Case Report

Anesthetists approach in a neonate with nesidioblastoma undergoing pancreatectomy

Kiran Patel, Mukta Shikare, Dilip Chavan, Pradnya Sawant

Department of Pediatric Anesthesiology, B. J. Wadia Hospital, Parel, Mumbai, India

Abstract

Persistent hyperinsulinemic hypoglycemia of infancy (PHHI) is rare, but an important cause of hypoglycemia in infants, associated with a number of structural abnormalities of the endocrine pancreas is collectively termed as "Islet cell dysmaturation syndrome." We present the anesthetic management in a clinically diagnosed case of PHHI in a 22 days old full term child, undergoing Subtotal Pancreatectomy. We have discussed the challenges faced in the intra-operative period in managing this neonate for pancreatic resection surgery with focus on intra-operative management of blood glucose levels.

Key words: Anesthesia, neonate, persistent hyperinsulinemic hypoglycemia

Introduction

Persistent hyperinsulinemic hypoglycemia of infancy (PHHI) is one of the rare causes of hypoglycemia in infancy. Infants with hypoglycemia may present with grunting, irritability, listlessness, nausea, vomiting, tachypnea, apnea, hypothermia, and with long-term sequel such as seizures, developmental delay, focal neurologic deficits or death secondary to severe, prolonged hypoglycemia.[1] Hence, it is a medical emergency, which needs immediate intervention and definitive management is surgical in most of the cases.[2] Anesthetic management of a 22-day neonate presenting with similar complaints, undergoing subtotal pancreatectomy, for PHHI, is described here.

Case Report

A 22-day neonate (4 kg) was admitted with a history of repeated episodes of convulsions since day 3 of life. She was delivered at full term by elective caesarean section. She had repeated episodes of generalized tonic clonic convulsions with blood glucose level as low as 21 mg/dl and was managed symptomatically with 10% dextrose at 10 ml/kg/min, to maintain blood glucose more than 40 mg/dl. Critical insulin sample analysis showed insulin:glucose ratio 0.7 (normal < 0.4). Ultrasonography Abdomen showed no significant findings. The biochemical and urinary analysis (serum metabolic screens, pH, lactate, ammonia and urinary ketones, amino acids, reducing-substance, serum cortisol, growth hormone levels during periods of normoglycemia) to rule out other metabolic and endocrinal conditions with similar presentation, were normal. The neurological assessment was unremarkable and no Electroencephalogram or other Imaging studies were performed. This led to a clinical diagnosis of PHHI. The neonate was managed with intravenous (IV) 10% dextrose10 ml/kg/min (150 ml/kg/day), two hourly feed through nasogastric (NG) tube, oral Diazoxide (8 mg/kg/dose) 8 hourly and hydrochlorothiazide (25 mg/alternate day). As hypoglycemia persisted even with maximum doses of diazoxide and hydrochlorothiazide, IV octreotide was started at 2 mcg/kg/once a day. This patient was scheduled electively for subtotal pancreatectomy due to persistence of symptoms in spite of aggressive medical management. The 2 hourly NG tube feeds were stopped 6 h prior to surgery and the IV infusion of 10% dextrose along with all the other drugs was continued. Blood sugar checked every 30 min by portable glucose analyzer remained between 100 and 200 mg/dl. 24 G IV cannula was secured on right upper limb. Anesthesia was induced with IV glycopyrolate (4 mcg/kg), fentanyl (2 mcg/kg) followed by propofol (2 mg/kg), atracurium (0.5 mg/kg)

Address for correspondence: Dr. Kiran Patel,
6 - Amber Palace, Chittaranjan Road, Vile-Parle (East),
Mumbai - 400 057, India.
E-mail: patelpkiran@gmail.com

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/0970-9185.117108

and airway secured with 3.5 uncuffed endotracheal tube. Anesthesia was maintained with oxygen, air, isoflurane with circle absorber system and intermittent doses of atracurium. Right internal jugular vein was cannulated by double lumen No. 4 Fr central venous catheter. Regional analgesia was provided with lumbar epidural catheter inserted by using 19 G Touhy's needle pediatric set at L3 ± L4 level and fixed at mark 9 cm. Bupivacaine 0.25% (4 ml) was used in epidural block as a bolus. Monitoring included electrocardiogram, non-invasive blood pressure, pulse-oximetry, capnography, central venous pressure, and temperature. Ringer's lactate 10 ml/kg/h was used as replacement fluid and glucose was supplemented as 4 mg/kg/min. The blood sugar was estimated every 15 min., which was always between 100 and 200 mg/dl as shown in Figure 1. Intra-operative blood loss was 20 ml. and surgery lasted for 75 min. Intra-operative hemodynamic parameters were stable and procedure was uneventful. Residual neuromuscular blockade was reversed with glycopyrrolate (8 mcg/kg), and Neostigmine (0.05 mg/kg). Trachea was extubated and patient shifted to neonatal intensive care unit. Blood sugar level was stabilized between 90 and 100 mg/dl with oral feeds over next 5 days. Post-operative analgesia was provided by 0.25% bupivacaine (1 ml/kg) 6 hourly for next 3 days along with the paracetamol suppository (20 mg/kg) 8 hourly. Histopathological examination of specimen confirmed diagnosis of PHHI.

