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EDITORIAL

Fueling growth and preventing stunting: the role of animal protein in achieving optimal nutrition - Indonesia's National Nutrition Day 2023 Theme

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Poor linear growth, currently defined as inadequate height to growth standards defined by the World Health Organization (WHO), is still a major problem in low-middle-income countries (LMICs) including Indonesia. The national survey results from 36.8% in 2007 to 30.8% in 2018 showed small differences in under-five years old children with height-for-age-Z-score less than -2 standard deviation (HAZ < -2 SD) from the growth reference or stunted.[1] Though the Indonesian Nutrition Status Survey results showed an improvement in the stunting rate to 21.6% in 2022, the data revealed large regional disparities, ranging from 8% in Bali to 35.3% in East Nusa Tenggara.[2]

It is known that for children with stunted growth in early life, the risk of impaired health, mortality, and delayed neurocognitive and motor development is heightened. Moreover, tend to have a long-term effect of decreased performance in education, lower productivity and socioeconomics, and a higher risk of chronic diseases in adulthood.[1,3]

Stunting has many associated factors, including socioeconomic inequality, geographic differences, maternal factors, such as education, age, nutrition status, and infection; short birth intervals, low birth weight, and preterm birth, food insecurity, practices of feeding, nutrient deficiencies, such as protein, iron, zinc, calcium, and vitamins, childhood morbidity, and environmental. Low birth weight and length, unimproved sanitation, and low protein intake are the leading risk factors in developing countries, especially in the horticulture area.[4,5]

The requirement for protein and amino acid is likely to be greater in environments where vulnerable populations such as children are commonly affected by ongoing or recurrent infections and impaired intestinal absorptive ability, despite the lack of overt clinical signs. Protein plays a role in the growth and maintenance of body tissues and replaces damaged cells. Inadequacy of protein intake during the growth period could arise nutritional problems and delayed growth.[6]

Linear growth retardation mostly occurs during the complementary feeding period of 6–23 months of age, when breastfeeding is no longer adequate to

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meet the child's nutritional needs. Adequate intake of energy, protein, and micronutrients is associated with a more diverse diet. However, epidemiological data suggest that infant feeding diversification after a period of exclusive breastfeeding is a problem; and that the nutritional quality of the solid food introduced is insufficient to meet the infants' caloric and nutrient needs.[3,7]A pooled analysis of Indonesia's Demographic and Health Surveys from 2007 to 2017 revealed that the percentage of children who consumed minimum dietary diversity was stagnant from 53.1% in 2007 to 53.7% in 2017, and less in rural areas.[8]

Protein adequacy among under-five Indonesian children was low. The Total Diet Study in 2014 found that 23.6% of children consumed less than 80% of the recommended dietary allowance for protein. Protein quality is crucial because of the main component of proteins, amino acids. Insufficient amino acids can disrupt protein synthesis and affect growth.[9,10] In LMICs, where staple foods such as rice, wheat, maize (corn), millet, sorghum, roots and tubers dominate infant and young child diets, there is a high likelihood of insufficient intake of essential amino acids and usable dietary protein to support overall growth. Animal-source foods could improve child nutrition through their rich content of high-quality protein, essential fatty acids, and micronutrients such as zinc, calcium, and vitamins A and B12 which have high bioavailability.[10,11]

A study by Limardi, et al[3] found that although there was no significant difference in dietary diversity between children with and without stunting, stunted children consumed a significantly lower proportion of flesh food and received significantly less protein from their diet. The findings of another study by Amalia, et al.[12] in East Java Indonesia showed that toddlers with improper complementary feeding practices are 7.87 times more likely to be stunted, while toddlers with protein deficit had a 6.5 times higher risk of stunting.

Sholikhah and Dewi[13] reviewed five studies from Indonesia to support arguments for the importance of animal protein source foods in stunting prevention. Three studies found animal protein source food consumption of children with stunted growth was lower compared to children with normal linear growth. Oktaviani et al.[14] found that children 2–4 years old who consumed an inadequate intake of animal protein have a higher risk of being stunted compared to children who consumed an adequate intake of animal protein by 6.059 ($p<0.001$). Afiah et al.[15] found that children under five years old who did not consume animal protein source food in the past week have a greater incidence of stunted compared to children who consumed animal protein source food in the past week ($p=0.023$, OR=9.000).

With a target to reduce the stunting prevalence to 14% in 2024, the Indonesian government has implemented various policies and programs through both 'nutrition-specific' (predominantly related to the health sector) and 'nutrition-sensitive' (related to non-health sectors) interventions.[16,17] A study in East Java revealed that access to adequate latrines was the nutrition-sensitive intervention that had the greatest impact on the incidence of stunting among children 6-24 months of age.[17]

The latest nutrition-specific intervention by raising theme for Indonesia's National Nutrition Day's 63rd anniversary on January 25th, 2023 was "Animal Protein Prevents Stunting", with slogans including "Animal Protein Food in Every Meal" and "My Plate is Rich of Animal Protein Food".[18] Indonesia still needs hard efforts to accelerate the reduction in the prevalence of stunting. In order to achieve adequacy of protein intake and proper complementary feeding for the children, women should be empowered to affect access to resources and allocations.[4,12] Further longitudinal studies, monitoring, evaluation, and maintaining the continuity of the programs are still needed to ensure the sufficiency of animal protein intake, thus determining the effects of animal protein intake adequacy on linear growth in children to prevent stunting.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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ORIGINAL PAPER

The correlation between knowledge and behavior of reading composition label of packaged food on public 2 JHS and Giovani JHS students in Kupang

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Abstract

Background: Labels of packaged foods are used as guidelines for buying packaged food products. School students are a group who are at high risk of getting illness through food and drink that they consume either at home, at school, or anywhere they can buy packaged food. This happens due to students at this age always get money from their parents to buy snacks at the school canteen or outside the school canteen. National data states that most of the snacks consumed by school students contain flavourings and some chemicals which are certainly not good for their health, such as flavoured foods (77.8%), sweets (68.1%), caffeinated (36.5%) and salty (24.5%). Poor knowledge in reading the composition on a food label and poor behaviour in choosing packaged food for school students can cause various health problems, such as food poisoning and obesity.

Objective : To determine the relationship between knowledge and behaviour of reading the packaged food label composition on Public 2 JHS and Giovanni JHS students in Kupang.

Methods: This is an observational analytical study with a cross sectional design conducted at two schools located in Kupang City, namely Public 2 JHS which is located at Tom Pello street No. 33 and Giovanni JHS which is located at Ahmad Yani street No. 50, Kupang City, East Nusa Tenggara Province, Indonesia. Both schools provide school canteens that sell some packaged foods to be purchased by students at both schools. 350 subjects were used in this study and divided into Group A consisting of 175 Public 2 JHS students and Group B consisting of 175 Giovanni JHS students, using a google form questionnaire. The respondents were chosen by cluster random sampling technique. This study was analyzed bivariately using the Spearman correlation test.

Results: The sample in this study amounted to 350 people consisting of 175 students at Public 2 JHS and 175 students at Giovanni JHS. The results of the study from 175 respondents at Public 2 JHS showed that in the knowledge variable, there were 172 (98.3%) respondents who had very good knowledge, and 3 (1.7%) respondents who had good knowledge. Meanwhile on the behavioural variable, there are 169 respondents (96.6%) who have very good behaviour and 6 respondents (3.4%) have good behaviour. The results of the research from 175 respondents of Giovanni JHS showed that in the knowledge variable, there were 172 (98.3%) respondents who had very good knowledge, and 3 (1.7%) respondents who had good knowledge. Meanwhile on the behavioural variable, there are 76 respondents (43.4%) who have very good behaviour and 99 respondents (56.6%) have good behaviour.

Conclusion: There is a significant correlation (p = 0.004) between knowledge and behaviour of reading the packaged food label composition on Public 2 JHS students and there is also a significant correlation (p = 0.046) between knowledge and behaviour of reading the packaged food label composition on Giovanni JHS students in Kupang.

Keywords: packaged food label composition, knowledge, behaviour

Introduction

Packaged food is referred to food whose container to protect the food product and acts as a label to provides information about the food product itself. Information label on packaged foods is given to buyers as a guideline for buying the products they want.[1] Studies have found that food literacy/nutrition literacy can have a critical role in shaping children's dietary behaviour and enabling them to have healthy food choices. In Iran, nutrition transition has taken place due to urbanization and rapid socio-economic changes and have resulted in a tendency toward a more westernized dietary pattern, especially among children and adolescents. This general shift in children's diet is characterized as low consumption of fruit and vegetables, fiber-rich foods and dairy products, as well as high consumption of fatty, sugary and convenience foods.[2] This culture of buying packaged food occurs in almost all social classes and ages, including school students in Indonesia.[3] School students are a group who is at high risk of getting illness through food and drink that they consume either at home, at school, or anywhere they can buy packaged food.[4] This happens due to students at this age always get money from their parents to buy snacks at the school canteen or outside the school canteen, without seeing and choosing what food to consume.[5] Most of the snacks they consume contain flavourings, preservatives and some chemicals which are certainly not good for their health and have no good nutrition for their growth.[4] National data states that the prevalence of risky foods that are consumed by the aged >10 years population is flavoured foods (77.8%), sweets (68.1%), caffeinated (36.5%) and salty (24.5%).[6] Based on data from the National Food and Drug Agency (BPOM), as of May 10, 2019, it has been found from 796 distributor warehouse facilities in Indonesia, as many as 170,119 food product packaging containing hazardous chemicals, damaged, and expired.[7]

Based on a survey conducted by the National Consumer Protection Agency (BPKN) in 2007 stated that only 6.7% of consumers in Indonesia who have knowledge in paying attention to labels when buying a packaged food product.[8] In 2015, a Community Food Safety Concern Study was conducted by the National Food and Drug Agency (BPOM), showed that only 25.3% of consumers had the behaviour to check the composition of packaged foods, while the other 37.1% often, 34.5% rarely and 3.1% even never checked the composition of packaged foods.[9]

Poor knowledge in reading the composition on a food label and poor behaviour in choosing packaged food for school students can cause various health problems, such as food poisoning and obesity. Based on data collected in 2019, from the Emergency Department (ER) of Hospitals and Health Centers in Kupang City, East Nusa Tenggara, informed that there were 98 incidents or cases of poisoning in Kupang. The poisoning cases mostly happened in aged 5 – 14 years population (29.59%) for about 29 patients.[10] According to National Food and Drug Agency (BPOM) in 2017, stated that the type of food that caused extraordinary events (kejadian luar biasa/KLB) as a result of food poisoning was mostly snack food (24,53%) and the most places where outbreaks occur due to snack food poisoning are in educational institutions (28.30%).[11]

The increase in the consumption of packaged foods is also associated with increasing incidence of obesity.[12] Basic Health Research Data (Riset Kesehatan Dasar) in 2018 stated that there was an increase in obesity with a prevalence of 31.0% in children aged <15 years, a prevalence of 21.8% in those aged >18 years and a prevalence of 13.6% of children who were overweight in East Nusa Tenggara Province. The problem of obesity and overweight in students have not become a priority problem yet, that needs be resolved in Kupang City.[13]

Inappropriate food intake can be at risk of causing various health problems such as food poisoning and obesity which eventually can caused degenerative diseases for those who consume it.[14] Research conducted by Indah Nasution et al.[15], on high school students at SMA Gajah Madah Medan in 2017 found that 62.2% of students had very good knowledge when they read packaged food labels. The students in this study had good knowledge because they had previously received

lessons about the content of ingredients in packaged foods and the nutritional value of packaged foods when they were in junior high school. This makes it easier for them to know about the composition of the ingredients and the nutritional value information contained on the labels of the packaged foods they consume.

Research conducted by Rezi Rafiki.[16] in 2012 on students at SMA Negeri 68 Jakarta found that students who had good knowledge about reading nutrition labels and food labels and were obedient in reading labels on packaged foods were 68 respondents (57.6%) and only 29 respondents (41.4%) had poor knowledge and were not obedient in reading nutrition labels and food labels of a packaged food. The results of the analysis showed that there was significant relationship between the level of knowledge and behaviour in reading food labels from packaged foods.

Based on research conducted by Christopher Sinaga and Sinta Fransiske.[17] in 2019 on students of SMK Farmasi Harapan Massa in Depok, it was found that although the overall proportion of respondents was more knowledgeable in reading labels on packaged foods, respondents still had poor behaviour in reading packaged food labels with a percentage by 81.0%. This resulted in no relationship between knowledge in reading packaged food labels with behavior in reading packaged food labels.

This study is an umbrella study with a study titled the correlation between knowledge and behavior in reading nutritional value information labels of food on Nusa Cendana University students. Therefore, the authors are interested in conducting a research with title: "The Correlation Between Knowledge and Behavior of Reading Packaged Food Label Composition on Students of Public 2 Junior High School and Giovanni Junior High School in Kupang".

Methods

This study is an observational analytic study using a cross-sectional research design. This study was conducted at two schools located in Kupang City. 350 subjects were used in this study and were divided into 2 groups, namely group A consisting of 175 students from Public 2 Junior High School and group B consisting of 175 students from Giovanni Junior High School, which included grades VII, VIII and IX from each of these schools.

In theory, Arikunto said that if the number of respondents <100, then all samples were taken. Meanwhile, if the respondent is >100, then the sampling is 10%-15% or 20%-25%. If the subject used is too large, the sample can be taken between 10%-15%, up to 20%-25% or more, depending on at least: [18]

a. The ability of researchers seen from the time, energy and funds.
b. The area of observation is narrow for each subject,
   because this involves a lot of data.
c. The size of the risk borne by the researcher. For high-risk research, of course, if the sample is large, the results will be better.

Based on this opinion, the sampling in this study was 25% of the existing population, because the total population exceeded 100, namely 1,403 students, the sample results were obtained from 25% X 1,403 = 350.75 so the sample used in this study was 350 students. The sampling technique in this study used cluster random sampling, namely randomization of groups, not individual subjects.

This study was conducted online through the zoom meeting and google form after received ethical clearance from Health Research Ethics Commission of Medical Faculty Nusa Cendana University. The number of the Ethical Clearance number was 70/UN15.16/KEPK/2021. Data collection started from August 20, 2021 until August 27, 2021 by filling out the informed consent form and both knowledge questionnaires and behavioural questionnaires about reading the composition of packaged food labels by 350 subjects who met the inclusion criteria. This study was analyzed univariately and then bivariately using Spearman correlation test.

Results

Table 1 showed that the most gender of respondents in group A and group B is female amounted to 198 (56.7%) respondents, compared to male amounted to 152 (43.3%) respondents. The

Table 1 Characteristics of respondents from Junior High School Students

Variable	n(%)		Total
	Group A	Group B	
Gender			
• Male	71 (20.2)	81(23.1)	152(43.3)
• Female	104 (29.8)	94(26.9)	198(56.7)
Age			
• 11 years old	6(1.7)	14(4.0)	20(5.7)
• 12 years old	68(19.4)	55(15.7)	123(35.1)
• 13 years old	61(17.4)	62(17.7	123(35.1)
• 14 years old	34(9.7)	44(12.6)	78(22.3)
• 15 years old	6(1.7)	0 (0%)	6(1.7)
Nutritional Status			
• Severe Underweight	19(5.4)	9(2.6)	28(8.0)
• Underweight	22(6.2)	17(4.9)	39(11.1)
• Normal	106(30.2)	119(34.0)	225(64.2)
• Overweight	22(6.2)	25(7.1)	47(13.3)
• Obesity	6(1.7)	5(1.4)	11(3.1)

age with the highest number of respondents from both groups is at the age of 12 years and 13 years with a total of 123 (35.1%) respondents, while the age with the least number of respondents from both groups is 15 years with a total of 6 (5.8%) respondents. The youngest age is at the age of 11 years and the oldest age is at the age of 15 years. The most nutritional status is normal, amounted to 225 (64.2%) respondents, while the least nutritional status is obesity with a total of 11 (3.1%) respondents.

Based on table 2, the distribution of respondent's characteristics based on counselling conducted at both schools is that a total of 193 (55,1%) respondents had previously received counselling about choosing a good snack food at each of these schools. Based on the behaviour of reading composition labels, as many as 242 (69.1%) respondents said they frequently read the composition label when buying packaged food. Based on the questionnaire question about get a stipend from parents, a total of 237 (67.8%) respondents said they frequently get a stipend to buy packaged food in the school canteen or outside the school canteen. Based on the questionnaire question about stipend with the amount of Rp.25.000,-, 226 (64.7%) respondents said they never get stipend with the amount of Rp.25.000,- to buy packaged food. Based on the habit of consuming foods containing sweet flavors, as many as 217 (61.9%) respondents said they don't have habit of consuming foods that contain excessive sweetness when buying packaged foods. Based on the habit of consuming foods containing salt and flavourings, as many as 231 (66.0%) respondents said they don't have the habit of consuming foods that contain excess salt and flavourings when buying packaged foods.

