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Original Article

ASSESSMENT OF SERUM LACTATE AND CREATININE KINASE TO EVALUATE MITOCHONDRIAL DYSFUNCTION IN AUTISTIC CHILDREN

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Abstract:

Background: *Mitochondrial dysfunction and autistic spectrum disorders (ASDs) are closely related with each other. It has also been mitochondrial dysfunction causes impairment in cellular function which may lead to lack of social communications, language deficits and abnormal energy metabolism in autistic spectrum disorder. These are associated with laboratory evidence of lowered mitochondrial function.*

Objective: *To observe the mitochondrial dysfunction and assess serum lactate and CK to in children with autistic spectrum disorder.*

Methods: *This case-control study was conducted in the Department of Physiology of Bangladesh Medical University (BMU), Shahbag, Dhaka from January, 2013 to December, 2013. For this study a total number of 100 male children with age range 3-8 years were randomly selected, among which 50 were normal children and 50 were diagnosed autistic children. The autistic children were selected from the Parent's Forum, Directorate Generals of Health Service (DOHS), Mohakhali, Dhaka and normal children were selected from some normal school. Serum lactate and creatine kinase (CK) were estimated in all children by standard laboratory method. For statistical analysis independent sample't' test were done as applicable.*

Result: *The mean of both the measured biochemical parameters were found significantly higher ($p<0.001$) in autistic spectrum disorder children. In addition, elevated levels of serum lactate and CK were found in 94% and 32% of autistic children respectively.*

Conclusion: *The result of this study revealed that mitochondrial dysfunction may occur in children with autistic spectrum disorder. The severity of the autistic spectrum disorder is directly related to the biochemical abnormality for mitochondrial dysfunction.*

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Keywords:
ASD, Mitochondrial dysfunction, Lactate, Creatine kinase

Introduction

Autism is a neurodevelopmental disorder which is associated with altered communication of a person. It usually appears within first three years of life.[1] Autism is a generalized term for a group of complex brain disorder having feature of impaired social interaction, verbal and non-verbal communication, repetitive and restricted behavior.[2] There is no boundary for these disorders occurrence, these affect all races, class, religion in all country.[3] Autism can occur due to dysfunction of mitochondria and abnormal brain bioenergetics.[4] Autistic spectrum disorders manifest disruption in multiple high energy organ system like central nervous system, muscular and gastrointestinal systems due to dysfunction of mitochondrial which lead to cellular function impairment.[5] A recent study

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revealed that 80% children with autistic spectrum disorder may have mitochondrial dysfunction.[6] Altered clinical, biochemical or neuropathological evidence of mitochondrial function can be associated with autism spectrum disorders and recent studies regarded mitochondrial disorders as a common metabolic disease in autistic children.[7] Classical mitochondrial diseases usually caused by genetic or respiratory pathway abnormalities. [8] Mitochondrial activity can be impaired by genetic mutation, cerebral folate deficiency, vitamin B6 or iron deficiency and also certain environmental toxin such as pesticides or heavy metals chemicals reduces mitochondrial activity.[9,10] Mitochondrial disorder is primary which may be due to direct genetic involvement that impairs ATP production and secondary which involved in metabolic abnormalities that impair ATP production ability of mitochondria.[11,12] In mitochondrial dysfunction excess ROS are produced and cells are more vulnerable to oxidative stress and damage from mitochondrial ROS.[13] Brain has high rate of oxygen consumption which lead to generation of ROS. Brain is very vulnerable to oxidative damage because of relatively low levels of antioxidants and antioxidant enzymes. In mitochondrial dysfunction reactive oxygen species level increase along with decrease energy level. [14] Mitochondrial disorder leads to impairment in neuronal function, imbalance in excitatory- inhibitory neurotransmitter and reduce neurotransmitter release in GABAnergic (gamma amino butyric acid) interneurons that have high firing rates and the programming of neurotransmitter also affected leading to long-term behavioral effects like autism. [15,16] The mitochondrial disorders are based on clinical, biochemical, molecular and histological findings. Biochemical parameters for mitochondrial dysfunction include increased serum lactate and creatine kinase (CK).[5,6] Several studies reported abnormal level of serum lactate and CK in autistic children.[1,17-23]

Autistic spectrum disorder children with mitochondrial dysfunction show impaired TCA cycle due to some enzyme deficiency, abnormal nutrients metabolism or nutritional deficiency. Impaired TCA cycle stops aerobic respiration which initiates anaerobic respiration causing increased level of lactate.[17]

In mitochondrial dysfunction decrease cellular ATP level causes impairment in Na+-K+ ATPase pump and cell volume cannot be maintained. It leads to loss of cellular integrity of certain organ such as muscle, brain and liver. Thus, creatine kinase level increase. [18,19,24]

In USA, serum lactate and CK found increased in 76% and 28% of autistic children compared to normal children. [24] Some researchers showed that serum lactate level increased in 35% of autistic children.[1] Again, another study found elevated plasma lactate level in 17% of autistic children.[25] Similarly, in 76.7% autistic children increased serum lactate levels were reported in another study.[20]