Discussion

Despite hypoglycemia is a commonly faced the problem in neonates, the threshold for hypoglycemia is still controversial. The operational threshold for hypoglycemia is defined as "that concentration of plasma or whole blood glucose at which clinicians should consider intervention, based on the evidence currently available in the literature."[3]

The operational threshold for hypoglycemia is considered when blood glucose level in Pre-term infants is <30 mg/dl,

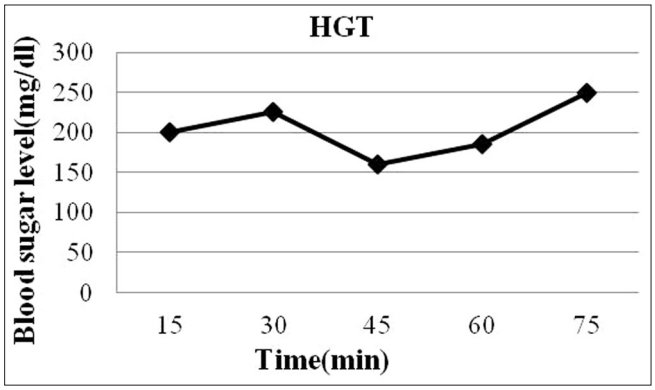

Figure 1: Intra-operative blood sugar levels

and <40 mg/dl in full-term infants -.[4] The differential diagnosis of neonatal hypoglycemia are shown in Table 1.[4]In neonatal hypoglycemia laboratory studies such as blood glucose, ketone, insulin levels, serum cortisol, growth hormone levels during periods of normoglycemia, and serum metabolic screens, pH, lactate, ammonia and urinary ketones, amino acids and reducing-substances, should be performed to arrive at a definitive diagnosis.[5] Hyperinsulinism in infancy (HI) is the most common cause of recurrent and persistent hypoglycemia in the neonatal period,[6] most cases of which are sporadic. It is characterized by the inappropriate and excessive secretion of insulin from the pancreatic β-cells. The most common cause of HI is due to mutations in the genes regulating the function of the K_{ATP} channel located on the β-cell membrane.[7] PHHI is associated with a number of structural abnormalities of the endocrine pancreas like multiple diffuse microadenomas, islet cell adenomas, islet cell dysplasia, islet cell hyperplasia (nesidioblastosis). All these conditions are collectively termed the "islet cell dysmaturation syndrome." The serum glucose level <60 mg/dl, non-ketotic hypoglycemia in association with elevated insulin levels (>10 μU/ml), Insulin/glucose ratio from 0.4 to 2.7 (normal <0.3), sustained glucose requirement in excess of 10 mg/kg/min are confirmatory findings in PHHI.[8] Though surgery is the treatment of choice for PHHI, optimization of blood glucose level prior to surgery is necessary to avoid adverse effects of hypoglycemia. These include seizures, developmental delay, focal neurologic deficits or death secondary to severe, prolonged hypoglycemia. Timely nasogastric feeds, dextrose infusion and drugs like diazoxide, octreotide etc., play an important role in blood glucose level optimization. The aim is to maintain blood sugar level more than 40 mg/dl.

Diazoxide, octreotide[9] and nifedipine[10] are the primary medications used in long-term treatment of PHHI. All these drugs increase serum glucose levels as a well-known adverse effect, but their other therapeutic actions may become a burden in patients with PHHI. Few of them are shown in Table 2. [11] Hence, the exact medication regimen, including doses and selection of drugs, must be highly individualized on the basis of therapeutic response, adverse-effect tolerance, and individual factors.

The Dextrose infusion rate can be calculated by following formulae:[12]

- Dextrose Infusion rate (mg/kg/min) = % of dextrose being infused x rate (ml/hr) body weight (in kg) x 6
- Dextrose Infusion rate(mg/kg/min) =IV rate (ml/kg/day) x % of dextrose/ 144

Table 1: Differential diagnosis of neonatal hypoglycemia[4]

PHHI	Hypopituitarism, hypothyroidism
Adrenal insufficiency	Infant of diabetic mother
Growth hormone deficiency	Multiple endocrine neoplasia
IUGR	Inborn error of metabolism
Small for gestational age	Patau syndrome, beckwith-wiedemann syndrome

IUGR=Intra uterine growth retardation, PHHI=Persistent hyperinsulinemic hypoglycemia of infancy

Table 2: Adverse effects of therapeutic agents used to increase blood sugar levels pre-operatively[11]

