Impact of arterial blood pressure on cerebral health: understanding the dynamics

Impacto de la presión arterial en la salud cerebral: entendiendo la dinámica

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Received: 01/20/2022 Accepted: 04/19/2023 Published: 05/12/2024 DOI: http://doi.org/10.5281/zenodo.11261096

Abstract

Aruan fish (Channa striata) is an endemic fish of Kalimantan that is widely used by the people in South Kalimantan Province. Haruan fish bone waste can be used for additional nutrition in pregnant women and can support the process of blood pressure regulation. Haruan fish bones contain minerals in the form of calcium, phosphorus, potassium, and magnesium. This study was conducted to investigate the effect of Haruan (Channa striata) fish bone powder during pregnancy and lactation on the blood pressure of Wistar rat (Rattus norvegicus) offspring. This study used a true experimental design with a post-test-only control group design. Group 1 (treatment) was given Haruan fish bone powder (Channa striata), and group 2 (control) was without Haruan fish bone powder (Channa striata) from the first pregnancy up to 22 days after the delivery. The systolic and diastolic blood pressure of the pups from both groups were measured and analyzed. Statistic test results showed a difference in blood pressure levels in rat pups between the control and the treatment group. In conclusion, there was an effect of giving Haruan fish bone powder (Channa striata) during pregnancy and lactation period on the blood pressure levels in Wistar rat pups (Rattus norvegicus).

Keywords: Fish bone powder; blood pressure; jaws and teeth development; mineralization

Resumen

El pez aruan (Channa striata) es un pez endémico de Kalimantan que es ampliamente utilizado por la gente de la provincia de Kalimantan del Sur. Los desechos de espinas de pescado de Haruan se pueden utilizar como nutrición adicional en mujeres embarazadas y pueden apoyar el proceso de regulación de la presión arterial. Las espinas de pescado Haruan contienen minerales en forma de calcio, fósforo, potasio y magnesio. Este estudio se realizó para investigar el efecto del polvo de espinas de pescado Haruan (Channa striata) durante el embarazo y la lactancia sobre la presión arterial de las crías de rata Wistar (Rattus norvegicus). Este estudio utilizó un diseño experimental real con un diseño de grupo de control únicamente post-prueba. El grupo 1 (tratamiento) recibió polvo de espinas de pescado Haruan (Channa striata), y el grupo 2 (control) no recibió polvo de espinas de pescado Haruan (Channa striata) desde el primer embarazo hasta 22 días después del parto. Se midió y analizó la presión arterial sistólica y diastólica de los cachorros de ambos grupos. Los resultados de las pruebas estadísticas mostraron una diferencia en los niveles de presión arterial en crías de rata entre el grupo de control y el de tratamiento. En conclusión, hubo un efecto de la administración de polvo de espinas de pescado Haruan (Channa striata) durante el embarazo y el período de lactancia sobre los niveles de presión arterial en crías de rata Wistar (Rattus norvegicus).

Palabras clave: Polvo de espinas de pescado; presión arterial; desarrollo de mandíbulas y dientes; mineralización

Introduction

Blood pressure regulation during pregnancy is crucial for the development of a healthy cardiovascular system. Blood pressure development begins during fetal development, typically between 6-8 weeks of gestation. The histological differentiation of blood vessels begins at around the 11th week of embryonic development. This stage is known as the cap stage, during which the endothelial cells develop. The bell stage begins at approximately the end of the 10th week of embryonic development. Angiogenesis and vasculogenesis occur during the bell stage and continue into later stages of blood vessel development. At the end of the 5th month of prenatal development, the blood vessels begin to form through a process called vasculogenesis. This is when calcium and other minerals are deposited onto the organic matrix that has been secreted by the endothelial cells and smooth muscle cells. The matrix apposition process occurs during this time, where the organic matrix is gradually mineralized, resulting in the formation of blood vessels. Any stressful events during pregnancy and childbirth can have an impact on blood pressure regulation, leading to the development of hypertension[1,2].

