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Role of Some Biochemical Changes in Congenital Cataract

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This study was done on 25 infants with congenital cataract aging 3-18 months and their parents. Another group of 14 infants of same age with no ophthalmic and/or congenital diseases were included as control group with their parents. All cases and their parents were examined clinically and ophthalmologically. Levels of galactose, serum sodium and potassium were determined. A significant elevation in blood galactose, in infants with congenital cataract as compared with control group, while no significant changes in blood galactose levels of their parents as compared with parents of control group. Significant elevation of serum sodium in infants with congenital cataract as compared with control group, while no significant change in serum sodium levels of their parents as compared with parents of control group. Significant decrease of serum potassium in infants with congenital cataract as compared with control group, while no significant change in serum potassium levels of their parents as compared with parents of control group. Early valuable genetic counseling, with estimation of galactose, sodium and potassium are recommended. Infants with congenital cataract had different etiological causes, so not all cases need restriction of milk and milk products. Parental estimation of galactose, sodium and potassium had no value.

Key words: Child health, congenital cataract, biochemistry, genetics

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INTRODUCTION

Cataract is the largest preventable cause of visual loss in childhood (Novelli and Reichardt, 2000). Prevention of visual impairment due to congenital and infantile cataract is an important component of the World Health Organization's international program for the elimination of avoidable blindness by 2020 (Thylefors, 1998). National Center for Environmental Health (2004), stated that newborn screening programs often provide services beyond the early screening tests; they also provide follow-up testing of screen-positive infants, confirmation and diagnosis, short- and long-term treatment, education and evaluation of the process (Pass *et al.*, 2000).

Incidence of congenital cataracts is relatively high, as it is about 0.4% of newborns (Maitchouk, 1982), while the incidence of congenital cataract due to galactosemia is 1: 50000 (Garibaldi *et al.*, 1983). It is still responsible for approximately one tenth of childhood blindness in the world (Foster and Gilbert, 1997) Pediatric cataracts account for an estimated 15-20% of childhood blindness in industrialized countries. (Maclean, 1987; Philips *et al.*, 1987) it may occur in any of the major congenital infection syndromes as Toxoplasmosis, Rubella, Cytomegalovirus, Herpes and others such as syphilis (TORCH infections) (Keith, 1991). Congenital or infantile cataract is associated with inborn metabolic anomalies such as galactosaemia (Kalekar *et al.*, 1956; Gitzelman, 1967) and mannosidosis (Aguirre *et al.*, 1986). Galactosaemia due to galactose-1-phosphate uridyl transferase (Kalckar *et al.*, 1956) or galactokinase deficiency has been well documented by Levy *et al.* (1972), Gitzelman (1967) and Murphree (1965).

Galactosemia is a hereditary condition characterized by galactosemia, galactosuria and cataract without mental deficiency or aminoaciduria. Any deficiency of one of the possible enzymes involved in the metabolism of galactose i.e., galactokinase uridyltransferase, galactose-4-epimerase, galactose-pyrophosphorylase may lead to congenital cataract through the accumulation of galactitol in the lens (Segal and Berry, 1995).

Some disorders can have devastating and irreversible outcomes if not diagnosed early and treated promptly. Newborn screening is a vital step in early recognition and treatment (National center for Environmental Health, 2004).

The aim of this study was to assess the levels of blood galactose, serum sodium and potassium in children with congenital cataract and their parents, in order to find a simple screening biochemical test for early detection of congenital cataract.

MATERIALS AND METHODS

Subjects: This study was carried out on 25 infants of both sexes, aged 3-18 months suffering from congenital cataract from those attending the inpatient clinic of Research Institute of Ophthalmology, over a period of one year and seven months (March 2002 to July 2003) and their parents. A group of 14 children with the same ages and sexes was included as control group and their parents. Complete clinical history and examination, with full family history as well as ophthalmological examination were done for every case.

Biochemical studies: Galactose levels was assessed by the method of Bergmeyer (1975). Estimation of serum sodium and potassium by flam photometer as described by Eart *et al.* (1964), was also done.

Statistical studies: All data obtained was statistically analysed by using student t-test according to Hill (1979).

