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Case Series

Neonatology Section

Clinical and Etiological Profile of Neonates with Persistent Hypoglycaemia

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ABSTRACT

Disturbances of glucose homeostasis that result in hypoglycaemia is a common metabolic issue encountered in newborn. Most of the times, awareness of various risk factors that predispose infants to hypoglycaemia allows for screening of those at risk newborns so that clinically undetectable hypoglycaemia can be treated promptly, thus preventing the development of severe or symptomatic hypoglycaemia, which is associated with adverse outcomes, but in certain conditions like the persistent, recurrent or severe hypoglycaemia may cause irreversible injury to the developing brain. Here we are reporting outcome of seven neonates who presented to us with varied symptoms of persistent hypoglycaemia.

Keywords: Glucose homeostasis, Irreversible neuronal injury, Hyperinsulinaemia

Glucose is one of the major source of energy for organ function. The high brain to body weight ratio in the newborn has shown to result in a proportionately higher demand for glucose, compared with the capacity for glucose production as compared in the adult, with cerebral glucose use accounting for about 90% of total glucose consumption [1]. Although, hypoglycaemia is associated with a number of physiologic changes, the most profound effects are seen in the brain, that includes selective neuronal necrosis in multiple brain regions, including the superficial cortex, dentate gyrus, hippocampus, and also caudate-putamen [1].

Hypoglycaemia is one of the most frequently encountered problems in the first 48 hours of life and low glucose concentrations are perhaps the most common biochemical abnormality seen by providers caring for newborns, glucose is the principal energy source for the neonatal brain and hypoglycaemia is known to cause irreversible neuronal injury when it is recurrent and severe. Hence, the neonatologist is advised to be proactive in suspecting and managing hypoglycaemia in the newborn.

CASE SERIES

From the case records of seven neonates presenting with hypoglycaemia (< 40 mg/dL) lasting for more than seven days or in infants who require higher amounts of glucose (>10-12 mg/kg/min) to maintain a normal glucose level for over a week, data was collected regarding the clinical presentation and results of laboratory evaluation done by standard biochemical assays as per the protocol were tabulated. Treatment given and outcome of those neonates were also recorded and data tabulated.

Out of seven neonates, four were term, two near term and one preterm. Four males and three female, most of them i.e., six were SGA ans one was LGA. Almost six neonates presented on day 1 and one presented on day 2. Three of them were

Case	1	2	3	4	5	6	7
GA	36	37	38	37	33	36	37
Sex	M	F	F	M	M	F	M
Birth Weight (Kg)	1.97	2.05	2.1	2.12	1.08	1.05	3.9
SGA/AGA/LGA	SGA	SGA	SGA	SGA	SGA	SGA	LGA
Onset of Hypoglycaemia	Day 2	Day 1	Day 1	Day 1	Day 1	Day 1	Day 1
Symptoms	Lethargy	Asymptomatic	Asymptomatic	Lethargy	Lethargy	Asymptomatic	Seizures

[Table/Fig-1]: Clinical profile of neonates with persistent hypoglycaemia.

Case	1	2	3	4	5	6	7
I:E	0.9	0.7	0.3	0.4	0.1	0.1	0.1
S.cortisol	Normal	Normal	Normal	Low	Normal	Normal	Normal

[Table/Fig-2]: Investigation profile of neonates with persistent hypoglycaemia.

Case	1	2	3	4	5	6	7
Max Dextrose Req (Mg/Kg/Hr)	23	28	18	20	24	20	22
Diazoxide Response	20 mg/Kg	15 mg/Kg	10 mg/Kg	15 mg/Kg	-	-	20 mg/Kg
Octreotide Req	Yes	No	No	No	No	No	Yes
Duration Of Dextrose Infusion	13	6	5	6	7	5	12
I:G RATIO	0.9	0.7	0.31	0.4	0.1	0.1	0.1
S.cortisol	Normal	Normal	Normal	Low	Normal	Normal	Normal
Diagnosis	Tyrosenemia	THI*	THI	THI	Sepsis	Sepsis	PHHI*
Outcomes	Expired	Well	Well	Well	Expired	Well	CP

[Table/Fig-3]: Treatment and outcome of neonates with persistent hypoglycaemia.
*THI-Transient Hyperinsulinaemia; PHHI-Persitent Hyperinsulinaemic Hypoglycaemia of Infancy

asymptomatic whereas, three were lethargic and one presented with seizures [Table/Fig-1].

[Table/Fig-2] shows investigation where the I:G ratio ranged from 0.1 to 0.9 and serum cortisol was found to be low in only one neonate.