A balanced and nutritious diet during pregnancy is crucial for the health and development of both the mother and the growing fetus. Pregnancy and lactation require additional energy, nutrients, and minerals such as iron (Fe), zinc (Zn), copper (Cu), calcium (Ca), phosphorus (P), magnesium (Mg), iodine, selenium, and vitamins: A, B1, B2, niacin, choline, pantothenic acid, B6, B12, C, E, and folates[3,4].

Calcium is indeed essential for the development of blood vessels and bones, particularly during pregnancy and lactation. It is needed for the formation and mineralization of blood vessels and bones, as well as for the growth and development of the fetal skeleton[5]. Magnesium is also an essential mineral for blood pressure regulation, along with calcium and other nutrients. It plays a crucial role by stimulating the activity of endothelial cells, which are responsible for blood vessel relaxation. Magnesium also activates enzymes from the phosphatase group, which are involved in the blood pressure regulation process[6]. Phosphorus is indeed the most abundant mineral, after calcium, and is a fundamental component of blood vessels and bones. Phosphorus helps to regulate the activity of endothelial cells and smooth muscle cells, which are involved in the process of blood pressure regulation[7]. Potassium, the ionic form of potassium, in trace amounts plays a vital role in blood pressure regulation by incorporated into the blood vessels, making them more resistant to vasoconstriction, which helps to prevent hypertension and maintain healthy blood vessels. They stimulate the proliferation of endothelial cells, the cells responsible for blood vessel relaxation, and inhibit the activity of vascular smooth muscle cells, the cells responsible for vasoconstriction, thus leading to a decrease in blood pressure and improved cardiovascular health[8].

A mineral intake can be fulfilled with one of the mineral-rich Haruan fish bones. Haruan fish bone is a form of waste generated from the fish processing industries. Fish bones are a good source of calcium and phosphorus, which are important minerals for blood vessel and bone development and maintenance. Additionally, fish bones contain other minerals such as magnesium, potassium, and trace elements like zinc and copper, which are important for various physiological functions in the body, especially during pregnancy and lactation. Fish bones are rich in hydroxyapatite, which is the main mineral component of bones and blood vessels.

Materials and methods

This research, conducted in vitro with a post-test control group design, received approval from the Health Research Ethics Commission of the Faculty of Dentistry, Lambung Mangkurat University (Approval No. 024/KEPKG-FKGULM/EC/II/2021).

Thirty Wistar rats (10 males and 20 females), aged 2.5-3 months and weighing 200-250g, were housed in iron cages for one week. They had access to standard food and water ad libitum. Lighting conditions were set to 12 hours of light and 12 hours of darkness, with a temperature maintained at 20-25°C. The rats were then paired with female rats at a ratio of 1:2 (male:female).

The rats were divided into two groups: Group 1 (treatment) received BR2 food and distilled water ad libitum along with Haruan fish bone powder (Channa striata) at a dose of 0.27 g/day. The Haruan fish bone powder, mixed with 2.5% CMC-Na suspension, was administered orally at a volume of 2 ml per day using a gastric tube. Group 2 (control) received BR2 food without Haruan fish bone powder.

On the 22nd day after weaning, the pups were anesthetized with ether inhalation anesthesia and subsequently decapitated. The jaws and teeth were collected, cleaned, dried, and ground into a fine powder.

Calcium levels were measured using the Titrimetry method. The tooth powder was dissolved in aquades with a red metal indicator, heated, and treated with NH4-oxalate solution. The resulting precipitate was filtered, washed, and titrated with 0.1 N KMNO4 solution to determine calcium content.

Phosphorus levels in dental samples were measured using UV-Vis Spectrophotometry at a specific wavelength of 422.7 nm. Prior to testing, the instrument was calibrated using standard phosphorus solutions.

Fluoride levels were determined by crushing dry samples and diluting them with aquadest. The solution was mixed with SPADNS to induce a color change, and the absorbance was measured using UV-Vis spectrophotometry. Calibration curves were used to determine fluoride concentration.

These findings contribute to understanding the effects of Haruan fish bone powder on calcium, phosphorus, and fluoride levels in dental tissues, potentially shedding light on its impact on arterial and cerebral blood pressure.