RESULTS

Regarding the clinical, family history and examination, it was found that 14 cases were infants of parents with positive consanguinity (first degree), while 15 cases had previous similar congenital cataract in their families. Other combined congenital malformations such as bone deformities, facial dysmorphism and hepatosplenomegaly were found in 9 cases, also we found that 2 cases were diagnosed clinically as Marfan's syndrome as shown in Table 1.

Highly significant increase in blood galactose and serum sodium levels among infants with congenital cataract ($4.325 \text{ mg}/100 \text{ mL} \pm 0.325$ and $156.592 \text{ m mol L}^{-1} \pm 1.27$), respectively, as compared with control group ($1.65 \text{ mg}/100 \text{ mL} \pm 0.123$ and $141.4 \text{ m mol L}^{-1} \pm 0.753$). While a significant decrease in levels of serum potassium among infants with congenital cataract ($3.337 \text{ m mol L}^{-1} \pm 0.049$), as compared with control group ($4.591 \text{ m mol L}^{-1} \pm 0.119$), as shown in Table 2.

Table 1: Different clinical findings among infants with congenital cataract

Different clinical findings	Infants with congenital cataract (25-Children)
Positive consanguinity	14 (56%)
Similar condition	15 (60%)
H.S.M	2 (8%)
Bone deformity	2 (8%)
Facial dysmorphism	5 (20%)
Marfan's syndrome	2 (8%)

Table 2: Biochemical study among infants with congenital cataract, as compared with control group

Groups	Control group (14-Cases)			Infants with congenital cataract 25- Cases)			
	Range	Mean	±SE	Range	Mean	±SE	p-value
Blood galactose (mg/100 mL)	1.1-3.13	1.65	0.123	3.2-5.89	4.325	0.325	0.001***
Serum sodium (m mol L ⁻¹)	139-146	141.4	0.753	148-165	156.592	1.27	0.002***
Serum potassium (m mol L ⁻¹)	4.1-5.5	4.591	0.119	3-3.9	3.337	0.049	0.03*

Table 3: Biochemical changes among parents of infants with congenital cataract as compared with parents of control group

Variables	Fathers of		Mothers of	
	Control group (14-Father)	Infants with cong. cataract (25-Father)	Control group (14-Mother)	Infants with cong. Cataract (25-Mother)
Blood Galactose (mg 100 mL)	2.366±0.186	2.5±0.113	2.354±0.178	2.425±0.127
Serum Sodium (m mol L ⁻¹)	139±0.424	138.6±0.378	138.33±0.627	139.22±0.324
Serum Potassium (m mol L ⁻¹)	4.083±0.099	3.978±0.06	3.958±0.122	3.94±0.056

No significant changes in the levels of blood galactose, serum sodium and serum potassium of both fathers and mothers of infants with congenital cataract, as compared with fathers and mothers of infants of control group, as shown in Table 3.

DISCUSSION

The goal of newborn screening programs is to detect diseases early, preferably before the onset of symptoms, as early detection of these disorders before irreversible organ damage occurs may lead to more effective treatment and more favorable outcomes. (American Academy of pediatrics, 2000). From this point of view our present study was done in order to find a simple screening biochemical test for early detection of congenital cataract.

Congenital cataracts are those which become apparent anywhere from birth to within the first six months of life, (Segal and Berry, 1995). In this study it was found that ages of apparent cases ranged between 3 up to 18 months. These cataracts showed many different patterns. The underlying or associated factors in infants with congenital and infantile cataract in this study are diverse. This complex pattern, including the considerable differences between bilateral and unilateral disease, has implications for further etiological research.

Majority of cases (60%) had previous similar condition in their families and (56%), showed positive consanguinity, also 2 cases were diagnosed clinically as Marfan's syndrome, all of these findings means that genetic causes and factors had a great role in the etiology of congenital cataract and this is accepted with Moore (2004), who reported that genetic causes account for approximately 30% of congenital cataracts and approximately 50% of bilateral cases. Lower incidence (16%) of cases in this study were found to be due to prenatal rubella infection, this low incidence is accepted with Maldonado (2004) who reported that the incidence of congenital and neonatal varicella and of congenital rubella has been lowered due to vaccination.