Methods

This case control study was conducted in the Department of Physiology of Bangladesh Medical University (BMU), Shahbag, Dhaka from January, to December, 2013. Total 100 male children with age range 3-8 years participated in this study. Fifty autistic children diagnosed by psychiatrist according to Childhood Autism Rating Scale (CARS)[26] taken from the Parent's Forum, Directorate Generals of Health Service (DOHS), Mohakhali, Dhaka and fifty control children was selected from some normal school. After selection of the subject, thorough information was given to their parents about the objective and study procedure. Their parents were encouraged for voluntary participation of their children. When their parents were agreed for participation then an informed written consent was obtained from their parents. The protocol of this study was approved by the Institutional Review Board of BMU. Children with epilepsy, turner syndrome, down syndrome and any kind of medication were excluded from this study. The parents of all subjects were requested to attend the Department of Physiology of BMU, Dhaka at 9:00 AM for examination of their children. Detail personal, medical, family, socioeconomic and dietary histories of the children were recorded in a data schedule. Thorough physical examinations of the subjects were done. Anthropometric measurement including height and weight was taken and BMI was calculated. Then under aseptic precaution, 5 ml of venous blood were collected from ante-cubital vein from each subject of both groups for estimation of biochemical test. Serum lactate level was measured in the laboratory of the Department of Biochemistry, BIRDEM General Hospital by colorimetric method. Serum creatine kinase (CK) level was measured in the laboratory of the Department of Biochemistry, BMU by auto analyzer using kit from IFCC (International Federal Clinical Chemistry). Data were expressed as mean + SE and also in percentage. Statistical analysis was done by

using SPSS for windows version 16. Independent samples't' test was used as the tests of significance as applicable. P value <0.05 was accepted as significant.

Results

All the subjects of this study were age and BMI matched (Figure 1).

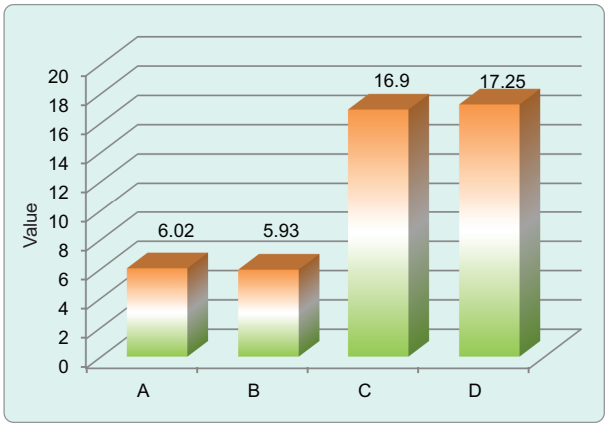

Figure 1: *Mean Age (years) and Body mass index (BMI) (kg/m2) of study subjects.*

In this study mean values of serum lactate and CK levels were significantly higher (p<0.001) in autistic children in comparison to that of normal children (Table I). Abnormally higher level of serum lactate and CK were found in 94% and 32% respectively in autistic children. No control children had elevated levels of these parameters (Table II).

Group A Apparently healthy children (control group)

Group B Autistic spectrum disorder male children (study group)

Table-I

Serum lactate and CK of both groups (n= 100)

Variables	Control (n=50)	Autistic (n=50)
Serum Lactate (mg/dl)	12.10 ±0.34 (8-17)	29.31±1.32*** (16-56)
Serum CK(U/L)	134.76+ 5.69 (67-230)	187.30+11.89 (70-456)

Data are expressed as Mean ±SE. Independent student't' test was used for statistical analysis. Figures in parentheses indicate ranges. ***p ≤ 0.001.

Table -II

Frequency of elevated levels of serum lactate and CK of study subjects.

Variables	Control (n=50)		Autistic (n=50)	
	No	%	No	%
Serum lactate	0	0%	0	0%
Serum CK	47	94%	16	32%

Discussion:

The present study was undertaken to observe some biochemical variables in male children with autistic spectrum disorders in order to evaluate their mitochondrial dysfunction. Mitochondrial dysfunction was assessed by estimating serum lactate and creatine kinase (CK) level in male children with autistic spectrum disorders. Both the variables were also studied in apparently healthy age and BMI matched male children for comparison. In this study, mean values of both the biochemical variables of control children were within physiological limit and were almost similar to those reported by different investigators.[1,5,17-23, 27]

It has been seen that defects in mitochondrial function cause critical deficiencies of energy metabolism. As autism is regarded as a general metabolic disorder so mitochondrial dysfunction may play an important role in pathogenesis of autism.[5]

It has been suggested that TCA cycle abnormality in mitochondrial dysfunction stops aerobic respiration which initiates anaerobic respiration causing increased level of lactate rise of serum lactate level .[17] Mitochondrial dysfunction also causes loss of some cellular integrity of muscle brain and liver and serum creatine kinase rises.[24]

In this study, serum lactate level was significantly higher in the study group than those of control group and this finding was supported several rechercher.[1,5,6,18,23,28]

In this present study, serum CK level was significantly higher in the study group compared to control group which was similar to several investigators' studies of different countries.[18,19,21,24]

In this present study, increased serum lactate level was found in 94% of study group, whereas serum lactate level was found within normal range in the entire control group which was consistent with other investigators. [1,5,18,24,25,27]

In addition, serum CK level was found higher in 32% of study group, whereas serum CK level was found

within normal range in the entire control group and it was supported by other studies. [18,19,21,24]

Conclusion:

From the result of this study, it may be concluded that mitochondrial dysfunction may occur in children with autistic spectrum disorder may occur in children with autistic spectrum disorder.

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