

# A randomized, blinded trial of uncooked cornstarch to diminish nocturnal hypoglycemia at Diabetes Camp'

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## Abstract

**Objective:** To determine if uncooked cornstarch, as part of the evening snack, can avert nocturnal hypoglycemia in type I diabetes. **Research Design and Methods:** Fifty-one campers and counselors at the American Diabetes Association Camp in San Bernardino, CA were randomly assigned to receive 5 g of uncooked cornstarch as part of the 21:00 evening snack vs. a standard snack of equivalent carbohydrate content. Each snack was given for five nights and the participants and medical personnel were blinded as to assignment. Midnight and 07:00 finger stick blood glucose levels were compared with values < 60 mg/dl defined as hypoglycemia and values > 250 mg/dl defined as hyperglycemia. **Results:** There were 218 midnight and 222 07:00 values for comparison. There were six episodes of hypoglycemia at midnight and nine episodes of hypoglycemia at 07:00 for the cornstarch snack nights vs. 30 hypoglycemia episodes at midnight and 21 at 07:00 for the standard snack nights ( $P < 0.001$  and  $< 0.05$ , respectively). There was no difference in the number of hyperglycemic events at midnight or 07:00 for the cornstarch vs. standard snack nights. At midnight, 12% of campers had hypoglycemia after the cornstarch snack vs. 46% after the standard snack ( $P < 0.001$ ), and at 07:00, 16% had hypoglycemia after cornstarch vs. 26% after the standard snack ( $P = 0.327$ ). **Conclusions:** These data suggest that uncooked cornstarch, as part of the evening snack, can diminish the nighttime and morning hypoglycemia associated with type I diabetes, without causing hyperglycemia.

**Keywords:** Uncooked cornstarch; Nocturnal hypoglycemia; Diabetes Camp; Type 1 diabetes

## 1. Introduction

Uncooked cornstarch is a complex carbohydrate composed of approximately 27% of the linear chain dextrose polymer, amylose, and 73% of the branched chain dextrose polymer, amylopectin. Uncooked cornstarch is slowly hydrolyzed by amylase and, therefore, slowly absorbed from the gastrointestinal tract. In this way, it can provide a continuous source of glucose for entry into the systemic circulation for up to 6-7 h.

Since 1984, it has been known that ingesting uncooked cornstarch can be useful to prevent the fasting and postprandial hypoglycemia associated with the glycogen storage diseases and other hypoglycemic syndromes [1,2]. When it became apparent that there were significant benefits to be realized by intensive diabetes management, but that intensive management was associated with a significant increase in hypoglycemic events, particularly during the night [3], we began to evaluate whether taking uncooked cornstarch, as part of the evening snack, would be of benefit to diminish the nocturnal hypoglycemia in patients with type I diabetes.

We performed an initial, pilot study in 13 children and adolescents who adhered to an intensive diabetes management regimen and had a mean HbA<sub>1c</sub> of  $6.8 \pm 0.7\%$  [4]. The study protocol consisted of comparing blood glucose levels for 2 weeks, at 02:00 and 07:00, during which time a standard evening snack was ingested, followed by a 2-week period in which the evening snack contained 5-7 g of uncooked cornstarch. The mean fasting (07:00) blood glucose levels determined were no different after the cornstarch snack ( $143 \pm 30$  mg/dl) compared to the standard snack ( $138 \pm 38$  mg/dl) ( $P > 0.10$ ). However, there was a significant decrease in the mean number of hypoglycemic episodes, as defined as a fingerstick glucose reading < 60 mg/dl, at both 07:00, and 02:00 a.m. At 07:00, with cornstarch, there were a mean of  $0.69 \pm 1.03$  hypoglycemic events compared to  $2.62 \pm 2.25$  with the standard snack ( $P < 0.010$ ). A similar change was seen at 0200 with a mean of  $0.61 \pm 0.87$  hypoglycemic events with cornstarch, compared to  $2.00 \pm 2.12$

with the standard snack ( $P < 0.025$ ). This suggested that cornstarch may be of benefit in reducing the nocturnal hypoglycemia associated with intensive diabetes management.

The present study was conducted to determine if uncooked cornstarch could diminish nocturnal and morning hypoglycemia in a larger cohort of type 1 subjects with varying levels of glucose control.

## **2. Materials and methods**

This study was conducted during the teen session at the American Diabetes Association sponsored Camp Chinnock, in the San Bernardino Mountains in Southern California. Fifty-one of a potential 115 campers and counselors entered the study after they were solicited with a letter, describing the study protocol, sent prior to camp and after they and/or their parents signed an informed consent. The subjects were 14-22 years of age, there were 20 males and 31 females, with a duration of diabetes from 6 months to 16 years. Half of the subjects were on two injections per day, while the remainder were on three or more, or used continuous subcutaneous insulin infusion.

