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Research Article

Maltodextrin Use in Persistent Neonatal Hypoglycemia; Audit Report of a Single Center Experience

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Abstract

Background: Neonatal hypoglycemia is known to cause significant neuronal damage and poor neurodevelopmental outcomes. Consensus guidelines are lacking for the management of persistent neonatal hypoglycemia and hyperinsulinism which often requires high concentrations of dextrose and medications. Although used in the pediatric population with persistent hypoglycemia, only a few case reports are published regarding the use of Maltodextrin supplementation in persistent neonatal hypoglycemia due to transient hyperinsulinism.

Objective: To audit the use of Maltodextrins in the management of persistent neonatal hypoglycemia due to transient hyperinsulinism in neonates.

Audit design: A retrospective chart review (CERNER electronic data) of all cases with persistent neonatal hypoglycemia who received Maltodextrin supplementation for a period of 3½ years between July 2018 and December 2021.

Results: A total of 18 neonates received Maltodextrin supplementation for neonatal hypoglycemia during the audit period. 16/18 (89%) neonates who received Maltodextrin supplementation were weaned off from intravenous dextrose within 1 week without major side effects or severe rebound hypoglycemia. Two out of 18 babies who received Maltodextrin needed Diazoxide supplementation for persistent hypoglycemia.

Conclusion: The results of our audit are promising, yet further research and randomized controlled studies are needed to systematically evaluate the findings of this audit regarding Maltodextrin supplementation for the management of neonatal hypoglycemia with transient hyperinsulinism.

More Information

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Keywords: Neonatal hypoglycemia; Hyperinsulinism; Maltodextrin; Oligosaccharide; Starch supplementation

Abbreviations: NICU: Neonatal Intensive Care Unit; AAP: American Academy of Paediatrics; PES: Paediatric Endocrine Society; RBS: Random Blood Sugar; GIR: Glucose Infusion Rate; SGA: Small for Gestational Age; PHHI: Persistent Hyperinsulinemic Hypoglycemia in Infancy; IUGR: Intrauterine Growth Retardation; IV: Intravenous

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Background

Neonatal hypoglycaemia is one of the common neonatal problems encountered in neonatal intensive care units (NICU) and post-natal wards. It's well known that hypoglycaemia can result in irreversible cerebral cortical injury and poor neurodevelopmental outcomes [1,2]. The guidelines for the definition and management of neonatal hypoglycemia kept changing over the years and are still debated [3]. American Academy of Paediatrics (AAP) defines neonatal hypoglycaemia as RBS < 2.6 mmol/dL during the neonatal period when Paediatric Endocrine Society (PES) defines hypoglycaemia as < 2.8 mmol/dL within 48 hrs and < 3.3 mmol/dL after 48 hrs of age [1,4]. It's often transient and asymptomatic cases can be managed with supplemental feeds. A significant number of cases might need intravenous dextrose therapy for a short period [2,4] Most cases of transient neonatal hypoglycemia recover within 48 – 72 hours, but a small percentage of such cases might need a high concentration of dextrose with a very high Glucose infusion rate (GIR), often associated with hyperinsulinism. [5,6]. Thus, if GIR is > 12 mg/kg/min after 48 hrs or hypoglycemia persists for > 5 – 7 days, persistent hypoglycemia may be considered, and further evaluations and management strategies should be planned [2,4]. Though metabolic or endocrine disorders are likely in cases of persistent hypoglycemia, transient neonatal hyperinsulinism is the most common cause of persistent hypoketotic hypoglycemia in neonates and infants and it is associated with a significant risk of permanent brain damage [7,8].

Several forms of congenital persistent hyperinsulinemic hypoglycemia (PHHI) with genetic mutations are described [6]. Transient neonatal hyperinsulinism is well described in Small for gestational age (SGA) and asphyxiated neonates along with poorly controlled diabetes mothers and genetic syndromes like Beckwith-Wiedemann syndrome [9–11] The mainstay of management of PHHI is by maintaining blood glucose > 3.3 mmol/L after 48 hrs, with high concentration dextrose preferably through a central venous line, frequent high-calorie diet and medications such as glucagon, corticosteroid, diazoxide, octreotide, and nifedipine which are tailored according to the patient need [12,13]. Diazoxide along with diuretics is the drug of choice in proven cases of hyperinsulinemic hypoglycemia [7,14].

