Paediatrica Indonesiana

VOLUME 55 September • 2015 NUMBER 5

Original Article

The role of exclusive breastfeeding in prevention of childhood epilepsy

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Abstract

Background Epilepsy affects 1% of children worldwide. The highest incidence is in the first year of life, and perinatal factors, such as hypoxic-ischemic injury, infection, and cortical malformation may play etiologic roles. Breast milk contains optimal nutrients for human brain in early life. Breastfeeding has been associated with lower risk of infections, better cognitive and psychomotor development. However, the role of breastfeeding in preventing childhood epilepsy remains unclear.

Objective To evaluate an association between exclusive breastfeeding and childhood epilepsy.

Methods A case-control study conducted from 1 May to 3 July 2013 involving children with epilepsy aged 6 months to 18 years who were attending pediatric outpatient clinic of Dr. Sardjito Hospital, Yogyakarta. Neurologically normal children, individually matched by age and sex, visiting the same clinic were considered as controls. Exclusion criteria were children with structural brain abnormality, history of epilepsy in family, and who had history of neonatal seizure, intracranial infection, febrile seizure, and head trauma before onset of epilepsy. History of breastfeeding was obtained by interviewing the parents. The difference of exclusively breastfeeding proportion between cases and controls was analyzed by *McNemar* test.

Results The total number of participants was 68 cases and controls each. Subjects with epilepsy had lower proportion of exclusively breastfed (48.5%) compared with controls (54.4%), but the difference was not statistically significant (P=0.541). Exclusively breastfeeding showed no statistical significance in decreasing risk of epilepsy (OR=0.71; 95%CI 0.32 to 1.61).

Conclusions Exclusive breastfeeding for 4-6 months has no effect against childhood epilepsy. **[Paediatr Indones. 2015;55:282-6]**.

Keywords: *breast feeding, epilepsy, risk factors, brain, child*

Epilepsy is one of the most frequent brain disorder. Each year, there are approximately 30-50 new cases of epilepsy every 100.000 people.[1] From a population of epilepsy worldwide, approximately 25% (5-10 million) are children under the age of 15 years. Forty percents of 3-5 million of new epilepsies each year are children, and more than 80% occur in developing countries.[2] The tendency of a child's brain to induce epileptic seizures is much greater than those in adults.[3] This condition is associated with the higher risk factors such as hypoxic-ischemic injury, meningitis, and cortical malformations. Pregnancy and perinatal conditions become important risk factors for epilepsy, such as eclampsia, complication of childbirth, perinatal infection, prematurity, asphyxia, birth trauma, cortical malformation, low birth weight, and infection of central nervous system.[4,5] These suggest that conditions in early life influence the risk of epilepsy in further life.

Brain development occurs most rapidly in the early years of life, in which the breast milk plays

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an important role because of its essential nutrient components, such as long-chain polyunsaturated fatty acid, cholesterol, and gangliosides, which are found in small amount or even not exist in formula milk. Breastfed babies are associated with better development of cognitive, mental, and psychomotor.[6] Studies also show that breastfeeding is associated with better IQ levels, development in total brain volume, and the development of brain white matter in children.[7] In addition to the benefit of contents in breast milk, factor related to breast-feeding state, which is the physical and psychological contact between mother and child, is also considered to be a positive effect on infant development.[8]

The role of breast milk against epilepsy in children is still unclear and several studies indicate different results. Some studies showed a decreased risk of epilepsy in children who were breastfed.[5,9,10] However, another study showed no association between breastfeeding and incidence of epilepsy.[4] The purpose of this study was to determine the effect of exclusive breastfeeding on the prevention of epilepsy in children.

