose (Arauz-Pacheco, et al., 1998).

Eating smaller meals and snacks throughout the day has not proven to be strategy that improves glucose control in people with type 2 diabetes (Beebe, et al., 1990). CGM has also been utilized in people with type 2 diabetes to monitor changes in glucose when comparing various carbohydrate intakes at meals (Pearce, et al., 2008). Fasting glucose concentrations were unaffected by these changes in carbohydrate distribution throughout the day. Finally, low-starch meals with emphasis on fruits and non-starch vegetables have been compared to high-starch and

usual starch meals that are comparable to the typical American diet (Gannon et al., 1998). Fasting blood glucose increased modestly for all types of meals and after a 24-hour fast. The 24-hour glucose response for the low-starch meal was significantly lower than the other treatments when compared to the 24-hour fast.

Variation in daily protein intake has also been examined in people with type 2 diabetes, but studies have shown mixed results. Gannon, et al. (2003) showed that a diet consisting of 30% kilocalories from protein can decrease overall glucose concentrations by measure of hemoglobin A1C, but cannot decrease pre-breakfast fasting glucose when comparing to a diet consisting of 15% kilocalories from protein. Navas-Carretero, et al. (2011) also showed that a diet consisting of 30% kilocalories from protein does not decrease pre-breakfast fasting glucose, but contrary to Gannon, et al. (2003), did not result in reduced hemoglobin A1C levels, either. These studies provide valuable information to guide healthcare professionals in making clinical practice recommendations regarding reducing pre-breakfast fasting and overall glucose control in diabetes.

Objectives

1) Using evidence-based research, identify best MNT strategies related to evening food composition for improving pre-breakfast fasting and overall blood glucose control in people with type 1 diabetes.

2) Using evidence-based research, identify best MNT strategies related to evening food composition for improving pre-breakfast fasting and overall blood glucose control in people with type 2 diabetes.

Steps to Conducting This Review

Identifying the objectives and purpose of the review was the first step prior to beginning

the comprehensive review of literature. Next, an extensive review of the literature dating back to the early 1980s was conducted in order to find relevant studies related to the objectives. After relevant studies were located, the quality of the studies was assessed to strengthen the review. This involved evaluating the study design, research questions, selection and description of the participants and research methods. Only research that was submitted to peer-reviewed journals was included in this review. Randomized studies were preferred. The evidence was then summarized according to topic, and finally, the findings were interpreted and conclusions were drawn that are applicable to clinical practice.

Definition of Terms

Continuous glucose monitoring (CGM) – well-recognized tool currently used by health professionals to identify timing and causes of hypoglycemia and hyperglycemic spikes with accuracy similar to that of self-monitoring of blood glucose; measures glucose concentrations in the interstitial fluid just under the skin and can be a useful tool to lower hemoglobin A1C in adults with type 1 diabetes (ADA, 2011; Pearce, et al., 2008)

Dawn phenomenon – abrupt increases in fasting concentrations of plasma glucose or insulin requirements or both between 5:00 A.M. and 9:00 A.M. in the absence of antecedent hypoglycemia; occurs both in people who use insulin and those who do not (Bolli & Gerich, 1984)

Fasting blood glucose – plasma glucose after at least 8 hours of no caloric intake (ADA, 2011)

Gluconeogenesis – the formation of glucose by the liver or kidney from noncarbohydrate precursors such as lactate, pyruvate, glycerol, and certain amino acids (Gropper, Smith, & Groff, 2008)

Glycogenolysis – the pathway by which glycogen is enzymatically broken down to glucose

(Gropper, et al., 2008)

Hemoglobin A1C – marker that reflects average blood glucose concentrations over a two to three month period (ADA, 2010)

Hyperglycemia – fasting plasma blood glucose ≥ 7.05 mmol/L (126 mg/dL) or random plasma blood glucose ≥ 11.20 mmol/L (200 mg/dL) (ADA, 2011)

Hypoglycemia – plasma blood glucose < 3.92 mmol/L (70 mg/dL) (ADA, 2011)

Insulin resistance – state of cellular resistance to insulin action; appears to be a syndrome that is associated with a clustering of metabolic disorders, which include non-insulin dependent diabetes mellitus, obesity, hypertension, lipid abnormalities, and atherosclerotic cardiovascular disease (DeFronzo & Ferrannini, 1991)

Kilocalorie – unit of energy; 1 kilocalorie = 1,000 calories (Gropper, et al., 2008)

Macronutrients – the dietary nutrients that supply energy, including fats, carbohydrates, and proteins (Gropper, et al., 2008)

Overnight blood glucose – for the purpose of this review, any blood glucose concentration measured after the evening meal or bedtime snack (final food intake prior to a fast) and prior to the breakfast meal

Postabsorptive state –the early fasting state; occurs during a time span of from 3 hours to about 12 to 18 hours following the meal (Gropper, et al., 2008)

Type 1 diabetes mellitus – previously referred to as insulin-dependent diabetes mellitus or juvenile-onset diabetes; develops from a cellular-mediated destruction of the pancreatic beta cells that make insulin (ADA, 2010)

Type 2 diabetes mellitus – previously referred to as non-insulin-dependent diabetes mellitus or adult-onset diabetes; involves insulin resistance and usually relative insulin deficiency (ADA,

2010)

Uncooked cornstarch – a complex carbohydrate composed of 27% amylase and 73% amylopectin; is converted into maltose and very small glucose polymers by pancreatic amylase and is slowly absorbed into circulation for up to seven hours (Kaufman, et al., 1995)

Limitations

Limitations to this current research review are outlined after each review topic and include limitations for studies involving both people with type 1 and type 2 diabetes.

Significance of the Review

Health professionals rely on evidence-based guidelines to educate and make recommendations for their patients. A recent review of evidence for MNT for type 1 and type 2 diabetes in adults answered nutrition practice questions and gave recommendations for diabetes care (Franz, et al., 2010). This review, however, did not include information and recommendations specifically related to evening food composition with regard to reducing pre-breakfast fasting and improving overall glucose control. Consensus is therefore lacking on this topic. Both people with diabetes and health professionals will benefit from a better understanding of how evening food composition affects blood glucose outcomes. This review provides guidance and helps to form recommendations surrounding this important topic and common clinical question.

Organization of Remaining Chapters

Chapter Two contains a review of the literature surrounding the following topics: 1) effects of evening food composition in type 1 diabetes; and 2) effects of evening food composition in type 2 diabetes. A limited number of research articles were found for this review, even though an extensive search was conducted. PubMed MEDLINE was primarily used to

search for literature, and additional articles were located from reference lists and personal communication. Key search words included fasting glucose, glycemic control, bedtime snack, uncooked cornstarch, and meals. A thorough literature search was conducted initially in 2008, and then repeated again in both 2010 and 2011. Few studies pertaining to this topic have been conducted in the past five years.

Study limitations are described after each topic in Chapter Two. Chapter Three includes discussion and conclusions derived from the literature review. It also contains recommendations for future research and recommendations for people living with diabetes. Finally, all references cited and summary tables are listed after Chapter Three.

CHAPTER 2. REVIEW OF LITERATURE

Pre-breakfast fasting hyperglycemia is a common occurrence observed in people with diabetes. This hyperglycemia can exert an adverse effect on overall glycemic control (Bolli & Gerich, 1984). Since it is a goal of MNT for people with diabetes to achieve plasma blood glucose concentrations in the normal or close to normal range, the relationship between evening food intake and glucose control should be thoroughly examined. The following review describes research related to evening food composition and its effects in both type 1 and type 2 diabetes. A total of eight studies for type 1 diabetes and nine studies for type 2 diabetes were reviewed. A summary of the literature findings is presented.

