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Effect of Administration of Mackerel Oil During Pregnancy on the Expression of Brain Derived Neurotrophic Factor (BDNF) in the Cerebrum of Newborn Mice

Sofiyanti Miftakhurohmah[1]*, Widjiati[1], Hermanto Tri Joewono[1]

[1]Universitas Airlangga, Indonesia

Abstract

Omega 3 contained in mackerel oil extract is an important constituent of neuron cell walls and the raw material for building fetal brain cells. DHA and EPA in omega 3 regulate BDNF synthesis through a p38-MAPK dependent mechanism. BDNF has a role in regulating cell survival and programming cell death (apoptosis) in the brain. This study aims to determine the effect of giving mackerel oil during pregnancy on BDNF expression in the cerebrum of newborn rats. Posttest research design only control group with true experimental type. A sample of 30 rats with 10 each per group. The first group was the control group (K), the second group was mackerel oil (P1), and the third group was omega 3 supplements (P2). BDNF expression examination methods with immunohistochemistry. The data were analyzed analytically with ANOVA and continued with post hoc LSD. There was a significant difference in the expression of BDNF cerebral newborn rats between groups with a value of p = 0.000 (2.780 ± 0.52 in the control group, 3.670 ± 0.36 in the mackerel oil group, and 3.670 ± 0.45 in the omega 3 supplement group) . The conclusion of this study was that the group given mackerel oil extract had a higher BDNF cerebral expression than the other groups.

Keywords

BDNF; cerebrum; mackerel oil; omega 3; pregnant rats

***Corresponding Author**: Sofiyanti Mifatkhurohmah (E-mail: cuphie15@gmail.com)

Introduction

Addressing nutritional and health problems to improve the quality of human resources is best during the pregnancy period. Pregnant women are a critical group and are vulnerable to malnutrition(Muniz et al., 2023). The good nutritional status of pregnant women will ensure healthy growth of the fetus and birth of the baby, postnatal nutritional reserves for the mother, as well as sufficient breast milk production to meet the baby's needs at the start of life.(WHO, 2012).

Fish is a source of nutrient-rich aquatic food for the human body that contains many nutrients. Mackerel contains omega 3 which is a long chain polyunsaturated fatty acid which is an important nutrient for the development of body cells. Nutrients play a vital role in the process of growth and development of neuron cells in the brain to provide the baby with intelligence. Omega 3 is an important element that makes up neuron cell walls. Apart from that, omega 3 is also a raw material for making fetal brain cells(Herlina & Nurjanah, 2017).

Brain growth and development begins in the womb where the processes of proliferation, migration, differentiation, synaptogenesis, apoptosis and myelination occur. (Rice & Barone Jr, 2000). The brain growth and development process is supported by Brain-Derived Neurotrophic Factor (BDNF) (Chen et al., 2013). Through the Tropomycin receptor kinase B (TrkB) receptor, BDNF can maintain the survival of neurons and regulate synaptic plasticity by increasing the number of dendritic spines and synapse formation.(Cunha et al., 2010). This molecular mechanism underlies that cognitive function is influenced by BDNF regulation(Lu et al., 2014). StudyCirulli et al., (2004)also proved that the group of mice injected with exogenous BDNF showed improved cognitive function than the control group of mice. Cognitive function was measured using the Morris Water Maze method.

This research is a series of studies to educate babies from the womb which aims to determine the effect of administering mackerel oil during pregnancy on BDNF expression in the cerebrum of newborn mice.

Methods

The white mice used in this research were the Sprague Dawley strain, aged 2-3 months. The treatment group was given mackerel oil and omega 3 on days 1 to 17 of pregnancy at a dose of 3.24 mg/day. Treatment is given orally using a sonde. On the 18th day, a caesarean section was performed. The mother rat was anesthetized with ketamine and acepromazine-xylazine, then sacrificed by cervical dislocation. Rat pups were born by caesarean section (SC), weighed, and 3 rats were selected from each mother with the heaviest, medium and lightest weights. The mother was sacrificed by decapitation and then preparations were made for histopathological examination. Immunohistochemistry was performed to examine BDNF expression. The child's brain tissue was observed under a microscope at a 5x field of view with a microscope magnification of 400x. The data was tested for probability using the ANOVA test and continued with Least Significant Difference (LSD) to see the differences in each group using SPSS software tools. Ethics have been obtained from the ethics committee of the Faculty of Veterinary Medicine, Airlangga University with the ethics number 2.KE.033.04.2020.

Results and Discussion

In this study, no mothers died when given treatment and no offspring died or experienced premature birth. This research used mothers who had an initial weight of 120-130 grams and a mother's body weight of around 231-240 grams when pregnant.

Based on table 1, it shows that the highest final body weight of the rat mother was 253.70 ± 94.49 in the mackerel oil group.

