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An analysis of the teratagenic effects that could possibly be due to alcohol consumption by pregnant mothers

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Full Text

Alcohol is one of the commonest teratogenic agents. The harmful effects of drinking during pregnancy have been recognized for more than a quarter of a century. However, this has not deterred women from consuming alcohol during pregnancy, due to a possible lack of information of decreased responsibiliy towards the developing fetus.

Alcohol can affect the developing fetus, giving rise to various malformations, the most extreme: of, which is a condition called Fetal Alcohol Syndrome (FAS). With the increasing incidence of FAS, there is a great variation in its clinical features as described in standard textbooks. The primary aim of this article is to describe in detail the various deformities induced in the developing fetus by alcohol. FAS is an irreversible condition. Some of the physical deformities are amenable to surgical correction. However, nothing much can be done about the mental defects in FAS. The only effective treatment is by institution of early rehabilitative measures. This makes it essential to diagnose FAS before or soon after birth. The article also aims to explore the various possible methods for an early diagnosis of FAS. The exact mechanism by which alcohol causes its deleterious effects is not known. The various aspects regarding the teratogenic potential of alcohol is also discussed based on the experimental evidence.

Clinical Features

FAS as described in standard textbooks is characterized by (a) physical and mental retardation (b) craniofacial anomalies such as maxillary hypoplasia, micrognathia and a thin upper lip (c) cardiac septal defects, mainly ventricular and (d) minor joint abnormalities. [1]

The physical growth retardation in cases of FAS is evident by the reduction in body weight, crown-rump length and read circumference. Though there is some catch up growth with age, children with FAS are usually smaller than their peers. Most of the children with FAS have a greater or lesser degree of mental retardation. At times this is noticed only when the child starts going to school. The conic monest abnormalities usually noted are mental retardation and seizures, probably due to an abnormality of the corpus callosum. Children with FAS also show a significant reduction in I.Q levels and achievement test scores. [2] This reduction persists into adulthood with an increase in discrepancy between the chronological age and the mental age. These children tend to be hyperactive or impulsive with a reduced attention span. The learning process is also impaired in cases of FAS. The impairment is more than that which can be explained by the degree in reduction in I.Q. levels. Due to these mental handicaps, many of these children end up as criminals or with abnormal habits and stereotypes. [3] Cardiac malformations have been noted in FAS, such as atrial and ventricular septal defects. A triad of venricular septal defect, unilateral stenosis of the pulmonary artery and pulmonary hypertension has also been seen. There is also report of a case of a newborn infant with FAS who died within 7 days due to an interruption of the aortic arch and an aortopulmonary window. [4] Reports of abnormal fetal heart rate patterns due to maternal alcohol consumption are also available. A continuous fetal monitoring showed an increased heart rate with a variable pattern. [5] The skeletal system also bears the brunt of the teratogenic effects of alcohol. The mean bone age is seen to be delayed in children with FAS, with little potential for catch up growth. A short stature was found to be a constant feature in 26 children followed till 14 years of age in females and 16 years in males. [6] Vertebral anomalies such as scoliosis and complex malformations of the cervical spine have been described, as also complete amelia of the limbs and unilateral defects of the ulna and tibia. [7] Since FAS is associated with craniofacial and ocular anomalies, a hearing and vestibular disturbance is at times associated with it. This is because all these structures have a common origin from the first and second branchiaJ arches. The types of hearing loss commonly seen are sensorineural and intermittent conductive deafness with a developmenal delay in auditory maturation [8] The development of hearing, language and speech are important landmarks in the mental development of a child. As the auditory and vestibular systems have the same peripheral apparatus, there are also vestibular, language and speech problems. Among the patients patients tested for speech and language ability, 90% had a speech pathology of which 76% had expressive language deficits and 82% had receptive language deficits. [9] The eye is one of the organs commonly involved in FAS, though not much mention of this is found in textbooks. Visual activity is often moderately or severely decreased. The external deformities commonly seen are short palpebral fissures, epicanthus, strabismus, nystagmus and ptosis. The internal defects include myopia and hypermetropia and a diffuse posterior haze on the cornea, which is usually bilateral. A unique pathological feature in these cases is an anomaly of the anterior banded zone of the Descemet's membrane, which is absent, poorly formed on thinned out in the peripheral and central cornea. This is often assn ciated with cases where the lens is fully opacified at birth. [10]

