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Systemic Review on Neonatal Diabetes

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ABSTRACT: neonatal diabetes mellitus It is defined by the onset of persistentHypoglycemiawithin the first six months of lifebut may presentupto 12 months of life a general mutation affecting pancreas beta cells or synthesis by secretion of insulin is present in more than 80% of the children with neonatal diabetes. Neonatal testingcan be transient , permanent or be a componentof syndrome. Genetic testing is important as a specific geneticmutation can significantly alter the treatmentand outcome. Patients with mutations of either KCNJ11 Or ABCC8 that encode sub units of the kAtpchannel gene mutation can bemanaged with sulfonyluriaoral therapy whilepatients with other genetic mutations require insulin treatment.

Key words : Neonatal diabetes , Hypoglycemia , KCNJ11, ABCC8 , sulfonyluria.

I. INTRODUCTION :

Neonataldiabetesis highly to be due to an underlying monogenic defect when it occurs under 6 months of age.Early recognition and urgent genetic testing are important for predicting thr clinical course and raising awareness of possible additional features, and in many cases these are essential for guiding appropriate and cost effective treatment. Neonatal diabetes can be either transient or permanent. Depending on the specific genetic mutation causing the condition.

Neonatal diabetes is a very rare condition. It is defined as hyperglycemia that requires insulin treatment, occurs during the first month of life , and last s more than two weeks.

Epidemiology : occuringinaroundone in 300,000 to 1 in 400,000 births . Out of the two types of neonatal diabtes that transient type is slightly more common effect in 50 – 60% cases of neonatal diabetes.

neonatal diabetes to the heads of all 230 pediatric departments and clinics in the former west Germany. About 60 % responded. They had seen 13 infants with neonatal diabetes who were born between 1977&1991& provided data in all them.
Incidents of neonatal diabetes mellitus is through to range from 1: 90,000to 1:160, 000lives births.
Neonatal diabetes is more common to develop in the first 3-5 days of life and resolve within 2-3 days of onset but can persist upto 10 days.

Types : transient diabetes & permanent diabetes
Transient neonatal diabetes is so called because it usually disappears within a year of birth but can coma back again typically during adolescent.
Permanent neonatal diabetes once diagnosed stays for the rest of life.

Complications :
Developmental delays such as muscle weakness and learning disabilities.
Diabetic ketoacedosis
Low birth weight Muscle weakness Epilepsy
Macroglossia – a larger a than normal tongue

Diagnosis : diagnosis is needs to be distinguished from autoimmune type 1 diabetes most patients diagnosed with diabetes after 6 months of age, and especially after 12 months of age will have autoimmune type 1 diabetes. 42 . 6 weeks (37.4-50.4) and 87.5% .
Most of these patients will test positive for at least one of the specific diabetes- related.
Persistent hyperglycemia, insulin deficiency are common features in making the diagnosis. Lack of immune markers for type 1 diabetes may be decieving for late onset presentation. The most important accept of the confirming the diagnosis is molecukar genetic testing. Some examples of the known mutations causing neonatal diabetes are : Glucokinase (GCK) , potassium channel (kCNJ11), ATP- binding cassette transporter sub family c

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member 8 (ABCC8) , Insulin (INS), Insulin promoter factor 1(IPF1), pancreas transcription factor 1 sub unit alpha (IPF1 A) , Hepatocyte nuclear factor 1 homeobox b (HNF1 B) , Fork head box (FOXP3) , Zinc finger 14 57(ZFP57).

Genetic testing : Genetic testing may play a important role in transfeeing therapy from insulin two sulfonyluriasince patients with certain mutations in the pancreatic ATP sensitive k + proteins like the sulfonyluria receptor one (SUR 1) and in ward rectifier k + channel may respond well to sulfonyluriatherapy (10- 13) instead of insulin .
it should strongly consideredconsidered for who have hyperglycemia . Most patients with mutations in KCNJ11and ABCC8 are responsible to sulfonyluria therapy.

