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Fetal Alcohol Spectrum Disorder — Study Review

Spektrum płodowych zaburzeń alkoholowych — przegląd badań

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Abstract

Fetal alcohol syndrome is regarded as a spectrum. Fetal alcohol spectrum disorder (FASD) might be surprisingly common, especially in vulnerable populations. Mental health problems, substance abuse, inappropriate sexual behavior, school and legal problems and unemployment might cooccur with FASD. Treatment of comorbidities might be helpful, however effects of stimulants in FASD are controversial. Women who drink during pregnancy might suffer from nutritional deficiencies, therefore try of compensation might be helpful for both mother and child. Moreover, nutrient of children with FASD might play an important role as a potential supportive therapy. In addition, physical exercise therapy might be beneficial for both mother and children because of neurogenesis induction potential. There is no established therapy for FASD, therefore further studies should focus on formulating one. (JNNN 2020;9(3):119–122)

Key Words: alcohol ingestion, brain development pathology, FAS, pregnancy

Streszczenie

Alkoholowy Zespół Płodowy jest uważany za spektrum. Spektrum Płodowych Zaburzeń Alkoholowych (FASD) może występować zaskakująco często, szczególnie w narażonych na to populacjach. Problemy ze zdrowiem psychicznym, nadużywanie substancji psychoaktywnych, niewłaściwe zachowania seksualne, problemy w szkole i z prawem oraz z odnalezieniem siebie na rynku pracy mogą współistnieć z FASD. Leczenie chorób współistniejących może być pomocne, jednak efektywność stymulantów w FASD jest kontrowersyjna. Kobiety pijące w czasie ciąży mogą cierpieć na niedobory żywieniowe, dlatego próba ich kompensacji może być pomocna zarówno dla matki, jak i dziecka. Ponadto, suplementy diety stosowane wśród dzieci z FASD mogą odgrywać ważną rolę jako potencjalne leczenie wspomagające. Co więcej, terapia oparta o wysiłek fizyczny może być korzystna zarówno dla matki, jak i dziecka, ze względu na możliwość indukcji neurogenezy. Nie ma sprecyzowanej terapii FASD, dlatego dalsze badania powinny koncentrować się na jej ustaleniu. (PNN 2020;9(3):119–122)

Słowa kluczowe: spożywanie alkoholu, patologia rozwoju mózgu, FAS, ciąża

Introduction

Alcohol consumption can harm not only the drinker, but also others [1]. A standard example of this harm to others is the negative consequences of alcohol consumption during pregnancy. Alcohol is a teratogen that can easily cross the placenta, causing damage to the brain and other organs of the developing children in the womb. It was found that alcohol consumption during pregnancy is a risk factor for various adverse pregnancy outcomes [2–6]. Health effects of prenatal exposure to ethyl alcohol have been considered under the general

concept of fetal alcohol spectrum disorder (FASD), which consist of 4 diagnostic units, fetal alcohol syndrome (FAS), partial FAS, alcohol-related neurodevelopmental disorder, and depending on the diagnostic guideline, alcohol-related birth defect. Alcohol can affect any organ or developing fetus, and as such, patients with FASD can suffer from wide range of comorbidities. Prenatal exposure to alcohol has long-term consequences, which care is expensive. Cost of living for a person with FASD in North America is estimated at over \$ 1 million [7].

Prenatal alcohol exposure is defined as at least one of the following: (1) six or more drinks per week for

two or more weeks during pregnancy; (2) three or more drinks on occasion two or more times during pregnancy; (3) social or legal problems related to alcohol during pregnancy; (4) intoxication during pregnancy documented by biochemical analysis of specimens; (5) presence of biomarkers for alcohol exposure during pregnancy (fatty acid ethyl esters, phosphatidylethanol and ethyl glucuronide in maternal hair, nails, urine or blood, or in the placenta or meconium); (6) increased prenatal risk associated with alcohol consumption during pregnancy, examined using screening tool [8].

The aim of the study is to present the pathophysiology, occurrence, supportive therapies in FASD and also impact of FASD in adolescent.

Pathophysiology

Based on animal models, alcohol exposure to seventh gestational day (GD) was particularly harmful to the medial forebrain areas [9]. Exposure on ethanol during eight GD effected in a disproportionate reduction in volume in the olfactory bulbs, hippocampus and cerebellum, and relative sparing of the pituitary and septum [10]. Exposure to ethanol during ninth GD caused a reduce of cerebellar volume, increase of ventricles, and disturbance of cerebral cortex, hippocampus and right striatum shapes [10]. In contrast, offspring exposed to alcohol at tenth GD showed increase in ventricles size and a disproportionate reduction in cortical volume [11]. Studies have indicated repetitively relationships between face measurements and brain structure in FASD [11]. Shorter palpebral fissures is related to reduction in the volume of the bilateral ventral diencephalon, lower size of anterior corpus callosum and a higher size of lower frontal cortex. The smoothness of the philtrum is related to decrease of size of thalamus and left pallidum. Children with greater facial dysmorphism noted significant disturbance in cerebral cortex growth.