The optic nerve seems to be particularly affected in FAS. It is frequently found to be hypoplastic, with a small optic disc. The condition is commonly associated with increased tortuosity of the retinal vessels, especially of the arteries. [11] The incidence of urinary tract anomalies is also high among children with FAS. The kidneys of children with FAS have been found to be consistently smaller. Quazi et al, 1979 while examing FAS cases found patients who had pyclonephritis with unilateral or bilateral renal hypoplasia, renal agenesis, hydronephrosis, as also tubular dysfunction and bladder diverticula. [12] The gastrointestinal system is also affected in cases of FAS. There is a report of one case of small intestinal atresia and abnormal insertion of the umbilicus. Microscopic studies of the liver of a 17 month old child with FAS showed hepatomegaly with parenchymal fat and portal and perisinusodal fibrosis, changes similar to that in alcoholic liver disease. FAS sis. [13] Thus it can be seen that al- has also been associated with features of congenital heppatic fibrocohol has the capacity to involve any organ system in the body. The reasons for this finding will be discussed later.

Diagnosis of Maternal Alcoholism and Fas

A probable diagnosis of FAS in a child can be made even before a child is born. This is possible by assessment of various characteristics of maternal alcoholism. These tests however, are not fully accurate and only serve as an alert for medical practitioners. There are instances where mothers who consumed alcohol during pregnancy delivered normal children. A definite diagnosis of FAS can be made by examination of a child just after birth or even at a later age.

An analysis of family history is at times useful. A retrospective study of clinical literature by Abel, 1988 reported that the incidence of the disorder among older sibs was 170 per 1000, whereas among younger sibs was 171 per 1000. Since the risk for FAS as determined by Abel was 1.9 per 1000 it clearly indicates the high risk of FAS among siblings, if one sib is diagnosed as having features of FAS. [14] The testing of pregnant mothers could provide an indication of prenatal alcohol abuse and chances of subsequent FAS in the child. Prenatal detection of four blood markers (blood-associated acetaldehyde, carbohydrate deficient transferrin, gamma glutamyl transpeptidase and mean red blood cell volume) in a woman have been used as an indicators of maternal alcoholism. Pregnant women with two or more of these markers usually had children with smaller birth weights and length and head circumference. Electrophoretic examination of gammma glutamyl transpeptidase in these cases showed a unique band following ethanol exposure. A substance called ethyl linoleate has been identified whose presence in the meconium during childbirth is supposed to be an indicator of maternal alcohol exposure. The reliability of these tests has, however, not been proved fully till date. [15]

The levels of serum gluytamyl transferase have been analyzed in pregnant women. However, the sensitivity of the gamma-glutamyl transferase test in identifying those who consumed more than 30 gm of alcohol in a day is only 25%. The levels of maternal alpha-fetoprotein (AFP), human placental lactogen (HPL) and pregnancy specific beta 1 glyco protein (SP-1) have also been studied in pregnant women. A low AFP predicted FAS correctly in 59% cases and low SP-1 in only 56% cases. HPL assay was useless in the detection of FAS. Carbohydrate deficient transferin (CDT) has also been tried as a marker of maternal alcoholism, but not found to be very specific [16] Efforts are now underway to develop a consistent method of dagnosis of FAS in a child. A useful tool is the "Discriminant function D" described by Clarren et al, 1987. In this the thickness of the upper lip, smoothness of the philtrum and the palpebral fissure length is measured for a child with suspected FAS, and compared against standard values. They have also suggested comparing other facial features with standard reference values for a particular age and community. [17] The eye has also been suggested as another tool for the diagnosis of FAS. The ocular length can be measured and compared with standards values, since girls with FAS have a shorter axial length than normal, and both boys and girls with FAS have a relatively smaller vitreous body of the eye. A steep corneal curvature has also been suggested as a consistent diagnostic characteristic. It was felt that a measurement of 46.00 diopters on greater of the horizontal corneal curvature was diagnostic of FAS. All this data data would again have to be compared with the standard values for a particular race, which have to be first determined. [11]