Table 2 Characteristics of respondents based on questionnaire questions

Variable	n(%)		Total
	Group A	Group B	
Snack food counselling			
• Yes	102 (29.1)	91(26.0)	193(55.1)
• No	73(20.9)	84(24.0)	157(44.9)
Behaviour of reading composition label			
• Yes	146(41.7)	96(27.4)	242(69.1)
• No	29(8.2)	79(22.6)	108(30.8)
Get stipend from parents			
• Yes	122(34.9)	115(32.9)	237(67.8)
• No	53(15.1)	60(17.1)	113(32.2)
Stipend amounted to Rp.25.000,-			
• Yes	76(21.7)	48(13.7)	124(35.4)
• No	99(28.2)	127(36.2)	226(64.4)
Habit of consuming sweet flavors			
• Yes	43(12.2)	90(25.7)	133(37.9)
• No	132(37.7)	85(24.2)	217(61.9)
Habit of consuming salt and flavourings			
• Yes	25(7.1)	94(26.9)	119(34.0)
• No	150(42.9)	81(23.1)	231(66.0)

Table 3 Distribution of knowledge levels in reading packaged food label composition on group A and group B students

Knowledge	n (%)	
	Group A	Group B
Very good	172 (98.3)	172 (98.3)
Good	3 (1.7)	3 (1.7)
Total	175 (100)	175 (100)

Table 4 Distribution of behavior of reading packaged food label composition on Group A and Group B students

Behavior	n (%)	
	Group A	Group B
Very good	169 (96.6)	76 (43.4)
Good	6 (3.4)	99 (56.6)
Total	175 (100)	175 (100)

Univariate Analysis

Based on **Table 3**, the distribution of knowledge levels about reading the composition of packaged food labels on students of Group A and Group B shows that students generally have a very good level of knowledge with a total of 172 (98.3%) respondents.

Based on **Table 4**, distribution of the behavior of reading composition on packaged food labels on students of Group A shows that students generally have very good behavior of reading packaged food label composition, with a total of 169 (96.6%) respondents. Meanwhile, Group B students generally have good behavior in reading composition on packaged food labels, with a total of 99 (56.6%) respondents.

Bivariate analysis

Table 5 shows that from 175 respondents, there are 172 (98.3%) respondents who have very good knowledge, divided into 167 (95.4%) respondents who have very good behavior and 5 (2.85%) respondents who have good behaviour; there are also 3 (1.7%) respondents who have good knowledge, divided into 2 (1.14%) respondents have very good behaviour and 1 (0.57%) respondent has good behaviour.

Table 6 shows that from 175 respondents of group B, there are 172 respondents who have very good knowledge, divided into 73 (41.7%) respondents who have very good behaviour and 99 (56.5%) respondents who have good behaviour; there are also 3 respondents who have good knowledge, and they are all 3 (1.7%) respondents have very good behaviour.

Discussion

Junior High School students are students aged 10-14 years who are categorized as teenagers. According to the World Health Organization (WHO), teenagers are those who have age range between 10 to 19 years and are both male and female who are in the transitional age between childhood and adulthood.[19]

Generally, junior high school teenagers frequently get allowance from their parents to buy snacks to fulfill their needs while attending school. Besides the frequency of getting allowance from parents, the amount of the given allowance can also determine the habit of purchasing snacks. Research conducted by Alamin et al.[20], regarding the amount of allowance and the consumption of snack foods at school for students in Semarang showed that the amount of allowance given by parents is related to the consumption of snacks at school. Based on table 2 that loads characteristics of respondents from group A and group B based on the questionnaire question whether they frequently get allowance with the amount of Rp.25.000,-, the results showed that most of the students from both schools are never got allowance from parents with amount of Rp.25.000,- to buy packaged food. The table data concludes that the amount of allowance is one of the factors that influence students' behaviour in choosing and buying snacks.

The data in Table 1 about the characteristics of the respondents from group A and group B students

Table 5 Analysis of the correlation between knowledge and behavior on group A students

Knowledge	Behavior						n(%)	*p*
	Very Good		Good		Deficient			
	N	%	N	%	N	%		
Very Good	167	95.4%	5	2.85%	0	0%	172 (98.3%)	0.004
Good	2	1.14%	1	0.57%	0	0%	3 (1.7%)	
Deficient	0	0%	0	0%	0	0%	0%	
Total	169	96.5%	6	3.42%	0	0%	175 (100%)	

Table 6 Analysis of the correlation between knowledge and behaviour on group B students

Knowledge	Behavior						n(%)	*P*
	Very good		Good		Deficient			
	N	%	N	%	N	%		
Very good	73	41.7%	99	56.5%	0	0%	172 (98.3%)	0.046
Good	3	1.7%	0	0%	0	0%	3 (1.7%)	
Deficient	0	0%	0	0%	0	0%	0%	
Total	76	43.4%	99	56.5%	0	0%	175 (100%)	

based on nutritional status showed that the students in this study generally have normal nutritional status with a total of 225 (64.2%) respondents, but also 28 (8.0%) respondents with severe underweight and 11 (3.1%) respondents with obesity. Based on nutritional status monitoring pocket book in 2017, the percentage of nutritional status of students and teenagers aged 5-12 years in NTT based on Body Mass Index (BMI)/Age are malnutrition with percentage of 7.8% and underweight with the percentage of 12.1%, while the national average percentage is 3.4% for malnutrition nutritional status and 7.5% for underweight. Based on data collected from Riskesdas 2018, for children aged 5-12 years, 6.8% children suffer from deficient nutritional status (underweight) and 2.4% of children suffer from poor nutritional status (malnutrition). The same data also stated that NTT has the most prevalence of children with deficient nutritional status for about 13,9% and the most prevalence of children with poor nutritional status for about 4,6%.[21]

According to Guthrie, undernutrition and poor nutrition in students are caused by negative imbalance between energy intake and nutritional needs.[22] According to WHO in 2011, overnutrition is a predisposing factor for chronic diseases such as heart disease and diabetes.[23]

Based on the results of the bivariate test, shows that there is a correlation between knowledge and behavior of reading the packaged food label composition on students of group A and group B. This is in accordance with the research conducted by Vania Candra et al.[24], which showed that there was a significant relationship between the respondents level of knowledge about reading packaged food labels and the practice of choosing packaged food, where respondents with very good knowledge

will practice good packaged food selection. This is also supported by research conducted by Maha Hoteit et al.[25], where there is a positive relationship between knowledge and buyer behaviour in Lebanon in reading packaged food labels when buying packaged food.

Knowledge of food composition labels in students is very influential on their behaviour, especially in choosing packaged foods that they will consume. Knowledge in students can be obtained both internally and externally. Knowledge that comes from their own self or based on life experience is knowledge that comes from internal knowledge, while the knowledge that comes from other people or mass media about the food they consume is knowledge that comes from external knowledge.[26] From the statement above, it found that the knowledge of the students of group A and group B is very good and in line with their behaviour in reading the label composition on packaged food they consume. This happens because from Table 2 about characteristics of respondents from group A and group B based on questionnaire question about counseling that have been held at each school, resulting that most students in both schools said that they had previously received counseling at school about selection of good snacks.

Very good level of knowledge can be obtained from higher education and from the information they get. Therefore, the level of knowledge is an important domain in the formation of behavior.[27] From the statement above, the behavior of the students of Group A and Group B is in the very good category and the good category, this is in line with their behavior in reading the composition on the packaged food labels they consume.

The limitation in this study is that the researchers did not conduct research on other schools and only chose 2 schools as research locations due to the pandemic situation. The distribution of questionnaires was carried out online through the zoom meeting application and google form by respondents due to the COVID-19 pandemic so that there were obstacles when conducting research such as explanations of research contents were not carried out directly so that it was possible to convey information to respondents to be ineffective and the research schedule was difficult to arrange because some respondents have teaching and learning activities in schools.

For further study, the researchers can do research about the factors that influence consumers' behaviour of reading the packaged food labels composition and conduct similar research on different populations or on different levels of education.

Conclusion

The level of knowledge about reading the packaged food composition label showed that the students from Public 2 Junior High School and Giovanni Junior High School in Kupang generally have a very good level of knowledge on that with the same total of 172 respondents and good level of knowledge with a total of 3 respondents.

The level of behaviour about reading the composition of packaged food labels in students of Public 2 JHS Kupang shows that 169 respondents have very good behaviour and 6 respondents have good behaviour.

The level of behaviour about reading the composition of packaged food labels in students of Giovanni JHS Kupang shows that as many as 76 respondents have very good behaviour and 99 respondents have good behaviour.

There is a significant correlation ($p < 0.05$) between knowledge and behaviour of reading the packaged food composition label on students of Public 2 Junior High School ($p = 0.004$) and Giovanni Junior High School ($p = 0.046$). with deficient nutritional status for about 13,9% and the most prevalence of children with poor nutritional status for about 4,6%.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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LITERATURE REVIEW

The role of dietary fiber or prebiotics in atopic dermatitis

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Abstract

Background: Atopic Dermatitis (AD) is a chronic inflammatory skin condition with itchy eczematous lesions, mostly found in children, and may affect a patient's quality of life. Individuals with AD were found to have dysbiosis of gut microbial, which may alter the immunologic tolerance of mucosa, causing inflammation and affecting skin conditions. Dietary fiber or prebiotics consumption may have a role in reversing dysbiosis and may have an effect on AD. In this literature review, the authors would like to further explore the role of dietary fiber or prebiotics in the prevention and alternative treatment for AD.

Methods: This study is a narrative literature review. The literature search was conducted in several sources: Pubmed, EBSCOHOST, Proquest, and Google Scholar, using keywords: "atopic dermatitis, atopic eczema, dietary fiber, prebiotic, nutrition". Our inclusion criteria were : 1) Studies in Randomized Clinical Trial (RCT), case report, case series, literarture review, systematic review, meta-analysis, cohort, and experimental studies, 2) available in full text, 3) written in English. Our exclusion criteria were : 1) Studies conducted more than 10 years ago (before 2012) and 2) lack of available data.

Discussion: Dietary fiber, particularly soluble fibers and those which can be fermented by gut bacteria (including prebiotics), plays a role in maintaining homeostasis of normal gut flora by producing SCFA, which increases the gut barrier, has anti-inflammatory properties, balances Th1/Th2 ratio, increases lymphocytes in *gut-associated lymphoid tissues* (GALT) system, and increases secretion of intestinal IgA. The role of dietary fiber/prebiotics in the prevention or decreasing rate of AD is still a matter of debate. Several studies showed no effect or correlation of prebiotic supplementation in decreasing the AD rate in pregnant women or babies with a high risk of atopy. On the other hand, several studies on prebiotic supplementation for babies and children have shown the benefits of prebiotic supplementation in preventing allergies (AD, rhinoconjunctivitis, and urticaria).

Conclusion: The role of dietary fiber or prebiotics in preventing or treating AD is still a matter of debate. Different study results make it difficult to conclude the clinical effect of prebiotics in allergy prevention, particularly AD. This may be caused by the heterogeneous studies and the limited number of studies on humans. Further studies (RCT) involving large-scale respondents are needed to define the effects of prebiotic supplementation in the prevention or alternative therapy for AD.

Keywords: atopic dermatitis, atopic eczema, children atopic dermatitis, dietary fiber, dysbiosis, elderly atopic dermatitis, prebiotic, nutrition

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin condition with a global prevalence of 20% in children and 5% in adults, presenting as dry, itchy skin and eczematous lesions with erosion, oozing,

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crusts with varying degrees of severity and may have an impact on quality of life.[1,2] The pathophysiology of AD has not been fully elucidated, although it was believed that the combination of the dysfunctional epidermal barrier, immune dysregulation, and environmental factors contribute to AD.[3] Furthermore, gut microbial are known to play a role in gut tissue and skin homeostasis. Dysbiosis on gut microbial diversity will alter mucosal immune tolerance and create an inflammatory microenvironment that will affect the skin condition. Several skin conditions, including acne vulgaris, psoriasis, rosacea, and AD, are associated with intestinal dysbiosis, manifesting in the skin through the gut-skin axis.[4,5] Decreased levels of microbiome such as *Lactobacillus and Bifidobacterium* and increased bacteria proportion of *E. coli, C.difficile*, and *S.aureus* are found in atopic patient's digestive systems. This condition could decrease the production of regulatory T cells and play important role in the pathogenesis of AD.[2,5]

The chronic natural history of AD and the need for long-term therapy with several adverse events potentials make patients, and their parents look for alternative therapies such as dietary modification.[3] Dietary fiber is defined as a carbohydrate group sourced from plant-derived food that cannot be completely broken down by human digestive enzymes and metabolized by microbes in the colon. Fiber consumption may increase the production of short chain fatty acid (SCFA), which increases the epithelial barrier function of the gut, improves immune system recruitment, and regulates inflammatory response.[4,6] In this literature review, the authors would like to dig deep into the role of fiber as the preventive or alternative therapy for atopic dermatitis.

Methods

This study is a narrative or traditional literature review. The literature search was conducted in several sources: Pubmed, EBSCOHOST, Proquest, and Google Scholar, using keywords: "atopic dermatitis, atopic eczema, dietary fiber, prebiotic, nutrition". Our inclusion criteria were : 1) Studies in randomized clinical trial (RCT), case report, case series, literarture review, systematic review, meta-analysis, cohort, and experimental studies, 2) available in full text, 3) written in English. Our exclusion criteria were : 1) Studies conducted more than 10 years ago (before 2012) and 2) lack of available data.

Discussion

Atopic Dermatitis

Atopic Dermatitis (AD), or commonly known as eczema, is a chronic inflammatory skin condition with increasing incidence in recent decades, particularly in developing countries.[7] According to the World Health Organization (WHO), AD affects 230 million people globally.[8] Atopic dermatitis is commonly found in children, with an estimated prevalence of 15-25%, and a varied prevalence of 1-10% in the adult population.[9] Atopic dermatitis is also commonly found in people with other atopic diseases called "atopic march," including allergic rhinitis, asthma, and food allergy.[10]

Atopic dermatitis is a multifactorial disease involving the interaction between genetic factors, immunity, and environmental factors. The strongest risk factor for AD is a family history of atopic disease, particularly AD. Other factors include living in urban areas, areas with low UV exposure, dry climate, diets with high consumption of sugar and polyunsaturated fatty acids, repeated consumption of antibiotics prior to 5 years of age, and higher socioeconomic status.[11] Pathogenesis of AD includes complex sequences involving skin barrier dysfunction, dysregulation of the systemic and cutaneous immune system, dysbiosis of the skin microbiome, and genetic factors.[12] Barrier dysfunction leads to chronic inflammation with epidermal hyperplasia and cellular infiltrates, including dendritic cells, eosinophils, and T cells. In the acute phase, there is a predominance of Th2-secreting IL-4, IL-5, IL-13, IL-25, and IL-31. Meanwhile, during the chronic phase, dominance switching occurs from Th2 to Th1.[7]

Microbiota diversity is known to decrease in individuals with AD's skin. Cutaneous colonization of Staphylococcus aureus occurs in 90% of AD patients, and the expression of virulence factors

have been proven to have a role in the pathogenesis of superficial or invasive infection, which contributes to AD exacerbation through the immune cell and keratinocyte regulation.[12] Aside from the skin, disturbance to gut microbiomes affects immune system homeostasis through metabolite production, which may create an inflammatory microenvironment. Combinations of these factors contribute to the development, persistence, and severity of AD through immunologic, metabolic, and neuroendocrine pathways, although few studies have shown conflicting results.[13]

Atopic dermatitis manifestation is characterized by acute eczematous flare-ups, oozing in the dry skin with an itching sensation. Chronic lesions may present as erythematous plaque to dried hyperpigmentation with lichenification or fissures. An itching sensation at night may cause sleep disturbances and fatigue and affect one's mental health.[14] To date, there is still no pathognomonic diagnostic test or laboratory biomarker to diagnose AD, so diagnosis is established based on history taking and physical examination. Several criteria have been used in diagnosing AD, with Hanifin and Rajka.[9] criteria being the most commonly used in the world.

