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Case report

Maltodextrin May Be a Promising Treatment Modality After Near-total Pancreatectomy in Infants Younger Than Six Months with Persistent Hyperinsulinism: A Case Report

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What is already known on this topic?
-Congenital hyperinsulinism is the most common cause of persistent hypoglycemia in newborns and infants.
-While several medical treatment agents are used to treat infants with congenital hyperinsulinism, hypoglycemia management has been quite difficult.

What this study adds?
- In the cases with congenital hyperinsulinemia, the maltodextrin addition in the early period enables us to achieve more stable serum glucose.
-Maltodextrin addition also shortens the patient's discharge period, prevents complications, and protects the patient from treatment side effects.
- Continuous glucose monitoring systems (CGMS) help manage patients' follow-ups more efficiently in this group.

Abstract
Persistent hypoglycemia in infants with congenital hyperinsulinism (CHI) can be challenging in approximately half of these cases, even after undergoing a near-total pancreatectomy. While maltodextrin has been recommended in the nutritional management of CHI cases younger than six months, facts about its efficacy in managing hypoglycemia are not yet clear. Here, we present a male infant with CHI who experienced persistent hypoglycemia even after undergoing a near-total pancreatectomy and despite multiple medical treatments. The infant's hypoglycemic episodes were successfully controlled by adding maltodextrin to his diet.
Keywords: congenital hyperinsulinism, ABCC8 gene, maltodextrin, near-total pancreatectomy, continue glucose monitoring systems

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Introduction
Congenital hyperinsulinism (CHI) is the most common cause of persistent hypoglycemia in newborns and infants (1). While several medical treatment agents are used for treating these infants, management of hypoglycemia has been quite difficult (2). It has been reported that persistent hypoglycemia can be seen in approximately 50% of cases with diffuse forms where a near-total pancreatectomy is performed, (3).
Adwick et al. reported that of the CHI cases who underwent a near-total pancreatectomy in their series, 31% had euglycemia, 20% had hyperglycemia, and 49% had hypoglycemia requiring treatment. Moreover, it has been emphasized that surgery for the diffuse form is not a cure but can only help hypoglycemia control (4).
Nutritional support is a critical milestone alongside medical treatment in cases with CHI. Frequent feeding with breast milk or formula is recommended for those who do not have oral intake problems (5). Uncooked cornstarch helps stabilization of serum glucose in cases above six months but it is not recommended for cases under six months because of its side effects. A small number of studies have reported the use of maltodextrin (Malt Extract, Wakodo, Fantomalt Nutricia) added to breast milk or formula in the nutritional management of cases younger than six months. However, none of these studies clearly demonstrated the effectiveness of maltodextrin in controlling hypoglycemia (6).
In this article, we present a male infant with CHI who was experiencing persistent hypoglycemia even after undergoing a near-total pancreatectomy and despite multiple medical treatments and whose hypoglycemic episodes were successfully controlled by adding maltodextrin to his diet.

Case presentation
A male patient was born with a weight of 4020 grams in the 37th week of pregnancy from a twenty-seven-year-old mother's first pregnancy. Critical blood samples taken due to seizure at the 3rd hour of life revealed a serum glucose level of 22 mg/dl, and a serum insulin level of 288 µU/mL. An intravenous (IV) dextrose infusion at a rate of 6 mg/kg/min was initiated along with frequent breastfeeding. Due to the persistent severe hypoglycemia in the follow-up, the IV infusion rate was gradually increased to 14 mg/kg/min. Due to the recurrence of hypoglycemia and the persistence of hyperinsulinism during

hypoglycemia, congenital hyperinsulinism was considered a factor and diazoxide treatment was started at a dose of 10 mg/kg/day. Subsequently, his hypoglycemic episodes persisted and he was transported to our clinic on the 30th day of life.

Preparation for surgery immediately began, diazoxide treatment was increased to 15 mg/kg/day, and octreotide was started at a dose of 5 mcg/kg/day and was gradually increased to 40 mcg/kg/day. Hypoglycemic episodes persisted during the treatment, and an IV infusion of glucagon was added. Facilities to carry out 18F-L-DOPA PET imaging were not available and so could not be performed on our patient and transfer to another center was considered inappropriate. A near-total pancreatectomy (95-98% resection) was performed on the 35th day of life. Histopathological samples showed diffuse nesidioblastosis. The genetic analysis revealed a previously reported heterozygous c.2113 C>T mutation in the ABCC8 gene which was known to be associated with diazoxide unresponsiveness.