Occurrence

The incidence of FASD in the populations of younger school-aged children can be as high as 20–50 cases per 1000 children [12]. Approximate incidence in the general population has been roughly estimated at about 1–2 cases per 1000 people for FAS [13] and about 9–10 cases per 1000 people for FASD [14]. Incidence of FASD could be at least ten times higher than the prevalence of FAS [15,16]. Alcohol related neurodevelopmental disorder is the broadest category; it is estimated that for each case of FAS there are three to four cases of alcohol-related neurodevelopmental disorders [17]. Two studies

have shown that the incidence of FASD is 23–47 cases per 1000 people and 40 cases per 1000 people in Europe [18,19]. In some subpopulations, the incidence of FASD is much higher than in the general population. In particular groups, such as children in care facilities (orphanages, foster families and childcare systems), the incidence of FASD presumably might be higher than in the rest of population [20]. Occurrence of FAS in children with special needs range in orphanage was ranged from 427 to 680 cases per 1000 people in Russia [21]. Alcohol consumption during pregnancy should be considered a global public health problem, because harmful effects of alcohol on the developing fetus illustrates many cases of disability that can be prevented [22].

Impact of FASD in Adolescent

FASD could be related to numerous brain structure and functioning malformations. In consequence, FASD could be related to disturbance in patients daily life functioning. Numerous comorbidities including mental health problems, substance abuse, inappropriate sexual behavior, school and legal problems and unemployment are reported [22].

Supportive Therapies

There is no treatment dedicated to FASD [23]. Conclusions from the recent study from Spain are that dog assisted therapy is promising supportive care for children and adolescents with FASD [24]. It was shown that from 50 percent to over 90 percent of patients with FASD meet diagnostic criteria for attention deficit/hyperactivity disorder (ADHD) [25,26]. The similarity between FASD cognitive and behavioral traits and other disease entities provides an opportunity to focus on symptom treatment, and daily life functioning improvement despite of the fact of not established treatment for FASD as an entity. One approach would be to treat people with FASD with drugs such as stimulants that have been successful in treating ADHD. Nevertheless, results of stimulant therapy in clinical studies of FASD are ambiguous. Treatment with stimulants may reduce hyperactivity, with little evidence of a beneficial effect on attention [27]. Other studies have reported variable effects [28] or even worse results [29] in FASD.

Some studies suggest that women who consume alcohol during pregnancy have nutritional deficiencies in comparison to control group. May and colleagues [30] examined the nutritional status of a group of South African mothers who gave birth to children with FASD,

compared with a group of mothers who gave birth to children without FASD. Deficiency in vitamins A, B6, choline, C, D and E; calcium, iron and zinc; and omega-3 fatty acids occurred more often in mothers of children with FASD. Potentially, it may contribute to abnormal fetal development [31] and further negative effects of ethanol on the developing embryo and fetus.

Nutritional status can also affect cognitive development throughout childhood [32]. Recent studies have focused on nutrient intake by children with FASD. Many children with FASD do not consume recommended daily omega-3 fatty acids and vitamin D [33,34].

Wheel accessibility significantly alleviates spatial learning and memory impairment in adult rats exposed to ethanol during development [35,36]. In addition, these post-exercise cognitive improvements are associated with physical exercise induced improvements in BDNF and hippocampal neurogenesis in adults who are both affected by developmental exposure to alcohol [37].

Conclusions

Fetal alcohol syndrome is regarded as a spectrum. FASD is relatively common, especially in vulnerable populations. Mental health problems, substance abuse, inappropriate sexual behavior, school and legal problems and unemployment might co-occur with FASD. There is no established therapy for FASD, therefore further studies should focus on formulating one.

Implications for Nursing Practice

FASD might be surprisingly common disorder. It is co-occurring with disturbances such as psychiatric disorders, addictions, inappropriate sexual behavior, decreased school performance and then problems finding their place on the labor market. There is no treatment dedicated to FASD. Treatment of comorbidities might be helpful, however effects of stimulants in FASD are controversial. Women who drink during pregnancy might suffer from nutritional deficiencies, therefore try of compensation might be helpful for both mother and child. Moreover, diet supplementation of children with FASD might play an important role as a potential supportive therapy. In addition, physical exercise therapy might be beneficial for both mother and children because of neurogenesis induction potential.