Effects of Evening Food Composition in Type 1 Diabetes

Schiffrin and Suissa (1987) examined the effects of an additional evening snack on the incidence of nocturnal hypoglycemia in 20 participants aged 13 to 20 years. All participants had type 1 diabetes and were on insulin pump therapy. Each person was randomly assigned to a control or experimental group; however, both groups followed an identical protocol for the first part of the study. Each participant was to consume an evening snack at 2100 and collect five capillary blood glucose samples via finger stick at home: 2100, 2230, 0000, 0400, and 0730 for three consecutive nights. Parents of the participants were asked to collect these capillary blood samples while their child was sleeping, in order to create a more usual environment at home. This same protocol was repeated a week later; however, the experimental group was instructed to have an extra snack at 2230 of eight ounces of milk if capillary blood glucose was 4.48 mmol/L (80 mg/dL) or less. If capillary blood glucose was between 4.48 and 6.72 mmol/L (80 and 120 mg/dL), six ounces of milk was to be consumed (Schiffrin & Suissa, 1987). The authors did not describe the protocol if capillary blood glucose was > 6.72 mmol/L (120 mg/dL), so it is

assumed that no extra snack was consumed. The control group did not consume an extra snack at 2230, no matter the glucose concentration. Bolus insulin was not given for any of the snacks; however, participants were instructed to give a bolus of one to two units of insulin if capillary blood glucose concentrations at 2100 were above 13.44 mmol/L (240 mg/dL). Findings of this study illustrated that ingestion of an extra snack at 2230 for capillary blood glucose concentrations less than 6.72 mmol/L (120 mg/dL) in the experimental group resulted in the absence of nocturnal or morning hypoglycemia, defined in this study as < 3.64 mmol/L (65 mg/dL). The incidence of hypoglycemia in the control group was 13 percent. The capillary blood glucose concentration at 2230 appeared to be highly predictive of the risk of overnight hypoglycemia, whereas the concentration at 2100 was not. The experimental group was continued for two months and resulted in unchanged hemoglobin A1C concentrations. Average hemoglobin A1C was $8.5 \pm 1.0\%$ at baseline and $8.4 \pm 0.9\%$ at completion of the study, indicating that unnecessary hyperglycemia did not occur in the group consuming an extra snack (Schiffrin & Suissa, 1987).

The Diabetes Control and Complications Trial (DCCT) was a prospective, randomized, multicenter trial aimed at comparing the use of intensive therapy to achieve near-normal blood glucose concentrations to conventional therapy on the development of long-term complications of type 1 diabetes. An ancillary study of the DCCT was conducted using a questionnaire to address various aspects of dietary behavior for the year prior for 623 intensively treated participants on insulin pump therapy or multiple daily injections of insulin (Delahanty & Halford, 1993). Participants were only eligible if they had been in the DCCT for at least 18 months, and ages ranged from 13 to 39 years. Average hemoglobin A1C of the participants was $7.15 \pm 1.0\%$ in the year prior to administering the questionnaire. During the DCCT trial, these

participants were instructed on a diet that consisted of 45-55% carbohydrate, 12-20% protein, and no more than 30-35% fat. The questionnaire asked participants about the frequency of an extra snack at night beyond the meal plan and how often they ate a snack at night. Results of the questionnaire showed that intensively treated people with type 1 diabetes who consumed an evening snack each day had lower hemoglobin A1C concentrations of 7.06 ± 0.93%, compared to 7.28 ± 1.20% for those who consumed an evening snack just two or less times per week. Those who consumed extra evening snacks (> 1 snack per evening) on three or more evenings per week had a higher average hemoglobin A1C concentration of 7.33 ± 1.12% when comparing to 7.01 ± 0.98% for those who consumed extra snacks less than one time per week (Delahanty & Halford, 1993). This showed evidence in favor of the consumption of a daily evening snack for blood glucose control for people with type 1 diabetes, but not for the consumption of extra nighttime snacks beyond this daily snack.

Studies have also been conducted to investigate the impact of bedtime snack nutrient composition, specifically uncooked cornstarch and protein, on blood glucose outcomes (Axelsen, et al., 1999; Kalergis, et al., 2003; Kaufman, et al., 1995; Kaufman, et al., 1997). An uncooked cornstarch snack was compared to a standard snack in 51 people with type 1 diabetes who were attending an ADA sponsored camp in Southern California (Kaufman, et al., 1995). Participants ranged from 14 to 22 years of age and included 20 males and 31 females. Half of the participants were taking two injections of insulin per day, and half were taking either three or more injections per day or were on insulin pump therapy. Hemoglobin A1C measurements prior to the camp were available for 40 of the 51 participants, with 30% of the values being less than 125% above the reported upper limit of the assay norm, 55% between 125% and 175% of the upper limit of assay norm, and 15% greater than 175% of the upper limit of the assay norm

(Kaufman, et al., 1995). All participants received a standard snack for five nights and an

uncooked cornstarch snack for five nights; these were given in random order and were blinded to

the participants and medical personnel. The uncooked cornstarch snack consisted of five grams

of uncooked cornstarch in 2.5 ounces sugar-free pudding, which equaled 17 of grams

carbohydrate and about seven grams of protein. The standard snack consisted of 4 ounces of

sugar-free pudding, which also equaled 17 grams of carbohydrate and about seven grams of

protein (Kaufman, et al., 1995). The participants checked blood glucose levels via finger stick

using their own blood glucose meters. Blood glucose concentrations were measured before

breakfast, before lunch, before dinner, before the evening snack, and between midnight and

0100. In addition, the participants were to measure blood glucose concentrations if they had

symptoms suggestive of hypoglycemia or hyperglycemia. The study showed that the standard

snack resulted in a significantly higher incidence of hypoglycemia, defined in this study as blood

glucose < 3.36 mmol/L (60 mg/dL). At midnight, the incidence of hypoglycemia was 2.2%

when consuming the uncooked cornstarch snack and 12.2% with the standard snack. At 0700

before breakfast the following morning, hypoglycemia incidence was 4.5% with the uncooked

cornstarch snack compared to 9.5% with the standard snack. There was no difference in the

incidence of hyperglycemia, defined as blood glucose > 14 mmol/L (250 mg/dL), between the

two study groups at midnight or at 0700 before breakfast (Kaufman, et al., 1995). This study

showed that an evening snack containing uncooked cornstarch could reduce the incidence of

hypoglycemia at midnight and the next morning without increasing hyperglycemia.

An additional study by Kaufman, et al. (1997) also determined that a snack containing

uncooked cornstarch could diminish the incidence of hypoglycemia in people with type 1

diabetes without causing an increase in overnight and fasting hyperglycemia. This study, similar

to Kaufman, et al. (1995) took place at an ADA sponsored camp in Southern California. There were a total of 79 participants, ages 14 to 30 years, of which 33 were male and 46 were female. The types of insulin therapy used were also similar to Kaufman, et al. (1995). Hemoglobin A1C concentrations were said to be reported in 73 of the 79 participants; however, these concentrations were not specified in the study. All participants consumed three meals and three snacks per day composed of 25% fat, 50% carbohydrate, and 25% protein (Kaufman, et al., 1997). Between the hours of 2100 and 2130, participants were randomly assigned to receive either a snack bar containing five grams of uncooked cornstarch or a bar containing no uncooked cornstarch; each snack bar contained a total of 22 grams of carbohydrate. Participants consumed each snack bar for five consecutive nights and were blinded to the type of bar they were consuming. The participants checked their own blood glucose via finger stick using either a One Touch^{TM} glucose meter or a Glucometer Elite^{TM} before breakfast, before lunch, before dinner, before evening snack, and finally between midnight and 0100. If the participant's finger stick blood glucose concentration was $\geq$ 6.72 mmol/L (120 mg/dL) before the evening snack, four ounces of milk was included with the snack bar. If the finger stick blood glucose concentration was 4.48 to 6.66 mmol/L (80 to 119 mg/dL), an additional 7.5 grams of carbohydrate and five grams of protein were added along with the snack bar. If the finger stick blood glucose concentration was 2.80 to 4.42 mmol/L (50 to 79 mg/dL), an additional 15 grams of carbohydrate and five grams of protein was included with the snack bar. Finally, if the finger stick blood glucose concentration was < 2.80 mmol/L (50 mg/dL), an additional 30 grams of carbohydrate and five grams of protein were given with the snack bar (Kaufman, et al., 1997). The study showed that the ingestion of the snack bar containing uncooked cornstarch resulted in a significantly lower rate of hypoglycemic events at midnight and in the morning before

breakfast when comparing the snack bar without uncooked cornstarch: 3.3% compared to 15.3% at midnight and 2.0% compared to 7.7% in the morning before breakfast. The bar containing uncooked cornstarch also resulted in a significant decrease in the number of hyperglycemic events at midnight and in the morning before breakfast: 6.4% compared to 11.1% at midnight and 5.1% compared to 8.2% in the morning before breakfast (Kaufman, et al., 1997). In this study, hypoglycemia was defined as finger stick blood glucose concentrations < 3.36 mmol/L (60 mg/dL), and hyperglycemia was defined as finger stick blood glucose concentrations > 14 mmol/L (250 mg/dL). Hemoglobin A1C was not reported in this study. Although the study authors did not describe if bolus insulin was given for either snack bar, there was no difference in total insulin dosage between the two bars during the study period. It was concluded that mixing uncooked cornstarch with other complex carbohydrate may have enhanced its prolonged glycemic effect, therefore reducing the incidence of hypoglycemia. In addition, the fat could have delayed gastric emptying, and the protein may have provided substrate for gluconeogenesis (Kaufman, et al., 1997).