After the surgery, octreotide and glucagon were continued, nifedipine was added, and the dextrose infusion was continued at a dose of 14 mg/kg/min. Despite full enteral nutrition and other parenteral treatments, the hypoglycemic episodes continued. Since the IV dextrose infusion could not be reduced, oral maltodextrin (1 measuring spoon of Fantomalt Nutricia® contains 5 grams of CHO) was added to each meal (12 times per day) at a total dose of 5 gram/kg/day. After the Addition of maltodextrin significantly controlled the patient's hypoglycemic episodes, and the dextrose support was gradually decreased. The dextrose treatment was discontinued on the 7th day following the addition of maltodextrin, and the patient was discharged.

Serum glucose monitoring was enabled using a continuous glucose monitoring system (CGMS) (Medtronic Guardian Connect CGM, Ca, USA) during both the inpatient and outpatient period. This system was off-labelly used after having informed consent from the parents to monitor glucose variability to prevent hypoglycemia using trend arrows, and to improve the efficacy of treatments. CGMS of the patient revealed that the hypoglycemic episodes had decreased significantly after the addition of maltodextrin (Figure 1 and 2). It was noticed that the percentage of serum glucose, which was below 70 mg/dL per day, decreased significantly after the addition of maltodextrin.

Glucagon and nifedipine treatments were discontinued after maltodextrin treatment, in the first and the fourth month respectively. The octreotide dose was reduced to 14 mcg/kg/day.

The patient’s neurological examination was comparable to his peers, while his body weight was 14 kg (SDS: 2,63), height 84 cm (SDS: 2,31), BMI 19,8 (SDS: 1,5) and head circumference 47 cm (SDS: -0.01) at the age of 12 months. He is still receiving octreotide and maltodextrin treatments without experiencing hypoglycemic episodes.

Discussion

CHI is a rare glucose metabolism disease that most frequently causes persistent hypoglycemia in the neonatal period. Early diagnosis is essential to prevent neurological damage due to hypoglycemia (7). It is emphasized that frequent feeding with high-caloric carbohydrates can reduce hypoglycemia attacks (5). Xu et al. stated that maltodextrin, a glucose polymer, can be used in the first six months of life. In contrast, uncooked corn starch is not used for the first six months due to its side effects (6). Cappella et al. reported that adding maltodextrin to the diet instead of increasing the IV glucose infusion is an effective procedure in the case of CHI (8). De Cosio et al. recommended that patients with CHI should be supported with maltodextrin (9).

In the literature, a limited number of articles regarding maltodextrin use in CHI were found. In one report, it was reported that maltodextrin was given to 4 CHI patients without any explanation regarding its efficacy (10).

Albeit maltodextrin is one of the most commonly known high-calorie formulae already being used in the feeding plan of CHI patients, the efficacy of maltodextrin on the hypoglycemic control of patients with CHI has not yet been studied in detail. There is no data on how adding maltodextrin to the diet effected the course of hypoglycemic episodes, the dosage, the feeding intervals and CGMS reports. Meanwhile possible side effects of maltodextrin are weight gain, gas, bloating and allergic reactions; none of these side effects were observed in our case (11).

In our case, the maltodextrin addition enabled us to achieve a more stable serum glucose, to change the treatment modalities and to shorten the discharge period of the patient. CGMS also helped us to manage the patient’s in/outpatient follow-ups more efficiently. The importance and efficacy of adding maltodextrin in the early period of hypoglycemia management was demonstrated in this CHI case by CGMS.

Conclusion

Management of CHI requires a multidisciplinary approach. Hypoglycemia can persist, even after a near-total pancreatectomy, especially in patients with diffuse form and potassium channel mutations. Our case suggests that the addition of maltodextrin in the early pre-op or post-op period would shorten hospitalizations, prevent complications, and even protect the patient from the side effects of treatments. More case series or case-control studies are needed to reveal the efficacy of maltodextrin supplementation in the management of infants with CHI.