References

- [1] Karriker-Jaffe K.J., Room R., Giesbrecht N., Greenfield T.K. Alcohol's Harm to Others: Opportunities and Challenges in a Public Health Framework. *J Stud Alcohol Drugs*. 2018;79(2):239–243.
- [2] Kesmodel U., Wisborg K., Olsen S.F., Henriksen T.B., Secher N.J. Moderate alcohol intake during pregnancy and the risk of stillbirth and death in the first year of life. *Am J Epidemiol*. 2002;155(4):305–312.
- [3] Henriksen T.B., Hjollund N.H., Jensen T.K. et al. Alcohol consumption at the time of conception and spontaneous abortion. *Am J Epidemiol*. 2004;160(7):661–667.
- [4] Albertsen K., Andersen A.M., Olsen J., Grønbaek M. Alcohol consumption during pregnancy and the risk of preterm delivery. *Am J Epidemiol*. 2004;159(2):155–161.
- [5] Patra J., Bakker R., Irving H., Jaddoe V.W., Malini S., Rehm J. Dose-response relationship between alcohol consumption before and during pregnancy and the risks of low birthweight, preterm birth and small for gestational age (SGA) — a systematic review and meta-analyses. *BJOG*. 2011;118(12):1411–1421.
- [6] O'Callaghan F.V., O'Callaghan M., Najman J.M., Williams G.M., Bor W. Maternal alcohol consumption during pregnancy and physical outcomes up to 5 years of age: a longitudinal study. *Early Hum Dev*. 2003;71(2):137–148.
- [7] Lange S., Probst C., Gmel G., Rehm J., Burd L., Popova S. Global Prevalence of Fetal Alcohol Spectrum Disorder Among Children and Youth: A Systematic Review and Meta-analysis. *JAMA Pediatr*. 2017;171(10):948–956.
- [8] Denny L., Coles S., Blitz R. Fetal Alcohol Syndrome and Fetal Alcohol Spectrum Disorders. *Am Fam Physician*. 2017;96(8):515–522.
- [9] Godin E.A., O'Leary-Moore S.K., Khan A.A. et al. Magnetic resonance microscopy defines ethanol-induced brain abnormalities in prenatal mice: effects of acute insult on gestational day 7. *Alcohol Clin Exp Res*. 2010;34(1):98–111.
- [10] Parnell S.E., O'Leary-Moore S.K., Godin E.A. et al. Magnetic resonance microscopy defines ethanol-induced brain abnormalities in prenatal mice: effects of acute insult on gestational day 8. *Alcohol Clin Exp Res*. 2009;33(6):1001–1011.
- [11] O'Leary-Moore S.K., Parnell S.E., Godin E.A. et al. Magnetic resonance microscopy-based analyses of the brains of normal and ethanol-exposed fetal mice. *Birth Defects Res A Clin Mol Teratol*. 2010;88(11):953–964.
- [12] May P.A., Gossage J.P., Kalberg W.O. et al. Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in-school studies. *Dev Disabil Res Rev*. 2009;15(3):176–192.
- [13] Public Health Agency of Canada (PHAC). *Fetal Alcohol Spectrum Disorder (FASD): A framework for action* (updated March 28, 2012). Retrieved August 23, 2020, from <https://www.canada.ca/en/public-health/services/reports-publications/fetal-alcohol-spectrum-disorder-fasd-framework-action.html>

