MANAGEMENT PROTOCOL OF HYPOGLYCEMIA IN INFANT AND CHILDREN BELOW 14

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Introduction and Literature review:
The definition of hypoglycemia and the threshold for treatment and continued management are controversial, however, a plasma glucose concentration of 47 mg/dl (2.6 mmol/l) was used in multiple studies. In 2015 the pediatric Endocrine society recommended that in the first 48 hours of life the target threshold plasma glucose concentration for treatment should be 50 mg/dl (2.8 mmol/L). also they make recommendation that in specific patients higher glucose target thresholds of 60 mg/dl (3.3 mmol/L) and 70 mg/dl (3.9 mmol/L). Despite being a very common problem after birth globally, consensus on how to manage low glucose concentrations in the first 48 hours of life has been difficult to establish and remains a debated issue. The main reason of that lack of extensive studies providing the data needed and agreed upon to establish a protocol or approach to hypoglycemia management.

Mainly the previous publications focused on aspects of managing low blood glucose concentrations in the patients most at risk for asymptomatic hypoglycemia- those born late preterm, large for gestational age, small for gestational age, or growth restricted, and those born following pregnancy complicated with diabetes mellitus.

The newborns with asymptomatic hypoglycemia due to late premature, large for Gestational age, intrauterine growth retardation and infant of diabetic mother it is not recommended to give bolus of dextrose at the rate of 200 mg/kg this recommendation cannot necessarily be generalized to the other group, especially those with symptomatic hypoglycemia or a defined or suspected serious metabolic hypoglycemia disorder, such as congenital hyperinsulinemic hypoglycemia or genetic conditions that lead to excessive glucose utilization (fatty acid oxidation disorders) or insufficient glucose production (hypopituitarism).

In Saudi Arabia Despite that hypoglycemia is a significant concern among neonatal and pediatric critical care specialists but we don’t have enough data about hypoglycemia in infancy that’s include the magnitude of the
problem, the risk factors, the prevention measures as well as management protocol. One study in Saudi Arabia assessed the prevalence, patterns, and risk factors for admission of term infants to a NICU to identify areas for quality improvement they found that the second common cause of admission was hypoglycemia accounts about 16.2%. Scattered studies focusing on the rare conditions causing hypoglycemia in neonates like ABCC8 gene mutation and phenotype in patients with congenital hyperinsulinism.

While experimental data confirm the neurological effects of hypoglycemia, available clinical data do not confirm a causal relationship between hypoglycemia and clinically significant adverse outcomes, such as neurological dysfunction, prolonged stay in ICU, or increased mortality. Reference no 2 However, presence of a guidance protocol will help in ameliorating the fear and controversy in management of hypoglycemia in children. At the shadow of this insufficiency we created our own protocol adopting the information and ideas from other protocols in the field as well as depending on our experience on dealing with such problem.

**Aim of the protocol:**
The goal of this protocol is to unify the approach to hypoglycemia in children and create guiding notes according to the best practice from all over the world and provide the physician in ministry of health with a unified protocol to ensure best services provided to our infants who suffered such health problem.

**Methodology:**
Development of Hypoglycemia protocol in children went through 4 phases over a period of 1 year as follows:

**Phase 1:** review the literature for Hypoglycemia in children protocols and guidelines worldwide and impact of implementing these protocol on health conditions as well as on cost. Then we payed special attention to the studies done in Saudi Arabia in regards to the prevalence and incidence of Hypoglycemia and the impact of this condition on health and cost. This phase has been done by panel of experts in the field of Endocrine and Diabetes, where The outcome is a unified Hypoglycemia management protocol according to the best evidence based practice.

**Phase 2:** the panel of experts has been extended to include pediatric and adult Emergency Medicine and intensive care units whom they reviewed the protocol developed in the first phase and put their input according to their experience in the specialty.

**Phase 3:** the protocol has been reviewed and amended by another panel of experts whom contributing in execution of the protocol as nurses, pharmacists, lab experts as well as quality improvement experts.

**Phase 4:** experts from the different specialties including (pediatric and Adult endocrinology and diabetes, pediatric and Adult emergency medicine, and pediatric and adult intensive care) from all the regions of kingdom of Saudi Arabia whom they reviewed the protocol and shared their opinion.
The protocol:

DEFINITION:
- For infants and children: plasma glucose <3.3 mmol/L or 60 mg/dl measured by accurate laboratory method
- For neonate: refer to MOH neonatal hypoglycemia protocol.