Another study also compared a bedtime snack containing uncooked cornstarch to a placebo snack (Axelsen, et al., 1999). This study of 12 people with type 1 diabetes included only those with a hemoglobin A1C ≤ 7.5%, a history of severe hypoglycemia during the last year or ≥ 1 nocturnal hypoglycemic episode, and a history of hypoglycemia unawareness (Axelsen, et al., 1999). All 12 participants completed this study in the outpatient setting, and all were taking at least four daily injections of insulin – intermediate-acting NPH at bedtime and regular insulin before meals. Participants were randomized to receive either an uncooked cornstarch-containing snack or a placebo snack at bedtime. This bedtime snack was consumed for four weeks. After a seven-week washout period, the participants then consumed the other bedtime snack for another

four weeks. The participants recorded their own daily fasting and bedtime blood glucose

concentrations throughout the study via finger stick using the Bayer Glucometer Elite™ blood

glucose meter. They were also instructed to measure finger stick blood glucose if they were

having any symptoms of hypoglycemia. In addition, they were responsible for checking and

recording finger stick blood glucose at 0300 every night during the second and fourth weeks of

each four-week period. The uncooked cornstarch and placebo snacks were both provided in jars

and appeared identical. The uncooked cornstarch snack was equal to 0.30 gram uncooked

cornstarch per kilogram body weight and was suspended in low-sugar fruit juice to total 0.32

gram carbohydrate per kilogram body weight. The placebo snack contained equivalent low-

sugar fruit juice in addition to food coloring and thickening agent to total 0.05 gram carbohydrate

per kilogram body weight (Axelsen, et al., 1999). In order to more closely monitor glucose

concentrations, nine out of the 12 participants also completed an overnight study in a hospital at

the end of the each snack period. During this portion of the study, arterialized blood samples

using a venous catheter were collected 30 minutes and zero minute prior to receiving the bedtime

snack at 2300. Following the snack, blood sample collection was continued hourly starting at

2300 and continuing until 0700. All glucose levels during the hospital portion of the study were

measured using an automatic glucose analyzer (Axelsen, et al., 1999).

    Axelsen, et al.'s study (1999) showed that bedtime finger stick blood glucose

concentrations in the outpatient setting were similar during the uncooked cornstarch and placebo

snack periods. At 0300, however, the finger stick blood glucose concentrations with the

uncooked cornstarch snack were an average of 1.91 mmol/L (34.20 mg/dL) higher compared to

the placebo snack. In addition, blood glucose persisted at a higher concentration throughout the

night with the uncooked cornstarch snack, and this resulted in a 1.11 mmol/L (19.80 mg/dL)

higher finger stick blood glucose concentration at 0700 before breakfast when compared to the placebo. Both of these increases were statistically significant. There was no significant change in hemoglobin A1C concentrations for either snack during the study period. Reported hypoglycemic episodes at 0300 totaled 11 during the placebo period, but this was significantly reduced to three during the uncooked cornstarch period (Axelsen, et al., 1999). During the hospital portion of the study, there were no significant differences in blood glucose concentrations when comparing the uncooked cornstarch and placebo snacks. There were, however, two episodes of hypoglycemia after consuming the placebo snack, compared to no episodes following the uncooked cornstarch snack. The authors stated that a firm conclusion could not be drawn regarding the effectiveness of uncooked cornstarch in preventing hypoglycemia. This was due to the fact that the placebo snack was virtually carbohydrate-free and therefore could not have prevented hypoglycemia. This study did show that an uncooked cornstarch snack could reduce the number of self-reported hypoglycemic episodes at 0300 without increasing hemoglobin A1C concentrations (Axelsen, et al., 1999).

Kalergis, et al. (2003) further investigated the impact of bedtime snack composition in nine men and six women with type 1 diabetes who were taking NPH insulin at bedtime and rapid-acting lispro insulin before meals. The participants' ages ranged from 23 to 65 years and duration of diabetes was eight to 43 years. Baseline average hemoglobin A1C concentration was $8.1 \pm 1.2\%$. This study was conducted at a hospital investigation unit in Quebec, Canada, and included four separate hospitalizations. This study aimed to determine whether a bedtime snack containing either uncooked cornstarch or protein would result in more favorable glycemic control. Participants were randomized to receive one of the following bedtime snacks at 2200: 1) a placebo drink sweetened with aspartame that contained no carbohydrate, protein, or fat; 2) a

standard snack consisting of two slices of white bread, one ounce of cheddar cheese, and a placebo drink to equal 30 grams of carbohydrate, 11 grams of protein, and three grams of fat; 3) an uncooked cornstarch-containing snack similar to the standard snack, but one slice of bread was replaced with 14 grams of raw uncooked cornstarch dissolved in the placebo drink to equal 29 grams of carbohydrate, 11 grams of protein, and three grams of fat; or 4) a protein-rich snack that replaced one slice of bread with 15 grams of protein in the form of a drink to equal 15 grams of carbohydrate, 24 grams of protein, and three grams of fat (Kalergis, et al., 2003). The participants and study nurse were blinded to the exact snack composition. It was not specified whether rapid-acting insulin was given for the bedtime snack. Blood glucose samples were collected via finger stick every hour starting at 2200, which was just prior to snack consumption, until 0700 using the Bayer Elite Glucometer[TM]. Since this was a crossover design study, participants received each of the four snacks on four different days during the study. They were instructed to leave a minimum of three days and a maximum of three weeks between each type of snack during the study intervention. Results of the study showed that the lowest incidence of morning hyperglycemia occurred in the group that received the placebo snack; however, the most episodes of overnight hypoglycemia also occurred with the placebo snack, especially when bedtime glucose concentrations were < 7.05 mmol/L (126 mg/dL). No hypoglycemia occurred with the standard or protein snacks. When finger stick blood glucose concentrations were > 10.08 mmol/L (180 mg/dL) at bedtime, 46% of the pre-breakfast fasting concentrations were elevated. The standard and uncooked cornstarch snacks followed the placebo with respect to the least morning hyperglycemia, and the protein-rich snack correlated with the highest incidence of morning hyperglycemia (Kalergis, et al., 2003). The authors concluded that the standard snack was the only snack that was able to prevent nocturnal hypoglycemia without significantly

impacting overnight and pre-breakfast fasting glycemia, especially when bedtime finger stick blood glucose concentrations were < 7.05 mmol/L (126 mg/dL).

Four different bedtime treatments have been compared against no treatment in the prevention of nocturnal hypoglycemia (Raju, et al., 2006). Twenty-one patients with type 1 diabetes and a mean hemoglobin A1C concentration of 7.1 ± 1.0% were studied at a clinical research center. Ten of the participants were women, and 11 were men. Eleven were on insulin pump therapy and 10 were on multiple daily injections of insulin. Participants continued their usual insulin regimens, and these were not altered by the study physicians. They were admitted to the research center overnight on five different occasions. On each occasion, the participants were randomized to either: 1) no treatment; 2) a conventional snack (200 kilocalories, 26 grams of carbohydrate, six grams of fat, and 11 grams of protein); 3) the same conventional snack plus an alpha-glucosidase inhibitor (acarbose), 100 mg orally; 4) one and one-quarter bar containing uncooked cornstarch (194 kilocalories, 39 grams of carbohydrate including 6.25 grams of uncooked cornstarch, four grams of fat, and four grams of protein); or 5) a beta$_2$-adrenergic agonist (terbutaline), 5.0 mg orally without a snack (Raju, et al., 2006). In previous studies, an alpha-glucosidase inhibitor has been shown to delay digestion of carbohydrates in the evening meal (McCulloch, Kurtz, & Tattersall, 1983; Taira, Takasu, Komiya, Taira, & Tanaka, 2000). Terbutaline at bedtime has previously been shown to more effectively reduce nocturnal hypoglycemia when compared to a conventional bedtime snack (Saleh & Cryer, 1997). Each treatment was administered at 2200, and blood samples for plasma glucose measurements using an intravenous line were drawn at 15-minute intervals from 2100 to 0700. These plasma glucose concentrations were measured using a glucose analyzer at the bedside. Results of the study showed that an absence of a bedtime treatment caused glucose concentrations to decline from 7 ±

0.60 mmol/L (126 ± 11 mg/dL) to 5.90 ± 0.80 mmol/L (106 ± 14 mg/dL) by 0700 the following morning. Only the terbutaline treatment raised glucose concentrations between 0245 and 0700 and resulted in a significantly higher mean morning (0700) glucose concentration when compared to no treatment. Mean nocturnal glucose concentrations were significantly higher with the conventional snack, the uncooked cornstarch-containing bar, and bedtime terbutaline, but not with the conventional snack plus acarbose (Raju, et al., 2006). Hypoglycemia was followed closely in this study. The no bedtime treatment group had plasma blood glucose concentrations of < 3.92 mmol/L (70 mg/dL) in 27% of the measured readings. Neither the conventional snack, nor the conventional snack with acarbose, nor the uncooked cornstarch-containing bar reduced this hypoglycemia. However, bedtime terbutaline did reduce plasma blood glucose concentrations of < 3.92 mmol/L (70 mg/dL) to less than 1% of the measured values. In addition, the conventional snack without acarbose and the uncooked cornstarch-containing bar seemed to shift low glucose concentrations to later in the night (Raju, et al., 2006). This effect was expected with the conventional snack containing acarbose, however did not happen. The authors concluded that although three of the four treatments did not cause an increase in morning glucose concentrations, none was acceptable clinically since they were unable to prevent nocturnal hypoglycemia. In addition, although terbutaline at bedtime was able to reduce nocturnal hypoglycemia, it was not recommended due to the hyperglycemic effects the following morning (Raju, et al., 2006).