Numerous scorings used to assess the severity of AD includes Eczema Area and Severity Index (EASI); SCORing Atopic Dermatitis (SCORAD); Physician Global Assessment (PGA). SCORAD >25 is considered mild AD, and SCORAD >50 is considered severe AD. Severe AD is associated with sleep disturbances, and in children, this leads to growth disturbances, low performance at school, attention disorder, and hyperactivity.[7,9] The treatment goal of AD is to alleviate the itching sensation and control this chronic disease in the long term so that the patient may function optimally at home, the workplace, and school. Listed below are the recommended therapy for AD patients based on European guidelines for the treatment of atopic eczema.[9]

Definition, Classification, and the Role of Dietary Fiber/Prebiotics

Dietary fiber definition has been a constantly evolving matter of debate.[15] Several countries define dietary fibers according to the Codex Alimentarius Commission definition in 2009, which definesdietary fibers as carbohydrate polymers with three or more monomeric units which are resistant to digestive enzymes (therefore, it does not get hydrolyzed and absorbed in the small intestine of humans) and meet the following criteria: (1) carbohydrate polymers naturally occurring from food such as fruits, vegetables, legumes, and cereals; (2) carbohydrate polymers obtained from food raw material which have physical, enzymatic or chemical effects on health; and (3) synthetic carbohydrate polymers proved scientifically to have physiological benefit.[15] The European Food Safety Authority (EFSA) defines dietary fiber as non-digestible carbohydrates plus lignin which includes non-starch polysaccharides (NSP) (cellulose, hemicelluloses, pectins, hydrocolloids (e.g. gums, mucilages, β-glucans)), resistant oligosaccharides, resistant starch, and lignin associated with the dietary fiber polysaccharides.[15]

Prebiotics is frequently associated with dietary fibers, but not all dietary fiber is prebiotics.[16] Currently, prebiotics is defined as undigested substance by digestive enzymes and acts as substrate for the growth and/or activity of one or more healthy bacteria species in the colon, particularly the growth of *bifidobacteria* and *lactobacilli* species.[16,17] Examples of prebiotics which are fibers that may be fermented and being studied to enhance the immune system are inulin, fructooligosaccharides (FOS), galactooligosaccharides (GOS), and xylooligosaccharides (XOS).[16]

Dietary fiber is classified based on the food source, chemical structures, solubility in water, viscosity, and fermentability.[16,18] Chemically, dietary fiber is classified as resistant oligosaccharides (Ros), including fructooligosaccharides (FOS) and galactooligosaccharides (GOS), resistant starch (RS), and non-starch polysaccharides (NSPs).[18]

Table 1 Treatment recommendation for AD patients.[9]

Atopic dermatitis severity	Treatment recommendations	
	Children	Adults
Baseline : basic therapy	Educational programs, emollients, bath oils, and avoidance of clinically relevant allergens	
Mild : SCORAD <25 or transient eczema	Reactive therapy with topical glucocorticoids class II or depending on local cofactors (topical calcineurin inhibitors, antiseptics inducing silver, silver coated textiles	Reactive therapy with topical glucocorticoids class II or depending on local cofactors (topical calcineurin inhibitors, antiseptics inducing silver, silver coated textiles
Moderate : SCORAD 25-50 or reccurent eczema	Proactive therapy with topical tacrolimus or glucocorticosteroids class II or III, wet wrap therapy, UV therapy (UVB 311 nm), psychosomatic counselling, climate therapy	Proactive therapy with topical tacrolimus or glucocorticosteroids class III, wet wrap therapy, UV therapy (UVB 311 nm, medium dose UV A1), psychosomatic counselling, climate therapy
Severe : SCORAD >50 or persistent eczema	Hospitalization, systemic immunosuppression : cyclosporine A, methotrexate, azathioprine, mycophenolate mofetil	Hospitalization, systemic immunosuppression : cyclosporine A, short course or oral glucocorticosteroids, dupilumab, methotrexate, azathioprine, mycophenolate mofetil, PUVA, alitretinoin

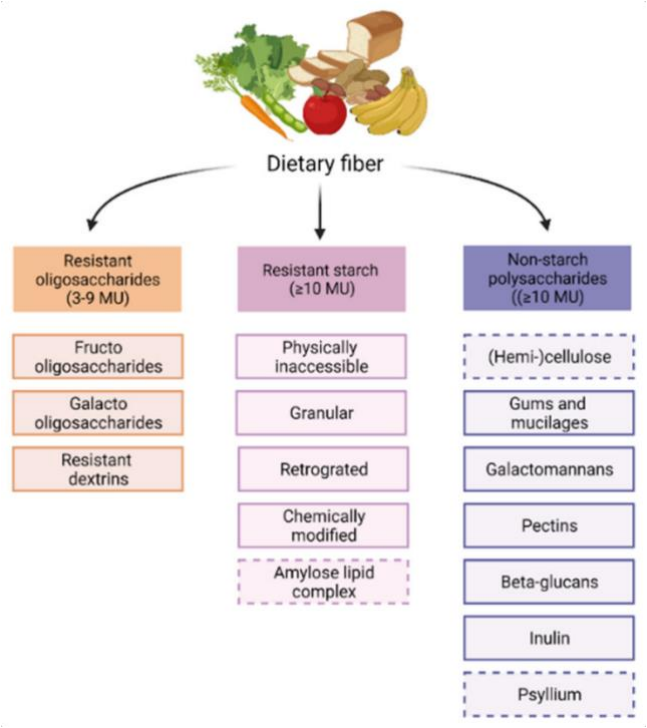

Figure 1 Classification of dietary fiber based on chemical structure. There are three groups of dietary fiber based on chemical structure: resistant oligosaccharides, resistant starch, and non-starch polysaccharides. The dotted square represents unfermented fiber.[18]

Soluble and insoluble fiber are commonly found in food sources such as legumes, vegetables, beans, seeds, fruits, and cereals. Meanwhile, RS can only be found in flour-containing foods such as cereals, legumes, tubers, and unripe fruits such as green bananas.[15,18] Insoluble fibers such as cellulose and hemicellulose are not fermented by gut bacteria but play a role in increasing transit time in the gut, solidifying the feces, and increasing the clearance process by defecation.[16,18] Soluble and fermented by gut bacteria fibers including Ros, all of RS (except amylose-lipid complex), and NSP (except hemi-cellulose and psyllium) have a role in immune system modulation. Dietary fiber containing non-digestible carbohydrates comes from polysaccharides plants, plants, or human milk-derived oligosaccharides.[16,18] These dietary fibers are resistant to the enzymatic and chemical digestive process, thus, cannot be digested or absorbed, reaching the colon and fermented by gut bacteria to become short-chain fatty acid, SCFAs: acetate, propionate, and butyrate, which has local and systemic anti-inflammatory properties.[15,17,18] Short-chain fatty acid (SCFA) and other metabolite products from fermentation by gut microbiota affect the immune system through several mechanisms: (1) enhancing intestinal barrier; (2) anti-inflammatory effect through activation of free fatty acid receptors such as G-protein-coupled receptor (GPR) 43, GPR41, and GPR109A which modulate homeostasis of the gut and regulate immune response; (3) inhibition of histone deacetylases which regulates rapamycin (mTOR)-S6K pathway for differentiation of T cell to effector and regulatory T cell and balance the ratio of Th1/Th2; (4) increasing the number of lymphocytes and/or leukocytes in gut-associated lymphoid tissues (GALT) and (5) increasing the secretion of intestinal IgA.[18–21]

Effect of Dietary Fiber/Prebiotics on Atopic Dermatitis

Diet influences dermatitis atopic.[15] Westernized diet commonly adopted in the modern world is dominated by processed food containing high calories, fat, and low fiber.[22] In a low-fiber diet, bacteria will break down the glycoprotein layer in the mucous layer of the gut as alternative energy, compromising the gut barrier.[5,22] A diet containing soluble fiber can be fermented by gut bacteria (prebiotics) and enhance the development of the gut microbiome in humans.[5,23] The gut microbiome plays a role in the maturation of Th1 cell and T cell regulator function and attenuates Th2 cell response, particularly in the fetal period.[2,16,17] Disruption in the homeostasis of normal gut flora (dysbiosis), particularly in the neonatal period, may result in an atopic cofactor, including atopic dermatitis.[24,25] Atopic dermatitis patients have increased gut bacteria such as *Escherichia coli*, *Clostridium difficile*, and *Staphylococcus aureus*; and decreased good bacteria such as *Lactobacillus* and *Bifidobacterium*.[17,25,26] The decreasing number of SCFAs-producing bacteria results in an imbalance production of T cell regulators, leading to an

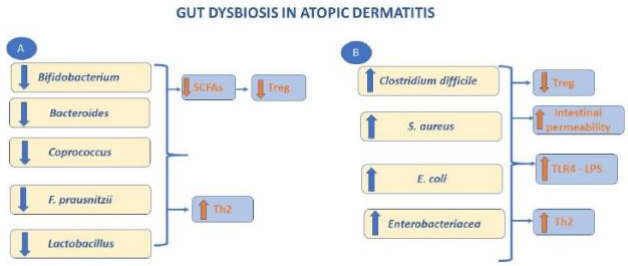

Figure 2 Gut dysbiosis in atopic dermatitis. (A) Decreased levels of microbiome such as *Lactobacillus and Bifidobacterium* and increased bacteria proportion of *E. coli, C.difficile*, and *S.aureus* in the digestive system in atopic patients. (B) *Bifidobacterium* and *Lactobacillus* metabolites have the ability to decrease cytokines associated with Th2 cells. Decreasing numbers of SCFA-producing bacteria cause decreased production of regulatory T cells.[25]

imbalance in the immune response of Th1/Th2, which results in increased Th2 cell and pro-inflammatory cytokines derived from Th2 cells.[17,25]

Modification of diet containing fibers/prebiotics may emend gut dysbiosis.[2,17] Prebiotics increase the production of SCFAs (acetate, propionate, and butyrate), which have anti-inflammatory properties, inhibition of pro-inflammatory cytokines from Th2 cells such as IL-4, IL-5, IL-6, IL-13, and decrease the level of IFN-γ (pro-inflammatory cytokines from Th1 cells), balancing out ratio of Th1/Th2, and increasing GALT system and intestinal IgA secretion.[2,17,19]

Dietary Fiber/Prebiotics Supplementation in Pregnancy and Lactation

There are still limited studies on prebiotic supplementation in pregnant and lactating women. Two preclinical studies conducted by Hogenkamp et al.[26] and another study by Fujiwara et al.[24] explored the effect of prebiotics supplementation during pregnancy on pulmonary resistance and atopic dermatitis-like skin lesion using model allergic mice. These three studies showed that there are decreased allergic responses in the model mouse given prebiotics, compared with the control group.[25] A recent study by Laigaard et al.[27] explored the effects of a prebiotic, xylooligosaccharide (XOS), on the gut microbiota and ear inflammation in an oxazolone-induced dermatitis model in BALB/c mice. This study reported that prebiotic supplementation in mice models resulted in increased levels of *Prevotella* bacteria in the gut and decreased serum IgE and pro-inflammatory cytokines in ear tissue biopsy.[27] These animal model studies showed the potential of prebiotic supplementation in pregnant and lactating women to decrease AD risk.

The first observational cohort conducted by Pretorius et al.[21] of 639 mother-infant pairs (all infants had a family history of allergic disease) investigated maternal intakes of total fiber, soluble fiber, insoluble fiber, resistant starch, and prebiotic fiber by a semi-quantitative food frequency questionnaire at 36–40 weeks of gestation. Infants then underwent clinical allergy assessment at 12 months of age through history taking, physical examination, and skin prick testing for common allergens.[21] This study showed that higher maternal dietary intakes of resistant starch were associated with reduced doctor-diagnosed infant wheeze, adjusted odds ratio (aOR) 0.68 (95% CI 0.49, 0.95, $p = 0.02$). However, in contrast, there were increased numbers of doctor-diagnosed eczema aOR 1.19 (95% CI 1.01, 1.41, $p = 0.04$) and parent-reported eczema aOR 1.27 (95% CI 1.09, 1.49, $p < 0.01$) in mothers who consume high dietary intakes of resistant starch.[21] However, this study has several limitations: this study did not divide maternal resistant starch dietary intakes into the four sub-types of resistant starch (RS1, RS2, RS3, RS4), which have different structural compositions and functional properties. Moreover, this study did not collect the infants' nor the mother's stool samples, did not collect detailed infant feeding data (especially exclusivity of breastfeeding and accurate infant formula use) between birth and 12 months of age, whereas breast milk is an important prebiotic in infants' gut microbiota.[21] In this study, the authors did not find an association between prebiotic consumption during pregnancy in reducing allergic events in infants. However, in this study, the average prebiotic consumption was only approximately 1.4 grams/day, which was lower than the recommended amount in the Mediterranean diet of 3-11 g/day, and was more similar to the recommended amount in the Western-style diet in the USA of 1-4 g/day.[21] Low

fiber intake, such as a Western diet, may cause changes in the gut microbiome and decreased levels of SCFAs, which have anti-inflammatory properties that maintain gut barrier function.[22]

The World Allergy Organization (WAO) does not recommend prebiotic supplementation during gestation and lactation as a preventive measure for atopic dermatitis due to its lack of valid scientific evidence.[17] Further studies, particularly in clinical trial settings, are needed to explore dietary fiber subtypes' effect on pregnant women's microbiomes, AD prevention, an association between metabolome (mother and infant) and the development of the infant immune system.

Dietary Fiber/Prebiotics Supplementation in Infants and Children

Prebiotics are naturally sourced from breast milk which contains minimal 200 Human Milk Oligosaccharides (HMO), which was not found in cow milk. Therefore, exclusive-breastfed infants have more abundant *Bifidobacteria* gut bacteria, particularly *B.Bifidum*, *B.longus*, and *B.Breve* compared with formulated milk.[4,24,25] Exclusive-breastfed infants have decreased risk of AD compared with infants not receiving exclusive breastfeeding. Infants not receiving exclusive breastfeeding are commonly fed with formulated milk. Therefore, prebiotic supplementation in formulated milk is developed and marketed to resemble the benefit of HMO.[24] A combination of *galactooligosaccharides* (GOS) and fructooligosaccharides (FOS) (scGOS 90% and LcFOS 10%) is the frequently studied prebiotic supplementation. Acidic oligosaccharides (AOS), Polydextrose (PDX) (with or without lactulose), oligofructose, and inulin are also studied in several studies.[24]

A review study conducted by Sestito et al.[24] (12 double-blind randomized controlled trial studies) compared the effect of prebiotic supplementation (particularly a combination of scGOS,lcFOS, PDX, pAOS) in standard formula or hydrolyzed/amino acid-based formula on AD. Included studies showed that prebiotic supplementation is still controversial in the prevention of allergy due to the heterogeneous studies and different types of prebiotics.[24] Several studies in that review: a cohort by Moro et al.[24,28] of 259 infants with a high risk of atopy found that a hydrolyzed protein cow's milk-based formula supplemented with 90% scGOS−10% lcFOS, (8g/L) given starting at 2 weeks at the age to 6 months of age significantly reduced AD at the age of 6 months compared to the placebo group (8g/L maltodextrin) [intervention group: 9.8 vs. 23.1% placebo group ($P < 0.05$)] and increased the number of fecal *bifidobacteria*. A long-term study with a follow-up duration of 2 and 5 years conducted by Aeslanoglu et al.[24,29] has shown the benefit of prebiotic supplementation as allergic prevention (i.e., atopic dermatitis, rhinoconjunctivitis, and allergic urticaria). Another RCT study found a 44% decreased incidence of AD at 1 year of life in infants at low risk of allergy fed with formula supplemented with GOS/FOS and specific pectin-derived acidic oligosaccharide compared to infants fed standard formula.[24]

Supplementation with prebiotics also showed a beneficial effect in children aged 1–4 years old.[30] In a double-blind, randomized, controlled trial, 125 children who were given cow's milk containing DHA, the prebiotics polydextrose (PDX) and galactooligosaccharides (GOS), beta-glucan, zinc, iron, vitamins A and D, were compared to 131 children fed with standard cow's milk for 28 weeks. Children who consumed milk enriched with prebiotics had significantly reduced episodes of allergic manifestation, including eczema and urticaria, allergic rhinitis and conjunctivitis, and wheezing when compared to the control group.[24,30]

Not all studies showed a beneficial effect of prebiotic supplementation on AD prevention.[24] Several studies showed that prebiotic supplementation did not have any benefit or effect on preventing or reducing AD incidence. A systematic review by Cueloo-Garcia et al.[31] reported that there was no strong evidence of prebiotic supplementation to prevent allergic risk, including AD.[1] A 2016 study conducted by WAO using Grading of Recommendations Assessment, Development, and Evaluation (GRADE) about prebiotic supplementation in non-exclusively breastfed infants found that there were no differences in numbers of eczema (RR; 0,57, 95% CI:0,30-1,08) in five meta-analysis studies

involving 1.313 infants.[32] Another study by Ranucci et al.[33] showed that formula supplemented with galactooligosaccharides/polydextrose (GOS/PDX) did not significantly decrease the cumulative incidence of AD in the first year of life, compared with standard formula and exclusive breastfeeding. Until now, from the study we have collected, there are no studies that make a benchmark for doses or types of fiber used for the prevention of atopic dermatitis because the study of fiber as prevention of atopic dermatitis still has various results (some provide benefits in the declining prevalence of atopic dermatitis, but some are not). It could be caused by the heterogenous studies, methods, and sampling.