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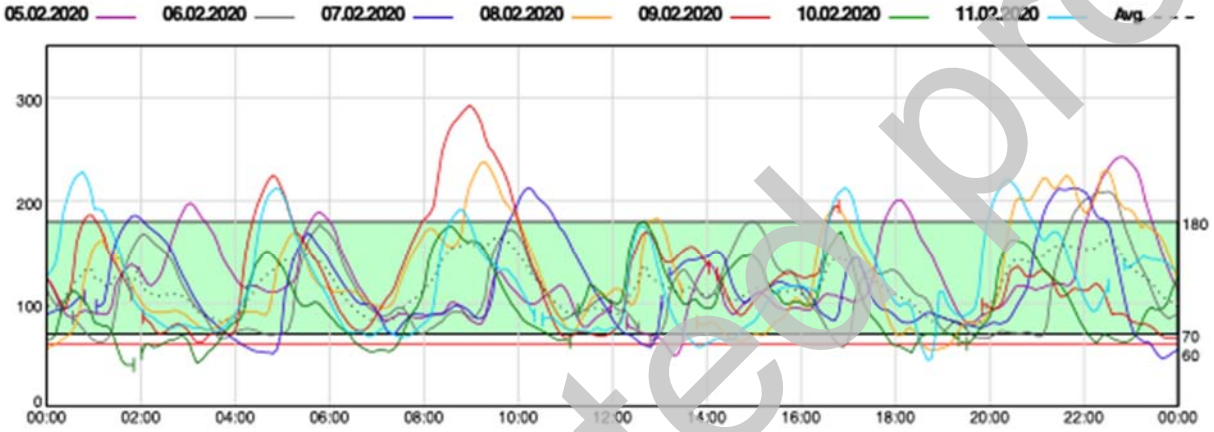
Figure 1: CGMS report: Before the addition of maltodextrin (It is noted that time in below range is 11%, the ratio of below <70 mg/dl)

Sensor Data (mg/dL)

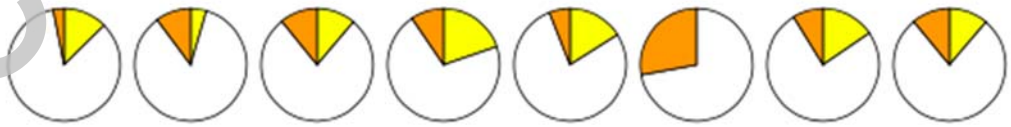


	Wed 5 Feb	Thu 6 Feb	Fri 7 Feb	Sat 8 Feb	Sun 9 Feb	Mon 10 Feb	Tue 11 Feb	Average / Total
# Sensor Values	285	284	285	283	249	287	284	1.957
High SG (mg/dL)	243	209	213	238	293	180	228	293
Low SG (mg/dL)	49	57	47	53	62	40	45	40
Average SG (mg/dL)	122	111	116	128	130	99	121	118
Standard Dev.	41	38	43	50	54	36	47	45
MAD %	3,8	1,8	3,3	9,9	8,4	20,9	6,3	8,9
# Valid Calibrations	1	2	2	2	3	4	2	16

Excursion Summary

	Wed 5 Feb	Thu 6 Feb	Fri 7 Feb	Sat 8 Feb	Sun 9 Feb	Mon 10 Feb	Tue 11 Feb	Average / Total
# Excursions	5	2	5	5	4	4	7	32
# High Excursions	4	1	3	4	4	0	5	21
# Hypo Excursions	1	1	2	1	0	4	2	11
AUC Above Limit	3,1	1,0	2,1	5,0	7,7	0,0	3,5	3,1
AUC Below Limit	0,3	0,4	1,3	0,7	0,2	2,8	0,6	0,9