Finally, a group of 10 children aged six to less than 18 years was studied to determine whether a bedtime snack with a higher fat content would provide greater protection against nocturnal hypoglycemia when compared to a snack with a lower fat content (DirecNet, 2008). All participants had been on insulin pump therapy for at least six months prior to the study

consent, and the FreeStyle Navigator^{TM} Continuous Glucose Monitoring System (CGMS) was utilized to measure glucose in the home setting. Average hemoglobin A1C at the beginning of the study was $6.9 \pm 0.5\%$. The participants were studied for a minimum of 12 nights; each participant consumed the low-fat snack for six nights and the high-fat snack on the other six nights. The high-fat snack consisted of potato chips equal to 30 grams of carbohydrate, 20 grams of total fat, five grams of saturated fat, and two grams of protein for a total of 320 kilocalories. The low-fat snack consisted of pretzels equal to 30 grams of carbohydrate, 1.3 grams of total fat, no saturated fat, and 2.5 grams of protein for a total of 138 kilocalories. The participants were instructed to check finger stick glucose prior to the bedtime snack using the Freestyle™ meter built into the CGMS. If the glucose concentration was < 4.48 mmol/L (80 mg/dL), carbohydrate was taken and glucose was rechecked until the concentration was ≥ 4.48 mmol/L (80 mg/dL). Bolus insulin to cover the bedtime snack was recorded, and this amount was calculated by the participants using their usual practices. The CGMS collected an average of 8.1 hours of glucose readings per study night. The mean pre-snack glucose concentration was similar between the two snack groups. On the high-fat snack nights, the average pre-snack glucose concentration was 9.13 ± 3.08 mmol/L (163 ± 55 mg/dL) as measured by the Freestyle™ meter and 9.07 ± 3.36 mmol/L (162 ± 60 mg/dL) as measured by the CGMS. On the low-fat snack nights, the average pre-snack glucose concentration was 9.18 ± 2.97 mmol/L (164 ± 53 mg/dL) as measured by the Freestyle™ meter and 9.24 ± 3.02 mmol/L (165 ± 54 mg/dL) as measured by the CGMS. Results of the study showed that mean glucose overnight was higher after consumption of the high-fat snack when compared to the low-fat snack. The high-fat snack nights resulted in an average glucose of 9.57 ± 2.58 mmol/L (171 ± 46 mg/dL) while the low-fat snack nights resulted in an average glucose of 8.73 ± 2.52 mmol/L (156 ± 45 mg/dL). Hypoglycemia of ≤ 3.92

mmol/L (70 mg/dL) occurred on 12 (19%) nights following the high-fat snack, compared to 13

(20%) nights following the low-fat snack, while hyperglycemia of ≥ 11.20 mmol/L (200 mg/dL)

occurred on 22 (35%) nights and 20 (30%) nights, respectively (DirecNet, 2008). It was

concluded that increasing the amount of fat in the bedtime snack had no impact on the risk of

nocturnal hypoglycemia, even though the glucose concentrations tended to be slightly higher on

those nights. In addition, the authors noted that the addition of an extra 182 kilocalories per day

at bedtime could result in undesired weight gain over time unless kilocalorie cuts were made at

other times of the day. These additional kilocalories were shown to provide no protective benefit

against hypoglycemia (DirecNet, 2008).

Table 2.1 includes a summary of the above studies involving people with type 1 diabetes.

Limitations of Current Research for Effects of Evening Food Composition in Type 1

Diabetes

Studies examining the effects of evening food composition on glucose control in type 1

diabetes are limited in number. In addition, the number of participants is generally small. Of the

eight studies reviewed, seven are of short duration, lasting less than three months. Only

Delahanty & Halford (1993), the ancillary study of the DCCT, provided information from a one-

year time period. Just three of the seven studies reviewed reported hemoglobin A1C results,

likely because the short durations of the studies would not have significantly impacted the

outcome. Fat content in the bedtime snacks was often not described, especially when milk was

consumed as part of the snack. A higher fat content could have provided substrate for

gluconeogenesis, which in turn could affect blood glucose results. Out of the seven studies that

measured blood glucose, only one utilized CGM; two analyzed frequent blood samples for

glucose as participants were admitted to a research center for at least one night. This frequent

Table 2.1 Studies reporting on evening food intake and type 1 diabetes

First Author, Year	Population / Duration of Study	Type of Study	Intervention	Major Findings
Extra bedtime snack intake (beyond 1 bedtime snack)				
Schiffrin, 1987	N = 20 / 3 days of one bedtime snack only followed by 3 days of same snack ± 6-8 oz milk; experimental group continued another 2 months	Randomized	Bedtime snack at 2100 vs. bedtime snack at 2100 plus 6-8 oz milk at 2230 if blood glucose ≤ 120 mg/dL	Addition of 6-8 oz milk eliminated overnight and pre-breakfast fasting hypoglycemia without ↑ A1C.
Delahanty, 1993	N = 623 / looked at diet behaviors over the past year in intensively controlled participants of the Diabetes Control and Complications Trial	Retrospective questionnaire	Frequency of a bedtime snack ± additional snacks above one daily bedtime snack	Consumption of a daily bedtime snack resulted in ↓A1C than when consuming a snack just 2-3 days/week; consuming additional snacks above this ↑ A1C.

Table 2.1 (continued)

CS bedtime snack compared to other snacks with equal CHO				
Kaufman, 1995	N = 51 / 5 nights of each snack	Randomized crossover	Bedtime standard snack without CS vs. snack containing 5 g CS	↓ Hypoglycemia overnight & pre-breakfast fasting with CS snack; no difference in hyperglycemia.
Kaufman, 1997	N = 79 / 5 nights of each snack	Randomized crossover	Bedtime snack bar without CS vs. bedtime snack bar with 5 g CS	↓ hypoglycemia and ↓ hyperglycemia at midnight and pre-breakfast fasting with bar containing CS.
CS bedtime snack compared to other snacks without equal CHO				
Axelsen, 1999	N = 12 / 4 weeks of each treatment plus an overnight stay for 9 participants	Randomized crossover	Bedtime CS snack mixed in low-sugar fruit juice vs. placebo low-sugar fruit juice	Outpatient results: ↓ hypoglycemia, but ↑ blood glucose at 0300 and 0700 following CS snack; no change in A1C. Overnight results: no significant differences in blood glucose; ↓ hypoglycemia with CS snack.
Kalergis, 2003	N = 15 / One day each of 4 treatments; 3 days to 3 weeks between each treatment	Randomized crossover	Placebo snack vs. Standard snack (30 g CHO, 11 g protein, 3 g fat) vs. CS snack (same as standard snack but with 14 g CS) vs. Protein snack (15 g CHO, 24 g protein, 3 g fat)	Standard snack only snack to prevent hypoglycemia and not cause significant hyperglycemia.

Table 2.1 (continued)

Raju, 2006	N = 21 / 5 separate overnights	Randomized crossover	No treatment vs. conventional snack (26 g CHO, 6 g fat, & 11 g protein) vs. conventional snack + alpha-glucosidase inhibitor vs. CS bar (39 g CHO including 6.25 g CS, 4 g fat, & 4 g protein) vs. a beta$_2$-adrenergic agonist	No treatment caused an increase in morning glucose but the beta$_2$-adrenergic agonist; no treatment was able to prevent nocturnal hypoglycemia. Beta$_2$-adrenergic agonist ↓ nocturnal hypoglycemia, but ↑ blood glucose the following morning.
Low-fat compared to high-fat bedtime snack				
DirecNet, 2008	N = 10 / 6 nights each of 2 treatments	Crossover (minimized algorithm used to determine ordering of the snacks)	Low-fat snack (30 g CHO, 1.3 g total fat, no saturated fat, & 2.5 g protein = 138 kcals) vs. high-fat snack (30 g CHO, 20 g total fat, 5 g saturated fat, & 2 g protein = 320 kcals)	High-fat snack ↑ blood glucose overnight compared to low-fat snack: 171 ± 46 mg/dL vs. 156 ± 45 mg/dL. No difference in hypoglycemia between groups

A1C = hemoglobin A1C   CHO = carbohydrate   CS = uncooked cornstarch
g = gram(s)   Kcal(s) = kilocalorie(s)

sampling of blood and disruption to sleep may have had an independent effect on blood glucose readings. Four of the studies used self-monitoring of blood glucose in the outpatient setting, which resulted in much fewer blood glucose readings when comparing CGM or overnight stays. Two of these four studies involved participants using their own glucose meters, but did not specify if these were calibrated for accuracy. Finally, only two of the studies specified whether bolus insulin was given for the bedtime snack, with one study instructing participants to give no bolus insulin, and the other instructing participants to give their usual dose of bolus insulin.