Dietary Fiber/Prebiotics Supplementation in Adults

There are not many studies that discuss the role of giving fiber in the prevention of atopic dermatitis in adults. One of the studies conducted by Lee et al.[6] who examined the relationship between dietary fiber intake and allergic diseases (asthma, allergic rhinitis, and atopic dermatitis) carried out on 10,479 adults, which is divided into 4 quartiles (Q1-Q4) based on the amount of fiber consumption using data from the Korean National Health and Nutrition Examination Survey (2010-2011), reporting that there was a decrease in the prevalence of asthma (Q4 OR: 0,656; 95% confidence interval (CI): 0,48-0,91, p for trend < 0,0001) and atopic dermatitis (Q3 crude OR: 0,746; 95% CI: 0,57-0,98; Q4 adjusted OR: 0,712; 95% CIL 0,50-1,01, p for trend < 0,0001) in groups that consumed higher dietary fiber.[6] The disadvantage of this study is that this study does not evaluate further the improvement of atopic dermatitis symptoms in patients who consume higher fiber, the results only find a decrease in the prevalence of atopic dermatitis patients in groups who consume higher fiber.[6] From the study we examined, no one explained the amount, dose, and type of fiber that adults must consume to prevent atopic dermatitis. This is because there is still a lack of research on the evaluation of dietary fiber intake and atopic dermatitis in adults. After all, research on fiber intake is more centered in the prenatal period and during the period of infants and children, where the incidence of atopic dermatitis is more in that period than in adults.

Conclusion

Supplementation of prebiotics/dietary fibers in the prevention and management of atopic dermatitis is still a matter of debate. Due to the heterogeneous studies and the limited number of studies done in humans, different study results make it difficult to conclude the clinical effects of prebiotics in allergy prevention, particularly atopic dermatitis. Therefore, further studies, particularly large-scale randomized controlled trials and meta-analyses on pregnant women, atopic infants, and infants with high risk of atopy, are needed to better understand the benefit of prebiotic supplementation in the prevention and non-pharmacological therapy of atopic dermatitis.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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CASE REPORT

The effectiveness of polydioxanone (PDO) thread-embedding acupuncture in adult patients with obesity: Case reports

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Abstract

Background: Obesity is a chronic condition defined as excess body fat which is diagnosed based on body mass index, abdominal circumference, and is associated with an increased risk of various diseases. Conservative management is often hard to comply with, unsuccessfully, and expensive, while acupuncture with its variety of modalities can be an option.

Case: A therapy with polydioxanone thread embedding on acupuncture points along with other acupuncture modalities were performed in three cases of obese patients according to their etiology and conditions.

Results: Based on the three cases of obese patients with PDO thread embedding acupuncture alone or combined with cupping, plum blossom and moxibustion modalities are beneficial in decreasing abdominal circumference. The effect after 2 months follow up respectively using abdominal circumference measurement 5 cm above the umbilicus -2 cm (from 110 to 99cm);- 3 cm (from 90 to 87 cm); -8 cm (from 88 to 80 cm), umbilicus to umbilicus -6 cm (from 107 to 101 cm); 10 cm (from 103 to 93 cm); 7 cm (from 93 to 86 cm), 5 cm below umbilicus -1 cm (from 106 to 105 cm); -5 cm (from 107.5 to 102.5 cm); -6 cm (from 104 to 98 cm). No serious side effects occurred in the three cases.

Conclusion: PDO thread embedding can be beneficial in treating obese patients. However, these results require further research.

Keywords: obesity, thread embedding acupuncture, PDO, plum blossom, cupping therapy, moxibustion

Introduction

Obesity is a chronic condition defined as excess body fat that is generally diagnosed based on body mass index (BMI) and is associated with an increased risk of various disease.[1] The World Health Organization (WHO) and the National Heart, Lung, and Blood Institute of the US National Institutes of Health have both stated that obesity is an epidemic.[2] Globally, this condition is reaching crisis proportions: nearly 30% of the population is obese or overweight, and this condition is expected to affect nearly half of the population by 2030.[3] Based on global survey data, the prevalence of obesity in women is greater than in men.[4,5] Thus, obesity is a worldwide epidemic associated with rapidly growing morbidity and mortality that has implications for both individual and public health.[6]

In 1980, Southeast Asia had the lowest prevalence of obesity, with Indonesia at 1.4%, Ethiopia at 1.2%, China and Bangladesh at 0.6% each, and Vietnam at 0.4%. However, in 2015, only Vietnam maintained an obesity prevalence below

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2%, at 1.6%.[7] Based on data from Riskesdas Indonesia, Indonesia's obesity prevalence increased from 10.5% in 2007 to 21.8% in 2015. In 2018, the prevalence of central obesity increased to 31%.[8] At Dr. Cipto Mangunkusumo Jakarta recorded 1,941 cases of obesity in outpatient installations and 369 cases in inpatient care in 2020.[9]

Body mass index is the measurement most often used to diagnose obesity. BMI is defined as mass in kilograms divided by the square of the height in meters.[2] According to the Asia Pacific criteria, a BMI of < 18.5 is underweight, 18.5–22.9 is normal weight, 23–24.9 is overweight, 25–29.9 is classified as obesity grade 1, while ≥ 30 is obesity grade 2.[10] The main cause of obesity is an imbalance between energy output and consumption. This imbalance is caused by several factors, including excessive eating, a sedentary lifestyle, in-utero effects (postpartum weight retention [PPWR] and gestational diabetes), as well as the complex relationship between biological, psychosocial, and behavioral factors, including genetic factors, socioeconomic status, and cultural influences. Increasing age, lack of sleep, endocrine problems, and pharmacological effects also play a part in causing this imbalance.[11,12]

Having a family history of obesity substantially increases a person's likelihood of developing obesity.[2] In particular, PPWR is defined as the body weight difference between pre-pregnancy and certain time periods after delivery. Measurements are usually performed serially at 3, 6, 9, 12, and 18 months postpartum. PPWR is a significant contributor to the risk of obesity in women one year after delivery, even among women who were of normal weight before pregnancy. Several studies have suggested that retention of excess weight one year after delivery is associated with long-term obesity. Postpartum weight retention averages at approximately 0.5–1.0 kg at 12 months, with variations ranging from a loss of 10 kg to an excess of 20 kg. Approximately 75% of women experience weight retention one year postpartum, with 47.4% retained weight of 4.54 kg and 24.4% retained weight more than 9.07 kg.[13-15]

Deposits of excess weight are most often found in central versus peripheral subcutaneous tissue, thus increasing the risk of cardiovascular disease,[13,14 ,15] hypertension, diabetes mellitus, dyslipidemia, glomerulonephritis, cholelithiasis, non-alcoholic fatty liver disease (NAFLD),gastroesophageal reflux disease (GERD), various cancers, obstructive sleep apnea (OSA), and osteoarthritis (OA), as well as increased mood disorders and anxiety.[2,16] Conservative management consists of lifestyle modification, pharmacotherapy, and surgery. However, the treatment of obesity is often difficult, unsuccessful, and expensive.[17] The use of pharmacotherapy has many side effects, while surgical operations require exorbitant costs and carry risks of serious complications.[18] Therefore, a social need exists to seek effective and safe therapy to deal with obesity.

Acupuncture has been widely used to treat various diseases, including obesity. The modalities used vary from manual acupuncture, thread-embedding, pharmaco-puncture, laserpuncture, press needle, cupping, plum blossom, and moxibustion.[19,20] Cupping therapy is a Traditional Chinese Medicine (TCM) therapy developed 2,000 years ago in which a hollow medium is attached to the skin's surface with suction for the purpose of preventing and curing disease. In general, cupping therapy is done on areas with thick muscles while avoiding uneven and hairy locations because the cups can come off easily. Cupping retention generally lasts 5–10 minutes.[21]

Moxibustion is based on the TCM technique of warming acupuncture points with burned moxa wool. Moxibustion is done to treat various diseases, such as fetal malposition, diarrhea, incontinence, fatigue, and problems related to the aging process.[22] Plum blossom is an acupuncture modality that relies on a small hammer with seven sharp, short needles measuring 4–5 mm with a diameter of approximately 0.5 mm. The hammer is lightly tapped on the skin to cause redness, which serves to tighten and strengthen tissues. Mechanical stimulation from plum blossom can induce changes in electrical charges and cause the release of various chemical mediators.[23] This action can also improve blood circulation, lymphatic flow, and cell nutrition.[24] Based on experimental research, plum blossom can reduce

pro-inflammatory cytokines, such as IL-2, IL-1α, IL-1β, TNF-α, and IFN-γ, thereby reducing inflammation and preventing the release of Matrix Metalloproteinases (MMPs) that can degrade the extracellular matrix and inhibit procollagen transcription.[25]

Many studies have shown that acupuncture is beneficial in reducing BMI and waist circumference and improving quality of life with minimal side effects. In particular, thread embedding at acupuncture points can induce continuous stimulation of peripheral receptors to the central nervous system and result in a therapeutic mechanism because this type of stimulation lasts longer with more intensive.[26] The materials that can be used for thread-embedding acupuncture are catgut, polylactic acid-glycolic acid (PGLA), PDO and medicinal thread.[27] Polydioxanone is an absorbable polymer from the α-hydroxy acid polymer family. Polymers that are ideal for biomaterial applications should not elicit undesired tissue responses disproportionately to their beneficial effects. Polydioxanone can be metabolized once it has served its purpose. It leaves no trace, is easy to manufacture, and has an acceptable shelf life. It can also be sterilized for in vivo use. The PDO thread-embedding technique can be used with penetrating and perpendicular acupuncture methods. The penetrating method can increase mechanical tensile strength and support the dermis structure.[28] Polydioxanone sutures have been found to degrade over a period of two months and are completely absorbed at 9 to 12 months. In contrast, the effects of collagen can last for more than 12 months.[29,30] The benefits of acupuncture therapy against obesity-related peptide hormones include regulating endocrine systems, such as leptin and ghrelin, improving insulin resistance, improving glucose and lipid metabolism and serum immunoglobulin levels, decreasing appetite,[20] improving digestion, and reducing oxidative stress and inflammatory response.[6]

CASE 1

A 26-year-old woman desired to reduce her abdomen size and lose weight. During a 9-year period (from high school grade 3 to college graduation) her body weight increased from 40 to 74 kg. It was found that the patient's diet was irregular with the consumption of carbohydrates other than rice 2 times a day at undetermined times, light snacks, and infrequent intake of vegetables and fruits. The patient had attempted two types of diets for 2 years at different times and experienced a weight loss of 2 kg in 2 months, but discontinued dieting because of frequent stomachache. The patient had a habit of chewing fast and a tendency to eat snacks when stressed out. She passed stools daily with soft (occasionally hard) consistency. She had a history of regular menstruation with 28–30-day cycles in general. The patient had no trouble sleeping. In addition, she had a history of gastritis for the last 2 years, and the last recurrence was 2 months prior. She had no history of hypercholesterolemia, high blood pressure, or diabetes. In the family history, the patient's mother and sister were also obese. From the patient's physical examination, her body weight was 75.8 kg and height was 155 cm, and her BMI was 31.55. Thus, she was diagnosed with grade 2 obesity. The abdominal circumference was measured with a tape measure horizontally 5 cm above the umbilicus, around the umbilicus and 5 cm below the umbilicus. The measurement is made at the end of normal expiration.

In this case, thread-embedding acupuncture was carried out on the abdomen, hands, and feet with a PDO thread using 27G × 50 mm at CV12 Zhongwan, CV4 Guanyuan, CV6 Qihai, ST25 Tianshu, SP15 Daheng, and ST28 Shuidao with a penetrating technique. Then, the PDO threads 31G × 25 mm were applied at TE6 Zhigou, BL20 Pishu, and ST40 Fenglong bilaterally using the perpendicular technique. Thereafter, a follow-up was implemented once a week. A week later, cupping therapy was added with dry-cupping technique implemented in the lower back area (the BL20 area to the sacrum). Cupping was performed for up to 5 minutes once a week. A week later, moxibustion therapy at the CV12 point was added to the weekly treatment. In addition, the patient was advised to adjust her diet and do physical exercise. After 2 months of follow-up, there was a 2-cm decrease in the diameter above the umbilicus (from 101 to 99 cm), whereas the diameter around the

umbilicus decreased by 6 cm (from 107 to 101 cm), and the diameter 5 cm below the umbilicus decreased by 1 cm (from 106 to 105 cm). However, the body weight increased slowly by 2 kg, from 75.8 to 77.8 kg.

CASE 2

A 37-year-old woman wanted to lose weight and slim down after giving birth to her third child 1.5 years ago. Her body weight started to increase from her first pregnancy (11 years ago) and increased from 50 to 62 kg. Then, during her second and third pregnancies, it increased up to 71 kg and, after 18 months (1.5 years), dropped to 70 kg. This patient had PPWR. She had undergone a low-carbohydrate diet and exercised on the treadmill on a regular basis 2–3 times a week for 30 minutes for 4 months (when the child was 9 months old) and her weight dropped to 63 kg, but she discontinued the diet and exercising for 6 months. Her daily diet rarely included breakfast, and even if she had it, she only consumed bread or bananas or milk at 06.30. Her lunch included a portion of rice, vegetables, and side dishes at 12.00. Her dinner was usually at 20.00 or 21.00 with ± 3 tablespoons of rice, non-fried vegetables, and side dishes, ending with fresh fruit such as oranges. Once a week, the patient consumed street food, such as pasta and tofu *martabak*. She had a bowel movement 2 to 3 times a week. As for her sleeping pattern, the patient slept around 01.00 and woke up at 05.00 for the past 2 years. When staying up late, she consumed bitter coffee and snacks. She had regular menstruation. She had no history of taking weight-loss drugs, and there was no history of using hormonal contraception. She had hypercholesterolemia for 6 years and never took medication. She also had a history of lower back pain for 20 years, along with stomach ulcers and diclofenac allergy. The patient's mother, father, and sister were also obese.

Upon physical examination, her vital signs were good; her body shape was that of an apple, and she weighed 70 kg at 151 cm of height, with a BMI 30.7 Kg/m^2. The abdominal circumference was measured with a tape measure horizontally 5 cm above the umbilicus, around the umbilicus and 5 cm below the umbilicus. The measurement is made at the end of normal expiration. Her circumference 5 cm above the umbilicus was 90 cm, while her circumference at the umbilicus was 103 cm and circumference 5 cm below umbilicus was 107.5 cm. The Indonesian version of the Food Craving Questionnaire-Trait-reduced (FCQ-T-r) questionnaire showed a score of 29/90 with a cut-off value >50, indicating food craving. The Pittsburgh Sleep Quality Index Indonesian version (PSQI-I) questionnaire scored 7, which indicated poor quality of sleep. Through examination, the GDS was 88 mg/dl, cholesterol 222 mg/dl 1 week ago, other laboratory results were within normal limits, and lumbosacral magnetic resonance imaging examination revealed the L4-S1 bulging with lumbar spondylosis and lumbar hyperlordosis. Thus, she was diagnosed with obesity grade 2, hypercholesterolemia, spondylosis, and lumbar hyperlordosis.

In this case, a treatment with the PDO threads 29G × 50 mm was carried out at the point CV12 Zhongwan toward CV8 Shenque, ST25 Tianshu toward SP15 Daheng, SP15 Daheng toward GB26 Daimai, CV6 Qihai toward CV4 Guanyuan, ST28 Shuidao toward CV4, and ST28 toward ST30 Qichong with a penetrating technique. Then, the PDO threads 31G × 25 mm were used at the acupuncture points TE6 Zhigou, BL20 Pishu, and ST40 Fenglong bilaterally with perpendicular technique. A week later, 6-cupping therapy was added in the BL20 to BL25 Dachangshu (T11–L4) area using the dry-cupping technique. The cupping lasted up to 5 minutes. The plum blossom therapy was also added and was performed in the front of the abdomen by tapping 10 to 15 times until erythematous occurred in 2 parallel lines right, left, above, and below the umbilicus. This was done once a week. A week later, moxibustion therapy was added to treatment at CV12 for 5–10 minutes until it felt warm and erythematous occurred. This therapy was also conducted once a week. The total thread-embedding therapy was only carried out once; cupping and plum blossom therapy were performed 4 times; moxibustion was performed 3 times. The patient was advised to adjust her diet and do physical exercise.