- [14] Roberts G., Nanson J. *Best Practices. Fetal Alcohol Syndrome/ Fetal Alcohol Effects and the Effects of Other Substance Use During Pregnancy*. Health Canada, Ottawa 2000.
- [15] May P.A., Gossage J.P., Kalberg W.O. et al. Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in-school studies. *Dev Disabil Res Rev*. 2009;15(3):176–192.
- [16] May P.A., Gossage J.P. Estimating the prevalence of fetal alcohol syndrome. A summary. *Alcohol Res Health*. 2001; 25(3):159–167.
- [17] Chudley A.E. Fetal alcohol spectrum disorder: counting the invisible - mission impossible? *Arch Dis Child*. 2008; 93(9):721–722.
- [18] May P.A., Fiorentino D., Coriale G. et al. Prevalence of children with severe fetal alcohol spectrum disorders in communities near Rome, Italy: new estimated rates are higher than previous estimates. *Int J Environ Res Public Health*. 2011;8(6):2331–2351.
- [19] Petković G., Barisić I. FAS prevalence in a sample of urban schoolchildren in Croatia. *Reprod Toxicol*. 2010; 29(2):237–241.
- [20] Lange S., Shield K., Rehm J., Popova S. Prevalence of fetal alcohol spectrum disorders in child care settings: a meta-analysis. *Pediatrics*. 2013;132(4):e980–995.
- [21] Пальчик А.Б., Легонькова С.В. Фетальный алкогольный синдром у детей: манифестация и динамика. *Обзорные Психиатрии и Медицинской Психологии имени В.М. Бехтерева [Bekhterev Rev Psychiatry Med Psychol.]*. 2011; 3:17–20.
- [22] Popova S., Lange S., Shield K. et al. Comorbidity of fetal alcohol spectrum disorder: a systematic review and meta-analysis. *Lancet*. 2016;387(10022):978–987.
- [23] Murawski N.J., Moore E.M., Thomas J.D., Riley E.P. Advances in Diagnosis and Treatment of Fetal Alcohol Spectrum Disorders: From Animal Models to Human Studies. *Alcohol Res*. 2015;37(1):97–108.
- [24] Vidal R., Vidal L., Ristol F. et al. Dog-Assisted Therapy for Children and Adolescents With Fetal Alcohol Spectrum Disorders a Randomized Controlled Pilot Study. *Front Psychol*. 2020;11:1080.
- [25] Bhatara V., Loudenberg R., Ellis R. Association of attention deficit hyperactivity disorder and gestational alcohol exposure: an exploratory study. *J Atten Disord*. 2006;9(3):515–522.
- [26] Fryer S.L., McGee C.L., Matt G.E., Riley E.P., Mattson S.N. Evaluation of psychopathological conditions in children with heavy prenatal alcohol exposure. *Pediatrics*. 2007; 119(3):e733–741.
- [27] Doig J., McLennan J.D., Gibbard W.B. Medication effects on symptoms of attention-deficit/hyperactivity disorder in children with fetal alcohol spectrum disorder. *J Child Adolesc Psychopharmacol*. 2008;18(4):365–371.
- [28] O'Malley K.D., Nanson J. Clinical implications of a link between fetal alcohol spectrum disorder and attention-deficit hyperactivity disorder. *Can J Psychiatry*. 2002;47(4): 349–354.
- [29] Frankel F., Paley B., Marquardt R., O'Connor M. Stimulants, neuroleptics, and children's friendship training for children with fetal alcohol spectrum disorders. *J Child Adolesc Psychopharmacol*. 2006;16(6):777–789.
- [30] May P.A., Hamrick K.J., Corbin K.D. et al. Dietary intake, nutrition, and fetal alcohol spectrum disorders in the Western Cape Province of South Africa. *Reprod Toxicol*. 2014;46:31–39.
- [31] Nyaradi A., Li J., Hickling S., Foster J., Oddy W.H. The role of nutrition in children's neurocognitive development, from pregnancy through childhood. *Front Hum Neurosci*. 2013;7:97.
- [32] Bryan J., Osendarp S., Hughes D., Calvaresi E., Baghurst K., van Klinken J.W. Nutrients for cognitive development in school-aged children. *Nutr Rev*. 2004;62(8):295–306.
- [33] Fuglestad A.J., Fink B.A., Eckerle J.K. et al. Inadequate intake of nutrients essential for neurodevelopment in children with fetal alcohol spectrum disorders (FASD). *Neurotoxicol Teratol*. 2013;39:128–132.
- [34] Werts R.L., Van Calcar S.C., Wargowski D.S., Smith S.M. Inappropriate feeding behaviors and dietary intakes in children with fetal alcohol spectrum disorder or probable prenatal alcohol exposure. *Alcohol Clin Exp Res*. 2014; 38(3):871–878.
- [35] Christie B.R., Swann S.E., Fox C.J. et al. Voluntary exercise rescues deficits in spatial memory and long-term potentiation in prenatal ethanol-exposed male rats. *Eur J Neurosci*. 2005;21(6):1719–1726.
- [36] Thomas J.D., Sather T.M., Whinery L.A. Voluntary exercise influences behavioral development in rats exposed to alcohol during the neonatal brain growth spurt. *Behav Neurosci*. 2008;122(6):1264–1273.
- [37] Gil-Mohapel J., Boehme F., Kainer L., Christie B.R. Hippocampal cell loss and neurogenesis after fetal alcohol exposure: insights from different rodent models. *Brain Res Rev*. 2010;64(2):283–303.

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