Effects of Evening Food Composition in Type 2 Diabetes

Similar to studies involving people with type 1 diabetes, research pertaining to a bedtime snack in people with type 2 diabetes has also examined the use of uncooked cornstarch (Axelsen, et al., 1999; Axelsen, et al., 2000; Dyer-Parziale, 2001). A study involving 24 people with type 2 diabetes was conducted to examine changes in blood glucose concentration when comparing two different bedtime snacks (Axelsen, et al., 1999). The 24 participants were split into two groups of 10 and 14, with an average hemoglobin A1C of 7.0 ± 0.9% and 6.8 ± 1.0%, respectively. Fasting blood glucose concentrations were also similar between the two groups at baseline: 8.2 ± 1.60 mmol/L (146.40 ± 28.60 mg/dL) and 8.40 ± 1.70 mmol/L (150 ± 30.40 mg/dL) (Axelsen, et al., 1999). Each group was studied overnight in a hospital setting and consumed the bedtime snack at 2200. The first group consumed a conventional bedtime snack consisting of whole grain bread with butter and meat, averaging 0.60 gram carbohydrate per kilogram body weight. The second group was studied twice in randomized order: once following the consumption of 0.55 gram per kilogram body weight of uncooked cornstarch dissolved in low-sugar fruit juice and once following the consumption of the placebo, which contained only the low-sugar fruit juice with thickening agents to equal an average of 0.10 gram carbohydrate per kilogram body

weight. Both the conventional and uncooked cornstarch snacks consisted of 50 grams of carbohydrate. Arterialized blood samples were collected using a venous catheter and blood glucose was measured using an automatic glucose analyzer. Blood samples were collected at 2150 and 2200 just prior to consuming the snack, and then at 2400, 0200, 0400, 0600, and 0700 (Axelsen, et al., 1999). Results showed a significantly higher blood glucose response from 2400 to 0400 with the conventional and uncooked cornstarch snacks when comparing the placebo. The ingestion of uncooked cornstarch at bedtime showed a lower average blood glucose peak of 2.92 mmol/L (52.20 mg/dL) compared to 5.24 mmol/L (93.60 mg/dL) for the conventional snack. There was also a delayed peak in blood glucose concentrations of 4.3 hours versus two hours when comparing the uncooked cornstarch and conventional snack, respectively. The authors concluded that both the conventional and uncooked cornstarch snacks significantly raised blood glucose concentrations between 2400 and 0400, but the conventional snack led to more rapid blood glucose elevations. The uncooked cornstarch snack had a delayed glycemic effect, with a moderate peak of blood glucose concentrations at 0400. There was no significant difference in blood glucose at 0700 the following morning between the uncooked cornstarch snack and the conventional snack; the placebo resulted in lower blood glucose the following morning (Axelsen, et al., 1999). The authors did not describe the frequency of hypoglycemia in this portion of the study.

A follow-up randomized, placebo-controlled, double-blind crossover study was then conducted to assess the effects of varying bedtime carbohydrate intake on glycemic control (Axelsen, et al., 2000). Both a high-dose and a low-dose uncooked cornstarch snack were studied separately versus a placebo. The high-dose snack consisted of 0.55 gram uncooked cornstarch per kilogram body weight for a total of 0.59 gram carbohydrate per kilogram body

weight. The low-dose snack consisted of 0.30 gram uncooked cornstarch per kilogram body weight for a total of 0.33 gram carbohydrate per kilogram body weight. The placebo contained no uncooked cornstarch and consisted of 0.10 gram carbohydrate per kilogram body weight in the high-dose study and 0.06 gram carbohydrate per kilogram body weight in the low-dose study (Axelsen, et al., 2000). Protein and fat content of the snacks was not provided. Fourteen people with type 2 diabetes participated in the high-dose study, and 24 participated in the low-dose study. Participants in the high-dose study were using diet alone or diet combined with either the oral diabetes medication metformin or a sulfonylurea for diabetes therapy, while the low-dose study excluded those using a sulfonylurea. Average hemoglobin A1C at baseline was $6.8 \pm 1.0\%$ in the high-dose study group and $6.1 \pm 0.9\%$ in the low-dose study group. The study was completed over 25 weeks, in which two seven-week periods were separated by an 11-week washout. Changes in hemoglobin A1C were recorded after seven weeks for the high-dose study group and after four and seven weeks for the low-dose study group. An overnight study was also conducted, in which arterialized blood samples were collected from a heated forearm every one-half hour from 2200-2400, every two hours from 0000-0600, and every one-half hour from 0600-1300. The snack was consumed at about 2200. Results showed that, similar to Axelsen, et al.'s study (1999), consumption of the high-dose snack was associated with an increase in blood glucose concentrations between 0200 and 0700. However, there were no significant changes seen in the hemoglobin A1C concentrations after seven weeks of the high-dose snack containing uncooked cornstarch. On the other hand, the low-dose snack with uncooked cornstarch was associated with significantly lower fasting blood glucose concentrations when compared to the placebo without uncooked cornstarch. Hemoglobin A1C concentrations were also not significantly different in the low-dose snack study group. This study showed a favorable effect

of a low-dose carbohydrate snack containing uncooked cornstarch on fasting blood glucose

concentrations in those controlling blood glucose with diet alone or diet plus metformin

(Axelsen, et al., 2000).

Dyer-Parziale (2001) once again examined the effects of uncooked cornstarch on

nocturnal blood glucose via finger stick in 28 adults with type 2 diabetes. Of these 28

participants, 13 were treated with oral diabetes agents, eight with insulin, and seven with a

combination of oral agents and insulin. Mean hemoglobin A1C at baseline was $8.21 \pm 1.28\%$

(Dyer-Parziale, 2001). The participants were randomly assigned to consume either a snack bar

containing uncooked cornstarch or a placebo bar without uncooked cornstarch for three nights

each. The time of snack consumption was not specified in the study. The snack bar contained

31 grams of carbohydrate, including five grams of uncooked cornstarch, and the placebo bar also

contained 31 grams of carbohydrate but no uncooked cornstarch. Protein and fat content was

similar in both bars, and the participants were blinded as to the type of bar they ingested. The

participants checked their own finger stick blood glucose concentrations at home using their own

glucose meter; these were to be obtained prior to the bedtime snack, at midnight, and prior to

breakfast. No hypoglycemia, defined in this study as < 3.36 mmol/L (60 mg/dL), occurred

throughout the duration of the study. The mean finger stick blood glucose concentrations both at

midnight and before breakfast were significantly lower with the snack bar containing uncooked

cornstarch when comparing the placebo bar. Mean finger stick blood glucose at midnight was

7.11 mmol/L (127 mg/dL) with the snack bar and 8.29 mmol/L (148 mg/dL) with the placebo

bar; mean finger stick blood glucose before breakfast was 6.38 mmol/L (114 mg/dL) with the

snack bar and 8.85 mmol/L (158 mg/dL) with the placebo bar (Dyer-Parziale, 2001). The snack

bar with uncooked cornstarch was suggested as a strategy to lessen nocturnal and morning

hyperglycemia in people with type 2 diabetes without increasing the risk of overnight or morning hypoglycemia.