At the end of the therapy, the patient's body weight decreased by 2 kg (from 70 to 68 kg),

whereas her BMI became 29.8 kg/m^2, diagnosed as obesity grade 1. On the follow-up 1.5 months following thread embedding, it was found that her body weight decreased to 67 kg, and cholesterol levels decreased to 187 mg/dl. A significant decrease also occurred in the patient's abdominal circumference after 2 months of follow-up; the circumference of 5 cm above the umbilicus decreased by 3 cm (from 90 to 87 cm), the circumference at umbilicus decreased by 10 cm (from 103 to 93 cm), and the circumference 5 cm below the umbilicus decreased by 5 cm (from 107.5 to 102.5 cm). Her cholesterol levels also decreased to 162 mg/dl at a 5-month post-therapy follow-up.

Case 3

A 40-year-old woman faced difficulty losing weight. She gained 4 kg during the last 2 years. Her weight before pregnancy 19 years ago was around 44 kg; however, it increased to 54 kg after her first pregnancy (18 years ago). She had 58 kg (16 years ago) during her second pregnancy, and during her third pregnancy (8 years ago), her weight increased to 60 kg and was 70.6 kg by the time of consultation. The patient had never tried any diet program before. She walked 30 minutes once a week but irregularly. Her daily morning diet routine included carbohydrates and coffee with 1 cup of milk. During the day, the patient ate 1 portion of rice with vegetables, *tempeh,* and tofu. At 17.00, she would eat chicken porridge/green bean porridge. Occasionally, she ate snacks 2–3 times a day (pudding/banana/bread/fruit). She had no sleep disturbances. She had regular bowel movements every morning. Her menstrual cycle was regular with a 28-day cycle. There were no symptoms leaning toward diabetes mellitus, asthma, hypertension, PCOS, sleep apnea, knee pain, urinary tract infection, dyspepsia, depression, and anxiety.

As seen from the patient's physical examination, her vital signs were good, her body shape was pear, and she had 70.6 kg at 152 cm, while her BMI was 30.55 kg/m^2, categorized as the obesity grade 2. The abdominal circumference was measured with a tape measure horizontally 5 cm above the umbilicus, around the umbilicus and 5 cm below the umbilicus. The measurement is made at the end of normal expiration. The circumference 5 cm above the umbilicus was 88 cm, the circumference as high as umbilicus was 93 cm, and the circumference 5 cm below the umbilicus was 104 cm. The Indonesian Version of the FCQ-T-r Questionnaire had a score of 37/90, indicating no food craving. Thread-embedding therapy in this case was carried out 1 time using the PDO threads 25G × 90 mm at the acupuncture points of ST25 Tianshu to SP15 Daheng bilaterally, SP15 Daheng to GB26 Daimaixue bilaterally, KI15 Zhongzhuxue to ST27 Daju bilaterally, PDO threads 27G × 60 mm at CV9 Shuifen to CV12 Zhongwan, ST24 Huaroumen toward mid SP16 Fuai and SP15 bilaterally, CV6 Qihai to CV4 Guanyuan, KI14 Siman to ST28 Shuidao bilaterally, using PDO 31G × 25 mm at BL20 Pishu and ST40 Fenglong bilaterally with perpendicular technique. The patient was advised to adjust her diet and do physical exercise.

The follow-up was carried out once a week, and it was found that the patient's body weight decreased with its highest peak at 4 weeks post-therapy, 5.4 kg less from the previous (70.6 to 65.2 kg), then it increased again. At 2 months of follow-up, her body weight was 68.2 kg. The circumference 5 cm above the umbilicus decreased by 8 cm (from 88 to 80 cm), the circumference as high as umbilicus decreased by 7 cm (from 93 to 86 cm), and the circumference 5 cm below umbilicus decreased by 6 cm (from 104 to 98 cm).

At 26 weeks of follow-up, there was a 3.4 kg (67.2 kg) decrease in body weight, and her BMI declined to 29.08, categorized as obesity grade I. There was still a decrease of abdominal circumference 5 cm above the umbilicus, umbilicus to umbilicus, 5 cm below the umbilicus by 4 cm (from 88 to 84 cm), 6 cm (from 93 to 87 cm), and 7 cm (from 104 to 97 cm). Laboratory results showed that there was a reduction in triglycerides before and after by 48 mg/dL (157 to 109 mg/dL), and HDL improved by 6 mg/dL (45 to 51 mg/dL).

Table 1 Summary of the cases

	Case 1	Case 2	Case 3
Age	26 years old	37 years old	40 years old
Etiology	Stress related obesity	PPWR	PPWR
Treatment	PDO threads with penetrating technique: • CV12 toward CV8, • ST25 toward SP15, • SP15 toward GB26, • CV6 toward CV4 • ST28 toward CV4, • ST28 toward ST30 PDO threads with perpendicular technique: • TE6, BL20, and ST40		PDO threads with penetrating technique : • ST25 toward SP15 • SP15 toward GB26 • KI15 toward ST27 • CV9 toward CV12 • ST24 toward mid SP16 and SP15 • CV6 toward CV4 • KI14 toward ST28, PDO with perpendicular technique : • BL20 and ST40
Additional treatment	• Cupping therapy at BL20 area to the sacrum • Moxibustion therapy at the CV12	• Cupping therapy at BL20 to BL25 • Plum blossom in the front of the abdomen • Moxibustion therapy at CV12	-
Result after 2 months follow up	**Abdominal circumference 5 cm above the umbilicus**		
	2 cm (from 101 to 99 cm)	3 cm (from 90 to 87 cm)	8 cm (from 88 to 80 cm)
	Abdominal circumference umbilicus to umbilicus		
	6 cm (from 107 to 101 cm)	10 cm (from 103 to 93 cm)	7 cm (from 93 to 86 cm)
	Abdominal circumference 5 cm below the umbilicus		
	1 cm (from 106 to 105 cm)	5 cm (from 107.5 to 102.5 cm)	6 cm (from 104 to 98 cm)
	Body weight		
	+2 kg (75.8 to 77.8 kg). Body weight tends to increase by 2 kg, the decrease in abdominal circumference occurs gradually and lasts up to 2 months.	2 kg (70 to 68 kg) Body weight lasts 1.5 months, abdominal circumference up to 2 months.	2.4 (70.6 to 68.2 kg) Body weight and abdominal circumference persisted up to 26 weeks post-therapy.

Discussion

Obesity is defined as excessive body fat, and fat distribution plays an important role in obesity. Several studies have found that fat in the middle or top of the body (apple-shaped obesity) is most closely associated with health risks such as insulin resistance in case of diabetes mellitus, hypertension, dyslipidemia, and cardiovascular disease. This risk is possible even when BMI does not increase sharply. In addition to BMI, waist circumference is a frequently used anthropometric measurement and is considered superior as a reflection of central obesity.[31] Postpartum usually causes approximately 6 kg of weight loss, including fluids and products of conception. From day 3, the body weight will decrease by about 0.3 kg/day until day 10. It will remain stable at week 10 about 2.3 kg of pre-pregnancy weight or 0.7 kg

in women who are breastfeeding. At 6–18 months following delivery, 1–2 kg of body weight will be retained, but one in five women can maintain 5 kg or more.[32] In PPWR, these excess weight deposits are found at the center of the abdomen (apple-shaped obesity), which can increase the risk of long-term obesity and cardiovascular disease. Postpartum conditions also contribute to the sagging of abdominal skin.

According to TCM, obesity can occur due to heat in the stomach and intestines, deficiency of the spleen and stomach, and renal insufficiency. Thus, acupoints BL20–BL25 can be used as Back Shu points of the spleen, stomach, kidneys, and intestines.[33] Obesity due to damp stagnation in the middle jiao, acupuncture can be performed on the back area as high as T7–L2.[23] One of the rapidly developing non-pharmacological obesity therapies is acupuncture with various modalities. Thus, PDO threads embedding acupuncture has recently become widely used because of their comparable effectiveness and fewer side effects compared to catgut suture.[34] Thread embedding using penetrating method also increases the mechanical tensile strength of tissues and supports the structure of the dermis and extracellular matrix, increasing the collagen and elastin components.[28]

The reason behind selecting these acupuncture points in our cases is because it has been proven by evidence-based medicine that acupuncture at point CV12 is used for regulating gastrointestinal function and gastric acid secretion according to the morphology in spinal ganglion T7–L2.[35] CV6 and ST25 regulate the sympathetic and parasympathetic nervous systems. Sympathetic nerve fibers inhibit gastric emptying, while parasympathetic nerve fibers increase intestinal peristalsis to reduce food absorption, thereby regulating gastrointestinal motility and suppressing perilipin expression via MAPK p44/42 and JNK. Decreased expression of perilipin causes increased lipolysis, facilitation of defecation,[36] reduction of abdominal distension, increase of intestinal peristalsis, and stimulation of gastrointestinal smooth muscle contraction. [35,37,38] ST25 and BL20 also have the function to increase PPARγ-mRNA and decrease total cholesterol, LDL, lipoprotein lipase liver, and triglyceride levels.[39] ST25, CV12, CV4, CV6, BL20, and SP15 regulate the endocrine system; increase gastric and small intestinal absorption; reduce oxidative stress; increase lipid metabolism by lowering total cholesterol and triglycerides; improve insulin thereby increasing PPAR-γ; reduce TNF-α in the blood; improve leptin resistance that leads to the reduction of NPY secretion, suppression of appetite, inhibition of fat synthesis, and increase of energy expenditure.[6,40] The BL20 point together with ST36 and ST25, can regulate lipid metabolism by increasing the expression of PPAR-γ mRNA in adipose tissue; activating lipoprotein lipase and hepatic lipase; and reducing total cholesterol and LDL cholesterol serum.[41] CV6, CV9, ST28, ST36, and KI14 can reduce body weight, waist and hip circumference, and triglycerides by improving leptin resistance.[40] ST40 is effective in regulating blood lipids and has proven to reduce IL-17, total cholesterol, triglycerides, and LDL, and increase HDL, stimulating an increase in the PPARγ activity, which will stimulate adipose tissue to secrete adiponectin, thereby activating PPARα in the liver that plays a role in fat metabolism. PPARα will upregulate apoA-I and apoA-II genes, and downregulate ApoC-III, resulting in increased catabolism by lipoprotein lipase.[42-44] GB26, KI15, ST24, and ST27 have proven to reduce body weight, BMI, hip circumference, waist circumference, waist-to-hip ratio, waist-to-height ratio, abdominal subcutaneous fat tissue thickness with a significant decrease in blood pressure, glycemia, LDL, uric acid as well as TNF α and IL-1β, and improve HDL significantly.[45] TE6 has been shown as effective in alleviating symptoms of ileus, abdominal pain, and distension, and increasing intestinal peristalsis. In this case, stimulation of the TE6 point can help maintain the bowel movement.[37] The PDO suture embedding has several advantages over chromic catgut sutures because it absorbs at a slower rate, so its stimulation in acupuncture points is longer and is superior to manual acupuncture or electroacupuncture in terms of the effectiveness in reducing BMI, waist circumference, and weight; hence, it reduces the frequency and duration of therapy, shows better ease of use, and has clinical benefits, and is faster than diet and exercise only.[46]

Thread-embedding acupuncture has proven as beneficial in treating obesity with minimal side effects. [26,35,46,47]

Furthermore, the cupping therapy on the BL meridian in the back combined with thread embedding can significantly reduce body weight, BMI, and waist and hip circumferences.[48] This can be caused by the improved subcutaneous blood circulation that stimulates the autonomic nervous system to further regulate fat metabolism and glucose in the blood associated with organs according to their dermatome, such as pancreas, stomach, intestines, and liver through the cutaneous-visceral reflex.[49,50] The use of thread-embedding acupuncture accompanied by cupping therapy in the BL area has a greater average therapeutic effectiveness of up to 90% in reducing weight, BMI, and waist and hip circumferences.[48] Furthermore, the plum blossom modality helps tightening the skin of the abdomen, and plum blossom is tapped on 2 lines right and left, above and below the umbilicus about 10–15 times until erythematous occurs. This action can release various chemical mediators,[23] increase blood circulation, improve lymphatic flow, and enhance cell nutrition.[24] Furthermore, it can prevent the release of MMP so that the extracellular matrix degradation process can be inhibited, and fibroblasts can be stimulated, resulting in the occurrence of procollagen transcription.[25] Moxibustion with 43°C–45°C temperature at point CV12 according to an experimental study conducted by Yang-Shuai et al. (2014) can inhibit gastric motility through the role of TRPV1.[51] The combination of several acupuncture therapy modalities can provide a greater effect than using only one modality.

An analysis of the three cases indicated that the effect of PDO thread embedding varies. In the first case, where the PDO with cupping and moxibustion were performed, there was only a reduction of abdominal circumference without being followed by weight loss. This can happen due to several possibilities. First, the acupuncture intervention is not synergized with advised dietary routine and physical exercise. The patients do not limit their food intake, so it is possible that the number of calories taken is still greater than their energy expenditure. Patients also tend to refuse any kind of physical exercise with the excuse of being busy and not having enough time. Meanwhile, in a systematic review by Kim et al. (2018), it is said that in general, acupuncture therapy combined with lifestyle modification has a high success rate. Namely, acupuncture therapy with various modalities is generally combined with diet and physical exercise to reach success.[20] Second, a stressed/depressed mind can affect the patients' diet. Patients tend to eat more snacks when they are under stress or pressure. It is argued that stress-related obesity is the result of an imbalanced interaction between cognitive factors (self-control), habits (diet, sleep, physical activity), physiology (HPA axis), and biochemical (leptin, ghrelin, and NPY).[52] Third, there is an effect related to the mechanism in PDO thread embedding in stimulating collagen formation, proliferation of myofibroblasts, and increasing fibrous tissue so as to strengthen subcutaneous fat tissue, improve tissue circulation, and localize denaturation of adipocyte cells in the abdominal area. Thus, the abdomen tightens along with the reduction of waist circumference.[30]

In the second case, the use of the PDO thread embedding modality combined with cupping, plum blossom, and moxibustion resulted in weight loss. According to the minimum clinically important difference, there was a weight loss of 2 kg, although it fluctuated afterwards due to irregular diet and exercise. Abdominal circumference (5 cm above, as high as and 5 cm below the umbilicus) showed a significant decrease of 3, 10, and 5 cm in 2 months, respectively. After 2 months, the patient's abdominal circumference began to increase. The effect of weight loss can last up to 1.5 months after the first therapy, while the effect of abdominal circumference can last up to 2 months after the first therapy. This may be caused by the tensile strength of PDO threads, which decreased to 25% after 6 weeks.[34]

The embedding of PDO threads alone was performed in the third case. The peak of weight loss was 5.4 kg at the 4th week of therapy, and it continued to increase afterwards. At the 26th week of follow-up, there was still a weight loss of 3.4 kg from before therapy and the abdominal

circumference 5 cm above, as high as and 5 cm below the umbilicus by 4, 6, and 7 cm, respectively. There was also an improvement in triglyceride results and an increase in HDL. The weight loss was then followed by weight gain because the patient did not regularly exercise and maintain the recommended diet, thus affecting the therapy results. This shows that PDO also had a shaping effect even though the increase in body weight was followed by a decrease in abdominal circumference. The PDO starts to degrade in about 60 days with complete degradation in 9–12 months.[29] In all three cases, there were no serious side effects other than pain in the right hand at the TE6 point implantation area on the same day of the procedure, which disappeared the next day, as well as soreness and tightness in the abdominal region on the 3rd day after the procedure, lasting till day 6. Afterward, no other complaints were reported.

Conclusion

This manuscript is a case report of obese patients using PDO thread embedding acupuncture. The original technique of thread embedding acupuncture is to use catgut thread, which has a higher risk of allergies. Not much research has been done using PDO thread embedding acupuncture, one of the advantages of this case report is the combination with various acupuncture modalities (cupping, plum blossom, and moxibustion) that provide benefits to the patient in reducing abdominal circumference due to biochemical and mechanical effects of PDO and no serious side effects occurred in the three cases examined. However, these results require further research.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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CASE REPORT

Metabolic effects of monounsaturated fatty acid–enriched diets on glycaemic control in patient with type 2 diabetes: an evidence-based case report

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Abstract

Introduction: Diabetes mellitus type 2 (T2D) is the most common type of diabetes. There is an ongoing debate as to whether nutrient quality or quantity is mainly responsible for the effects on hyperglycaemic control of patients with T2D**.** Monounsaturated fatty acid (MUFA) has a metabolic effect in reducing the risk factor for metabolic syndrome to prevent and control hyperglycaemia in patients with T2D and is recommended by professional organizations.

Methods: Literature searching was conducted by advanced searching in Pubmed, Cochrane Library, Scopus, and ProQuest database using MeSH Terms combined with Title/Abstract. After removing duplicates, the literature were screened based on the eligibility criteria. Critical appraisal and level of evidence of the selected literature were determined based on Oxford Centre for Evidence-Based Medicine.