Drug	Mechanism of action	Side-effects
Diazoxide	Inhibits pancreatic insulin release	Hypotension, fluid and Na retention, hyperglycemia, tachycardia
Nifedipine	Ca channel blocker	Edema, dizziness, flushing
Octeotride	Somatostatin analog; decreases GH secretion	Dysglycemia, hypothyroidism, ECG changes
Chlorothiazide	Inhibits Na reabsorption in distal renal tubules	Hyperglycemia hypotension hyperuricemia
Glucagon	Insulin antagonist, accelerate hepatic glycogenolysis	Nausea vomiting

GH=Growth hormone, ECG=Electrocardiogram

In these patients, maintenance of blood sugar level is the main concern. In the normal neonate the glucose requirement is 4-6 mg/kg/min and the fluid requirement is 100-150 ml/kg/day. To balance both these requirements, a 5-10% dextrose solution is the maintenance fluid for neonates. In hyperinsulinemia, glucose requirement increases to 10 mg/kg/min.[12] When glucose is supplemented with boluses of high concentration dextrose containing fluid, blood glucose level could exceed renal threshold for glucose causing glycosuria and osmotic diuresis. Hence, it is preferred to use the dextrose containing fluid as maintenance and ringer lactate as replacement solution. We need to be very careful while supplementing dextrose as use of increased volume can cause volume overload in neonates. Maximal concentration of glucose that can be given through peripheral IV line is D12.5%. If infant requires IV dextrose concentrations >12.5%, insertion of central venous catheter is helpful.[4] Utmost care should be taken not use D25% or D50% IV or large IV volume boluses as this creates rebound hypoglycemia and hyperosmolarity in infants who are hyperinsulinemic.[4] Intra-operatively blood glucose level can also act as a guide for tumor removal.[13]

Conclusion

Avoiding long term complications of hypoglycemia like neurological damage is of prime importance in management of PHHI. Though uncommon but PHHI is clinically important cause of hypoglycemia in neonates, and must be considered in a patient with a presumptive pre-operative diagnosis of insulinoma.[14]

References

1. Cryer PE. Glucose homeostasis and hypoglycemia. In: Wilson JD, Foster DW, editors. Williams Textbook of Endocrinology. 8th ed. Philadelphia: WB Saunders Company; 1992. p. 1223-53.
2. Aynsley-Green A. Disorders of blood glucose homeostasis in the neonate. In: Roberton NR, editor. Textbook of Neonatology. 2nd ed. Edinburgh: Churchill Livingstone; 1992. p. 777-98.
3. Cornblath M, Hawdon JM, Williams AF, Aynsley-Green A, Ward-Platt MP, Schwartz R, *et al*. Controversies regarding definition of neonatal hypoglycemia: Suggested operational thresholds. Pediatrics 2000;105:1141-5.
4. Marles SL, Casiro OG. Persistent neonatal hypoglycemia: Diagnosis and management. Paediatr Child Health 1998;3:16-9.
5. Desai MP, Khatri JV. Persistent hyper insulinemic hypoglycemia of infancy. Indian Pediatr 1998;35:317-28.
6. Hussain K, Aynsley-Green A. Management of hyperinsulinism in infancy and childhood. Ann Med 2000;32:544-51.
7. Glaser B, Thornton P, Otonkoski T, Junien C. Genetics of neonatal hyperinsulinism. Arch Dis Child Fetal Neonatal Ed 2000;82:F79-86.
8. Aynsley-Green A. Hypoglycemia. In: Brook CG, editor. Clinical Pediatric Endocrinology. 1981. p. 637-59.
9. Thornton PS, Alter CA, Katz LE, Baker L, Stanley CA. Short-and long-term use of octreotide in the treatment of congenital hyperinsulinism. J Pediatr 1993;123:637-43.
10. Baş F, Darendeliler F, Demirkol D, Bundak R, Saka N, Günöz H. Successful therapy with calcium channel blocker (nifedipine) in persistent neonatal hyperinsulinemic hypoglycemia of infancy. J Pediatr Endocrinol Metab 1999;12:873-8.
11. McGowan JE. Neonatal Hypoglycemia. Pediatr Rev 1999;20:e6.
12. Berry FA. Practical aspects of fluid and electrolyte therapy. In: Berry FA, editor. Anesthetic Management of Difficult and Routine Pediatric Patients. 2nd ed. Edinburgh: Churchill Livingstone; 1990. p. 110.
13. Muir JJ, Endres SM, Offord K, van Heerden JA, Tinker JH. Glucose management in patients undergoing operation for insulinoma removal. Anesthesiology 1983;59:371-5.
14. Witteles RM, Straus II FH, Sugg SL, Koka MR, Costa EA, Kaplan EL. Adult-onset nesidioblastosis causing hypoglycemia: An important clinical entity and continuing treatment dilemma. Arch Surg 2001;136:656-63.

How to cite this article: Patel K, Shikare M, Chavan D, Sawant P. Anesthetists approach in a neonate with nesidioblastoma undergoing pancreatectomy. J Anaesthesiol Clin Pharmacol 2013;29:384-6.
Source of Support: Nil, **Conflict of Interest:** None declared.