Measurement of magnesium levels using the Titrimetry method. Approximately 350 mg of the sample is weighed accurately, then dissolved in dilute hydrochloric acid. Add to the solution with sodium hydroxide until a steady mist forms then add 5 ml of ammonia buffer. Titrate with dinatrium edetat.0.05M uses eriochrome black to blue indicators. The following reactions occur at this measurement:

$Zn^{++} + (H_2Y)^{=} > (ZnY)^{=} = 2H^{+}$ (1)

$HlIn^{=} + Zn^{++} > ZnIn^{-} + H^{+}$ (2)

$ZnIn^{-} + (H_2Y)^{=} > (ZnY)^{=} + HIn^{-}$ (3)

Results

Blood pressure levels of Wistar rat offspring are shown in Figure 1. The results showed levels of systolic and diastolic blood pressure in Wistar rat offspring (Rattus norvegicus) were decreased. There were differences in the rat pups' blood pressure including systolic and diastolic blood pressure levels in treatment and control group. The pups' blood pressure level in the treatment group was lower than the control group.

The data collected were analyzed using Independent Sample T-test for systolic and diastolic blood pressure because the normality test was. The result of T-test showed that there were significant differences ($p<0.05$) in the average of pups' systolic blood pressure ($p=0.000$) and diastolic blood pressure ($p=0.000$) between the treatment and control group. Mean arterial pressure was analyzed using Mann Whitney test because the normality test result was $p>0.05$. The result of Mann Whitney test showed that there was a significant difference ($p<0.05$) between the treatment and control group ($p=0.002$). It can be concluded that Haruan (Channa striata) fish bone powder supplementation can significantly decrease blood pressure levels of pups (Table 1).

Figure 1. Mineral level of treatment and control group

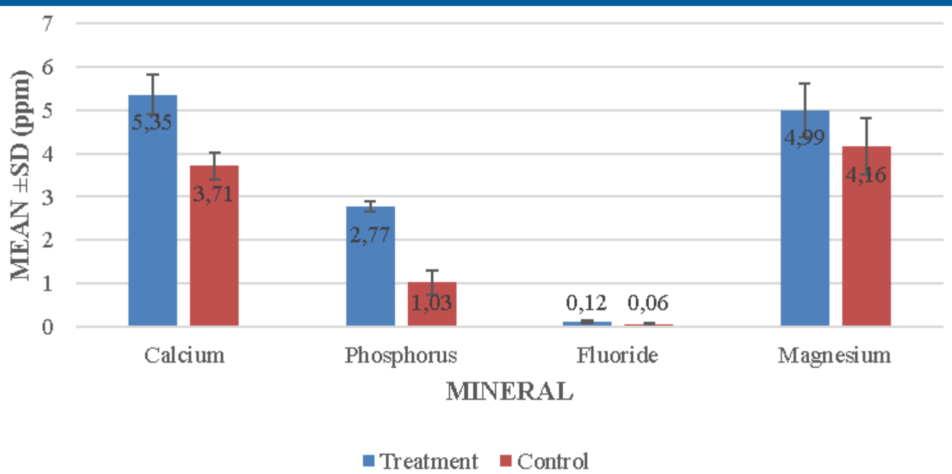

Table 1. The results of statistical tests of mineral

Mineral	Group	N	Signification value (p)
Calcium	Treatment	17	0.000*
	Control	17	
Phosphorus	Treatment	17	0.000*
	Control	17	
Fluoride	Treatment	17	0.000*
	Control	17	
Magnesium	Treatment	17	0.002*
	Control	17	

(*) significant $p<0.05$

The results of this study are in accordance with previous research which stated that maternal supplementation with Haruan fish bone powder could decrease the risk of hypertension in offspring. It is essential for pregnant and breastfeeding women to consume a balanced diet for the growth and development of the cardiovascular system. This includes an adequate intake of essential nutrients and minerals. Unlike vitamins, minerals cannot be synthesized by the body and must be obtained through the diet or supplements[11,12]. Adequate intake of essential minerals from Haruan fish bones can meet mineral needs during pregnancy and lactation.