Results: Two selected literature were relevant to answer our clinical question, both literature are systematic review/meta-analysis studies. The first literature is a study by Fumiaki et al. (2016), while the second is by Frank Qian et al. (2016). All literature provided evidence that a diet high in MUFA could improve glucose-insulin homeostasis among patients with T2D. These effects were marked by lower fasting blood glucose and haemoglobin A1c (HbA1c), and insulin level in the enriched MUFA diet group compared to PUFA.

Conclusion: Nutrient quality is mainly responsible for the effects on glycaemic control profile in patients with T2D, with a high MUFA diet consistent with favourable effects to improve fasting glucose and HbA1c.

Keywords: T2D, MUFA, glucose fasting, HbA1

Case scenario

A 55-year-old woman was treated at Sumber Waras hospital with a diagnosis of acute gastroenteritis, hyperglycaemic diabetes mellitus, acute kidney injury, grade II hypertension, electrolyte imbalance and anemia gravis. Five days before being hospitalized, she felt fatigued after she traveled out of town. During the trip, she could not control her food intake and forgot to take her regular medication for diabetes. When she arrived home, she immediately checked her blood sugar level, and the result was 280 mg/dL; after that, she took her medicine regularly. She checked her blood sugar level two days before hospital admission, showing 230 mg/dL.

The patient has had diabetes for 10 years, and her sugar level has never been below 200 mg/dL. In the hospital, the doctor analyzed her dietary

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habits and found that she liked to eat fried food, coconut milk, and bread for snacking. She was recommended to change her dietary habits by replacing the source of fat with olive oil, which is known to be able to control blood sugar levels for patients with diabetes mellitus.

Introduction

Diabetes mellitus is a global health burden with a worldwide prevalence of 9%. Type 2 diabetes (T2D) is the most common type of diabetes and accounts for approximately 90% of all cases. The prevalence of T2D has increased rapidly in both developed and developing countries over the last few decades. The number of T2D incidences has globally reached 425 million (8,8% of adults), with an additional 352 million at risk of developing T2D.[1,2] In China, the morbidity of T2D sharply increased from 2.5% in 1994 to 10.9% in 2013.[2] Based on the 2018 *Riset Kesehatan Dasar* (RIskesdas) data in Indonesia, there is also an increased prevalence of T2D to 8.5%.[3]

Risk factors for developing T2D are divided into two, unmodifiable (age and family history of diabetes) and modifiable factors (dietary habits and physical activity).[1,4] Epidemiological evidence has consistently demonstrated that diet is a key modifiable risk factor for T2D prevention.[1,2] There is an ongoing debate as to whether nutrient quality or quantity is mainly responsible for controlling hyperglycaemia in patients with T2D. Currently, energy-dense foods rich in saturated fatty acid (SFA) are considered the main culprit of the epidemic rise of obesity, T2D, fatty liver and cardiovascular diseases.[5] The fatty acid composition appears to play an important role in lipid-induced metabolic alteration, which is supported by the finding of higher liver triglyceride (TG) content and insulin resistance. International organizations and the 2015 USDA Dietary Guidelines for Americans have advocated substituting SFA with unsaturated fatty acid (MUFA AND PUFA). The recommendation is mainly based on the effect, especially MUFA, for preventing and controlling T2D. [2,6]

The association of MUFA consumption with the risk of T2D development remains limited and controversial. Moreover, nutrition recommendations still differ.[2,7] The current recommendation by the American Diabetes Association emphasizes the inclusion of MUFA and PUFA in the diet of individuals with T2D over intake of SFA. However, the evidence for the quantity of total fat intake is inconclusive. Meta-analyses of randomized controlled trials demonstrated that high MUFA diets were effective in reducing glycaemic control, lipid serum, and blood pressure compared to a high carbohydrate diet. In contrast, most of the previous cohort studies in European/American countries reported non-significant associations.[2,8]

The effect of MUFA on glycaemic control in patients with T2D is still inconclusive, and there is no consideration for a specific daily amount of MUFA; therefore, the author wanted to explore this topic through an *Evidence-Based Case Report* (EBCR).

Clinical question

The population target of this study is adult patients with T2D. The discussion of this study is high MUFA diet, compared to PUFA, as diet factors can control glycemic index in patients with T2D. The clinical question is, "In a patient with T2D, could a high MUFA diet effectively control blood glucose levels?"

P : Adult with T2D
I : High MUFA diet consumption
C : High PUFA diet consumption
O : level of HbA1c, fasting glucose and plasma insulin.

Methods

Literature searching was conducted by advanced searching using a combination of both Mesh Terms and Title/Abstract in four databases: Pubmed, Cochrane Library, Scopus, and ProQuest. Keywords that were used include "type 2 diabetes" or "type II diabetes" or "non-insulin diabetes," "monounsaturated fatty acid" or "MUFA," and "glycemic" or "glucose" or "HbA1c", and "systematic review" or "randomized" or "trial." Authors used Oxford Centre for Evidence-Based

Medicine as a guide to critically appraise the literature and determine the level of evidence.

Eligibility criteria

Inclusion criteria
1. Aged ≥ 18 years old
2. Subject with T2D diagnosis.
3. Subject with an intervention of enriched MUFA diet ≥ 12% total daily calories
4. An intervention of enriched MUFA diet ≥ 2 weeks
5. Study design: Systematic review-meta analysis or RCT
6. Article published up to the last ten years.
7. Articles published in English.

Exclusion criteria
1. Subject with insulin therapy
2. Study not in the human subject.
3. Study results did not include HbA1c, fasting glucose and plasma insulin levels.

Results

The author found 19 literature from Pubmed database, 6 from Cochrane Library, and 6 from ProQuest (Table 1). Duplicate removal was done using the Covidence application. Lastly, literature were assessed for eligibility based on PICO and eligibility criteria (Figure 1). We selected two articles from Fumiaki et al.[9] and Frank Qian et al.[8]

Table 1 Literature searching strategy

Database	*Search Strategy*	*Hits*
Pubmed	#1: (((((type 2 diabetes mellitus[MeSH Terms]) OR (diabetes mellitus, non insulin dependent[MeSH Terms])) AND (acids, monounsaturated fatty[MeSH Terms])) OR (fatty acids, monounsaturated[MeSH Terms])) OR (monounsaturated fatty acids[MeSH Terms])) OR (polyunsaturated fatty acids[MeSH Terms])) AND (hb a1[MeSH Terms]) #2: (((((type 2 diabetes mellitus[MeSH Terms]) OR (diabetes mellitus, non insulin dependent[MeSH Terms])) AND (acids, monounsaturated fatty[MeSH Terms])) OR (fatty acids, monounsaturated[MeSH Terms])) OR (monounsaturated fatty acids[MeSH Terms])) OR (polyunsaturated fatty acids[MeSH Terms])) AND (hb a1[MeSH Terms]) #1 AND #2	19
Cochrane Library	#1 ("type 2 diabetes mellitus"):ti,ab,kw OR ("non insulin dependent diabetic"):ti,ab,kw AND ("monounsaturated fatty acid"):ti,ab,kw AND ("polyunsaturated fatty acid"):ti,ab,kw AND ("glucose control"):ti,ab,kw AND ("systematic review"):ti,ab,kw #2 ("type 2 diabetes mellitus"):ti,ab,kw OR ("non insulin dependent diabetic"):ti,ab,kw AND ("monounsaturated fatty acid"):ti,ab,kw AND ("polyunsaturated fatty acid"):ti,ab,kw AND ("glucose control"):ti,ab,kw AND ("randomized clinical trial"):ti,ab,kw #1 AND #2	6
Scopus	Type 2 diabetes OR type II diabetes OR non insulin diabetes AND monounsaturated fatty acid OR MUFA AND glycemic OR glucose OR hbA1c AND systemic review OR randomized OR trial AND Limit (PUBYEAR 2013) TO (pubyear 2022) AND (medical) AND exclude (animal) OR exclude (child) OR exclude (depression) OR exclude (diabetes Mellitus Type 1)	0
ProQuest	ti(Type 2 Diabetes Mellitus) AND ti(monounsaturated fatty acids) AND ti(polyunsaturated fatty acids) AND ti(blood glucose control) OR ti(glycemic) OR ti(hba1c) AND ti(a systematic review) OR ti(a randomized trial)	6

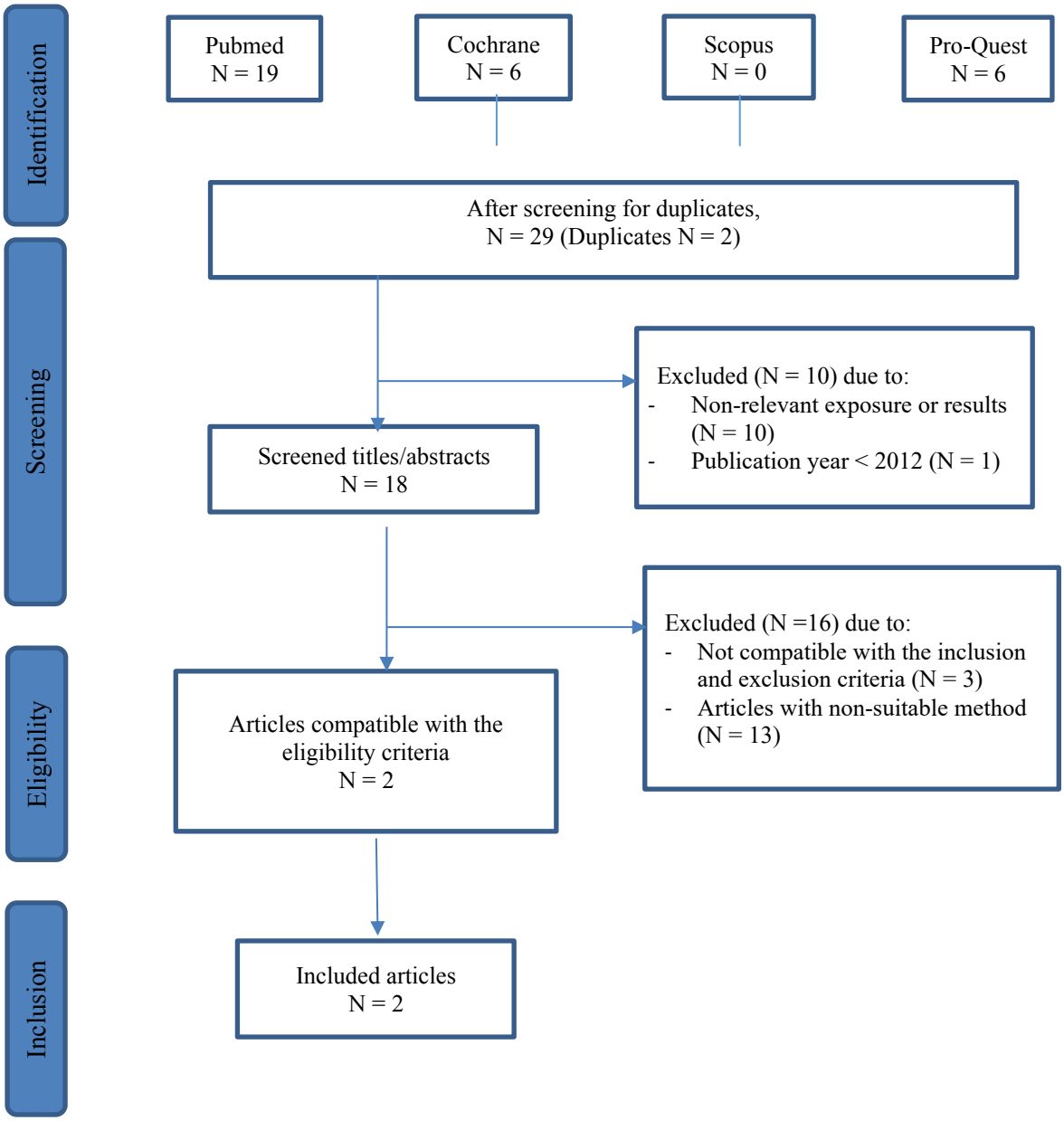

Diagram 1 Prisma's flow chart

Table 2 The Characteristics of the Literature

Articles	Study design	Population	Outcome
Fumiaki et al. (2016)	Systematic review and Meta-analysis of Randomized Controlled feeding trials	4220 subjects (45% men). 11 trials evaluated the two-hour post-prandial glucose test or insulin, 13 trial tests of intravenous infusion to evaluate the sensitivity of insulin. 10 trial tests of intravenous infusion to evaluate the capacity to secrete insulin.	Reduced HbA1c levels, 2-hour insulin post-challenge (HOMA IR), fasting insulin levels and improved insulin secretion capacity. Reduced HbA1c levels, 2-hour insulin post-challenge (HOMA IR), fasting insulin levels and improved insulin secretion capacity. Replacement of 5% dietary energy from carbohydrate or SFA to MUFA lowered HbA1c. Replacement of SFA with PUFA decreased fasting glucose levels.
Frank Qian et al. (2016)	Systematic review and Meta-analysis of Randomized Controlled Trials	Full-text screening was conducted and resulted in 53 studies, 28 studies were included with 24 studies for MUFA vs carbohydrate diet with a total participant of 1460 and 4 studies for MUFA vs. PUFA diets with a total of 44 participants.	Enriched MUFA diet significantly reduced fasting glucose plasma levels, triglyceride, weight and systolic blood pressure, also with a significantly increased HDL.

Table 3 Validity criteria

Article	Common point	Follow up	Outcome	Adjustment	Outcome over time	Precision	Applicability	Clinically important	Result
Fumiaki et al.[9]	+	+	+	+	+	+	+	+	A
Frank Qian et al.[8]	+	+	+	+	+	+	+	+	B

Table 4 The Similarity of Articles with PICO

	Similarity Population	*Similarity Determinant*	*Similarity Outcome*
Fumiaki Imamura *et al.*[9]	+	+	+
Frank Qian *et al.*[8]	+	+	+

A : This result showed that replacing 5% of energy with MUFA could reduce HbA1c levels (-0.09%; -0.12,-0.05: n=23), 2-hour challenge insulin level (-20.3 pmol/L; -32.2, -8.4; n= 11) and the homeostasis of insulin resistance (HOMA-IR) (-2.4%; -4.6,-0.3; n=30).

B : This result showed that enriched MUFA diet consumption could improve the metabolic risk factors in patients with type 2 diabetes mellitus compared to enriched PUFA diet, with a significant result in reducing fasting blood glucose -0.87 (-1.67,-0.07) WMD (95% CI)

Discussion

Optimizing the control of glycemic parameters in patients with type 2 DM is an essential procedure to reduce long-term complications. The United Kingdom Prevention study showed that hyperglycemia is the biggest factor for coronary heart disease.[7] Many observational studies have reported improved glycemic control and insulin resistance in subjects who consumed enriched MUFA diets.[8] MUFA is classified as a fatty acid with one double bond, with a higher melting point than PUFA (two double bonds or more).[10]

Qian et al.[8] conducted a systematic review and meta-analysis that compared the effect of an enriched MUFA diet to an enriched carbohydrate diet in glycemic control, lipid serum, and systolic blood pressure in patients with type 2 diabetes mellitus. The study showed improved glycemic control in patients who consumed MUFA, particularly when the enriched MUFA diet was used as a replacement for a carbohydrate diet. This is in line with a study by Scwingshackl et al.[8] who reported a significantly reduced HbA1c level when comparing an enriched MUFA diet with an enriched carbohydrate diet. Most outcomes in this study showed a statistically significant reduced fasting blood glucose (WMD −0.44 mmol/L (95% CI −0.74, −0.14)). This indicated that food composition has its own metabolic effect.[8]

An enriched MUFA diet is a proper choice for nutritional management in patients with glucose and lipid metabolism issues. MUFA can affect the function and composition of cellular membrane's fatty acid, including membrane fluidity, ion permeability, and insulin membrane receptor's affinity, thus, accelerating glucose intake into the cells. MUFA stimulates the improvement of insulin sensitivity; this mechanism is associated with the insulin signaling process involving IRS-1/PI3K. This pathway is associated with the influence of inflammatory mediators such as C-reactive protein (CRP), tumor necrosis factor (TNF-α), and interleukin, which have a central role in increasing insulin resistance. An enriched MUFA diet is expected to reduce CRP and/or TNF-α levels.[11]

Another systematic review and meta-analysis by Fumiaki Imamura et al.[9] were conducted by replacing a 5% carbohydrate diet with SFA, MUFA, and PUFA, followed by an evaluation of metabolic components such as glucose, 2-hour glucose plasma, HbA1c, and insulin levels. By replacing the 5% carbohydrate diet with MUFA, an improved HbA1c level of 0.1% and a reduced complication incidence of type 2 DM of 0.1% by 22% were found (95% CI = 15.9, 28.4%).[9] The physiological mechanism that provides metabolic effects by replacing carbohydrate diet with MUFA is reduced glycemic load, leading to reduced insulin needs and increased insulin sensitivity.[8]

A study from KANWU (Kuopio, Aarhus, Naples, Wollongong and Uppsala) in 162 healthy subjects reported a reduced insulin sensitivity with an enriched SFA diet for 3 months; they conducted a comparison by replacing SFA with an enriched MUFA diet, which showed improved insulin sensitivity. This result was obtained with a total fat consumption of <37% of the total energy, with a high-MUFA fat type. The recommended daily intake of fatty acids in the United States is MUFA 13-14% of the total energy, SFA 11-12%, and PUFA ≤7% of the total energy. The total fat consumption in the Mediterranean diet should be

33-40% of the total energy with a total MUFA of 16-29%, with olive oil as the main source of fat.[10] Based on PERKENI in Indonesia for patients with type 2 DM, the recommended total fat intake is 20-25% of the total caloric requirement and should not exceed 30%, with a composition of SFA <7% of the caloric requirement, PUFA <10%, and MUFA 12-15% of caloric requirement. The recommendation for saturated fat : monounsaturated fat : polyunsaturated fat = 0.8 : 1.2 : 1, and the recommended caloric consumption is <200 mg/day.[3]

MUFA can be obtained from oils derived from plants such as olive oil, canola oil, hazelnut oil, and sunflower oil. Several fruits also contain high MUFA, such as avocado. Nuts and seeds can also be sources for MUFA, including macadamia nuts, hazelnuts, and pecans. As for animal-based protein, it is still in debate whether this source of protein can be consumed in high amounts although containing MUFA; for example, 100g of meat contains 5.7g MUFA; however, it also contains a high SFA level of 16.3 g. Therefore, it is recommended to consume plant-derived MUFA.[10]

In conclusion these literature, provides novel quantitative evidence for effects of major dietary fats on glucose-insulin homeostasis. The results support guidelines to increase MUFA intake to improve glycaemia and insulin resistance, with possibly stronger effect among patients with type 2 diabetes. These findings help inform public health and clinical dietary guidelines to improve metabolic health. Most of the trial in these literature review were conducted among Western population, which may limit the generalizability of our findings to other population. Hence we cannot completely rule out the possibility that the metabolic differences were attributable to some unmeasured dietary component. Our result and available evidence support the importance of future experimental studies with large number of research subject population.