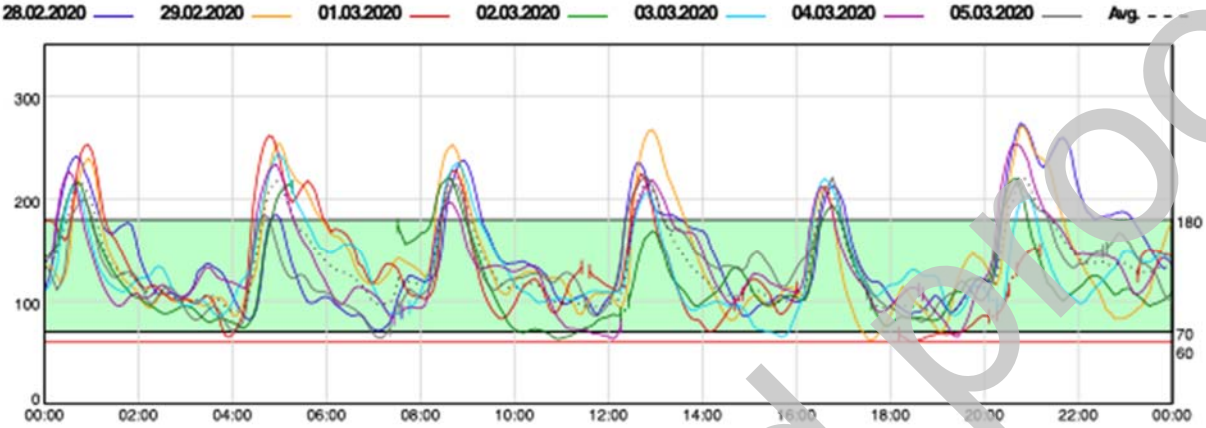
Duration Distribution (hh:mm)



Above 180	3:00	13%	1:05	5%	2:40	11%	4:40	20%	3:20	16%	0:00	0%	3:40	15%	18:25	11%
Within (70 - 180)	20:00	84%	20:10	85%	18:30	78%	16:40	70%	16:10	78%	17:15	72%	17:55	76%	126:40	78%
Below 70	0:45	3%	2:25	10%	2:35	11%	2:15	10%	1:15	6%	6:40	28%	2:05	9%	18:00	11%

Figure 2: CGMS report: After the addition of maltodextrin (It is noted that time in below range is 3%, the ratio of below <70 mg/dl)

Sensor Data (mg/dL)

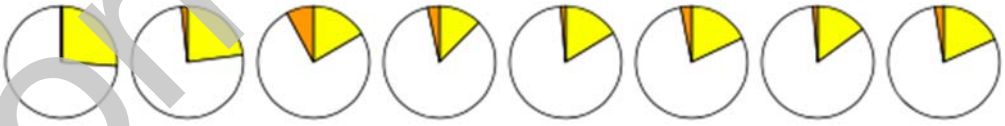


	Fri 28 Feb	Sat 29 Feb	Sun 1 Mar	Mon 2 Mar	Tue 3 Mar	Wed 4 Mar	Thu 5 Mar	Average / Total
# Sensor Values	287	288	241	264	288	289	288	1.945
High SG (mg/dL)	274	271	262	222	243	253	222	274
Low SG (mg/dL)	71	62	60	63	65	63	64	60
Average SG (mg/dL)	145	141	130	121	132	135	133	134
Standard Dev.	50	53	49	42	41	44	38	46
MAD %	8,1	6,0	2,0	8,7	1,6	5,0	2,8	4,7
# Valid Calibrations	2	2	3	2	2	2	2	15

Excursion Summary

	Fri 28 Feb	Sat 29 Feb	Sun 1 Mar	Mon 2 Mar	Tue 3 Mar	Wed 4 Mar	Thu 5 Mar	Average / Total
# Excursions	2	2	1	4	4	4	5	22
# High Excursions	2	2	1	4	4	4	5	22
# Hypo Excursions	0	0	0	0	0	0	0	0
AUC Above Limit	9,2	10,3	6,5	2,9	4,4	5,3	3,1	6,0
AUC Below Limit	0,0	0,1	0,3	0,1	0,0	0,1	0,1	0,1

Duration Distribution (hh:mm)



Above 180	6:15	26%	5:30	23%	3:20	17%	2:45	12%	3:55	16%	4:20	18%	3:35	15%	29:40	18%
Within (70 - 180)	17:40	74%	18:05	75%	15:10	75%	18:30	85%	19:45	83%	19:00	79%	20:05	84%	128:15	79%
Below 70	0:00	0%	0:25	2%	1:35	8%	0:45	3%	0:20	1%	0:45	3%	0:20	1%	4:10	3%