Glucose polymers mixed with water are mentioned as part of the nutritional therapy in congenital hyperinsulinism, but recommendations or reports for its use in neonates are lacking [15,16] A limited number of articles regarding Maltodextrin (Fantomalt and Polycose) use in congenital hyperinsulinism were found, the efficacy of such high-calorie formulae has not been studied well in neonates [6,17]. Polycose and Fantomalt are Maltodextrins marketed by Abbott and Nutricia respectively, each delivering 380 kcal/100 gm and osmolarity of 97 mOsmol/L. Polycose is added with electrolytes such as Na, Ca, K, Ph, and chloride at minimal levels as Fantomalt contains sugars as polysaccharides and minimal Sodium [18]. These Maltodextrins will act as an easy source of glucose through the action of amylase and maltase [19]. Glucose polymer supplementation is not a standard practice in transient hypoglycemia due to concerns about osmotic load and lack of evidence [20,21] A Literature search did not show any evidence or recommendations on its routine use as an oral supplement to prevent hypoglycaemic episodes during the weaning of intravenous glucose intake in hypoglycaemic neonates.

In this single-center level II NICU, neonatal hypoglycaemia accounts for < 10% of all admissions, and persistent hypoglycaemia is rarely encountered. Neonates receiving > 12 mg/kg/minute for > 48 hours and requiring a high concentration of dextrose > 12.5% are managed with intravenous dextrose through the central vein. If attempted weaning of GIR fails, hyperinsulinism is suspected and further evaluations are done routinely in collaboration with a pediatric endocrinologist. Maltodextrin supplementation is arranged with the involvement of an experienced dietician who calculates the calorie intake, GIR, and feeding concentration and prescribes the dose of Maltodextrin which is titrated according to the needs of the baby. Over the last several months, we observed successful use of such Maltodextrin supplementation without major side effects and we managed to wean intravenous dextrose promptly and reduced the central venous catheter dwelling time in cases of persistent hypoglycemia due to hyperinsulinism. Hence we wanted to evaluate our experience by doing this audit to look at the impact of Maltodextrin in weaning the dextrose concentration and prevention of rebound hypoglycemia in persistent neonatal hypoglycemia. Also to study the need for medications in proven cases of hyperinsulinism who received Maltodextrin supplementation and explore the side effects associated with Maltodextrin use in neonatal hypoglycemia

Materials and methodology

Patients

This audit was done by a retrospective chart review of electronic (CERNER) data. Cases were collected for a period of 3 ½ years (July 2018 – Dec 2021) from the database maintained for the auditing of NICU morbidities. All neonates who received Maltodextrin for persistent hypoglycemia were selected. Neonates born outside our hospital and all neonates with or without hypoglycemia but did not receive Maltodextrin supplementation were excluded from the data review.

Data

An Excel data collection sheet was designed to collect data regarding the birthweight, risk factors for hypoglycemia, maternal HbA1c, Random blood sugar (RBS) at admission, lowest RBS reading, highest GIR, and Dextrose concentration by intravenous (IV) intake, need for central line, biochemical results including insulin level, metabolic work up and medications used. The starting day of Maltodextrin supplementation, day of discharge, and post-natal follow-up visits were noted. Any side effects such as feed intolerance or loose stools abdominal distension or NEC-like presentation during the Maltodextrin supplementation were searched for and documented. Descriptive statistics using SPSS version 27 was used for the statistical analysis of the data.