Table 1. Mean and standard deviation of final BW of rat mothers for each group

Group	Final Mean BB (grams)±SD
No Treatment	231.60 ± 45.87
Mackerel oil	253.70±94.49
Omega 3 supplement	240.00 ± 52.01

Based on table 2, it shows the highest average value of BDNF expression in the group given mackerel oil when compared to other groups, namely 3.670 ± 0.36. To see whether there were differences between groups, the Anova test was carried out and continued with the LSD test.

Table 2. Mean and standard deviation of BDNF expression in the cerebrum of rat pups for each group

Group	Mean±SD
No treatment	2,780 ± 0.52
Mackerel oil	3,670 ± 0.36
Omega 3 supplement	3,190 ± 0.38

From table 3, the results of the Anova test show a p value = 0.000, which means there is a significant difference in the expression of BDNF in the cerebrum of newborn mice. Then the LSD test analysis was carried out and the results showed that in all comparisons for each group there were significant differences (p<0.05).

Table 3. Results of Anova test and LSD test of BDNF expression in children's cerebrum Rattus norvegicus

Group	Test LSD		Anova test
	Mackerel oil	Omega 3 supplement	
No treatment	0,000	0.043	0,000
Mackerel oil		0.019	

A comparison of the BDNF expression of the fetal brain in groups (K, P.1, P.2) can be seen in Figure 1. The red arrow indicates BDNF expression in the cerebrum which is indicated by the brown color of the chromogen. Based on this research, it was found that the expression of BDNF given mackerel fish oil was higher than that given no treatment. This is in accordance with research fromLim & Kwak (2019)which explains that DHA and EPA in fish oil can increase the stimulation of BDNF production thereby increasing synapse development, synapse plasticity and cognitive function.

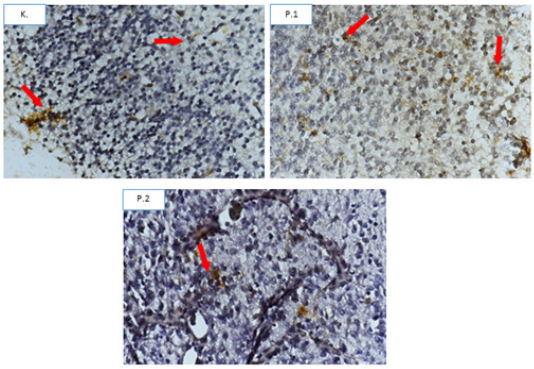

Figure 1. Comparison of images of fetal brain BDNF expression in groups (K, P.1, P.2).

The use of mackerel fish is widely used by the wider community because mackerel fish contains a lot of omega which is good for brain intelligence. Omega 3 is included in essential polyunsaturated fatty acids which are useful for increasing brain intelligence(Irmawan, 2009). The use of omega-3 fatty acids can be obtained from consuming mackerel (Rastrelliger kanagurta) fish oil, so mackerel has the potential to produce fish oil which is rich in omega-3 fatty acids.

Fish oil contains about 25% saturated fatty acids and 75% unsaturated weak acids(Widiyanto et al., 2015). Natural fatty acids including omega-3 are eicosapentaenoic acid (EPA) and docosahexaethanoic acid (DHA). The main function of the fatty acids DHA, ARA and EPA is to help the process of brain growth and development (intelligence), fetal development and nerve development.(Nadeak, 2013).

Omega-3 fatty acids in brain cells play

a role in preventing neuronal apoptosis by increasing phosphatidylserine in cell membranes which will activate the phosphorylation of Akt/PI3 kinase, this process will inhibit caspase 3. Apart from that, DHA also regulates BDNF synthesis through a p38- MAPK dependent mechanism. . The neurotrophin BDNF plays a role in synapse development, synapse plasticity, and cognitive function. During brain development, BDNF plays a role in regulating cell survival and programmed cell death (apoptosis). Omega 3 consumption increases BDNF resistance so that the ability of apoptosis decreases and makes neuron cells become better or the rate of decline in cognitive function will be slower even if exposed to external factors such as stress (Hermawan, 2010;Gultom et al., 2008).

Omega-3 fatty acids in the form of EPA and DHA can stimulate transcription factors in the hippocampus which will regulate the level of snaptic plasticity of brain neurons, Peroxisome Proliferator-Activated Receptors (PPARs).(Kuratko et al., 2013). Adequate n-3 PUFA status can support the maintenance of optimal nerve integrity and function. DHA influences neural plasticity and cognition. Consumption of omega 3 supplementation has been found to increase hippocampal BDNF levels and improve cognitive function in rodent models of brain trauma(Gomez-Pinilla et al., 2008).

DHA is thought to improve cognitive capacity by accelerating synaptic plasticity and modifying synaptic membrane fluidity. DHA is also thought to be directly linked to improving brain health in the central nervous system through a number of potential mechanisms. In addition, DHA moderates the expression of genes that regulate various biological functions that are potentially important for learning/memory(Sydenham et al., 2012)

Conclusion

There was a difference in BDNF expression in the cerebrum of rat offspring between those who were not treated and those who were given mackerel fish oil extract and omega 3 supplements. The group given mackerel fish oil extract had higher BDNF expression in the cerebrum than the other groups.

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