Methods

We conducted a case-control study in the outpatient clinic of Department of Child Health Dr. Sardjito Hospital, Yogyakarta during the period from May 1 until July 3, 2013. All outpatients, aged between 6 months to 18 years, with history of term birth ($\geq$37 gestational weeks), birth weight $\geq$2500 g, and had been diagnosed as epilepsy were included in the study as the case group. Clinical diagnosis of epilepsy was determine based on the definition of the *International League Against Epilepsy* (ILAE, 1989), which is the presence of recurrent (two or more) epileptic seizures unprovoked by any immediate identified cause such as hypoglycemia and imbalance of electrolytes, and with the inter-seizure interval of more than 24 hours.[11] while the control group consisted of other patients without neurological disorders, visiting the same clinic, and were individually matched by age and sex. Subjects were taken by consecutive sampling to meet the required sample size. Exclusion criteria were children with congenital anomalies, metabolic disorders, severe structural brain abnormalities (such as cortical malformations, cerebral palsy, and brain tumors), history of epilepsy in the family, and those who had history of neonatal seizures, intracranial infections, febrile seizures, and head trauma before the onset of epilepsy, as well as subjects who did not obtain clear data on the pattern of breastfeeding from birth.

Information on history of breastfeeding were obtained by direct interview to the parents, and confirmed by other family members whenever possible. The duration of breastfeeding was expressed in units of months. Exclusive breastfeeding was defined as giving to the infants only breast milk with no other food or drink except multivitamins, minerals, and medicines, at the age of 0-4 months (in subjects born before 2003) or the age of 0-6 months (in subjects born in 2003 and thereafter) in accordance with Indonesian government policy.[13,14]

Data were statistically analyzed using a computer program. Basic characteristics of the study subjects were presented as frequency, mean, and standard deviations. Difference of proportion of exclusive breastfeeding between the matched cases and controls were analyzed by *McNemar* test. Difference of duration of breastfeeding between groups were analyzed by *Mann-Whitney* test. The study was approved by the Medical and Health Research Ethics Committee of the Gadjah Mada University Medical School/ Dr. Sardjito Hospital. Parents of children who were willing to join the study had signed informed consents.

Results

During the study period, we identified 70 children with epilepsy who fulfilled the inclusion criteria and did not meet the exclusion criteria. Two patients were excluded from the study because the parents failed to remember the history of breastfeeding practice. Sample size obtained was 68 epilepsy patients as the case group, and 68 patients with non-epileptic as the control group, adjusted individually for age and gender. The basic characteristics of subjects are shown in **Table 1**.

The proportion of exclusive breastfeeding in two groups are shown in **Table 2**. The proportion of exclusive breastfeeding in the case group (48.5%) was lower than the control group (54.4%), however, the

Table 1. Basic characteristics of study subjects

Characteristics	Case group N=68	Control group N=68
Mean age (SD) years	8.1 (5.26)	8.1 (5.23)
Gender, n (%)		
Male	38 (55.9)	38 (55.9)
Female	30 (44.1)	30 (44.1)
Mean number of children in family (SD)	2.2 (1.06)	2.5 (1.62)
Maternal age at delivery, n (%)		
< 25 years	21 (30.9)	20 (29.4)
≥ 25 years	47 (69.1)	48 (70.6)
Median duration of breastfeeding, months (IQR)	19.0 (14.25)	14.0 (15.75)

IQR=interquartile range

Table 2. Proportion of exclusive breastfeeding in case and control groups

	Case group	Control group	OR (95% CI)	P value
Exclusive breastfeeding, n (%)	33 (48.5)	37 (54.4)	0.71 (0.32 to 1.61)	0.541
Non-exclusive breastfeeding, n (%)	35 (51.5)	31 (45.6)		

difference was not statistically significant. Exclusive breastfeeding had no role in decreasing risk of epilepsy [OR 0.71; 95% CI 0.32 to 1.61 (P=0.541)].Similarly, the duration of breastfeeding showed no significant difference in both groups (**Table 3**).