In clinical practice, patients may believe that a large supper can lead to elevated fasting blood glucose the next morning. Arauz-Pacheco, et al. (1998) examined the effects of a large supper meal in 17 people with type 2 diabetes with pre-existing fasting hyperglycemia. Oral diabetes medications were stopped two weeks prior to the study to produce a hyperglycemic state, and baseline fasting plasma glucose concentrations had a mean of 12.30 ± 0.90 mmol/L (223 ± 16 mg/dL). Average hemoglobin A1C among the participants was $9.9 \pm 0.5\%$ (Arauz-Pacheco, et al., 1998). Participants received three separate meal protocols in random order spaced one week apart: 1) small supper: seven kilocalories per kilogram ideal body weight (IBW) breakfast, seven kilocalories per kilogram IBW lunch, and 14 kilocalories per kilogram IBW supper; 2) large supper: seven kilocalories per kilogram IBW breakfast, seven kilocalories per kilogram IBW lunch, and 28 kilocalories per kilogram IBW supper; and 3) no supper: seven kilocalories per kilogram IBW breakfast, 14 kilocalories per kilogram IBW lunch, and no supper (Arauz-Pacheco, et al., 1998). Meals were provided in frozen form after being prepared at a metabolic kitchen at a research center. Each meal consisted of a macronutrient distribution of 50% carbohydrate, 30% fat, and 20% protein. Meal times were specified as follows: breakfast between 0700 and 0730, lunch between 1200 and 1230, and supper, when applicable, between 1900 and 1930. Fasting plasma glucose was measured using a glucose analyzer at the research center between 0700 and 0900 the day following the randomized meal. Results of the study showed that fasting plasma blood glucose concentrations after the large supper were 1.30 ± 0.50 mmol/L (23.50 ± 9 mg/dL) higher than after no supper, and 1.00 ± 0.50 mmol/L (18.10 ± 9 mg/dL) higher than after the small supper. There was no significant difference in plasma blood

glucose concentrations between no supper and a small supper. This showed that a large evening meal can result in a significant, but modest, elevation in fasting plasma blood glucose concentrations in people with type 2 diabetes with pre-existing fasting hyperglycemia. In addition, the authors concluded that a large meal with high amounts of protein may provide gluconeogenic substrates and stimulate glucagon and growth hormone, which may result in enhanced hepatic glucose production (Arauz-Pacheco, et al., 1998).

Another study tested the hypothesis that altering the kilocalorie distribution of meals and time intervals between these meals could have a significant effect on plasma blood glucose control (Beebe, et al., 1990). The suggestion to eat small meals with snacks in-between is commonly given to people with type 2 diabetes. It is thought that this meal pattern would help improve plasma blood glucose, whereas consuming most kilocalories in the latter part of the day is thought to cause hyperglycemia. Beebe, et al. (1990) examined various kilocalorie and meal distributions on six participants with type 2 diabetes not using insulin therapy. Participants continued taking their oral hypoglycemic medications throughout the study. Mean hemoglobin A1C among the six participants was $8.9 \pm 0.5\%$ (Beebe, et al., 1990). The study was performed at a research center at which participants stayed on three separate occasions for 26 hours each time, beginning at 0700 and ending at 0900 the following morning. Each participant received a different kilocalorie distribution on each occasion in randomized order, and each occasion was separated by a two-week interval. During every 26-hour period, the macronutrient composition remained constant for all meals and snacks, with 50% of kilocalories from carbohydrate, 35% of kilocalories from fat, and 15% of kilocalories from protein (Beebe, et al., 1990). However, during each study period, the kilocalorie distribution at meals and snacks changed as follows: 1) 30% at breakfast, 40% at lunch, and 30% at supper with no snacks; 2) 20% at breakfast, 20% at

lunch, and 30% at supper with 10% each for three snacks between meals; or 3) 10% at breakfast, 20% at lunch, and 70% at supper with no snacks. Meal times were 0800, 1300, and 1800. Blood samples were collected at 15 to 30 minute intervals throughout the 26-hour study period using an indwelling catheter, and plasma glucose was measured using a glucose analyzer. Results showed that pre-breakfast fasting plasma blood glucose concentrations, as well as mean concentrations of glucose from midnight to 0300 and 0300 to 0600, did not differ significantly across the study groups. When kilocalorie distribution was spread more evenly between meals and snacks, a slight increase in mean glucose concentrations was seen, but sharp, meal-induced peaks of glucose were blunted. It was also noted that the effects of the dawn phenomenon appeared to be lessened when a late snack or a large supper was consumed. The glucose concentrations did not increase at dawn, or the increase was of smaller magnitude (Beebe, et al., 1990). Overall, this study showed that widely varying meal and eating patterns produce only modest variation in overall plasma blood glucose concentrations, and that spreading food intake into small meals and snacks does not improve glucose control.

In addition to studying variations in kilocalorie distribution at meals, research has also examined widely varying distribution of carbohydrate at meals using CGM in type 2 diabetes (Pearce, et al., 2008). Twenty-four men and women participated in this study, and diabetes treatment strategies included diet-only, oral hypoglycemic medications, and/or insulin. The participants had a mean hemoglobin A1C of 8.6 ± 1.6% and a mean fasting blood glucose concentration of 7.50 ± 2.20 mmol/L (134 ± 39.30 mg/dL). This study consisted of four three-day randomized treatments in which total daily carbohydrate intake was kept consistent at 40% of total kilocalories. Protein and fat were also kept consistent at 34% of total kilocalories and 26% of total kilocalories, respectively (Pearce et al., 2008). All treatments included identical

foods that were provided to participants, but the foods were allocated differently at each meal, as follows: 1) CARB-E: carbohydrates evenly distributed at all meals, which was about 68-70 grams per meal; 2) CARB-B: carbohydrates loaded at breakfast, which was 128 grams while the other two meals consisted of about 38 grams; 3) CARB-L: carbohydrates loaded at lunch, which was 125 grams while the other two meals consisted of about 39-40 grams; or 4) CARB-D: carbohydrates loaded at dinner, which was 123 grams while the other two meals consisted of about 41-44 grams (Pearce, et al., 2008). Meals were able to be consumed at anytime the participants wanted, but they had to be consumed six hours apart. The CGMS, which measured glucose levels in the interstitial fluid, measured interstitial glucose every 10 seconds, which resulted in 288 readings per day. The participants were blinded to the CGM results. Fasting glucose using the CGMS was recorded at 0530 every morning. Results of this study showed that fasting glucose concentrations did not differ significantly between days, by treatment, or by time. The lowest daily postprandial peak glucose was seen in the CARB-L treatment, followed by the CARB-E treatment, suggesting that lunchtime is the most favorable time to consume carbohydrates. An even distribution of carbohydrate was not shown to be optimal for minimizing postprandial glucose peaks (Pearce, et al., 2008).

Glucose outcomes after ingestion of a diet high in fruits and vegetables have also been examined in people with type 2 diabetes (Gannon, et al., 1998). Six men with an average hemoglobin A1C of $9.5 \pm 0.8\%$ and an average fasting glucose of 8.60 ± 0.80 mmol/L (155 ± 13.90 mg/dL) were studied in a special diagnostic and treatment unit. None of the men had been treated with oral hypoglycemic medications or insulin before the start of the study, and all had consumed a diet containing at least 200 grams of carbohydrate per day for three days before the study began. Participants were admitted to the treatment unit and completed an overnight fast.

Each participant then consumed each type of three test meals in random order on days one, four, and seven of the study. One meal consisted of 15% kilocalories from protein, 30% kilocalories from fat, and 55% kilocalories from carbohydrate, with an emphasis on starch-containing foods (referred to as high-carbohydrate, high starch). The second meal consisted of 20% kilocalories from protein, 40% kilocalories from fat, and 40% kilocalories from carbohydrate; this kilocalorie distribution was referred to as the typical American diet (referred to as usual carbohydrate, usual starch). The third and final meal consisted of 22% kilocalories from protein, 34% kilocalories from fat, and 43% kilocalories from carbohydrate, with an emphasis on fruits and vegetables (referred to as usual carbohydrate, low-starch) (Gannon, et al., 1998). The same test meal was consumed for breakfast, lunch, and dinner at 0800, 1200, and 1700, respectively. A bedtime snack was also given at 2100, which varied in macronutrient composition depending on the test meal day; however, the kilocalories remained the same for all study days. The participants consumed a regular hospital diet ad libitum on non-study days, and one 24-hour period of water intake only was used to determine fasting baseline response. Blood samples were collected at 0730, 0745, 0800, 30 minutes after each meal, and hourly throughout the remainder of each study day. Concentrations of plasma glucose were determined by a glucose analyzer. Results of the study showed that mean fasting glucose concentration remained stable throughout the entire week of the study at 8.80 ± 0.34 mmol/L (158 ± 6.10 mg/dL). Compared to this average baseline fasting blood glucose concentration, the mean 24-hour glucose response for the high-carbohydrate, high-starch meal was 34% higher when compared with the usual carbohydrate, usual starch meal. The 24-hour response for the usual carbohydrate, low-starch meal was significantly lower at only 3-4% of both the high-carbohydrate, high starch and usual carbohydrate, usual starch meals. When comparing to average baseline fasting blood glucose

concentrations after ingestion of water only, the 24-hour glucose response for the usual carbohydrate, low-starch meal still remained significantly lower than the other meals. It was concluded that a diet high in fruits and vegetables, although not likely to be acceptable on a long-term basis, may be useful for people with type 2 diabetes (Gannon, et al., 1998)

