International Journal of Contemporary Pediatrics
Dawn I et al. Int J Contemp Pediatr. 2017 Sep;4(5):1803-1806
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20173789

Original Research Article

Assessment of non-ketotic hypoglycaemia in new born attending in Malda Medical College and Hospital

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Received: 12 June 2017
Accepted: 08 July 2017

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ABSTRACT

Background: Blood glucose level of <40/dl irrespective of period of gestation is known as hypoglycaemia. Nonketotic hypoglycaemia is associated with disorders of fructose or galactose metabolism, hyperinsulinism, fatty acid oxidation and GH deficiency. Aim of our study to detect the new born having clinical manifestations of hypoglycaemia, measure the capillary blood glucose and urinary ketone bodies in neonates with sign and symptoms of hypoglycaemia and to perform detail work up of neonates having non ketotic hypoglycaemia.
Methods: It is hospital based cross-sectional study carried out for one calendar year extending from 01.01.2015 to 31.12.2015.
Results: Thirty-five patients were identified as hypoglycemic Nine patients were diagnosed with non ketotic hypoglycemia for a prevalence of 8.5/100, 00. Two patients had the low growth hormone (GH) levels (0.4 ng/ml and 0.5 ng/ml). Three patients had increased Asparate Aminotransferase (AST) and Alanine Aminotransferase (ALT) level. Three patients increased urinary acetyl-carnitine level.
Conclusions: Patient suffering from different congenital disorder and an extensive and overzealous workup for endocrinopathy or inborn error of metabolism is necessary.

Keywords: Capillary blood glucose, New born baby, Non-ketotic hypoglycaemia, Urinary ketone-bodies

INTRODUCTION

Blood glucose level of <40/dl irrespective of period of gestation is known as hypoglycaemia. Glucose has a central role in fuel economy and is a source of energy storage in the form of glycogen, fat and protein. It is essential for cerebral energy metabolism because it is usually the preferred substrate and its utilization accounts for nearly all the oxygen consumption in the brain.[1,2] The infant is born with a blood glucose concentration of 60-70% of the maternal level and it falls during first 24 hours, the lowest value is seen at the age of 3 hours followed by a transient rise in blood glucose during next 24 hours and again low levels at the age of 3-4 days before stability achieved.[3] Hypoglycaemia is manifested by jitteriness, tremor, twitching and convulsion, episodes of cyanosis, tachypnea, tachycardia, sweating and irregular breathing.[4] Causes of hypoglycaemia are idiopathic, inadequate intake, small for gestational age, prematurity, birth asphyxia, hypothermia, septicemia, maternal diabetes mellitus, erythroblastosis fetalis, Beckwith- Weidemann syndrome, Transposition of great vessels, hyperinsulinemia, inborn error of metabolism and maternal therapy with beta-agonist and beta blocker.[5] The long- term sequel of severe, prolonged hypoglycaemia are mental retardation, recurrent seizure activity or both.[6]

Before birth, the foetus receives glucose through the maternoplacental circulation at a daily amount of 7 g/kg.[7] When the umbilical cord is clamped, the neonate must meet several metabolic challenges, two of which are the

maintenance of adequate circulating levels of glucose or alternate fuels to the brain and other organs, and adaptation to intermittent milk feedings. If these processes fail to occur, neonatal hypoglycaemia develops.[8]

Maintenance of physiological plasma glucose concentration depends on a normal endocrine system that integrates and modulates substrate mobilization, interconversion and utilization. Enzymes of glycogenolysis, gluconeogenesis and other metabolic fuels must be functional, and there must be an adequate supply of endogenous fat, glycogen and gluconeogenic substrates (amino acids, glycerol, lactate).[9] Preterm, small for gestational age and intrauterine growth-retarded infants, and infants with hyperinsulinism (infants of diabetic mothers, Beckwith-Wiedemann syndrome), asphyxia, sepsis or other medical conditions, such as cardiopulmonary disease, are at risk of developing hypoglycaemia.[8-11] However, when a full term, apparently healthy neonate without the predisposing signs and symptoms of the above conditions develops hypoglycaemia, the aetiology may not be immediately obvious. The more uncommon causes of hypoglycaemia, such as inborn errors of metabolism, should be considered. The clinical diagnosis of inborn errors of metabolism presenting as hypoglycaemia is often difficult because blood and urine samples may not be helpful unless collected at the time of the acute symptoms. This difficulty in diagnosis occurs because the disorder may produce only intermittent abnormalities.[12]

Nonketotic hypoglycaemia is associated with disorders of fructose or galactose metabolism, hyperinsulinism, fatty acid oxidation and GH deficiency. Ketotic hypoglycaemia is associated with organic acidurias, maple syrup urine disease, glycogen storage disease and adrenal insufficiencies of central or peripheral origin.[13]

Aim of our study to detect the new born having clinical manifestations of hypoglycaemia, measure the capillary blood glucose and urinary ketone bodies in neonates with sign and symptoms of hypoglycaemia and to perform detail work up of neonates having non ketotic hypoglycemia

METHODS

It is hospital based cross-sectional study carried out for one calendar year extending from 01.01.2015 to 31.12.2015. The pediatric patients admitted in the Malda Medical College and Hospital. All the patients of neonatal age group suffering from hypoglycemia. Capillary blood glucose level were estimated and urine were analyzed for Presence of ketone bodies. Serum asparate aminotransferase (AST), alanine aminotransferase (ALT). insulin. GH also analyzed. Urine also analyzed for acetyl carnitine. Technique of data collection: Data were analyzed by suitable statistical test published.

RESULTS

Thirty-five patients were identified as hypoglycemic. Mean blood glucose was 34.2 mg/dl. Prevalence of hypoglycemia among population seeking care in our hospital was 33.3/100, 00 visits. Nine patients were diagnosed with non ketotic hypoglycemia for a prevalence of 8.5/100, 00. Non ketotic hypoglycemia demographics were: 5 males, 4 females.