PRESENTATION
- In newborn: apnea, cyanosis, poor feeding, sweating tremors, jitteriness, irritability, convulsion, coma.
- Infant and children: irritability, dizziness, blurred vision, difficulty speech, headache, confusion, feeling faint, personality changes, palpitations. Hunger, Nausea, Sweating, Anxiety, Tremulousness, Nervousness, Ataxia, drowsiness, convulsion, coma.

DIAGNOSIS:
Reliable blood sugar estimation during symptoms.

ASSESSMENT

History:
- Neonate: prematurity, IUGR, maternal diabetes, perinatal stress eg. birth asphyxia, sepsis, shock, fasting hypoglycemia or hypoglycemia after meal (hyperinsulinemia)
- Diabetes Mellitus, renal insufficiency/failure, hepatic cirrhosis/failure, other endocrine diseases, or recent surgery
- Drug History: Insulin usage or ingestion of an oral hypoglycemic agent, toxic ingestion, new medications
- The social history may include intake and nutritional deficiency
- Review systems for: weight reduction, nausea, vomiting, headache, etc...
- Look for other symptoms suggesting infection

Examination:
- Physical findings are nonspecific in hypoglycemia and generally are related to the central and autonomic nervous systems.
- Height, weight (thin stature- ketotic hypoglycemia.
- Assess vital signs for hyperthermia, tachypnea, tachycardia, hypertension, and bradycardia (neonates)
- The head, eyes, ears, nose, and throat examination may indicate blurred vision, pupils normal to fixed and dilated, icterus (usually cholestasis due to hepatic disease)
- Cardiovascular disturbances may include tachycardia (bradycardia in neonates), hypertension or hypotension, and dysrhythmias.
- Midline congenital anomalies: Ambiguous genitalia, micropenis, facial anomalies, cleft palate, central incisor, nystagmus, etc.
- Respiratory disturbances may include dyspnea, tachypnea,
- GI disturbances may include nausea and vomiting, dyspepsia, and abdominal cramping Hepatomegaly-glycogen storage disease. Any abdominal mas.
- Skin may be diaphoretic and warm or show signs of dehydration with decrease in turgor, hyperpigmentation.
- Neurologic conditions include coma, confusion, fatigue, loss of coordination, tremors, convulsions, and diplopia and Cataract in case of galactocaemia.
INVESTIGATIONS
• Obtain 5-10 ml blood red top and 20 ML urine for further investigation to be safe for 48-72 hr
• Critical Sample: Acute Blood and Urine Tests at time of Hypoglycemia

Blood
• Chemistry panel with bicarbonate
• Insulin, C-peptide
• Cortisol, growth hormone
• Free fatty acids, β-hydroxybutyrate, acetoacetate
• Lactate, ammonia
• Total and free carnitine
• Acyl carnitine profile saves serum tube

Urine: the first urine voided during or immediately after the hypoglycemic event should be collected and tested for ketones (if blood ketones van not be measured) and urine organic acid.

MANAGEMENT PLAN:

Hypoglycemia Blood sugar < 3.3 mmol/l
Collect blood sample for investigations (blood gas, insulin, BOHB, lactate, FFA)

Conscious & Asymptomatic
• Send blood sample for glucose
• Offer feed or sugary drink for older children
• Recheck blood sugar by 15 min

Impair consciousness, convulsion or coma
• Collect sample of blood for investigations.
• IV glucose 10% dextrose normal saline
  5 ml/kg over 3-4 minute followed by D10 normal saline in maintenance IVF Repeat blood sugar after 15 minute if there is No Response
  Repeat D10 % dextrose bolus if still No Response
  Increase rate and concentration of glucose infusion. If >12.5% of glucose infusion is needed to maintain normal blood sugar
  insertion of central line is advisable. If No response start Glucagon injection as follows:
  The weight of the child <20 Kg give 0.5 mg SC/IM/IV
  The weight of the child >20Kg give 1 mg SC/IM/IV
  The dose of glucagon may be repeated in 15 minutes if necessary
• Repeat blood sugar every 15 minutes
• Once blood sugar is control, oral feeding should be Started glucose infusion should gradually discontinued.
• Try to find the cause of hypoglycemia
• Consult pediatric endocrinologist
Ketotic hypoglycemia

- It is the most common cause of childhood hypoglycemia
- It usually presents between the age of 18 months and 5 years and remits spontaneously by 8 to 9 years of age
- Hypoglycemia usually occurs during illness when food intake is limited
- Diagnosis is confirmed by fasting for several hours under close supervision and collecting blood samples for testing. At the time of hypoglycemia,
  - there is associated ketonemia & ketonuria
  - S.alanine levels are reduced
  - Treatment consists of frequent feedings of a high-protein, high carbohydrate diet.
References:


