Case Report

Transient neonatal diabetes in a very small sick newborn: A case Report

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Abstract

Hyperglycemia in neonatal period is a common metabolic disorder, especially seen in preterm low birth weight and critically ill newborns. The estimated incidence of this condition is around 45%–80%. But Neonatal diabetes mellitus (NDM)is a rare neonatal disease, which has an incidence of approximately 1 in 90,000–160,000 neonates worldwide. Herein we report an extreme preterm, extreme low birth weight, male neonate with transient neonatal diabetes mellitus who was treated with intravenous insulin initially and then subcutaneous insulin Glargine. An adequate glycemia was achieved at 3 weeks of life.

Key words: Transient neonatal diabetes, very small sick newborn

Introduction

Blood glucose supply and metabolism has a significant importance for growth and normal brain development in the fetus and newborn. Abnormality in it can result in hypo or hyperglycemia. Neonatal hyperglycemia is a common metabolic disorder found in NICU Usually seen in preterm low birth weight and critically ill newborns[1]. The estimated incidence of this condition is around 45%–80%[2,3]. But Neonatal diabetes mellitus (NDM) is a rare disease of newborn, with an approximate incidence of 1 in 90,000–160,000 newborns worldwide[4]. Hyperglycemia in neonate is common on 3 to 5th day of birth, but it is unusual for it to persist beyond 10 days. Premature infants are more prone to develop hyperglycemia because they lack adequate insulin secretion from the pancreas and some of them exhibit insulin- resistance[4,5].

NDM can be either transient or permanent. Transient NDM (TNDM) comprises about 50% of all NDM cases; this persists for a median of 12 weeks and usually resolves by 18 months of age. However, about 50% of TNDM cases relapse in late childhood or adolescence. But permanent NDM (PNDM) cases require lifelong medical treatment and the disease does not resolve[4,5,6]. The neonates with NDM are usually born before date, small for gestational age or intrauterine growth retarded and may present with reluctant to feed, signs of dehydration, weight loss, and glucosuria with or without ketoacidosis or ketonuria[1].

Herein we report an extreme preterm, extreme low birth weight, male neonate with transient neonatal diabetes mellitus who presented with respiratory distress immediately after birth and then developed persistent hyperglycemia and glycosuria at 7 days of life. The baby was treated as per NICU protocol. Hyperglycemia was treated with intravenous insulin initially and then subcutaneous insulin Glargine. An adequate glycemia was ensured at 3 weeks of life.

Case Presentation

B/O Nusrat Jahan, a male neonate was delivered by a 26-year-old mother at ad-Din Medical College & Hospital,

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who was extremely preterm (27+2 weeks of gestation), extremely low birth weight, and appropriate for his gestational age. The mother had no prior medical history of systemic sickness and had received appropriate prenatal treatment. Neither consanguinity nor a major medical history of diabetes existed in his family. The newborn was active and let out a spontaneous cry as soon as it was born. His Apgar scores were 8 at 1 minute and 10 at 5 minutes. His measurements at birth were 930 g (3rd–5th percentile), 24 cm (10th–25th percentile), and 31 cm (10th–25th percentile) for weight, length, and head circumference, respectively.

As he exhibited extreme preterm, extreme low birth weight, he was admitted to our neonatal intensive care unit for further evaluation. After several hours of admission, he developed Respiratory distress (grunting, tachypnoea, desaturation, cyanosis). CXR was done showing ground glass shadowing with air bronchogram. We diagnosed the case as respiratory distress syndrome and was treated with respiratory support (NIPPV) and other supportive managements. The initial blood glucose level was 4.2 mmol/ L. Following 3 days baby's clinical condition improved, baby was shifted from NIPPV to LFNC, developed neonatal jaundice and was treated with phototherapy. ECHO revealed a small PDA and was treated accordingly. On day 7 we observed one episode of hyperglycemia (11.3mmol/L). On that day neonate was getting IVF 5% dextrose with electrolytes, GIR was 4.9 mg/kg/min, urine output was 4.2ml/kg/hr and vital signs were normal. We monitored blood glucose 3 hourly and rest of readings were normal. On the following day (day 8) blood glucose level was rising (12- 24 mmol/L). On that day GIR was 6.3mg/kg/min. We have done septic work up, VBG revealed pH 7.26, PCO2 32.4, HCO3 14.3, BE -11.4. We continued treatment with IVF: 5% dextrose with electrolytes, added Injectable antibiotics and gave 2 shots of insulin bolus 0.1 U/kg. Blood glucose level falls in normal range after 2 boluses.

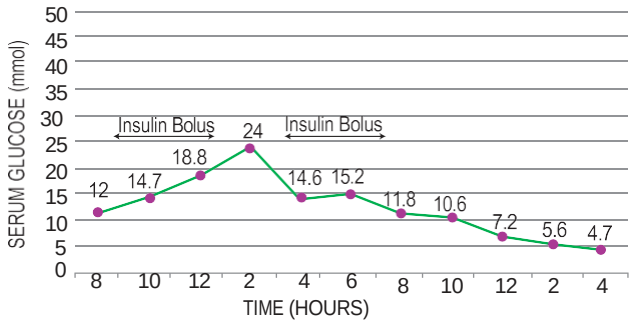

Figure-1: Rising of Blood glucose level

From day 9 the baby developed persistent hyperglycemia (11-22.5 mmol/L). We have rechecked IVF and other medications. GIR was 5.9mg/kg/min. Septic work up revealed nothing significant. So, we started continuous intravenous regular insulin infusion (0.1units/kg/hr) according to hyperglycemia treatment protocol but he remained hyperglycemic for the next several days.

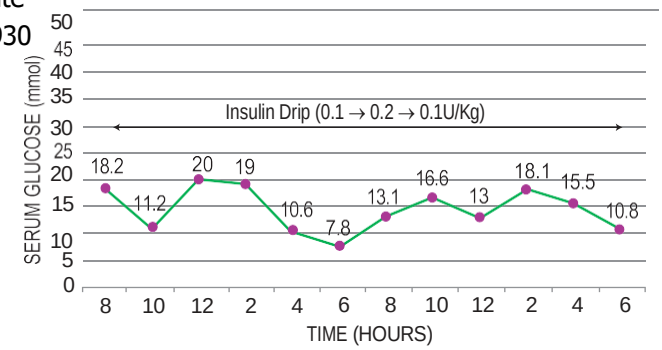

Figure-2: Fluctuation of Blood glucose level

During that period, he developed polyuria and lost 25% of birth wt. We considered the possibility of NDM and scheduled additional laboratory tests. His baseline biochemistry, including serum blood urea nitrogen 15.3 mg/dL, creatinine 0.9 mg/dL, aspartate aminotransferase 38 U/L, alanine aminotransferase 16 U/L and complete blood count reports were within the normal ranges. Urinalysis revealed a 4+ glucose level but no ketones. Moreover, no sign of ketoacidosis was found. Ultrasonography of the whole abdomen revealed no structural abnormalities.

As there was persistent hyperglycemia despite continuous intravenous regular insulin infusion. We decided to stop continuous infusion rather than giving insulin Glargine, a long-acting insulin subcutaneously. After giving 1st shot of insulin Glargine (0.45 U/kg/ dose) baby developed hypoglycemia (1.9 mmol/L) which was treated with 10% dextrose bolus. On the following day we again gave insulin Glargine and repetition of same events occurred.

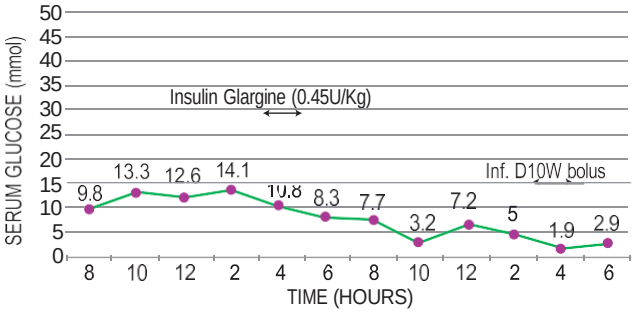

Figure-3: Normalization of Blood glucose level after Insulin Glargine

But from day 18 blood glucose level became in normal range (5.3- 8.4mmol/L). So, we stopped giving insulin.

As the neonate obtained adequate glycemia (5.6-8.9 mmol/L) with expected weight, he was discharged on PMA 39^{+4} weeks with weight: 1300 gm on enteral feedings without any insulin or hypoglycemic treatment.

Discussion

Neonatal hyperglycemia is a common metabolic disorder, especially seen in low birth weight preterm and critically ill newborns[1]. The definition of hyperglycemia is uncertain. For practical management, a BG value of 3.88–8.33 mmol/L (70–150 mg/dl) is considered as a safe range[7]. In PT babies, BG up to 10 mmol/L is commonly observed with parenteral glucose administration. This may not require any treatment and would only need close glucose monitoring. However, BG >10–11.1 mmol/L are of great concern in neonates as this can lead to complications[8]. When a newborn experiences prolonged hyperglycemia that lasts longer than two weeks and necessitates insulin treatment —NDM is diagnosed; typically occurs due to abnormalities in insulin secretion and beta-cell development[9]. Intrauterine growth retardation, volume depletion, severe hyperglycemia, glycosuria, polyuria, ketonuria and ketoacidosis are typical symptoms of NDM. Permanent neonatal diabetes mellitus (PNDM) and transient neonatal diabetes mellitus (TNDM) are the two kinds of neonatal diabetes mellitus[1]. Gene mutations associated with the ATP-sensitive potassium channel are the main cause of PNDM. This subtype requires lifetime treatment and has no period of remission[10]. 50% of NDM instances are TNDM cases. In 90% of cases, TNDM is known to be caused by three mechanisms. The altered expression of genes on chromosome 6 is a component of all the mechanisms. The three methods are as follows: (1) imbalanced duplication of 6q24 on the paternal allele; (2) paternal uniparental disomy of chromosome 6 (UPD6pat); and (3) 6q24 maternal hypomethylation defect[1,10]. The TNDM course varies greatly. Throughout the first few weeks or months of life, permanent resolution takes place. A small percentage of patients may relapse into a permanent form of diabetes mellitus during their childhood or adolescence[1,10]. Insulin and oral sulfonylurea drugs are effective treatments for TNDM, and after a year, the condition spontaneously remits. However, a small percentage of patients experience relapses in adolescence and adulthood[1,10]. Later in life, 50% of patients with 6q24-related TNDM develop permanent diabetes mellitus[1]. Although PNDM is less prevalent than TNDM, therapy for it must be lifelong[10]. Early detection and management of newborn diabetes mellitus are important because proper management of hyperglycemia encourages appropriate weight gain and development. Our patient displayed TNDM; he was born before date, that is a common trait of NDM. His TNDM symptoms could not explained otherwise and Insulin Glargine, a subcutaneous long-acting insulin, proved to be an effective treatment. The only side effect we experienced was acute hypoglycemia.

In conclusion, we present a case of TNDM in a premature newborn who responded well to subcutaneous Insulin Glargine treatment. Numerous studies suggest that Glargine's release pattern— a true "peak-less" insulin— makes it most suited for managing type 1 diabetes in newborns and early infancy, when patients are frequently or continuously fed. Long term close surveillance (until adolescence) is needed with an emphasis on any relapses of diabetes.

References

1. Pun P, Clark R, Wan KW, Peverini R, Merritt TA. Neonatal diabetes mellitus: The impact of molecular diagnosis. Neo Reviews 2010;11:e306-10.
2. Rozance PJ, Hay WW Jr. Neonatal hyperglycemia. NeoReviews 2010;11:e632-38.
3. Binder ND, Raschko PK, Benda GI, Reynolds JW. Insulin infusion with parenteral nutrition in extremely low birth weight infants with hyperglycemia. J Pediatr 1989;114:273-80.
4. Dahl A, Kumar S. Recent advances in neonatal diabetes. Diabetes Metab Syndr Obes 2020;13:355-6.
5. Lemelman MB, Letourneau L, Greeley SA. Neonatal diabetes mellitus: an update on diagnosis and management. Clin Perinatol 2018;45:41-59.
6. Flanagan SE, Patch AM, Mackay DJ, Edghill EL, Gloyn AL, Robinson D, et al. Mutations in ATP-sensitive K+ channel genes cause transient neonatal diabetes and permanent diabetes in childhood or adulthood. Diabetes 2007;56:1930-7.
7. Şimşek DG, Ecevit A, Hatipoğlu N, Çoban A, Arısoy AE, Baş F, et al. Neonatal Hyperglycemia, which threshold value, diagnostic approach and treatment? Turkish neonatal and pediatric endocrinology and diabetes societies consensus report. Turk Pediatri Ars 2018;53:S234-8.
8. Beardsall K, Vanhaesebrouck S,Ogilvy Stuart AL. Prevalence and determinants of hyperglycemia in very low birth weight infants: Cohort analyses of the Nirture study. J Pediatr 2010;157:715 9.
9. Polak M, Cave H. Neonatal diabetes mellitus: a disease linked to multiple mechanisms. Orphanet J Rare Dis. (2007) 2:12. doi: 10.1186/1750-1172-2-12
10. A. Kataria, R. Palliyil Gopi, P. Mally, and B. Shah, —Neonatal diabetes mellitus: current perspective,‖ Research and Reports in Neonatology, vol. 4, pp. 55–64, 2014.