Procedure

The decision for Maltodextrin supplementation was taken by a team of consultants and specialist neonatologists after reviewing the clinical context and available investigations for neonates suspected of hyperinsulinism. It was administered with the help of a clinical dietitian who calculated the calorie intake, GIR, feeding concentration, and the dose of Maltodextrin to be used. The Maltodextrin module had 0.96 g of carbohydrate and 3.84 kcal per gram. Maltodextrin was mixed in Expressed breast milk (EBM) or a 20 kcal per ounce formula. The amount added was decided based on the GIR needed and the concentration to be met. A maximum increase of 0.1 kcal/ml concentration was attained every 24-48 hours to ensure feeding tolerance. The concentration of feed was gradually increased until the target range of blood glucose level was reached. The maximum increase of GIR in pre-term infants was 1-2 mg/kg/min, whereas in term infants it was 1-3 mg/kg/min. The concentration used ranged between 1.25 gm in 60 ml milk (1/4 scoop in 60 ml) to 2.5 gm in 45 ml milk (Range used: 0.02 – 0.06 gm/ml). Neonates were observed

closely for tolerance and dose adjusted individually based on each infant's symptoms and GIR need. Once the blood glucose level was normalized and maintained within normal values, the module was weaned off slowly.

Results

There were a total of 18 cases who received Maltodextrin (Fantomalt) during the study period. The demography of cases is shown in Table 1. The median gestational age of the infants was 36 weeks (Range: 32 – 40 weeks). The lowest gestational age neonate was born at 32 weeks. The lowest birth weight was 1440 gm and the highest weight noted was 3800 gm. 2/3rd of cases admitted were delivered by LSCS. Out of 18 cases, 13 neonates were intrauterine growth retardation (IUGR) neonates. Only 5 out of 18 neonates had gestational diabetes as a risk for hypoglycemia. The single case with asphyxia was mild asphyxia and did not require therapeutic hypothermia. All the neonates with hypoglycemia were admitted within 2 hrs of birth except one case which was admitted at the age of 5 hrs. The lowest RBS at admission was noted as 0.4 mmol/dL. The highest dextrose concentration used was 20% and 61% of cases needed central venous access (Table 1).

Wide variation in biochemical evaluation was noted for these cases with persistent hypoglycemia. 61% (11/18) neonates had insulin level and cortisol done, yet serum ketones were assessed for 8 neonates and a Growth hormone assay was done for 7 neonates. All the cases that had a biochemical evaluation, were shown to have detectable levels or elevated levels of insulin and hypoketonemia suggesting hyperinsulinism. The median Insulin level of this audit population was 16 μunit/ml (Range: 2 - 106).

Maltodextrin supplementation

All neonates received Fantomalt as Maltodextrin supplementation (Table 2). The earliest supplementation was on the 3rd day of life when the babies were already on full oral feeding. The delayed supplementation of Maltodextrin was for the preterm born at 32 weeks, which was started on the 10th day of life. Only one neonate needed restarting of IV dextrose during weaning due to rebound hypoglycemia. Three other neonates had mild rebound hypoglycemia during weaning while on Maltodextrin, but they did not require restarting of IV fluid. One neonate had loose stool after starting Maltodextrin which improved within 24 hrs and the supplementation was restarted without further intolerance. Two neonates had suspected features of sepsis for which antibiotics were needed. These two neonates did not improve with Maltodextrin and needed Diazoxide supplementation and later transferred to the tertiary center. All the other neonates who received Maltodextrin supplementation were weaned off from IV dextrose within 1 week, except for 1 neonate (preterm 32 weeks). The duration of Maltodextrin supplementation ranged from 2 – 14 days.

Table 1: Demography.

Parameters		Median (Range) or Frequency (%)
Gestational age (weeks)		36 (32 – 40)
Mode of delivery	LSCS	12/18 (67%)
	Vaginal delivery	6/18 (33%)
Weight (grams)		2350 (1440 - 3800)
Dextrose concentration needed (%)		14.5 (10 – 20)
Central venous access (UVC or PICC)		11/18 (61%)
GIR (Glucose infusion rate needed) mg/kg/min		11.1 (6.7 – 17)
Insulin level (μ unit/ml)		16 (2 - 106)
IV dextrose weaning after Maltodextrin (days)		5 (1 - 10)

Table 2: Maltodextrin supplementation.