Table 3. Bivariate analysis of breastfeeding duration between the case and control groups

	Median duration (IQR), months	P value
Case group	19.00 (14.25)	0.334*
Control group	14.00 (15.75)	

IQR= interquartile range

*Mann-Whitney test, statistically significant if P<0,05

Discussion

The proportion of exclusive breastfeeding in this study were higher than the national's prevalence, which was 32% according to data from the *Indonesian Demographic and Health Survey* 2007, and 15.3% according to data of Basic Health Research (*Riskesdas*) 2010.[14,15] Based on the *Health Data Profile* of Indonesia 2011, coverage of exclusive breastfeeding in the province of Yogyakarta Special Region was higher than the national average, which was 71.0%.[16] The definition of exclusive breastfeeding in this study was giving breast milk without any additional food or drink for 6 months in accordance with the Indonesian government policy. However, because this new policy was recommended since 2003,[14] a definition of exclusive breastfeeding for 4 months was given for subjects born before 2003.

The results of this study indicate that exclusive breastfeeding is not a protective factor against epilepsy in children. This is in contrast to some previous studies which suggest that breastfeeding can reduce the risk of epilepsy.[5,9,10] All of these three studies had prospective cohort designs with large numbers of subject. Both of these aspects need to be considered for future study. In epidemiology, the three studies were conducted in developed countries. More than 80% of new epilepsies occur each year in developing countries, which predominantly affected children in rural areas and low socioeconomic society.[2,17,18] One of the main reasons of this higher incidence is because of the more risk factors that can lead to permanent brain damage, including meningitis, malaria, neurocysticercosis, pre- and perinatal complications, and malnutrition.[1] In the purpose to avoid bias in our study, patients with history of intracranial infections, head trauma, low birthweight, and history of neonatal seizures had been excluded. However, other factors such as perinatal asphyxia, birth trauma, and complications of childbirth can not be excluded due to difficulty of obtaining such data by retrospective study design.

The protective mechanism of breastfeeding against epilepsy has not been yet clear, but it was suggested that the contents of polyunsaturated fatty acids (PUFAs) such as arachdonic acid (AA) and docosahexaenoic acid (DHA), cholesterol, and sialic

acid, play an important role in brain development and stabilization of neuronal membranes by the neuroprotective mechanism and increasing the seizure threshold.[19,20] The level of fatty acids in breast milk is affected by maternal weight gain, nutritional status, and diet during pregnancy.[21,22] It also varies based on the triceps skin fold thickness, arm circumference, and body mass index of the mother during pregnancy. A study showed polyunsaturated fatty acids (PUFAs) and triglyceride content of breast milk in women with higher socioeconomic status were significantly higher than those with lower socioeconomic status, which was likely related to maternal nutritional status.[23] In our study, there was no analysis of the levels of blood PUFAs.

Information on exclusive breastfeeding in this study was only based on the parents' recall, however, previous study revealed that the maternal recall for information of initiation and duration of breastfeeding practice in the past had high validities and reliabilities, even up to a period of 20-22 years.[24] Futhermore, the same study also revealed that the recall of mothers of the age at introducing solid foods and fluids other than breast milk was less accurate than recall of the initiation and duration of breastfeeding, with the agreement between the first and subsequent interviews only around 37% - 66% and 13% - 45% in terms of introducing solid foods and formula milk, respectively. Because the criteria of exclusive breastfeeding is giving breastfeeding alone without other food or drink for a certain period, this may lead to recall bias in our study. We suggest further studies using prospective cohort design for a better control of some confounding factors such as pre-and perinatal complications. In addition, prospective design can also reduce recall bias regarding the duration of exclusive breastfeeding.

Exclusive breastfeeding for 6 months still become the policy of the Indonesian government and WHO recommendation to date.[13] A systematic review concluded that exclusive breastfeeding for 6 months, compared with 3-4 months or less, significantly decreases the incidence of gastrointestinal infections in children, helps the postpartum weight loss, and prevents early pregnancy, but does not have strong evidence for the long-term protective effect against allergic disease, growth, obesity, cognitive ability, and behavior. Considering the benefits of breast milk, recommendation of exclusive breastfeeding for the first 6 months, both in developed and developing countries should be sustained.[25]

We conclude that exclusive breastfeeding for 4-6 months has no effect on prevention of epilepsy in children.

Conflict of interest

None declared.

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