Symptoms : shakiness , persistent thirst, Blue color of lips & Low body temperature ,
Floopy muscle tone ,Unable to feed , frequent urination, rapid breethinhbreething, dehydration. Lack of insulin,

Treatment : sulfonyluria therapy,
Metformin, intravenous dextrose.

Management of acute hyperglycemia : neonates with diabetes mellitus can present with significant hyperglycemia, electrolyte disturbance, dehydration and ketoacedosis. The initial management fluid resuscitation with isotonic electrolyte solutions, to treat the dehydration that results from osmotic diuresis. The appropriate fluid therapy is calculated on an individual bases and administrated slowly over a period of 24 - 48 hours to avoid cerebral edema that results from too rapid correction. Neonates & infants presenting with diabetic ketoacedosis should be managed in an intensive care unit, under the supervision of a pediatric endocrinologist, with frequent monitoring of blood glucose, electrolytes, and neurological status. Neonatal diabetic ketoacedosis is managed according to same principles guiding the therapy for the children and adolescent with diabetes mellitus.

Insulin therapy : It is crucial to obtain satisfactory weight gain and growth, especially in babies with IUGR, but the treatment of NDM is complex due to the paucit of subcutaneous fat and the need for the low doses of insulin. Insulin is administrates as on intravenous infusion, intermittent subcutaneous therapy, or as continues subcutaneous insulin infusion. It is often delivered initially by an intravenous infusion as this enables better titration of doses based on the blood glucose levels. After the initial treatment of the diabetic ketoacedosis, the intravenous infusion of regular insulin should be continued in infants with persistent hyperglycemia, despite reductions in glucose infusion rates, and in those with persistent glucose excursions, while others are transitioned to an appropriate regimen subcutaneous insulin. Finding a suitable regimen is usually not an easy task as few data are available on the most appropriate insulin preparations for youth infants. Patients are transitioned to injection of badal insulin or a combination basal / bolus insulin regimen.

Continuous glucose monitoring sensor : A continues glucose monitoring sensor (CGMS) consist of an electrode sensor that catalyzes glucose oxidation, generating an electric current that is recorded by a monitor. The CGMS is inserted subcutaneously and allows continues measurement of glucose in the insterstetial fluid. The sensor is especially usefull in preterm babies and in small for gestational babies who are at risk for wide excertions in blood glucose levels. The CGMS is programmed to give alerts when glucose levels are either lower or higher than acceptabke limits, and this feature enables the caregiver to respond promptly. The prompt care is clinically important as both hypoglycemia and hyperglycemia are associated with acute neuro physiological abnormalities and later neuro developmental impairment. However, despite its proosed advantages for continues blood glucose measure ment, there limited experience with its use, or accuracy in new borns.

Diet :
All new borns with NDM should receive a high caloric diet along with an adequate amount of insulin to promote satisfactory weight gain and growth. Any reduction of glucose and calories to improve hyperglycemia in these babies significantly effects their weight gain. A high caloric diet can be achieved with the help of the dietician, who can assist in calculating the calories in determining the carbohydrate content of breastmilk Or formula. The carbohydrate content of human milk and standard infant formula ate similar (approximately 70 – 75 g/L), and the carbohydrate content of human milk fortifier is negligable (

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<0.1g/packet) the dietary management requires a team approach to address the caloric needs ans carbohydrate counting.

Follow up : Frequent monitoring of blood glucose and the maintenance of bolld glucose in the appropriate range is essential to prevent accute and long term complications. The HbA should be monitored every three months and the level maintained between 7.5% 8.5% all patients with TNDM need -long -term follow up due to the potential for recurrence of diabtis in later life . If there is reccurence, the treatment various between diet, oral hypoglycemia agents, a d insulin. Patients need annual screening for the chronic complications of diabetes, including urinanalysis for micro albumin uria and opthamologicexamination for retinopathy.

