The prevalence of chromosomal translocation t (1; 4) (p21; p14) in Iranian patients with mental disability

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Abstract

Introduction: Intellectual disability or intellectual retardation is a condition in which total mental functioning is distinctively below average and there are disabilities in adaptive behaviors during growth. According to the definition of American Mental Disability Community in 1992 a person is considered intellectually disabled if he or she has an IQ (intelligence quotient) of less than 70 and has a limitation in one or multiple adaptive skills. There are many different causes of intellectual disability that one of them is the genetically and chromosomal abnormalities. The aim of this paper was to study translocation breakout t (1; 4) (p21; p14) in a number of mental retardation patients in Iran.

Materials and methods: This descriptive study was carried out on 100 persons with light mental disability by using cytogenetic methods. Lymphocytes were cultured in the dedicated environment by G-Banding karyotype of each person after obtaining patient's blood sample. The data were statistically analyzed by logistic regression.

Results: The findings showed that none of the patients with a mental disability was afflicted to the chromosomal translocation, (1; 4) (p21; p14).

Conclusion: The lack of translocation in this study was equivalent with the obtained frequency in the same studies which have been carried out on the subjects suspected to have a translocation. Also, it seems that chromosomal analysis may be a usefulness diagnostic tool for children with mental retardation.

Keywords: Mental disability, Translocation, Karyotype

Introduction

Prevalence of mental disability in population of Iran is 2-3% (1). Genetic causes are the most common of intellectual disability. About of 10% mental retardation is from include chromosomal abnormalities, 15% are single chromosomal abnormalities and 5% are genetic syndromes, environmental factors including teratogens which include 1% of causes, events of during pregnancy, problems at birth and problems after birth (2). About 1 infant from 200 has been born with a chromosomal abnormality that 3% is because of genetic causes and chromosomal abnormalities. According to 14 years studies on affected children, it has recognized that 31.5% (3) was due to chromosomal abnormalities. High rates of chromosomal abnormalities show the importance of surveying cytogenetic in an affected person with or without dimorphic symptoms and congenital disorders (4). Chromosomal abnormalities exist in 10% of mild mental disability and 40% of

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severe mental disability (5). Chromosomal abnormalities involve two kinds of disorders: numerical and structural (6). In structural changes, breakage is created in chromosomes in which the numbers of chromosomes are fixing, but their structure is altered (7). As a result of the chromosomal break, it is possible that the broken pieces are not attached together and, as a result, this piece is missing without centromere or attached to the other pieces that in such condition genetically exchange occurs and the broken piece may replace in its first place (8). Changes in chromosome structure include: deficit (means declining genetic material and this is the first chromosomal abnormality), duplication (extra copies of a piece of chromosome unnaturally, the copied piece could be transferred to another homologous or non homologous chromosome), inversion (the amount of genetic material is fix, but the gene order is changing and a new combination of chromosome is creating), translocation (transferring a piece of chromosome to a non-homologous chromosome (9).

There are two different types of translocation, reciprocal translocation and Robertsonian translocation (10). In a reciprocal translocation, the numbers of chromosomes are not changed. This translocation is not harmful, but has a high risk of unbalanced gametes and disable children (11). Reciprocal translocation is common and it is found in about 1 child from 600 children, as well as in women who had a few abortions and in infertile men (`12).In robertsonian translocation, only acrocentric chromosomes involve information. One example that has seen in human is translocation between chromosomes 9 and 22 that is seen in 95% affected persons by chronic myelogenous leukemia. In this type of translocation a piece of the long arm of chromosome 22 is separating and transferred into the end of the big arm of chromosome 9 (13- 14). Due to reliability and high accuracy of karyotype in the identification, this study has conducted by this approach to decide the rate of frequency of this type of translocation in persons with mental disability.

Materials and methods

A total of 100 patients (66 male and 34 female) was included in this study. All children were referred to pediatric centers of Tehran, Kermanshah, the east Azerbaijan and Kurdistan. The psychological evaluation revealed mental retardation (IQ<70). All clinical genetic syndromes like congenital anomalies, dimorphic features were recorded, then 2ml intravenous blood taken in a heparinized tube from each child.

Cytogenetic method: Phytohemaglutinin stimulated lymphocyte cultures for G-banding method of karyotyping were set up using the peripheral blood using 2 ml sodium heparinized intravenous blood, harvested and the slides for metaphase study were prepared. The slides were stained using Giemsa stain. A separate lymphocyte cultures were also set up for High Resolution Banding using Ethidium bromide method, which shows more chromosomal bands (about 400-600), in comparison with the routine G-Banding Method (about 250-300). It helped in studying structural variations better than G-banding. Metaphases were studied under oil immersion lens (100 X) in Zeiss microscope and were captured using KaryoImager Version V1.0. For each sample. 40-50 metaphases were screened for abnormal chromosomal changes, which were designated according to the International Standard Nomenclature. The length of the Y chromosome was measured using the Y/F index ratio.