Haruan fish bone is one of the raw materials that can be used to fulfill nutritional needs during pregnancy and breastfeeding because it has organic and inorganic components. In addition, the bones of the Haruan fish contain a lot of mineral salts such as calcium phosphate and creatine phosphate. The main mineral content found in Haruan fish bones consists of calcium, sodium, phosphorus, magnesium, fluoride, iron, zinc, potassium, and copper[13,14].

Blood pressure regulation begins during fetal development. The process of blood vessel development involves the formation of vascular tissue, which includes both the endothelium and the smooth muscle. Once the blood vessels have formed, the cells within them begin to differentiate and multiply, forming the various layers of vascular tissue. Blood pressure regulation, which is the process of maintaining a healthy blood pressure, also begins during fetal development and continues after birth as the cardiovascular system matures. The blood pressure regulation process is a complex and tightly regulated process, and any disruptions or imbalances in the availability of minerals or the activity of the regulatory cells can result in developmental defects or abnormalities in blood pressure. Therefore, the nutritional status of the mother during pregnancy and lactation plays an important role in the development, formation, and regulation of blood pressure[15–17].

During fetal development, there is an exchange of nutrients between the mother and the fetus, which allows for the formation and regulation of the developing cardiovascular system. Minerals such as calcium, phosphorus, magnesium, and fluoride, which are important for blood pressure regulation, are circulated in the bloodstream of the fetus and are taken up by specialized cells called vascular smooth muscle cells. These cells are responsible for the regulation of blood pressure, and they use the circulating minerals to create a healthy blood pressure[18]. Tricalcium phosphate is a key component of this regulatory process, and it eventually converts to hydroxyapatite crystals, which are very hard and durable[19].

Calcium, sodium, magnesium, phosphorus, and potassium are considered major minerals due to their abundance in the body[20]. Calcium is an essential mineral for the regulation of blood pressure, just as it is for bone health. Calcium is deposited onto the vascular smooth muscle cells during the blood pressure regulation process. Calcium is also an important component of the vascular endothelium, which provides structural support to the blood vessels[21-23].

Calcium absorption is particularly important during pregnancy for the development of the fetal cardiovascular system, and during pregnancy, the demand for calcium increases as the fetal cardiovascular system develops. The mother has mechanisms to increase calcium absorption from the diet to meet the increased demand during pregnancy. For example, the hormone estrogen, which is produced in higher levels during pregnancy, increases calcium absorption from the intestines. The body produces more of an active form of vitamin D during pregnancy to help with calcium absorption and utilization. The recommended daily intake of calcium varies between countries and organizations, but generally falls within the range of 900-1200 mg/day for adults. The World Health Organization (WHO) of the United Nations specifically recommends a dietary intake of 1000 mg/day of calcium for non-pregnant adults between ages 19-50 and 1200 mg/day for pregnant women[24,25].

Phosphorus is another important mineral for blood pressure regulation. Phosphorus plays a key role in the formation and regulation of the cardiovascular system, and it is required for the development of the fetal cardiovascular system. It is primarily found in the form of phosphate in the body. Within the cardiovascular system, phosphorus and calcium work together to form hydroxyapatite crystals. In the human body, approximately 85% of phosphorus is stored in the form of phosphoproteins and hydroxyapatite crystals in bones and teeth[26]. Phosphorus is regulated by the hormones PTH, 1,25(OH)2 D3, and FGF23. PTH increases the release of phosphorus from bone, while 1,25(OH)2 D3 increases intestinal absorption of phosphorus and FGF23 decreases renal reabsorption of phosphorus. Inorganic phosphorus, in the form of phosphate ions, is an essential component for the formation of hydroxyapatite crystals in the cardiovascular system[27].

The recommended daily intake of phosphorus for pregnant and lactating women is higher than that for non-pregnant adults. The "Recommended Dietary Allowances" or RDA data determine the recommendations for daily micronutrient intake for a pregnant woman. The recommended daily intake of phosphorus for pregnant and lactating women is 700 per day[12,28].