II. DISCUSSION :

The combination of neonatal diabetes mellitus with phosphoribosyl – ATP pyrophosphatase hyperactivity leads to gout and urolithiasis in early adulthood. The reports on children with this disorder from four families mention prenatal growth retardation, motor and mental retardation, ataxia, hypotonia, hearing impairment, and disturbed speech development, but not diabetes.

Forty – seven of the patients had neonatal diabetes with hyperglycemiarequiring insulin therapy that began during the first month of life, and 10 additional infants had hyperglycemia that began between the 42nd& 85 th days of life. We excluded all infants with transient hyperglycemia of less than two weeks duration that could be attributed to such factors asmay cause the body to produce chemicals called ketones, resulting in a potentially life – threatening condition called diabetes ketoacedosis.cerebralhemorrhage, or meningitis and encephalitis.

Among infants with neonatal diabetes, some have permanent diabetes, other have remission of their diabetes and later recurrence, and still others have apparently permanent remission. Since diabetes may recur after a prolonged period, however, one should hesitate to consider a remission permanent, and neonatal diabetes should probably be considered as a prediabeticstate. The two brothers described here are classified as having permanent diabtes, although each had remissions of their hyperglycemia.

Neonatal diabetes has some similarities to insulin – dependent diabetes as it occurs in older children : heredity plays an important part, and HLA haplotypes typical for insulin – dependent diabetes may be present. Two brothers (patients 50 and 51) had HLA – DR3 and DR4, and other patients had HLA- DR3 (patients 31, 33 &38) or DR4 (patients 26 and 27).

At least half the patients did not appear to have the usual type of insulin – dependent diabetes that simply developed unusually early in life. Insulin – dependent diabetes is thought to be an autoimmune disease with a genetic predisposition, in which some causative factor initiates an autoimmune process that leads to destruction of the beta cells and insulin deficiency. It is unlikely that this process would not only begin but also become well – advanced in utero. Since only one mother had insulin – dependent diabetes herself, transplacentalpassage of maternal anti – islet – cell antobodies was probably not a factor affecting batao cell function in most infants. Finally, permanent or prolonged remissions are very unusual in insulin – dependent diabetes but quit frequent in neonatal diabets. Many infants with neonatal diabetes were small for their gestatiknal ages, and some were extremely small. One may speculate that intrauterine growth retardation may cause neonatal diabetes, and low birth weight may be associated with decreased beta – cell function in adults. The possible importance of intrauterine growth retardation is supported by the occurrence of neonatal diabetes in one neonate who had atwin brother whose birth weight was normal and who was diabetic. The infants with onset of diabetic in the second and third month of life for whom we obtained data usually had normal birth weights (and permanent diabetes).

The results indicates that among newborn infants with diabtes mellitus, the diabetes will be transient in about 50 percent of cases. The presence of HLA - DR3 & DR4 increases the likelihiid of permanent diabetes, as does onset after the age of one month. The presence of the Wolcott – Rallison syndrome or phosphoribosyl ATP pyrophosphatase hyperactivity appears to be associated with a poor prognosis with respect to remission of diabetic as well as to longevity and the occurrence of additional problems. Nevertheless, the overall prognosis for general health and normal intellectual development is usually good.

III. CONCLUSION :

Neonatal diabetes mellitus is causing by a single mutation. These patients will mist often present within the first six months of life, but less

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commonly may present upto 12 months of life. Early clarification of the molecular etiology by genetic testing is paramount. Patients with channel mutations such as KCNJ11 and ABCC 8 , can be transitiined to sulfonyluria agents, allowing for simplified administration, decreased treatment costs and potential neurodevelopmental improvements. Genetic testing may also guide longitudinal monitoring for other associated problems in forms with syndromic features, as well as for screening of family members. Patients with 6q24 have transient hyperglycemia in infants with onset of diabetic in adolescents. It is important distinguish monogenic neonatal diabetes mellitus from other causes of hyperglycemia in the newborn. Insulin – dependent hyperglycemiathat persists longer than a weak to ten days, should raise suspecion for an underlying monogenic cause of diabetes and prompt genetic testing.

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