Conclusion

Based on the critical review of both literature, there is a significant association between enriched MUFA-typed fatty acid consumption with glycemic control, especially in reducing fasting blood glucose and HbA1c level. This finding could be a base to educate and answer clinical questions from patients, which is an association between an enriched MUFA diet with glucose control in patients with type 2 DM. Patient is advised to replace 5% of their carbohydrate intake with foods high in MUFAs such as canola oil, avocados, nuts such as Brazil nuts, sunflower seeds, hazelnuts, macadamia nuts, or walnuts, reduce intake of SFA and simple carbohydrates such as deep fried foods, flour, biscuits, or cakes.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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LITERATURE REVIEW

Zinc as an inhibitor of NMDA receptor can exhibit antidepressant effect

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Abstract

Background : New antidepressant strategies are needed, due to unsatisfactory clinical efficacy and many side effects of commonly used drugs. Recent studies linking the pathophysiology of depression with glutamatergic imbalance. There is hyperactivity of the main excitatory system (glutamatergic) to its inhibition (GABAergic). N-methyl D-aspartate (NMDA) receptors as a part of glutamatergic synapses are potential targets for intervention. Antagonist administration for glutamatergic systems, such as zinc, can exhibit antidepressant effects.

Objective : To observe the effect of zinc administration on NMDA receptors in depressed subjects

Methods : In this paper, we provide a literature review. The method to achieve the objective consists of using literature exploration, which was conducted from February to June 2022 by searching the relevant studies from several databases.

Results : Study trials both in human and animal subjects reveal that depression is associated with a lower concentration of zinc. Comparison between the lowest zinc intake with the highest zinc intake had significantly lower incidence of developing depression. Dietary zinc deficiency induces depression along with upregulation of the NMDA receptor complexes. Zinc's antidepressant effects might be mediated through its action reducing NMDA channel-opening frequency.

Conclusions : The presence of zinc may downregulate the glutamate response in binding to NMDA receptors. Because of numerous studies about the connection between zinc and depression, it seems that zinc may have the potency to develop new antidepressants. Since the capability of zinc administration to reduce depressive symptoms, it is expected leading to increased medication adherence, lower costs and better outcomes.

Keywords : zinc, antidepressant, depression, NMDA

Introduction

Depression causes significant morbidity and mortality affecting around 280 million people worldwide.[1] The World Health Organization (WHO) stated that depression is a leading cause of disability worldwide and is a major contributor to the overall global burden of disease.[2] Depression is different from mood fluctuations or short-term emotional responses to daily life. When depression happens recurrently with moderate or severe intensity, it can be a serious health condition. This causes the affected person to suffer greatly and can have a negative impact both at work or at school and in family.[2] Associated with reduced quality of life, depression causes more than 700,000 suicide deaths per year. Suicide is the fourth leading cause of death among 15-29 year olds.[1]

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Generally, people are lack aware of the connection between nutrition and depression. Depression is more often thought of as an illness that is emotionally rooted.[3] Though nutrition can play a key role in the onset, severity and duration of depression. Poor eating patterns are easily seen in people with depression, such as skipping meals, decreased appetite, or a dominant desire to consume sweet foods.[4] Currently, several researchers in the field of nutritional neuroscience are highlighting nutritional factors related to human cognition, behavior, and emotions.[3] In addition, when it comes to treating depression, most prescription drugs, including antidepressants, cause side effects. In some cases, chronic use or higher doses may lead to drug toxicity. An effective way for psychiatrists to deal with these problems is with alternative treatment, such as complementary nutritional therapy.[5]

One of the nutrients that affect the incidence of depression is zinc. Zinc plays a role in DNA replication, transcription and protein synthesis, influencing cell division and differentiation.[6] The highest amounts of zinc are in the brain, especially in the hippocampus and cerebral cortex.[7] In the central nervous system, zinc exists in two forms, first bound to protein, and second in free form. Free zinc resides in the cytoplasm of neurons, packaged as vesicles. Under normal conditions, zinc is released from the presynaptic vesicles, modulating postsynaptic receptors. Zinc deficiency can lead to an increased risk of neurological disorders, affect neurogenesis and increase neuronal apoptosis, resulting in memory deficits.[8] Zinc insufficiency is also associated with neuropsychiatric manifestations that can appear as changes in behavior and cognition, decreased ability to learn, and depression.[9] Thus, disruption of zinc homeostasis is considered as risk factor for depression.

Zinc might influence depression through its interaction with NMDA receptors. The NMDA receptor is a type of ligand-gated ion channel, one of ionotropic glutamate receptors, the other being the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor and kainate receptors.[10] Considerable evidence indicates that glutamate homeostasis is dysregulated in depressive disorder. Several lines of studies, both in humans and in animal models, support the concept that neurotransmission via the NMDA receptor is disrupted in depression. Thus, the NMDA receptor has become a target of interest in research related to depression.[11] Dietary zinc deficiency induces depression along with upregulation of the NMDA receptor complexes. Zinc's antidepressant effects might be mediated through its action reducing NMDA channel-opening frequency.[12] Furthermore, a review will be made to give a possible explanation of the mechanisms by which zinc interacts with the NMDA receptors in the context of depression.

Methods

This review was designed as a literature study to analyze the existing information about the effect of zinc administration on depression. Literature was explored from the following electronic databases: PubMed, ScienceDirect, Web of Science and Google Scholar. All databases were searched from February to June 2022. A combination of key words addressing "zinc deficient" or "zinc diet", "NMDA receptors" and "depression" or "depressive disorder" were used. There were no language restrictions set in the search strategy. The titles and abstracts of relevant articles were screened first, then the full articles were read and further observed to identify the eligible studies.

This review summarizes important clinical and basic science evidence for zinc's role in depression and draws connection to NMDA receptors. The abstracts, titles and full texts of all retrieved studies were comprehensively reviewed independently. The included studies were required to meet the following criteria: (1) the study design is observational study, experimental study, cohort prospective study, meta-analysis, randomized controlled trials, case reports, or systematic review; (2) the study included both human and animal subjects; (3) the association between dietary zinc intake and NMDA receptor; (4) depression status as the outcome were reported. The exclusion criteria were listed as follows: duplicated or irrelevant articles and letters.

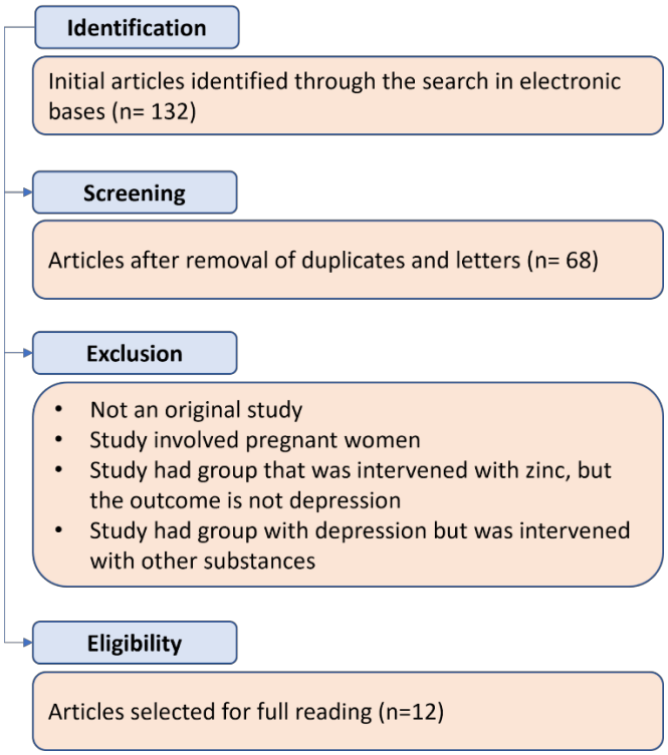

Figure 1 Scheme of article's extraction

The searching results from each included study were extracted independently. The eligible study included the following information about the first author, year of publication, location, age, gender, animal model, sample size, study design, dietary zinc assessment, exposure, and diagnostic criteria of depression. The appropriate information also clarified the connection between zinc and NMDA receptors. Detailed article's extraction was represented in **figure 1**.

Results

Numerous study trials both in human and animal subjects reveal that depression is associated with a lower concentration of zinc. A meta-analysis of human observational studies demonstrated the concentration of zinc in the peripheral blood of depressed patients to be approximately 1.850 µmol/L lower than in healthy controls, with significant inverse associations between depression severity scores and serum zinc concentrations.[13] Cross-sectional study involving postmenopausal women who were not using menopausal hormone therapy reported that the women with higher levels of zinc serum had less depressive symptoms.[14] Dietary zinc has an inverse association with risk of depression. Comparison between the lowest zinc intake with the highest zinc intake had significantly lower incidence of developing depression with a reduction of about 30-50%.[15] Zinc supplementation significantly improved mood, reduced depression scores, and facilitated the treatment outcome in cases with antidepressant treatment-resistant patients.[16] Randomized controlled trials reveal the potency of zinc as adjunctive therapy for improving mood in depressed individuals through increasing BDNF levels. Higher serum zinc and greater reduction in Beck Depression Inventory (BDI) score was found in the zinc-supplemented group, and there was significant positive correlation between serum BDNF and zinc levels at baseline.[17]

The relationship between zinc and depression may be linked to its action on NMDA receptors. Zinc restriction in rats causes behavioral alterations that refer to some similarities to the pathophysiology of depression. In addition, depressive-like behavior led by zinc deficiency is related with the changes in NMDA receptor signaling pathway.[18] Since zinc is involved in pathophysiology of depression, it is sufficient to consider that disturbances of zinc homeostasis might occur in the brain tissue. Based on research conducted on suicide victims due to depression, although there was no alteration of zinc level in the hippocampal tissue compared to controls, however there is a statistically significant decrease in the potency of zinc to prevent the activity of NMDA receptors in the hippocampal tissue of suicide subjects.[19] Antagonist activity of zinc to NMDA receptor has antidepressant-like effects, attributed to inhibition of NMDA-sensitive glutamate channels. It was observed that zinc administration in rats and mice reduced the number of NMDA receptor complexes, which in turn led to their downregulation.[20] Conversely, a zinc deficient diet induces an upregulation of the NMDA receptor complex.[18] Besides NMDA, zinc also can potentially be beneficial to help

depression through its action to influence other types of receptors, such as the AMPA receptor, metabotropic glutamate receptor (mGluR) and gamma-aminobutyric acid (GABA) receptor. It is hypothesized that zinc may have the ability to maintain homeostasis between excitatory and inhibitory systems via GPR39 as a zinc receptor, which seems to be a promising target to improve depressive symptoms.[21]

Depressive-like effects are thought to be consequences of altered NMDA receptor subunits levels.[22] Research on the effects of antidepressants on NMDA receptors also supports the consideration of changes in the receptor complex during depressive disorders.[23] Chronic antidepressant treatment decreases glycine affinity and function of the NMDA receptor complex in the hippocampus.[23] Chronic antidepressant treatment was also observed altering mRNA expression of the genes encoding for the NMDA receptor subunit, as a result there was downregulation of expression and/or function of NMDA receptor, which in turn to help protect against glutamate-mediated excitotoxicity.[20] Chronic antidepressant treatment not only caused changes in the human NMDA receptors, but also zinc levels that were previously decreased, apparently normalized.[24] Since the hippocampus is the main site of synaptogenesis, where zinc levels are markedly reduced in depressive disorders, increasing hippocampal zinc concentrations after antidepressant treatment promotes neurogenesis as well as in neuroprotection.[24]

Discussion

Zinc is the second highest trace element after iron in the human body. Human adults have 2 to 3 grams of total zinc, most of which is stored in bone, brain, and skeletal muscle, whereas in plasma, zinc levels are only 0.1%. Usually, levels of zinc plasma are used to estimate nutritional status of zinc.[25] Zinc is necessary for different biological roles. It is involved in enzyme activation, gene expression, cell division, cell growth, and it is needed for the immune system to function correctly. Recommended dietary intake of zinc for adults is between 8-11 mg/day. Food sources to meet daily zinc requirements can be found in beef, lamb, nuts, whole grains, legumes, and yeast. Zinc is also found in most multivitamins and mineral supplements. Tolerable intake levels of zinc supplements should be below 40 mg/day.[26] Although it is not recommended to take zinc supplements beyond 40 mg/day, zinc is considered nontoxic. There is no standard treatment to overcome zinc overdose. Zinc taken in large amounts can manifest nausea, vomiting, diarrhea, abdominal cramps, lethargy, and fatigue within 3 to 10 hours of consuming the supplement. An extremely high intake of zinc also can result in copper and iron deficiency.[27]

In the central nervous system, zinc is the most prominent micronutrients. Zinc concentration is highest in the brain compared to other organs in the human body, where it is about 150 μmol/L, this level is 10 times higher than serum zinc. Mostly, zinc in the brain presents as a structural component of proteins, and about 10–15% of brain zinc exists in a chelatable form. In addition, in brain extracellular fluids, chelatable zinc occurs at much lower concentrations, it is estimated only about 500 nM.[28] One of the essential functions of zinc is its role as a neuromodulator. During synaptic transmission, zinc is released then it binds to synaptic membrane receptors.[29] In synaptic cleft, zinc reacts with excitatory NMDA and AMPA receptors, as well as the inhibitory GABA receptors.[30] Moreover, extracellular zinc effects on various voltage-gated ion channels, with the result that alteration of neuronal excitability.[31]

The NMDA receptor is a ligand-gated ion channel receptor that is permeable to calcium and, to a lesser extent, also permeable to sodium and potassium.[23] In general the structure of the NMDA receptor includes two glycine-binding subunits (NR1) and two glutamate-binding subunits (NR2).[32] NMDA receptors are located on the postsynaptic neuron membrane and collaboratively modulate glutamate-stimulated post-synaptic transmission.[23] Magnesium ion (Mg^{+2}) is located at the entrance of a NMDA

channel. At resting state, it forms a plug that blocks the channel. In order to depolarize a postsynaptic neuron, both glutamate and glycine must bind to their respective sites on NMDA, releasing Mg^{+2} and allowing Ca^{+2} entry.[33] NMDA receptors activation results in long-term potentiation and increased synaptic plasticity.[32] In contrast, when zinc is present at the synapse, NMDA receptor activation is inhibited.[19] Therefore it becomes a consideration that antidepressant effects of zinc are managed via zinc-containing neurons. Neurons that contain zinc ions in their presynaptic vesicles are predominantly glutamatergic, and are generally called zinc-enriched neurons (ZEN). Hippocampus is the area of the brain where the highest concentrations of zinc are found.[34] Zinc penetrates the brain through the blood brain barrier systems (BBB). The BBB dissociates plasma zinc from the brain under physiological conditions. Zinc, iron – regulated transporter like protein (ZIP) and zinc transporter (ZnT) are two proteins that have been identified to regulate zinc concentration and maintain zinc homeostasis in the brain. ZIP protein increases zinc uptake by the brain so that plasma zinc concentrations decrease, whereas ZnT protein exports zinc out of the brain thereby increasing plasma zinc concentrations.[35]