Results

The results showed that which of them had not chromosomal translocation t (1; 4) (p21; p14). On the base of these results in 10% of children with mental disability,

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their parents were relative and 90% were not. Foremore, 32% had a background in their relatives and 68% had not, 69% lived in city and 31% in the village and 80% had the poor economic condition and 20% were in good economic condition.

Discussion

On the results of this study in 100 disable children in Iran showed that none of affected persons haven't Translocation t (1; 4)(p21; p14). On the base of its results 10% of parents with disable children were relative and 90% were not. 32% of them had background in family and 68% had not.69% lived in the city and 31% in the village. 80% of them had the poor economic condition and 20% had the good economic condition. The national committee of disabled children was established in the US in 1950 and then this illness defined and classified in 1973. After that the classification was complete in 1980 and finally it was altered and a distinguished code determined for this disease on which the affected person should have low mental ability compared with normal one and has a limit in one or multiple adaptive skills at 18 ages or fewer than (15). The causes of mental disability divided into three groups: before birth, during birth, and after birth. In various studies, the frequency of before birth causes 8/1~61% has reported that most of them is genetic diseases and chromosomal abnormalities. The most common chromosomal abnormality is followed" id="errorNo_15">that is followed by mental disability is Trisomy or Down syndrome that its chance of repetition is 1-2% at next pregnancies. It seems that Down syndrome has relation with mother's age. Prevalence of this syndrome is increase with women age less than 20 and more than 35 (16). Fragile X Syndrome is the other chromosomal abnormality that can cause mental disability. Womb infections are one of the causes of mental disability before birth called Torch syndrome that affects fetus especially in early months of pregnancy.as well as mother's metabolic abnormalities such as Diabetes and hypothyroid may affect fetus brain and causes mental disability. It is possible that medical factors and ray radiation especially in fifth to the eighteenth week of pregnancy cause mental disability. Inherent metabolic abnormalities such as phenylketonuria and galactosemia diseases are because of inherent noun autosome. If there is positive relative background in respect of disease type, parents' blood relation, the possible of their prevalence in such family increases up to 50% (8). Chromosomal abnormalities in human are the main causes of inherent diseases which involve50~60% of Spontaneous abortions before the13th week of pregnancy, 7% of the death of baby inside the womb and 3~4% of infants' disorders (11). Such diseases occur when the amount of genetic material (DNA) decrease or increase (12).Totally cytogenetic abnormalities are 50~70% of repeated abortions. The most common chromosomal abnormalities followed by repeated abortion involve Trisomy autosomal (60%), Monosomy X (20~29%), Poly Ploidy (20%), imbalanced translocations (4%) and Trisomy 21 accompaniment of Monosomy X (5%). In most studies, the most common autonomy has been Trisomy 16 that in 20 to 30% of products, the repeated abortion has seen and followed it Trisomy 22,21,15,13 are most common (17). Genetic translocation reported for the first time in 1926 (18).Reciprocal chromosomal translocations reported in 1% of human (19-20).The risk of imbalanced chromosomal abnormalities has been reported in 8/9% of the affected person children (21). Balanced chromosomal translocation could be because of the neutral gene in the broken chromosome that has a direct relation with broken areas and causes disease phenotype. Studies on molecular cytogenetic in 70% of persons with balanced chromosomal translocation showed no genetic change on the surface

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of the chromosome that is the especial symptom of the disease (21). Balanced chromosomal translocation in one of the parents increases the possible repeated abortion to 3~5. This possibility Robertson two times more than the father, if the mother has a translocation. About half of chromosomal abnormalities in women balanced reciprocal translocation. 24% of cases are Robertsonian and 12% are Mosaism of chromosomes and other cases involve inversion and sundry abnormalities. Studying on 1760 affected persons and considering all their chromosomal abnormalities showed that 377 men (67/9%) and 178 women (32/1%) had chromosomal abnormality among them 5/7% had both reciprocal and Robertsonian translocations (18-22). Understand the main areas in chromosomes in terms of genotype and phenotype is very useful. Determining the karyotype of these critical areas and occasionally various congenital abnormalities we can see chromosomal abnormalities (23). The place of responsible genes in human abnormalities could be obtained from studying the effects of phenotype and chromosomal abnormalities. Therefore, studying molecular mutation is necessary to define more disorder. It is of importance to diagnose genetically by using cytogenetic screening as well as consulting with parents and the manager of places where children with mental disability are protected. However, genetic consultation for affected people or who are carriers of this defective gene is of importance. Couples shall be referred to the genetic expert for consultation about trance location. Finally, the important of surveying this disease is that physicians often order abortion as they see trance location or Inorganic or duplication at Amino synthesis while it is possible that structural abnormalities have no phenotype influence because of genes locations and this study show the role of different chromosomal abnormalities on mental disability.

Conclusion

The lack of translocation in this study was equivalent with the obtained results in the same studies which have been carried out on the subjects suspected to have a translocation. Also, the results shows that chromosomal analysis may be a useful diagnostic tool for children with mental retardation, emphasizing the importance of cytogenetic method on the diseases.

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