Original Article

NEONATAL HYPOGLYCEMIA: PREVALENCE AND CLINICAL MANIFESTATIONS IN TEHRAN CHILDREN'S HOSPITAL

Nasrin Dashti[1], Nahid Einollahi[2], Sakineh Abbasi[3]

ABSTRACT

Objective: To measure the prevalence of hypoglycemia among newborn infants in Children Hospital using a standard laboratory glucose method and to evaluate the evidence of clinical manifestations of hypoglycemia, designing appropriate strategies for prevention and treatment.

Methods: The study population consisted of 673 neonates in Tehran Children's Hospital and was conducted between June 2004 and March 2005.

Results: The incidence of neonatal hypoglycemia in the present study group was 15.15% live births. The clinical features which remained significantly associated with the hypoglycemic neonates were refusal of feeding (45%), hyporeflexia (36.2%), irritability (30%), cyanosis (28.4%), tackypnea (24.5%), seizure (16.6%), weak cry (15.8), apneic spels (9.8%), pallor (1.9%), cardiac arrest (9.1%) and sweating (1%).

Conclusion: Hypoglycemia does occur frequently in newborn infants and requires careful monitoring and therapy of serum glucose.

KEY WORDS: Hypoglycemia; Neonate; Prevalence; Treatment protocols.

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INTRODUCTION

The definition of neonatal hypoglycemia has remained elusive amongst the text books, pediatricians and experts in this field.[1-5] After birth, the normal newborn infant's plasma glucose concentration falls quickly to levels below those prevalent in fetal life. This is part of the normal transition to extra uterine existence and partly triggers the endocrine and metabolic events associated with normal adaptation.[6-9] When adaptation fails, for example through immaturity or illness, limitation of substrate supply may disturb cerebral function.

Severe hypoglycemia is a dangerous condition, which if not properly treated, and may cause neonatal death. Even in less severe cases, it can cause permanent brain damage and neurological sequelae. Thus, the treatment of real hypoglycemia is imperative.[7] Causes of hypoglycemia can be divided into five major categories of glucose metabolism disruption:

1) Failure to receive or absorb nutrients;
2) Decreased production or release of hepatic glycogen;
3) Limited substrate for gluconeogenesis;
4) Decreased alternate fuel production;
5) Increased utilization of glucose.

Of these five major categories, neonates will usually fall into three or four of these states. In general transient forms of hypoglycemia is usually corrected within three to seven days of life and require glucose infusion equal to normal glucose production rates. Persistent

1. Nasrin Dashti, Ph.D
2. Nahid Einollahi, Ph.D
3. Sakineh Abbasi, Ph.D
1-3: School of Allied Health Medicine
Tehran University of Medical Sciences
Tehran- Iran

Correspondence

Nahid Einollahi
E-mail: einolahn@sina.tums.ac.ir

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forms of hypoglycemia are more protracted and severe than transient forms and require prolonged treatment. Infants with a disorder in any of these categories will present with hypoglycemia as the primary problem.[8] The prevalence and association of hypoglycemia have not been accurately described. The prevalence of hypoglycemia in different populations is difficult to compare because of differing definitions, populations, labor room practices, infant ages and technical methods.[9] Symptoms of hypoglycemia are often vague and unspecific. Hypopnea, bradycardia and hypothermia are common findings and may be signs of both cerebral dysfunction and adaptation to low-energy availability. Hypoglycemia can also be present without any apparent symptoms, the so- called "asymptomatic hypoglycemia" found in neonates at risk of hypoglycemia.[7] In this study the prevalence of hypoglycemia was measured among newborn infants using a standard laboratory glucose method and evidence of clinical manifestations of hypoglycemia, designing appropriate strategies for prevention and treatment were evaluated.

PATIENTS AND METHODS

The study population consisted of 673 neonates in children's hospital in Tehran. Full verbal explanation was given to mothers and their permission sought for enrolment in the study. The first postnatal glucose testing was performed 1-3 hours within the first 24 hours of life. The blood glucose levels of ≤35 mg/dL were considered hypoglycemic. Subsequent measurements of neonatal blood glucose were performed within 3- 24 hours and also after 24 hours of life. The blood glucose levels of ≤40 mg/dL and ≤45 mg/dL were considered hypoglycemic respectively. Testing of neonatal glucose was performed in capillary blood that was obtained by heel stick with a reflectance meter (Roche Diagnostics, Mannheim, Germany). Glucose values of ≤40 mg/dL were confirmed in laboratory measurements by the glucose oxidase method (Ziest Chimi Diagnostics, Tehran, Iran). All hypoglycemic neonates were checked for clinical signs such as refusal of feeding, hyporeflexia, irritability, cyanosis, tackypnea, seizures, week cry, apneic spels, pallor, cardiac arrest and sweating. The immediate management of hypoglycemic neonates was directed towards maintaining blood glucose above 45 mg/dL. This was achieved through the following treatments. All hypoglycemic neonates were given an intravenous infusion of 25% glucose in water (1gm/kg) at a rate of 1 ml/kg/min followed by a continuous infusion of glucose at a rate of 2.4 to 14 mg/kg/min. Neonates developing recurrences after glucose therapy, received intravenously administered hydrocortisone at a rate of 2.5 mg/kg/46 hr before normalization of serum glucose was attained. Neonates developing recurrences after glucose and hydrocortisone therapy, received diazoxide at a rate of 10-15 mg/kg/24 hr. All statistical analysis was performed using SPSS software version.[11]