Since there is no definite treatment of FAS, the only remedial measures are by correction of the deformities. Many of the physical deformities are corrected by the normal process of growth and development of the child. In certain cases, however, effective surgical measures need to be instituted do pending on the extent and nature of the problem. The mental retardation seen in FAS is a greater cause of concern. Since not much is known about the effect of alcohol on the nervous system only rehabilitative measures can be instituted in most cases. Since most of the children are slow learners with attentional problems, they need special care to aid their learning process. Vocational training is important, or order to enable such children to lead independent lives when they mature into adults.

Discussion

It can be seen that there are many more clinical features attributable to the teratogenic effects of alcohol than were earlier described. This could be due to a greater awareness and recognition of the condition by medical practitioners. The cause of many abnormalities in children that were earlier unexplained has now been identified to be due to prenatal alcohal exposure. An explanation of the manifold effects of alcohol can be found by a closer look at the process of development of the human fetus. The ectoderm, mesoderm and the endoderm are the three primitive cell layers from which all the organ systems in the organ systems in the human body are developed. The cells of the ectodermal and mesodermal germ layers are derived from the epiblast layer of the bilaminar germ disc. Some of the cells of the endoderm are also derived from this epiblast layer. Alcohol has been shown to disrupt cells of the epiblast layer with decreased intercellular adhesion and formation of blebs. [18] Since the epiblast cell layer is responsible for formation of most of the organ systems, the deleterious effect of alcohol on this cell layer could account for many of the malformations seen in FAS. The mesodermal layer gives rise of the urinary and musculoskeletal system. Alcohol has been shown to inhibit the rate of cell division and migration of mesodermal cells. [19] It must be noted that though the epiblast cell layer gives rise to many of the organ systems, all the organ systems are not equally involved in FAS. The selective susceptibility of certain organ system to the harmful effects of alcohol is, however, not known.

It is obvious that there is no diagnostic test for maternal alcoholism, which is fully accurate. The increased number of tests is an indication of the limited effectiveness of each test. Hence a probable diagnosis of maternal alcohol abuse is possible only by corroboration of all the findings. The presence of even one of the risk factors would serve as an alert to medical practitioners. It would however, be very wrong to rely on these diagnostic tests alone. A routine examination of pregnant women for features of maternal alcoholism is of course helpful. However, for reasons of increased expenditure the exercise would be worthwhile only in communities that have a high incidence of female alcoholism and children affected with FAS. The diagnosis of FAS features in a child is now possible by a proper examination of the child. However, an awareness of the condition is essential among medical practitioners and health workers to be able to recognize the condition soon after birth, so that rehabilitative measures can be instituted early. Corrective measures are obviously needed to manage cases of FAS. In the absence of much knowledge regarding the exact mechanisms of action of alcohol not many remedial measures can be instituted. Hence more effect needs to be directed towards understanding these mechanisms. Only this would enable the adoption of adequate measures for the prevention and treatment of FAS.