Maltodextrin supplementation (Fantomalt)	Mean (SD) or Median (Range)
Number of neonates successfully weaned off IV dextrose after Maltodextrin supplementation	16/18 (89%)
Day of starting (day of life)	5 (3 – 10)
Concentration/dose (1.25 gm in 60 ml – 2.5 gm in 45 ml)	0.02 – 0.06 (gm /ml)
Successful IV dextrose weaning after Maltodextrin (days)	5 (1 - 10)
Duration of Maltodextrin use (days)	7 (2 - 14)
Day of discharge (day of life)	13 (6 - 26)
Medication use (Diazoxide)	2 cases

Discussion

There were 18 cases in this single-center audit experience of Maltodextrin use for persistent neonatal hypoglycemia and this is the first audit report for its use to treat persistent hypoglycaemia in neonates. This audit finds that 16/18 (89%) neonates had successful weaning of IV dextrose shortly after initiation of Maltodextrin supplementation and hence reduced the need for central venous access. Only two out of 18 cases needed Diazoxide after starting Maltodextrin despite having laboratory evidence of hyperinsulinism in neonates who had insulin levels done. Only one neonate experienced rebound hypoglycemia necessitating restarting of IV dextrose. One neonate developed loose stools after starting Maltodextrin but improved after 24 hours and tolerated the supplementation subsequently. Two neonates had developed features of sepsis needing antibiotics, but whether it was related to the Maltodextrin supplementation is not clear. A follow-up of these neonates at 12 months showed that 14 of them were having normal development. One baby was noted to have a speech delay and 3 cases were lost for follow-up. It was observed that 72% of these cases with persistent hypoglycemia were IUGR and GDM as a risk for hypoglycemia was found only in 27% of cases. All the IUGR neonates had further evaluations including chromosome microarray and TORCH workup, but they were normal. Another interesting observation was that 50% of the cases had thrombocytopenia and two of them received platelet transfusion too. If this finding is related to IUGR alone or associated with persistent hypoglycemia needs to be studied further.

Glucose polymer supplementation such as corn starch is reported to be used in the dietary management of congenital hyperinsulinism in children over 1 year of age, but a literature search did not show evidence of routine use or recommendation of Maltodextrin use in neonates with transient hyperinsulinism [22]. Case report published in August 2021 from Turkey reports about a single infant diagnosed with persistent hypoglycemia even after near total pancreatectomy which was successfully controlled by adding Maltodextrin to its diet [17]. Michelle Blanco et al reported a neonate who was preterm IUGR with persistent hypoglycemia and thrombocytopenia which needed IV fluids for 18 days, continuous NGT feeds for > 1 month with normal insulin level [23]. Transient hyperinsulinemic hypoglycemia diagnosis in that infant was confirmed by exaggerated glycaemic response to glucagon despite normal levels of insulin and the neonate needed Diazoxide for persistent hypoglycemia [23]. However, there is no data on the dose, the feeding intervals, or the course of hypoglycaemic episodes during its use [17,20]. Oral glucose gel use has recently been found to reduce the NICU admission rates in high-risk neonates and it is recommended for prophylaxis and treatment of neonatal hypoglycemia, but no reports were found on its use in persistent neonatal hypoglycemia [13,24].

Conclusion

This single-center audit of transient hyperinsulinemic hypoglycemia of neonates is the largest case experience of Maltodextrin supplementation in persistent neonatal hypoglycemia. The audit findings of this case series with persistent hypoglycemia and transient hyperinsulinism suggest that Maltodextrin supplementation may be beneficial without major side effects in term neonates. However, evidence or recommendations on its routine use as an oral supplementation are very much limited. Hence this report prompts the need for further research and randomized controlled studies to systematically evaluate the effects of Maltodextrin supplementation in the management of persistent hypoglycemia due to transient hyperinsulinism in neonates.

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Ethical considerations

Since this is an audit report, institutional review board approval was not applicable.

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