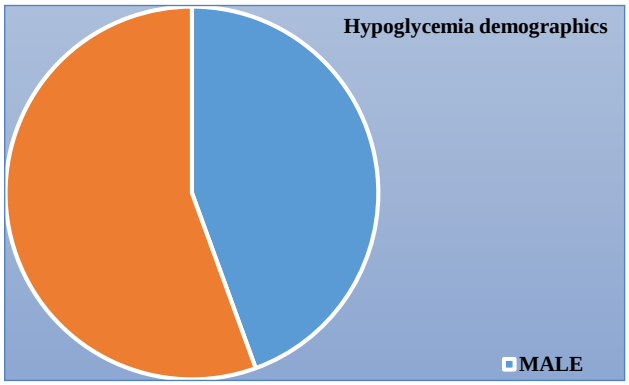

Figure 1: Hypoglycaemia demographics.

One of the 9 non ketotic hypoglycemia patients had increase insulin levels 12µU/mL) and. insulin to glucose ratio is 41.7 pmol/L:mmol/L. Two patient had the low growth hormone (GH) levels (0.4 ng/ml and 0.5 ng/ml). Three patients had increased Asparate Aminotransferase (AST) and Alanine Aminotransferase (ALT) level. Three patients had increased urinary acetyl-carnitine level.

DISCUSSION

Hyperinsulinism, regardless of the cause, increases glucose utilization and glycogen formation. It reduces the gluconeogenic precursors, including amino acids, free fatty acids and ketone bodies. The diagnosis is confirmed when the insulin to glucose ratio is greater than 38.7 pmol/L:mmol/L.[14-16] Glucagon produces an elevated glycaemic response because of the large glycogen stores.[14]

The anterior pituitary hormones are important in energy production. Growth hormone (GH) acts to stabilize glucose and stimulate the release of free fatty acids from adipose tissue during episodes of hypoglycaemia,

Galactosemia may be associated with abnormal AST, ALT.Galactose-1-phosphate-uridyl-transferase deficiency, the cause of classical galactosemia, presents with vomiting and diarrhoea within a few days of the introduction of milk; hypoglycaemia may be associated.[13]

Elevated AST, ALT, suggests fructose 1,6-bisphosphatase deficiency. Fructose, a six-carbon reducing sugar, is used in the liver, kidney and small intestine because it can be converted into intermediates for the glycolytic-gluconeogenic pathway. Of course,

symptoms only occur after fructose is introduced into the diet; it is present in some infant formulas. Fructose 1,6-bisphosphatase is a key enzyme for gluconeogenesis because it allows the endogenous formation of glucose from lactate, glycerol and amino acids such as alanine.[17,18] In the first week of life, the neonate is very dependent on gluconeogenesis for glucose production.[19]

The mitochondria play a major role in energy production because this is the organelle where fatty acids are degraded by the sequential removal of two-carbon fragments (known as acetyl-CoA) from the carboxyl terminal end of the molecule. This process is known as beta oxidation. The liver uses 90% of its acetyl-CoA to form ketone bodies that can be used as auxiliary fuel for many tissues, including the brain. Fatty acids are also metabolized in peroxisomes and in the cytoplasm by omega oxidation.[20]

Fatty acid oxidation defects usually show hypoketosis, urine organic acid abnormalities, and carnitine and acylcarnitine abnormalities. Medium chain acyl-CoA dehydrogenase (MCAD) deficiency, an autosomal recessive condition, is the most common defect of fatty acid oxidation with an incidence of 1/20,000 (1/16,400-1/46,000).[21] It may present as early as day four of life, usually following a prodromal illness with episodic hypoketotic hypoglycemia, apnea, Reye-like encephalopathy or sudden infant death syndrome.[22] Metabolic acidosis, hyperammonemia, elevated liver function tests, elevated acylcarnitine: free carnitine ratio and secondary carnitine deficiency are associated laboratory findings. The acylcarnitine profile is unique because cis-4-decenoate is seen in the plasma of patients when ill or well.[16] The gene is located on chromosome 1p31, and the most common mutation is A985G.[18] The combination of DNA analysis and acylcarnitine profile can reliably detect all patients with MCAD deficiency.[18]

Carnitine palmitoyltransferase deficiency types I and II (CPT I and CPT II) may present in the neonatal period with hypoketotic hypoglycaemia. The plasma carnitine is normal to increased and the plasma acylcarnitine is normal in CPT I. The plasma carnitine is decreased and the plasma acylcarnitine is increased in CPT II.[19]

Long chain 3-OH acyl-CoA dehydrogenase (LCHAD) deficiency may present as early as the first day of life with hypoketotic hypoglycaemia, liver dysfunction, hypotonia and variable hypertrophic cardiomyopathy. Metabolic acidosis and urine dicarboxylic aciduria may be associated. When the fetus has LCHAD deficiency, the heterozygous mother may have had HELLP (hemolysis, elevated liver enzymes and low platelets), hyperemesis gravidarum or fatty liver of pregnancy.[19]

CONCLUSION

Non-ketotic hypoglycaemia is the rare cause of hypoglycemia in children in the infancy period. Non-ketotic hypoglycemia may be associated with disorders of fructose or galactose metabolism, hyperinsulinism, fatty acid oxidation and GH deficiency. An extensive and overzealous workup for endocrinopathy or inborn error of metabolism is necessary.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Dawn I, Jeauddin Sk, Biswas G, Jana JK. Assessment of non-ketotic hypoglycaemia in new born attending in Malda Medical College and Hospital. Int J Contemp Pediatr 2017;4:1803-6.