GALACTOSAEMIA - PRESENTATION, DIAGNOSIS AND MANAGEMENT

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Galactosaemia is a rare autosomal recessive metabolic disorder. It presents in early life with hypoglycaemia and encephalopathy or progressive jaundice followed by liver failure. Cataract may be visible on naked eye examination. Diagnosis is highly suggested by detecting reducing substances in urine without glycosuria in an infant with hepatic dysfunction. Dietary therapy by elimination of galactose is the mainstay of treatment. The outcome for treated galactosaemia is not yet optimal. This paper reports the experience of presentation, diagnosing and management of galactosaemia at The Childrens Hospital & the Institute of Child Health, Lahore. This paper presents a prospective, observational study from January 1999 to April, 2004. Diagnosis was made on the criteria including (a) clinical presentation of a neonate with hepatic dysfunction, (b) strongly positive urine reducing substances with the absence of glycosuria as determined by negative Clinistix test and (c) rapid clinical improvement on elimination of galactose from the diet of infants. Diagnosis of galactosaemia was made in 18 infants over the study period. Their age at presentation ranged from 35 days – 9 months (median 10 weeks). There were 12 males and 6 females (M: F ratio 2:1). Most common mode of presentation was fulminant hepatic failure (FHF). Cataract was present in the majority of patients. Laboratory values showed raised bilirubin and universal coagulopathy. Fourteen patients responded to galactose elimination and showed initial dramatic improvement in clinical and lab parameters. Four patients (22 %) died. Galactosemia is not uncommon in our community; diagnosis needs to be suspected in sick neonates and infants with severe hepatic dysfunction. Early galactose elimination from diet leads to dramatic clinical improvement.

INTRODUCTION

Galactosaemia is a rare autosomal recessive metabolic disorder due to galactose-1-phosphate uridyltransferase (GLUT) deficiency1. Nation-wide newborn screening for galactosaemia is performed in many countries[2,3]. It presents in early life with hypoglycaemia and encephalo-pathy or progressive jaundice and liver failure[4-7]. Cataract may be visible on naked eye or slit lamp examination. These infants are also prone to E. coli septicaemia. Diagnosis is highly suggested by finding reducing substances in urine without glycosuria in an infant with hepatic dysfunction. It can be confirmed by finding reduced GLUT enzyme activity in erythrocytes if available[8].

Dietary therapy by life long elimination of galactose from diet is the mainstay of treatment in galactosaemia[9,10]. The outcome for treated galactosaemia is not yet optimal. It has good prognosis, if detected in neonatal period or early infancy. However, there are long-term complications of the disease such as speech disorders, mental retardation, ataxia and in females hypergonadotropic hypogonadism[11]. This paper reports the experience of presentation, diagnosis and management of galactosaemia at a tertiary referral centre.

PATIENTS & METHODS

This is a prospective, observational study including all cases, in whom diagnosis of galactosaemia was made, admitted to the Department of Paediatric Gastroenterology-Hepatology, the Children's Hospital & the

Institute of Child Health, Lahore. The study spans the time period from January 1999 to April, 2004. Diagnosis was made on the following three criteria. 1. Clinical presentation of a neonate with hepatic dysfunction i.e. signs of liver failure, early onset of ascities and cataracts. 2. Strongly positive urine reducing substances with absence of glycosuria as determined by negative Clinistix test, which is specific for glucose. 3. Rapid clinical improvement on elimination of Galactose from the diet of infant. Facilities for the confirmatory erythrocyte GLUT enzyme assay are not available in this country. A note was made of age at presentation, clinical features, and outcome of dietary therapy.

RESULTS

Diagnosis of galactosaemia was made in 18 infants over the study period. Their age at presentation ranged from 35 days – 9 months (median 2 ½ months)**.** There were 12 males and 6 females (M: F ratio 2:1). Most common mode of presentation was fulminant hepatic failure (FHF) (Table 1). Although cataracts were present in the majority of patients, they were not the reason for referral. Laboratory values (Table 2) showed raised bilirubin and universal coagulopathy. Fourteen patients responded to galactose elimination and showed dramatic improvement in clinical and laboratory parameters. Four patients (22 %) died due to FHF. Survivors are being followed up for their developmental assessment to determine the long term cognitive and hepatic impairment.

Table 1: Clinical Presentation of 18 cases of galactosaemia

Symptom / Sign	No of cases
Signs of fulminant hepatic failure progressive jaundice & early ascities	16
Septicaemia with jaundice	2
Cataract	16
Ascities alone	1

Table 2: Laboratory tests in 18 cases of galactosaemia

Test	Result
Serum bilirubin	ranged between 10-28 mg /dl
Transaminases	raised between 5-10 times
Coagulopathy	Universal 100% had PT >10 seconds control
Urinary reducing sugars	strongly positive in all

DISCUSSION

We don't know the true incidence of galactosaemia in our country but high incidence of consanguineous marriages in our community does make it 'not an uncommon' disorder. Although newborn screening for galactosaemia is practiced in many parts of the developed world[1-3], this approach has obvious financial and logistic restraints and yield from such testing is not very high. However galactosaemia needs to be suspected strongly in sick neonates and infants with jaundice, early ascities and other signs of hepatic failure[4] like deranged coagulation parameters, hypoglycaemia and low albumin. Before these sick neonates are put "nothing by mouth" it is imperative that a urine sample is collected and tested for reducing sugars. It has been found by experience that this is best done expeditiously by inserting (and removing) a sterile urinary catheter for urine specimen collection.

Although there is an urgent need for a 'central metabolic laboratory' in our country, currently our best way of making a diagnosis is showing non-glucose reducing sugar in urine of a sick neonate with hepatic dysfunction and its rapid reversal with galactose free feeds (e.g. Soya based milk formulae). Early diagnosis is imperative to prevent fatal liver damage and affects eyes. Death of 4 patients from fulminant hepatic failure is largely the result of delayed referral in our setup.

There is evidence that long-term outcome depends upon particular genetic alleles rather than strict dietetic control[11]. This series does not have a follow-up long enough to answer this question especially in the absence of genetic analysis. However these infants are being followed up carefully over time to see the incidence of mental retardation and other neurological sequelae.

CONCLUSION

In conclusion, galactosaemia is not uncommon in our community. Diagnosis needs to be suspected in sick neonates and infants with severe hepatic dysfunction. Early galactose elimination from diet leads to dramatic clinical improvement.

ACKNOWLEDGEMENTS

I am thankful to the Dean of the Children Hospital for his patronage. I am also thank my house staff for proving me all the necessary help during this study.

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