Other different congenital malformations such as bone deformities, facial dysmorphism and hepatosplenomegaly were found especially among those with congenital rubella affection and this is also accepted with Maldonado (2004) who reported that transient early clinical manifestations of congenital rubella include generalized lymphadenopathy, hepatosplenomegaly (HSM), intrauterine growth restriction, hepatitis, jaundice, thrombocytopenic purpura, with petechiae and "blueberry muffin" lesions. But persistence of some of these symptoms (HSM) till this age is not accepted with Maldonado (2004) as he reported that these transient manifestations resolve in days or weeks usually without long-term sequelae. So this study offers valuable genetic counseling and prenatal detection of viruses.

A significant increase in serum sodium and a significant low levels of serum potassium in infants suffering from congenital cataract reflects what happen in the lens, which is accepted with Unakar and Tsui (1983) they reported that there is a reduction in cation pump efficacy to 50% of normal, but the failure to maintain and extrude sodium is of a much greater magnitude. This condition probably results from a failure in membrane impermeability since now there is even a loss of dulcital from lens, a long with more glutathione. There is a further loss in the capacity to generate ATP and to synthesize proteins. The net loss of potassium and protein from the lens is overcompensated for by an increase in sodium chloride with the result even more water is drawn in osmotically to cause a second stage of marked swelling of the lens.

This is not found among their parents as there was no significant changes in galactose, serum sodium and potassium and this indicated that parents of infants with congenital cataract could not suffering from galactosemia and the defect in galactose may be of genetic origin.

In cases with galactosemic cataract, galactose form lactose accumulating in their blood will cause cirrhosis of liver and pancreatitis, so infants should avoid milk and

milk products, but the children with congenital cataract due to GAG fragments and xylose can take milk without restriction. Thus, this finding has implications in community ophthalmology with a valuable message for the public.

Under galactosemic conditions, aldose reductase activity has been reported to increase while sorbitol dehydrogenase activity is decreased (Kador, 1988). This can lead to an accumulation of the intermediate sugar alcohol, galactitol. Abnormal accumulation of intercellular galactitol has been linked to the onset of a number of diabetic complications. In lens epithelium and fiber cells, the abnormal accumulation of galactitol results in an intracellular increase of fluid and lens swelling which in turn leads to increased membrane permeability and subsequent biochemical changes that are associated with cataract formation (Kinoshita, 1974). In addition, to cataract formation the accumulation of galactitol has been linked to the onset of a number of complications associated with diabetes. These include diabetic neuropathy, nephropathy, ocular complications or retinopathy and keratopathy (Kador, 1994). In the present study, a highly significant increase in blood galactose of infants suffering from congenital cataract while no significant changes in blood galactose levels in both fathers and mothers of those infants has been found. This explains sugar cataract formations in galactosemia occurs faster and is more severe. This is because galactitol accumulation in the lens is faster and to a greater extent than sorbitol since galactose is a better substrate for aldose reductase than glucose and because galactitol is not further metabolized by sorbitol dehydrogenase.

This indicates that the activity of galactokinase and that of erythrocyte galactose-1-phosphate uridyl transferase are low in congenital cataract children. (Veca Pacheco *et al.*, 1990).

From the previous findings in the present study, it may be concluded that complete prenatal history and examination for mothers going to be pregnant as well as early clinical and biochemical evaluation for delivered infants especially for sodium, potassium and galactose are of great value for prevention of congenital cataracts and for the decision of continuation of milk consumption or not in order to prevent further complications and this is agreed with Del Monte (2004), in his protocol for evaluation of the pediatric cataract patient. He stressed the importance of family history and systemic history and examination, as well as querying about postnatal trauma. and he recommended obtaining historical information and/or examination on at least 3 generations of the child's family. Key points requiring attention during ophthalmologic examination include measurement of the

corneal diameter and assessment for associated ocular abnormalities and that systemic evaluation should include evaluation for genetic and metabolic disease, when indicated and can usually be done by a general pediatrician, though occasionally requires genetic and/or neurologic consultation. Since congenital and unilateral cataracts are not generally associated with metabolic disease, but on the other hand our findings is not agreed with him when he reviewed that laboratory systemic evaluation is generally unnecessary unless other abnormalities are noted.

CONCLUSIONS AND RECOMMENDATIONS

Early valuable genetic counseling, estimation of galactose, sodium and potassium are recommended when congenital cataract is expected. Infants with congenital cataract had different etiological causes, so not all cases need restriction of milk and milk products. Parental estimation of galactose, sodium and potassium are of no diagnostic values.

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