Assessment of glycemic control prior to camp, as measured by glycated hemoglobin and reported in the camp form, was available on 40 of the 51 subjects. Thirty percent had a glycated hemoglobin level  $< 125\%$  above the reported upper limit of the assay norm, 55% had a level between 125-175%, and 15% had a level  $> 175\%$  of the upper limit of the assay norm.

### *2.1. Study intervention*

Study subjects were randomly given five nights of the cornstarch snack and five nights of the standard snack. The cornstarch snack included 5 g of uncooked cornstarch (Kingsford, CPC International, Englewood Cliffs, NJ) in 2.5 ounces of sugar-free Jello pudding (White Plains, NY) to be equal to 17 g of carbohydrate, plus one protein exchange. The standard snack included 17 g of carbohydrate as 4 ounces of sugar free Jello pudding and one protein exchange.

Study subjects were grouped by cabin assignment and each cabin was randomly assigned to receive the cornstarch snack or the standard snack. Each snack was given for five nights and all attempts were made to ensure that the snacks were consumed. The campers, staff, dieticians and physicians deciding the insulin dosages and treatments for hypoglycemia were blinded as to the type of snack assignment. Only the dieticians responsible for dispensing evening snacks were aware which campers had consumed cornstarch, but they had no other role in diabetes management.

The goal of the medical management of the participants of this study was the same as that for the remainder of the campers during the camping session: to maintain blood glucose levels in the targeted range of 70-150 mg/dl, with avoidance of extremes of glycemic excursion if possible. Insulin dosage adjustment, according to an algorithm, was therefore done daily by medical staff under the supervision of a pediatric endocrinologist. All participants ate three full meals and three snacks per day. The diet was standardized at 1900 calories with 25% fat, 500/6 carbohydrate and 25% protein, but subjects consumed between approximately 1200 and 4200 calories as recorded by dieticians after talking to the campers after their meals. All subjects routinely tested their blood glucose levels with a glucose meter five times per day, before breakfast, lunch, dinner, evening snack, and between midnight and 01:00.

The subjects participated in the full range of camping activities without restrictions. Additional blood glucose levels were measured if subjects had symptoms suggestive of hypoglycemia or hyperglycemia. Hypoglycemia was treated according to a standard protocol, so that additional simple and complex carbohydrate and protein were given to correct the blood glucose level, and to attempt to avert further abnormalities of glycemia.

Comparisons of the number of hypoglycemic events, as defined as a blood glucose level  $< 60$  mg/dl, and the number of hyperglycemic events, as defined as a blood glucose level  $> 250$  mg/dl, obtained at midnight and at 07:00, were made for the cornstarch snack nights versus the standard snack nights. Statistical analysis to compare blood glucose levels was done with the Fisher's exact test. McNemars' test was used to

compare blood glucose levels for individual campers, comparing cornstarch vs. standard snack midnight and 07:00 values. Analysis of hypoglycemic events by glycated hemoglobin level was done using the Fisher's exact test and the Cochran Mantel-Haerizel test.

### 3. Results

There were available for comparison 218 midnight and 07:00 glucose levels after the cornstarch snack, and 222 readings after the standard snack. Data points were not available for some subjects on some evenings due to passes from camp, or intercurrent illness that necessitated dietary alteration or intravenous hydration.

There were six episodes of hypoglycemia at midnight and nine episodes at 07:00 for the 218 cornstarch nights vs. 30 hypoglycemic episodes at midnight and 21 at 07:00 for the 222 standard snack nights ( $P < 0.001$  and  $< 0.05$ , respectively). As shown in Fig. 1, this translated to an average incidence of hypoglycemia of 2.2% for midnight levels with cornstarch vs. 12.2% for the midnight levels with the standard snack. The average incidence at 07:00 was 4.5% with cornstarch vs. 9.5% with the standard snack.

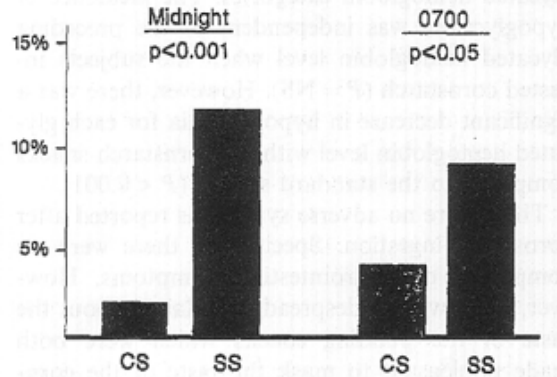


Fig. 1. Incidence of hypoglycemic events.