Other studies involving people with type 2 diabetes and have focused on protein intake and glucose control. Gannon, et al. (2003) provided evidence that a higher protein, moderate carbohydrate diet can improve overall glucose control, but have no effect on pre-breakfast fasting glucose when comparing a lower protein and higher carbohydrate diet. Twelve participants with type 2 diabetes on no diabetes medication with a mean hemoglobin A1C of 8.0% were studied during a 10-week period in a unit similar to a research center. After random assignment, all participants were studied for five weeks each on a high-protein diet and a control diet. Participants were provided with all meals. The high-protein diet consisted of 40% of total kilocalories from carbohydrate, 30% of total kilocalories from protein, and 30% of total kilocalories from fat. The control diet consisted of 55% of total kilocalories from carbohydrate, 15% of total kilocalories from protein, and 30% of total kilocalories from fat. Carbohydrate amounts for the high protein diet were reported as follows: 65 grams at breakfast, 49 grams at lunch, 22 grams for afternoon snack, 67 grams for supper, and 20 grams for bedtime snack. Carbohydrate amounts for the control diet were reported as follows: 82 grams for breakfast, 69 grams for lunch, 36 grams for afternoon snack, 79 grams for supper, and 33 grams for bedtime snack (Gannon, et al., 2003). All participants were admitted to the unit on the evening before the study began. The following day, participants were all provided with the same three meals containing the nutrient composition of the control diet. The participants then spent another night at the unit, and the following day they were again fed the same standardized meals, including

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afternoon and bedtime snacks at 1400 and 2100, respectively. Blood samples were taken at a total of 46 time points on the second day of the study and plasma blood glucose was analyzed using a glucose analyzer. Participants were then sent home with 2-3 days of either the high-protein diet food or the control diet food, depending on the randomization group. They returned every two to three days during the five-week period to pick up more food, and hemoglobin A1C was measured at each of these times. At the end of the five weeks, participants were again admitted to the unit to repeat blood sample collections as described above. They continued to receive the same diet in the unit that they had been following at home. Finally, after a two to five-week washout period, this entire study process was repeated with the participants consuming the other diet they had not followed during the first five-week period (Gannon, et al., 2003). Results of the study showed no significant difference in mean fasting glucose after five weeks of either diet. There was, however, a consistently lower overall glucose concentration after five weeks of the high-protein diet. This was further shown by a statistically significant decrease in hemoglobin A1C from $8.1 \pm 0.3\%$ to $7.3 \pm 0.2\%$ after the high-protein diet; the control diet resulted in a more modest decrease of $8.0 \pm 0.2\%$ to $7.7 \pm 0.3\%$ (Gannon, et al., 2003).

A final study provided evidence in favor of weight loss benefits of a moderately high protein content diet, but not for reduction of fasting glucose or hemoglobin A1C in people with type 2 diabetes (Navas-Carretero, et al., 2011). This study, which followed a longitudinal design, totaled 17 participants that were studied over two consecutive periods of four weeks each. The participants were between the ages of 45 and 75, and the only medication used to control type 2 diabetes was metformin. The first study period was a free living period in which participants followed their usual dietary pattern. The second study period was the intervention

phase in which structured meal replacements were used in place of the participants' usual breakfast, morning snack, and afternoon snack. These meal replacements had a moderately high protein content consisting of 40% of kilocalories from protein, 30% of kilocalories from carbohydrate, and 30% of kilocalories from fat. Participants were asked to complete two 72-hour dietary records during each study period. Fasting serum glucose and hemoglobin A1C concentrations were assessed before and after the entire study, but not between study periods. Results of the study showed a statistically significant reduction in body weight of one kilogram during the intervention period. According to the dietary records, distribution of kilocalories switched from 15-55-30 (% protein-% carbohydrate-% fat) in the free living period to 40-30-30 during the intervention period. Mean hemoglobin A1C at the beginning of the study was 7.0 ± 1.3% compared to 7.2 ± 1.5% at the end of the study; this was not a significant change. Fasting serum glucose concentrations also did not significantly change, with an average of 8.90 ± 3.50 mmol/L (159.20 ± 62.20 mg/dL) at the beginning of the study compared to 8.80 ± 3.30 mmol/L (156.70 ± 59.40 mg/dL) at the end of the study. This showed that a high protein diet had no effect on fasting or overall glucose concentrations (Navas-Carretero, et al., 2011).

Table 2.2 includes a summary of the above studies involving people with type 2 diabetes.

Limitations of Current Research for Effects of Evening Food Composition in Type 2 Diabetes

The number of studies investigating the effects of evening food composition on glucose control in type 2 diabetes is limited in number. In addition, although the number of participants in these studies tends to be larger than the majority of studies involving people with type 1 diabetes, it is still limited. The largest number of participants out of all the studies reviewed totaled 38. Just one of the nine studies had duration of greater than three months. Diabetes

medication regimens varied among the studies and many times were not reported at all. Within one of the studies, different medications were allowed between the two study treatments being compared. Similar to studies in people with type 1 diabetes, hemoglobin A1C was measured in just three of the nine studies. Again, this is likely related to the short duration of study intervention. CGM was used in just one of the studies reviewed; however, a majority of the studies were conducted in a research center where multiple blood glucose values could be obtained. Two of the studies relied on participant-reported food intake information, which has been shown to result in under-reporting or over-reporting (Lutomski, van den Broeck, Harrington, Shiely, & Perry, 2011). Finally, uncooked cornstarch as part of a bedtime snack seems to be over-studied and may not even be an edible option for people outside of the research setting. Further studies involving different bedtime snack options are warranted.

Table 2.2 Studies reporting on evening food intake and type 2 diabetes

First Author, Year	Population / Duration of Study	Type of Study	Intervention	Major Findings
CS bedtime snack compared to other bedtime snacks with varying CHO				
Axelsen, 1999	N = 24 / 1 day each of 2 treatments	Randomized (partially)	Conventional snack (0.6 g CHO/kg body wt) vs. CS snack (0.55 g CS/kg body wt) vs. Placebo snack (0.1 g CHO/kg body wt)	Both conventional and CS snacks significantly ↑ blood glucose between 2400 and 0400 compared to placebo. No difference at 0700 between the 2 snacks; ↑ blood glucose at 0700 compared to placebo.
Higher dose CS bedtime snack compared to lower dose CS bedtime snack				
Axelsen, 2000	N = 28 / 25 weeks total: Two 7-week periods with 11-week washout between; also included an overnight study	Randomized crossover	High-dose CS snack (0.55 g CS/kg body wt) vs. Low-dose CS snack (0.3 g CS/kg body wt) vs. Placebo snack (no CS; 0.6-0.1 g CHO/kg body wt)	Low-dose CS snack resulted in ↓ fasting blood glucose compared to placebo. High-dose CS snack ↑ fasting blood glucose. No significant change in A1C from beginning to end in any study group.
CS bedtime snack compared to other bedtime snacks with equal CHO				
Dyer-Parziale, 2001	N = 28 / 3 nights of each treatment	Randomized crossover	Bedtime snack bar without CS vs. bedtime snack bar with 5 g CS	No hypoglycemia with either treatment. CS bar ↓ midnight and fasting blood glucose compared to no CS (127 mg/dL vs. 148 mg/dL at midnight and 114 mg/dL vs. 158 mg/dL fasting the following day).

Table 2.2 (continued)

Varying kcal distribution at meals and/or snacks				
Arauz-Pacheco, 1998	N = 17 / 1 day of each treatment spaced 1 week apart	Randomized crossover	Small kcal supper (14 kcals/kg IBW supper) vs. Large kcal supper (28 kcals/kg IBW) vs. No supper	Large supper ↑ pre-breakfast fasting glucose when compared to small supper and no supper (241 mg/dL vs. 223 mg/dL vs. 219 mg/dL). No significant difference between small supper and no supper.
Beebe, 1990	N = 6 / 3 separate occasions of 26 hours each; separated by 2-week intervals	Randomized crossover	3 meals per day with no snacks (30% kcals breakfast, 40% kcals lunch, and 30% kcals supper) vs. 3 meals per day with 3 snacks (20% kcals breakfast, 20% kcals lunch, and 30% supper with 10% kcals each for three snacks) vs. Large kcal supper with no snacks (10% kcals breakfast, 20% kcals lunch, and 70% kcals supper)	Evening snack and large kcal supper appeared to lessen dawn phenomenon. Fasting and mean overnight blood glucose not significantly different among treatments.
Varying CHO distribution at meals				
Pearce, 2008	N = 24 / 3 days	Randomized	CHO evenly distributed at meals (~70 g CHO per meal) vs. CHO loaded at breakfast (~125 g CHO) vs. CHO loaded at lunch (~125 g CHO) vs. CHO loaded at dinner (~125 g CHO).	No significant difference in fasting blood glucose among the treatment groups. Lunchtime most favorable time to consume CHO.