RESULTS

A total of 673 neonates were studied. Ages ranged from 6 hours of life to 25 days with an average age of 5.5 days. The mean birth weight was 3085 grams. The incidence of neonatal hypoglycemia in the present study group was 102/673 (15.15%) live births. The clinical features which remained significantly associated with the hypoglycemic neonates were, refusal of feeding (45%), hyporeflexia (36.2%), irritability (30%), cyanosis (28.4%), tackypnea (24.5%), seizure (16.6%), weak cry (15.8%), apneic spels (9.8%), pallor (1.9%), cardiac arrest (9.1%) and sweating (1%). About 6.8% of the hypoglycemic neonates were asymptomatic. 28.7% of all hypoglycemic neonates responded to intravenous infusion of 25% glucose in water. The mean duration of treatment was 6.5 days. Again 44.5% of hypoglycemic neonates developing recurrence after glucose therapy received intravenously administered hydrocortisone at a rate of 2.5 mg/kg/46 hours. The mean duration of treatment was 12.85 days. About 26.8% of three hypoglycemic neonates developing recurrences after glucose and hydrocortisone therapy received diazoxide at a rate of 10-15 mg/kg/24 hours.

The mean duration of treatment was 19.11 days.

DISCUSSION

The earliest reporting of neonatal hypoglycemia in neonates of nondiabetic mothers was in 1937 by Hartmann and Jaudon, the researchers who first observed that neonatal hypoglycemia occurred quite regularly during the first four or five days of life in the normal newborn.[11,12] Over the next 50 years, most of the research on neonatal hypoglycemia was conducted on fasting infants at risk, or infants of diabetic mothers. Unfortunately past research has rarely focused on neonatal hypoglycemia in normal, exclusively breast fed newborn.[13] Literature provides clear evidence of a postnatal metabolic adjustment period that, when experienced by the healthy neonate, includes a self limiting blood glucose nadir occurring at 1-2 hours of age.[10] Research evidence concludes that this transient hypoglycemic condition is self-correcting, with the glucose concentration gradually increasing from 3 hours of birth and continuing over the subsequent days as the neonate adjusts from an absolute dependence on placental nutrition to metabolic and nutritional independence via intermittent enteral feedings and the use of several exclusive breast feeding has been demonstrated in the literature to safely meet the nutritional needs of the newborn. Glucose screening is a preliminary test of a large sample of the population to detect the concentration of glucose in a blood sample that may represent a disorder requiring further investigation.[14]

Hypoglycemia does occur frequently in newborn infants.[15] The prevalence of hypoglycemia in the present study was found 102/673 (15.15%) live births. However Gutberlet and Cornblath estimated the prevalence of hypoglycemia as 4.4 per 1000 live births.[16] Lubchnco and Brad havereported an incidence of 11.4% of blood sugar less than 30 mg/dl in a general nursery population when screened before the first findings at 6 hours of age.[17] The prevalence of hypoglycemia (15.5%) was higher in this study when compared with the studies from industrialized countries. Our figures would probably be higher if we had studied a rural population in which health and nutrition is usually poor. Therefore it is necessary that the definition and criteria for the diagnosis of neonatal hypoglycemia be modified in order to encompass different situations. It is equally important that while employing an accurate diagnostic method close and careful observation of the infant is ensured for evidence of clinical manifestations of hypoglycemia.[10] The literature refers to numerous clinical features with low plasma glucose Concentrations.[18] They include pallor, sweating, apnea, cyanosis, seizures, hyporeflexia and refusal of feeding.[19-28] Almost 8.35% of the hypoglycemic neonate in this study showed significant clinical features of hypoglycemia. The significance of this symptomatic hypoglycemia is that if it is allowed to go untreated the infant may die or subsequently develop serious neurological handicaps.[19-23] However a proportion of hypoglycemic neonates were asymptomatic (6.8%) due to an increased utilization of alternative substrates, such as lactate, in combination with intracerebral storage of glycogen. This may be a situation for some children of diabetic mothers with transient hyper-insulinemia secondary to maternal hyperglycemia. Lactate is produced in the adipose tissue in the presence of insulin.[29] Lactate is high in subcutaneous adipose tissue in neonates and may be a source of circulating lactate, which in turn can serve as an alternative fuel for the brain during hypoglycemia.[30-32] Furthermore, astrocytes can store glycogen and directly supply the neurons with glucose.[33] The immediate priority in medical treatment is to provide an adequate amount of carbohydrate to ensure that blood glucose is maintained in normal range.[20] All hypoglycemic neonates should undergo careful surveillance including careful monitoring and therapy of serum glucose.[34-38]

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