Summary and Conclusion

It can be concluded that alcohol is definitely harmful to the developing fetus. The effect can manifest in various ways, the most extreme of which is a condition called Fetal Alcohol Syndrome (FAS). The diagnosis of maternal alcoholism leading onto cases of FAS is difficult due to absence of accurate diagnostic tests. The diagnosis of FAS in a child is easier by a proper examination. There is no specific treatment of FAS in a child. The only management is by institution of corrective and rehabilitative measures. The exact mechanism of the teratogenic action of alcohol is not known. It is probably due to the harmful effect of alcohol on the epiblast layer of the bilaminar germ disc. In the absence of adequate knowledge regarding FAS, not much can be done to remedy the deleterious effects of alcohol. Hence, a word of advice to all pregnant women is to avoid drinking during pregnancy.

References

1 Behrman RE, Robert MK, Jenson HB. Nelson's Textbook of Pediatrics P 531. WB Saunders Company. Philadelphia 2000.

2 Streissguth AP, Randels SP, Smith DF. A test-retest study of intelligence in-patients with fetal alcohol syndrome : implications for care.J Am Acad Child Adolesc Psychiatry, 1991;30:584-7.

3 Coles CD, Platzman KA, RashkindHood CL et al. A comparison of children affected by prenatal alcohol exposure and attention deficit, hyperactivity disorder. Alcohol Clin Exp Res 1997;21:150-161.

4 Lewis DD, Woods SE. Fetal alcohol syndrome. Am Fam Physician 1994; 50:1025-32.

5 Silva PD, Miller KD, Madden J, Keegan KA Jr. Abnormal fetal heart rate pattern associated with severe intrapartum maternal ethanol intoximation J Reprod Med 1987:32:144-6.

6 Habbick BF, Blackely PM, Houston CS et al. Bone age and growth in fetal syndrome. Alcohol Clin Exp Res 199p:22:1312-6.

7 Azouz EM. Fetal alcohol syndrome and bilateral tibial exostoses. A case report. Pediatr Radiol 1993;23:615-6.

8 Church, MW, Kaltenbach JA. Hearing, speech, language and vestibular disorders in the fetal alcohol syndrome. Alcohol Clin Exp Res 1997; 21:495.512.

9 Church MW, Abel EL. Fetal alcohol syndrome. Hearing, speech, language and vestibular disorders. Obstet Gynecol Clin North America 1998;25:85-97.

10 Ehongo A, Cordonnier M, Zanen A, van Bogaert P, Dunac A. Fetal alcohol syndrome and bilateral uniform posterior haze of the cornea. Bull Soc Belge Ophtalmol 1995;259: 67-76.

11 Hellstorm A, Svenson E, Stromland K. Eye size in healthy Swedish children and in childrne with fetal alcohol syndrome. Acta Opthalmol Scand 1997;74:423-8.

12 Qazi Q, Masakawa A, Milman D et al. Renal anomalies in fetal alcohol syndrome. Pediatrics 1979;63:886-9.

13 Lefkowitch JH, Rushton AR, FengChen KC. Hepatic fibrosis in fetal alcohol syndrome. Pathologic similarities to adult alcoholic liver disease. Gastroenterology 1983;85: 951-7.

14 Abel EL. Fetal alcohol syndrome in families. Neurotoxicol Teratol 1988;10:1-2.

15 Stoler JM, Homes LB. Under-recognition of prenatal alcohol effects in infants of known alcohol Alcohol exposure in utero and functional deficits in children during the first four years of life. Ciba Found Symp 1999;105:176-96.

16 Bearer CF, Lee S, Salvator AE et al. Ethyl linoleate in meconium.; a biomarker for prenatal alcohol exposure. Alcohol Clin Exp Res 1999; 23:487-93.

17 Clarren SK, Sampson PD, Larsen PD et al. Facial effects of fetal alcohol syndrome exposure: assessment by photographs and morphometric analysis. Am J Med Genet 1987;26:651-66.

18 Nakatsuji N, Johnson KE. Effects of ethanol on the primitive streak stage mouse embryo. Teratology 1984;29:369-75.

19 Sulik KK Critical period for alcohol teratogenesis in mice, with special reference to the gastrulation stage of embryogenesis. Ciba Found Symp 1984;105:124-141.