[Table/Fig-3] shows the various treatment modalities and outcome in the seven neonates. Diazoxide response was seen for the doses ranging 10-20 mg/Kg, and two of them required octreotide, duration of glucose infusion was max 13 days in some neonates. Tyrosenemia was diagnosed in one, two of them were sepsis, three of them Transient Hyperinsulinaemia (THI), and one had Persitent Hyperinsulinaemic Hypoglycaemia of Infancy (PHHI). Two expired, remaining four had good outcome and discharged as well baby. During follow-up at six months, only one had cerebral palsy as sequelae.

DISCUSSION

Hypoglycaemia is found to be most frequently encountered problems in the first 48 hours of life of a newborn and most common biochemical abnormality seen by clinicians managing newborn is the low glucose concentrations.

Definition of hypoglycaemia and screening guidelines in neonatal period still remain controversial. The operational threshold for hypoglycaemia has been defined as that concentration of plasma glucose or whole blood glucose at which clinician has to consider the intervention, based on the evidence available in literature currently [2].

This so called operational threshold value that is currently accepted for defining hypoglycaemia in newborn is blood glucose value of less than 40 mg/dL (plasma glucose less than 45 mg/dL, till we get proper evidence [3].

Recurrent/resistant hypoglycaemia will be considered in an infant in whom despite a GIR of 12 mg/Kg/min, we fail to maintain normal BGL or when stabilisation is not achieved following seven days of therapy. High levels of glucose infusion may be needed in the infants to achieve euglycaemia. Causes of resistant hypoglycaemia include congenital hypopituitarism, adrenal insufficiency, hperinsulinaemic states, galactosaemia, glycogen storage disorders, inborn errors of metabolism like maple syrup urine disease, fatty acid oxidation defect etc., [3].

Clinically, low glucose levels in neonates may not manifest and be totally asymptomatic. However, a smaller proportion of infants with hypoglycaemia can be symptomatic. Hypoglycaemia can be presenting with variable clinical signs and may include stupor, jitteriness, sometimes tremors and apathy, episodes of intermittent apnoeic spells or tachypnoea, weak cry or high pitched cry, limpness and lethargy, occasionally episodes of cyanosis, convulsions, difficulty in feeding and eye rolling some times, episodes of sweating, sudden pallor, hypothermia and cardiac arrest have also been reported in newborns with hypoglycaemia [3] .

Generally, transient forms of hypoglycaemia are corrected within three to seven days of life and usually require glucose infusion equal to normal glucose production rates.

Persistent neonatal hypoglycaemia forms of hypoglycaemia are more protracted and severe than transient forms and require prolonged treatment and at risk of irreversible brain injury [4].

Neonates with persistent hypoglycaemia should be evaluated with serum insulin levels, serum cortisol levels, growth hormone levels, blood ammonia, and blood lactate levels. Urine ketones and reducing substances, urine and sugar amino acidogram, free fatty acid levels, galactose-1-phosphate uridyl transferase levels etc., as per the etiology suspected [3].

Apart from increasing GIR for resistant hypoglycaemia, we can

use certain drugs like hydrocortisone, diazoxide, glucagon and octreotide [3].

In infants with recurrent hypoglycaemia lasting for five or more days, risk of cerebral palsy, development delay and low mental scores at 18 months of age has been shown to be high.

Pathological changes of NHBI include swelling of the neuronal and glial cells, necrosis, gyrus atrophy and white matter demyelination [5]. Neonatal hypoglycaemic brain injury is found to predominantly affect the parieto-occipital regions as evidenced by MRI scans [6].

Glucose is the principal energy source for the neonatal brain and hypoglycaemia is known to cause irreversible neuronal injury when it is recurrent and severe; As first few months of life are the most vulnerable period for developmental disability, which occurs in 25%-50% of children with congenital hyperinsulinism. Early recognition and treatment are crucial for preventing these sequelae [7,8].

CONCLUSION

The evaluation and management of hypoglycaemia in newborn differ in several respects from that in adults. Firstly, persistent hypoglycaemia mostly results from a congenital or genetic defect that regulates secretion of insulin, sometimes deficiency of cortisol and/or growth hormone or defects in the metabolism of glucose, glycogen, and fatty acids. Secondly, it is difficult to identify and distinguish newborn infants with a persistent hypoglycaemia disorder from those with transitional low glucose levels in the initial 48 hours of life. Third, the first few months of life are found to be the most vulnerable period for developmental disability that occurs in 25%-50% of children with congenital hyperinsulinism. Early recognition and treatment are very crucial for preventing these developmental sequelae.

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