Table 2.2 (continued)

Gannon, 1998	N = 6 / 1 day (3 meals per day) each of 3 different test meals; spread out over 1 week and also included one 24-hour fast	Randomized crossover	High-CHO, high-starch meals (15% kcals protein, 30% kcals fat, 55% kcals CHO) vs. Usual CHO, usual starch meals (20% kcals protein, 40% kcals fat, 40% kcals CHO) vs. Usual CHO, low-starch meals (22% kcals protein, 34% kcals fat, 43% kcals CHO)	Fasting blood glucose ↑ modestly for all treatments and after 24-hour fast. Compared to the baseline 24-hour fast, the 24-hour glucose response for the usual CHO, low-starch meal was significantly ↓ than the other treatments.
Varying daily kcals from CHO and protein				
Gannon, 2003	N = 12 / 5 weeks of each treatment; separated by a 2-5 week washout period	Randomized crossover	High-protein diet (40% kcals CHO, 30% kcals protein, and 30% kcals fat) vs. Control diet (55% kcals CHO, 15% kcals protein, and 30% kcals fat). CHO for the high protein diet: 65 g breakfast, 49 g lunch, 22 g afternoon snack, 67 g supper, and 20 g bedtime snack. CHO for the control diet: 82 g breakfast, 69 g lunch, 36 g afternoon snack, 79 g supper, and 33 g bedtime snack.	No significant difference in fasting blood glucose after either treatment. Significant ↓ in A1C after high-protein diet (8.1 to 7.3%). Less modest ↓ in A1C after control diet (8.0 to 7.7%).

Table 2.2 (continued)

Navas-Carretero, 2011	N = 17 / 2 consecutive periods of 4 weeks each	Longitudinal	Free-living period followed by meal replacements moderately high in protein (40% kcals protein, 30% kcals CHO, and 30% kcals fat).	A1C and fasting blood glucose did not significantly change even though % of kcals from protein and CHO did (from 15% kcals protein in free-living period to 40% using meal replacements and from 55% kcals from CHO in free-living period to 30% using meal replacements).

A1C = hemoglobin A1C   CHO = carbohydrate   CS = uncooked cornstarch
g = gram(s)   IBW = Ideal Body Weight   Kcal(s) = kilocalorie(s)
Wt = weight

CHAPTER 3. DISCUSSION, CONCLUSIONS, AND RECOMMENDATIONS

Blood glucose control in diabetes is essential to prevent or delay both acute and long-term complications. MNT has shown to be an effective and essential therapy in the management of blood glucose in both type 1 and type 2 diabetes. Achieving and maintaining blood glucose concentrations in the normal or as close to normal range as safely possible is an important goal of MNT for people with diabetes. It is imperative that nutrition recommendations in diabetes are evidence-based. This review has summarized the evidence surrounding the effects of MNT strategies that aim to improve pre-breakfast fasting and overall glucose control in type 1 and type 2 diabetes.

In people with type 1 diabetes, eight clinical trials have examined the relationship between a bedtime snack and pre-breakfast fasting glucose. These studies have shown that a snack containing a mixture of carbohydrate and protein can reduce the incidence of overnight hypoglycemia without causing pre-breakfast fasting hyperglycemia. Uncooked cornstarch has shown to be effective in preventing overnight hypoglycemia, but may result in pre-breakfast fasting hyperglycemia; however, hemoglobin A1C concentrations, when reported, have not significantly changed. A bedtime snack with a higher fat content may increase mean glucose overnight without significantly reducing hypoglycemia; therefore, a bedtime snack lower in fat is preferred. Finally, studies have shown both a positive and negative effect on blood glucose outcomes following consumption of an extra bedtime snack beyond a daily snack.

Fewer studies have investigated the relationship between a bedtime snack and pre-breakfast fasting blood glucose concentrations in people with type 2 diabetes. The studies that have been conducted have mainly only examined the effects of uncooked cornstarch. A dose of 0.30 gram uncooked cornstarch per kilogram body weight (total of 0.33 gram carbohydrate per

kilogram body weight) in a bedtime snack appears to prevent overnight hypoglycemia and reduce pre-breakfast fasting hyperglycemia when compared to snacks without uncooked cornstarch. A higher protein diet has not been shown to reduce pre-breakfast fasting glucose, but may result in reduced hemoglobin A1C. Finally, a larger caloric intake at supper has shown to produce a modest increase on pre-breakfast fasting blood glucose concentrations; however, a larger carbohydrate supper meal has not.

Future research should include studies of longer duration and larger sample sizes to solidify evidence-based nutrition recommendations that clinicians give surrounding evening food intake with a goal of reducing pre-breakfast fasting and overall glucose. Ideally, each study treatment should last for two straight months so that hemoglobin A1C can be assessed. Researchers should utilize current blood glucose monitoring techniques such as CGM. Powers, Cuddihy, Wesley, and Morgan's study (2010) showed the value of using CGM in food studies and provided a robust description of the glycemic response to various food intakes. This description includes not only peak glucose concentrations after consuming a particular meal or snack, but also time to peak, time to return to baseline, and area under the curve. Recent studies also emphasize the detrimental effects of oscillations in glucose levels as they are correlated with complications of diabetes (Ceriello, et al., 2004). Thus, nutrition research should more fully examine the glycemic response to food in a manner that decreases stress on the patient. CGM offers this benefit as it does not require an individual to have blood samples drawn or finger stick blood glucose testing performed frequently overnight in order to assess glycemic response.

Research conducted with people with type 2 diabetes is affected by the individual's degree of insulin resistance and insulin deficiency, since both insulin resistance alone and insulin deficiency alone can alter plasma glucose levels (Ferrannini, 1998). Diabetes research is also

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affected by the diabetes medications the participants may take. Thus, it is recommended that studies with people with type 2 diabetes focus research on a specific and similar group of persons in order to better translate the results.

Fixed meals are also important part of diabetes research, in order to reduce blood glucose variability caused by differences in the percentage of daily macronutrient consumption among participants. Finally, more commonly consumed bedtime snacks should be studied, including those containing carbohydrate only, carbohydrate plus protein, carbohydrate plus fat, and carbohydrate plus protein and fat.

Until further research is conducted, health professionals can advise people living with type 1 diabetes to consume a daily bedtime snack. Compared to no bedtime snack, this MNT strategy has shown to prevent overnight hypoglycemia without increasing fasting hyperglycemia or hemoglobin A1C. This daily snack should be composed of carbohydrate and protein, but not high in fat, since a higher fat snack does not protect against hypoglycemia and may result in higher fasting pre-breakfast blood glucose. A bedtime snack containing uncooked cornstarch and carbohydrate may be favored over a carbohydrate snack without uncooked cornstarch as it appears to reduce the incidence of overnight hypoglycemia. The decision to use or not use rapid-acting insulin prior to consuming this snack should be determined by the healthcare team.

People with type 2 diabetes may not benefit from a bedtime snack, since studies have shown that omission of this snack does not cause overnight hypoglycemia. In addition, since type 2 diabetes may be accompanied by insulin resistance and obesity, adding additional kilocalories may not be favorable. Until further studies are conducted, if a person with type 2 diabetes chooses to consume a bedtime snack, the snack could contain a low dose of uncooked cornstarch (approximately 0.30 gram uncooked cornstarch per kilogram body weight).

Increasing protein intake would not benefit a person with type 2 diabetes who is seeking a MNT strategy to reduce pre-breakfast fasting blood glucose levels, since studies have not shown this benefit; however, this strategy may be effective in reducing hemoglobin A1C. Finally, it should be recommended that people with type 2 diabetes avoid a supper meal high in kilocalories, but not necessarily high in carbohydrate. This is because a higher kilocalorie supper meal may result in a modestly higher pre-breakfast fasting glucose, but a higher carbohydrate intake at supper will not.

If people with diabetes would like to evaluate the effects of evening food composition on their pre-breakfast fasting and overall glucose control, the following steps should be considered: 1) Choose a bedtime snack or supper meal to consume at a consistent time each evening. 2) If a home blood glucose meter is to be used, it should be calibrated to ensure accuracy. Blood glucose should, at minimum, be measured at midnight, 0300, upon first waking, and immediately prior to breakfast. CGM is the preferred method of glucose analysis, if available. 3) Continue this meal or snack for at least one week to ensure adequate data. 4) Repeat previous steps, however without consumption of a bedtime snack, or with a different variation of the supper meal or bedtime snack (such as reducing the kilocalories of the supper meal or adding a source of protein to the snack). 5) In order to evaluate the effects on hemoglobin A1C, this supper meal or bedtime snack would need to be consumed for a minimum of two straight months without alternations with other meals or snacks. 6) Review the results with a physician, a Registered Dietitian, or a Certified Diabetes Educator.

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