Fluorides, in trace amounts, are considered essential for proper cardiovascular development.8 Fluoride stimulates vascular smooth muscle cells, the cells responsible for blood pressure regulation, and helps to increase blood vessel density. Fluoride can also inhibit the activity of vascular smooth muscle cells, which can help maintain blood pressure[29]. Fluoride ions can be incorporated into the hydroxyapatite crystals in the cardiovascular system, making them more resistant to blood pressure changes[30]. Fluoride has been shown to stimulate blood pressure regulation by increasing the activity of vascular smooth muscle cells, the cells responsible for synthesizing new blood vessels. At the same time, fluoride also decreases blood pressure by inhibiting the activity of vascular smooth muscle cells, the cells responsible for constricting blood vessels. This results in a net decrease in blood pressure, which can reduce the risk of hypertension and other cardiovascular-related problems. Identification of vascular smooth muscle cells[8,31,32]. In the cardiovascular system, fluoride can be incorporated into apatite crystals through a process called ion exchange. This process leads to the formation of fluoroapatite[8].

Fluoride may be supplemented during pregnancy until blood pressure regulation is completed. During pregnancy and breastfeeding, mothers should take 1 mg fluoride a day. Even though fluoride is an important mineral in the development of the cardiovascular system, excess intake of fluoride during pregnancy can lead to fluorosis in the developing cardiovascular system of the fetus. Therefore, it is important for individuals to maintain a balanced fluoride intake and follow recommended guidelines to ensure the health and strength of their cardiovascular system, while also minimizing the risk of unwanted side effects.

Magnesium (Mg) plays a crucial role in blood pressure regulation, although it is not as well-known as calcium and potassium in this regard. Magnesium is mainly stored in bones and muscle and is also found in smaller amounts in soft tissues and extracellular fluids. Magnesium is involved in the regulation of blood vessel tone, as well as in the contraction and relaxation of vascular smooth muscle cells, including those involved in cerebral blood flow[34]. Vitamin D and the parathyroid hormone (PTH) influence the regulation of magnesium in blood pressure control. Vitamin D increases the expression of magnesium transporters in the blood vessels, which leads to vasodilation and decreased blood pressure. On the other hand, parathyroid hormone increases magnesium levels in the blood, which in turn promotes vasodilation and decreased blood pressure by stimulating the production of active vitamin D in the kidneys[35,36].

Magnesium ions play a crucial role in maintaining healthy blood pressure by acting as a cofactor for enzymes involved in the regulation of vascular tone. Magnesium also contributes to the structural integrity of blood vessels and can affect their responsiveness to vasoactive stimuli by affecting the morphology and structure of vascular smooth muscle cells. In addition to its role in blood pressure regulation, magnesium is also present in the cerebral vasculature, where it plays a critical role in maintaining proper cerebral blood flow and preventing hypertension-related cerebrovascular damage.

Conclusions

Intake of magnesium significantly impacts blood pressure regulation through its role in enhancing vasodilation and improving endothelial function. Magnesium acts as a catalyst in converting vitamin D into an active form, thereby promoting the production of vasodilators like nitric oxide, which effectively lower blood pressure levels. Conversely, a decline in magnesium levels prompts an increase in parathyroid hormone activity, leading to vasoconstriction within blood vessels. Persistent vasoconstriction can result in elevated blood pressure levels and contribute to the onset of hypertension.

During pregnancy, maintaining adequate magnesium intake is crucial, with recommended daily amounts falling within the range of 350-400 mg/day. This intake level is vital for sustaining healthy blood pressure levels and mitigating the risk of hypertension-related complications in both the mother and the fetus. Ensuring sufficient magnesium intake during pregnancy not only supports maternal cardiovascular health but also fosters optimal fetal development and well-being.

ACKNOWLEDGEMENTS

The authors were very grateful to Direktorat Jenderal Pendidikan Tinggi Kementerian Pendidikan dan Kebudayaan Indonesia and Faculty of Dentistry, Lambung Mangkurat University, Banjarmasin for giving the authors opportunity to conduct research.

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