There was no difference in the number of hyperglycemic episodes between the two groups at midnight or at 07:00. There were 13 hyperglycemic episodes at midnight over the 218 cornstarch nights vs. 23 with the 222 standard snack nights ( $P = 0.112$ ); while there were 26 hyperglycemic events at 07:00 with the cornstarch snack vs. 19 with the standard snack ( $P = 0.273$ ).

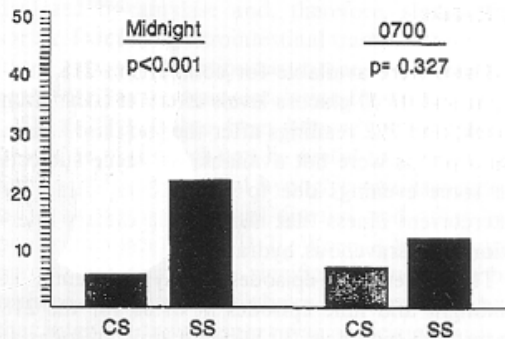


Fig. 2. Number of campers to experience at least one hypoglycemic event.

Assessment of individual campers, shown in Fig. 2, revealed that there were six of the 51 campers, or 12%, that had a low blood glucose level at midnight over the entire study period with the cornstarch snack compared to 23 of 51 campers, or 46%, with the standard snack ( $P < 0.001$ ). There were eight subjects, or 16%, who experienced hypoglycemia at 07:00 with the cornstarch snack, compared to 13 subjects, or 26%, who had hypoglycemia with the standard snack ( $P = 0.327$ ).

There was no effect on the incidence of hypoglycemia by glycated hemoglobin level. With cornstarch, there was a 5.7% incidence of hypoglycemia in the subjects with glycated hemoglobin  $< 125\%$  above the upper limit of the assay, there was a 3.2% incidence in the group with glycated hemoglobin level between 125 and 175% and a 4.5% incidence in the category  $> 175\%$ . With the standard snack, there was a 16.6, vs. 11.8, vs. 13.0% incidence of hypoglycemia in the three glycated hemoglobin categories. The incidence of hypoglycemia was independent of the preceding glycated hemoglobin level when the subjects ingested cornstarch ( $P = NS$ ). However, there was a significant decrease in hypoglycemia for each glycated hemoglobin level with the cornstarch snacks compared to the standard snacks ( $P < 0.001$ ).

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There were no adverse symptoms reported after cornstarch ingestion. Specifically, there were no complaints of gastrointestinal symptoms. However, there were widespread complaints about the taste of the pudding snacks which were both made unpleasant to mask the taste of the cornstarch.

These data suggest that uncooked cornstarch, when given as a component of the evening snack, and equivalent to 1/3 portion of a bread exchange, can diminish the incidence of hypoglycemia and the number of subjects experiencing hypoglycemia at midnight, 3-4 h after ingestion. In addition, the incidence of hypoglycemia can be decreased in the morning, 9-10 h after ingestion. This decrease in hypoglycemia was not accompanied by an increase in hyperglycemia at those time periods. Therefore, this inexpensive dietary adjunct may be of benefit in subjects wishing to achieve intensive diabetes management, but who are limited in achieving that goal by the development of excessive hypoglycemia.

Since during this study all subjects were managed with an intensive protocol aimed at keeping blood glucose levels in a narrow range, campers experienced hypoglycemia regardless of their antecedent glycemic control. Therefore, in patients who begin intensive management with the risk of developing hypoglycemia, cornstarch ingestion may be beneficial in reducing that risk. In addition, the beneficial response to the cornstarch snack in subjects with elevated glycated hemoglobin levels suggests that there is a role for cornstarch ingestion in those who are less than optimally managed and who might still experience hypoglycemia.

It appears important to have the cornstarch mixed with other simple and complex carbohydrates and protein to allow for effectiveness. In 1993, Ververs et al., evaluated uncooked cornstarch in water in subjects with diabetes [5]. The cornstarch snack was compared to a standard snack of equal carbohydrate content. In this study, cornstarch did not completely prevent hypoglycemia, although there was a reduction in hypoglycemic episodes, possibly because cornstarch was given as the entire snack without other mono- or disaccharides or protein.

Unfortunately, the taste of the cornstarch snack was not appealing to the subjects in this study. However, the other known side effects of cornstarch ingestion, which include diarrhea, abdominal distention and increased flatulence [6], were not experienced by study participants. This is likely due to the low dosage consumed in this study, compared to the significantly increased dosage used in patients with glycogen storage disease. Therefore, if this simple and inexpensive dietary intervention could be made more palatable, it might become a routine part of the diabetes regimen to diminish hypoglycemia, which is the limiting factor for most patients already following or attempting to initiate intensive diabetes management.

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