Zinc is released simultaneously with glutamate by ZEN and rapidly reaches the micromolar levels required for synaptic modulation. Mechanism of the antidepressant action of zinc is direct inhibition of the NMDA receptor. The dynamics of zinc binding to the NR2 subunit of the NMDA receptor varies according to the glutamate-binding isoform. NR2A has high sensitivity to extracellular zinc and requires only nanomolar concentrations to produce voltage-independent inhibition.[36] In contrast, NR2B subunit binds zinc at 100-fold lower affinity than NR2A to produce voltage-dependent inhibition.[32] Besides modulating NMDA receptor activity via allosteric site binding, zinc provokes the release of the inhibitory neurotransmitter i.e. GABA from interneurons to inhibit presynaptic glutamate release.[37] Since less glutamate at the synapse, glutamate binds to the NMDA receptor will be reduced. Furthermore, another potential mechanism of zinc to act as antidepressant is the indirect inhibition of the NMDA receptor by promoting mGluR inhibition. When zinc inhibits mGlur, it will result in a decrease of intracellular release of Ca^{+2} from neuronal stores. Ca^{+2} increases the activity of NMDA receptors, so that the role of zinc in reducing the availability of Ca^{+2} will further reduce the functionality of the NMDA receptors (**figure 2**).[38]

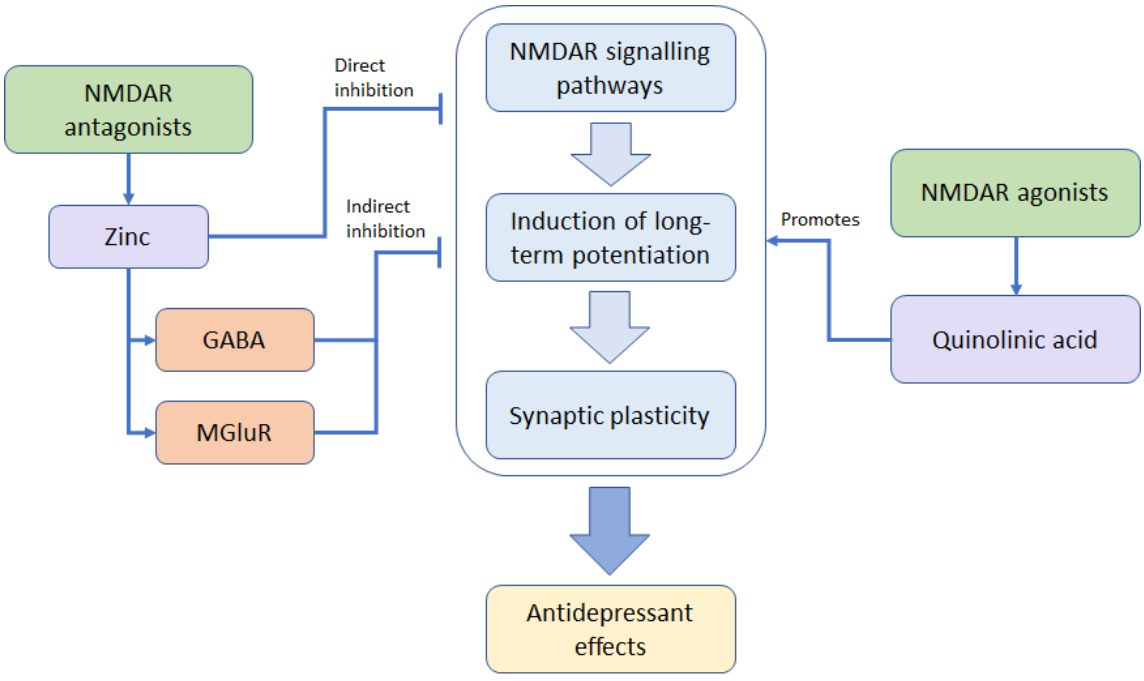

Figure 2. Mechanism of NMDA receptor inhibition and promotion
Figure explanation: NMDAR: N-methyl D-aspartate receptors, GABA: gamma-aminobutyric acid, MGluR: metabotropic glutamate

Patients with depression who do not show any response to antidepressants, or have a recurrence are suggested to consume zinc supplementation as an adjunct to antidepressant drugs to improve their therapeutic effects.[39] In addition, some studies have shown the low serum zinc levels in depressed patients are normalized during treatment with antidepressants.[40,41] One of the symptoms of depression is lack of appetite, therefore it lessens zinc intake. However, instead of finding a decrease in serum zinc levels, on the contrary, normal serum zinc levels were found in depressed patients during treatment with antidepressants. It can be inferred that the enhanced serum zinc up to normal levels may be due to antidepressants. Antidepressants are thought able to stimulate zinc release from the body's stores such as muscles and bones, besides that, zinc supplementation on these patients restored the zinc pools in blood circulation.[41] In a study on patients with major depression who were given imipramine combined with supplementation of 25 mg zinc revealed a significantly reduced rate of depression. These patients were resistant to antidepressant medication, so that zinc supplementation may help to facilitate treatment with antidepressants.[42] A meta-analysis study that determines whether zinc supplementation or placebo can improve depressive symptoms in children, adolescents, or adults, also concludes that zinc supplementation may have a contribution reducing depressive symptoms in individuals treated with antidepressant drugs for clinical depression. [43]

Antidepressant's effect of zinc in inhibiting NMDA receptors is also observable through its involvement in the inflammatory process. Proinflammatory cytokines levels, such as interleukin 6 (IL-6) and tumor necrosis factor a (TNF-a) increase when zinc deficiency occurs.[44] The presence of proinflammatory cytokines may cause depression by altering serotonin regulations in the brain. Increasing number of proinflammatory cytokines are associated with indoleamine 2,3-dioxygenase (IDO) activation. IDO will reduce the level of amino acid tryptophan which is necessary for serotonin synthesis. IDO catalyses the conversion of tryptophan to metabolites kynurenine. Subsequently, kynurenine will be metabolized to quinolinic acid by kynurenine 3-monooxygenase.[45] Augmentation of quinolinic acid metabolism over kynurenine facilitates neurodegeneration, including depression. Quinolinic acid is a neurotoxic metabolite which is considered as an NMDA receptor agonist that causes excessive release of glutamate in hippocampus, striatum, and cortex (**figure 2**).[46]

Conclusions

Glutamatergic system disruption, i.e. imbalance condition between excitatory and inhibitory systems leads to the development of depressive symptoms. Since there is numerous evidence about decreased zinc levels in depressive disorders, it is possible that zinc may have the potency as a state marker of that disease. The presence of zinc can downregulate the glutamate response by inhibiting NMDA receptors. This inhibitory activity is impaired under conditions of zinc deficiency. The ability of zinc as an NMDA inhibitor can be a chance to develop new antidepressants, but further research is still needed. Considering that pharmacotherapy has potential adverse side effects, this review suggests that zinc can be used as an adjuvant to help reduce depressive symptoms in individuals with a clinical diagnosis of depression. Zinc supplementation is also expected to lessen the amount of required psychotropic medication, thereby leading to increased medication adherence, lower costs, and better outcomes.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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ORIGINAL PAPER

External validation test of body height estimation on outpatient radiotherapy clinic of Dr. Cipto Mangunkusumo General Hospital

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Abstract

Background : Stature is required to calculate body mass index and determine the energy needs of patients in nutritional medical therapy. Difficulty was found to obtain stature data in patients who are unable to stand. Therefore, there are some height estimation formula to predict the actual height using knee height. This study aimed to validate the Chumlea formula on outpatient clinic of Dr. Cipto Mangunkusumo General Hospital, Indonesia.

Methods : This cross-sectional study used 90 respondents selected by consecutive sampling. Actual height, knee height, age and gender data were collected. Estimated height using the three of Chumlea formula. Pearson correlation was used to see the correlation between actual height and estimated height. Paired t-test were used to determine the difference significance.

Results : The average age of the subjects was 45±10 years old with actual height 157±10 cm, and knee height 48.8±3.5 cm. A strong positive correlation was found between actual height with all estimated height on male ($p=0.000$; $r > 0.8$) and female subjects ($p=0.000$; $r > 0.6$). However, comparison between actual height and estimated height showed no significant differences only in Chumlea L1 formula ($p=0.087$) and Chumlea L3 formula ($p=0.824$) on the male subjects.

Conclusions : Chumlea L1 and Chumlea L3 formula was a valid fomulation for calculating the estimated body height in adult male patients. There was no valid Chumlea's formulation to estimate body height in female patients.

Keywords: Body height, Stature estimation, Knee height, Chumlea formula

Introduction

Measurement of stature is a part of the anthropometric examination. Measurement and recording of body height is one component of calculating the body mass index (BMI), which is useful for assessing the risk of malnutrition in hospitalized patients.[1] Tonder, et al.[2] revealed that the prevalence of malnutrition in hospitals was up to 78%, and almost a quarter was already malnourished at the time of admission.[2,3] Knowing the high number of malnutrition, anthropometric data at the time of admission is necessary. Nonetheless, not all patients admitted to the hospital have complete anthropometric data.

Assessing nutritional status is important for nutritional medical therapy interventions, especially in patients treated in hospitals.[4] Therefore, stature data is needed to calculate the patient's energy needs, which are included in nutritional medical therapy.[5]

Difficulty was found to obtain body height data in patients who are unable to stand.[6] Measurement tape can be used for measuring body height

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estimation, by obtaining the body length, but its validity is still doubtful. In addition, anthropometric measurement using tools also require calibration process periodically.[7] Some of these reasons certainly affect hospital costs.
There are some estimated height calculations have accomplished in previous studies. This study aims to validate three of the equations developed by Chumlea to estimate stature of the patients.

Methods

Research Design

This research was an analytical study with cross sectional design.

Recruitment

This study used 90 subjects selected by consecutive sampling. The population that fulfilled the research criteria were accepted as the respondents of the study until the required number of samples was reached in accordance with the calculation of the number of samples. Respondents that fulfill the research criterias were given an information sheet, explained the aim of the study and the examination to be accomplished.

Furthermore, subjects who were responsible to participate in the study were asked to fill out and sign the consent form to participate in the study. General and demographic data collection was completed by interview to regarding the characteristics of the subjects. Then, the subjects were measured for actual height and knee height. Subjects were all patients who were able to stand and did not have any postural deformities in outpatient unit Radiotherapy Clinic Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia. Data collected in the period August-November 2019. The sample were part of the accessible population who are willing to participate in the research and fulfill the research criterias. The number of ethical approval is KET-368/UN2.F1/ETIK/PPM.00.02/2019.

Data collection

Height (cm) was measured to the nearest centimeter using a microtoise, along a surface as flat as possible such as a door or a wall. Measurement of height was carried out twice and the results were the average of the two measurements. Knee height (cm) was measured once per person with a knee height caliper (SECA® 207) to the nearest centimeter on the right side with an angle of 90° between the thigh and the leg according to Chumlea,et al[8]. The caliper was placed in line with the lateral malleolus and the head of the fibula, with the soft tissue compressed, the distance from the sole of the foot to the top of the thigh immediately above the condyles of the femur was measured.

Table 1 Chumlea formulation for estimate the stature[8,9]

Formulation	Equation
Male Stature	
First Chumlea's formulas for Caucasian people (L1)	H (cm) = 64.14 + (2.02 × KH [cm]) − (0.04 × age [y])
Chumlea's formulas for white people (L2)	H (cm) = 71.85 + (1.88 × KH [cm])
Chumlea's formulas for black people (L3)	H (cm) = 73.42 + (1.79 × KH [cm])
Female Stature	
First Chumlea's formulas for Caucasian people (P1)	H (cm) = 84.88 + (1.83 × KH [cm]) − (0.24 × age [y])
Chumlea's formulas for white people (P2)	H (cm) = 70.25 + (1.87 × KH [cm]) − (0.06 × age [y]
Chumlea's formulas for white people (P3)	H (cm) = 68.1 + (1.86 × KH [cm]) − (0.06 × age [y])

Formula analysis

Estimated height (H) is obtained from calculations using the Chumlea formula[8,9] according to sex, age (y) and knee height (KH) measurement. The formulation can be seen in the **Table 1**.

Data Analysis

The data were collected from the research subjects were recorded on each research form, edited, and coded. The data was entered into a computer and processed using the Statistical Package for Social Sciences (SPSS) program. Statistical analysis was performed using the paired t-test and Pearson Correlation test.

Results

Data were collected on 90 patients in the radiotherapy clinic of Dr. Cipto Mangunkusumo General Hospital. The distribution of subjects can be seen in **Table 2**. The patients involved in this study were in the range age of 45 ± 10 years old, with 44 men (49%) and 46 women (51%). The height of all patients in the range of 157 ± 10 cm, with the height of men 165 ± 6.7 cm and women 150 ± 6 cm. The knee height of all patients was found to be 48.8 ± 3.5 cm with the knee height of men 51.4 ± 2.6 cm and female 46.3 ± 2.3 cm. Table 3 shows the correlation between actual height and estimated height using the Chumlea formula,

Table 2 Distribution of patients' age, actual height, and knee height (n=90)

Variables	Result
Age (year)	45±10*
Gender	
Male, n (%)	44 (49)
Female, n (%)	46 (51)
Actual Height (cm)	
Male	165±6.7*
Female	150±6*
Knee Height (cm)	
Male	51.4±2.6*
Female	46.3±2.3*

*mean ± standar deviation

Table 3 Correlation between actual stature and estimated stature using formula r = Pearson Correlation; *Statistically Significant (p<0.05)

Variable	r	p
Male Stature		
Chumlea L1	0.834	0.000*
Chumlea L2	0.833	0.000*
Chumlea L3	0.833	0.000*
Female Stature		
Chumlea P1	0.662	0.000*
Chumlea P2	0.755	0.000*
Chumlea P3	0.755	0.000*

Pearson correlation showed a strong correlation in both the male and female groups with p 0.000 in all formulas.

Table 3 shows that among all Chumlea formula, only Chumlea L1 and Chumlea L3 formulas for male patients did not have a significant difference with the actual height measurement, with p-value of 0.087 for Chumlea L1 and p-value of 0.824 for Chumlea L3. Meanwhile, in female patients, all of the Chumlea formulas showed a significant difference between the actual height and the estimated height.

Discussion

Determination of nutritional status for patients in hospital is very important for malnutrition screening and therapy. Nutritional status is also an important clinical outcome to be monitored during the patient's stay in the hospital. One component of determining nutritional status is height. To measure body mass index (BMI), for example, height data is needed. In hospital, height measurement is often difficult, especially in patients who are unable to stand or have deformities or postural abnormalities. There are several alternatives to determine the estimated height using the formulas generated from previous studies using components of body parts measurements such as knee length, ulna length, arm-span, demi-span and so on.

Table 4 Comparation between actual stature and estimated stature using formula

Formula	Mean± SD/ Median (Minimum-Maximum)	p
Male		
Actual Stature	165±6.7	
Chumlea L1	166±5.3	0.087t
Chumlea L2	168.5±4.9	0.000 t*
Chumlea L3	165.5±4.64	0.824 t
Female		
Actual Stature	150±6	
Chumlea P1	158±4.7	0.000 t*
Chumlea P2	154±4.3	0.000 t*
Chumlea P3	151±4.2	0.000 t*

t Paired T Test
*Statistically Significant ($p<0.05$)

This study compared the actual height measurements using microtoise and estimated height measurements using several formulas developed by Chumlea that use knee length as the component of the formula.[8,10] Knee length is often used because it does not decrease due to age.[11]

This study measured the actual height and the estimated height using all the Chumlea formulas showed that male adult subjects are taller than women. This is aligned with previous studies in various countries and races which found that men's height is higher than women's. Moelyo et al.[12] showed that in 1995 the male's height was taller (165.8 cm) than female (153.6 cm) and consistent for the last 40 years (1955-1995) both in rural, small cities, and large cities, with positive secular trends from 1955-1995 for males 95% CI 1.3 (1.1-1.4) cm and for females 95% CI 0.9 (0.8-1.0) cm. Genetic factors played role in sexual dysmorphism, which make males 8% taller than females over the last 110 years.[12] Adult male subjects in this study have an average height of 165±6.7 cm and knee height of 51.4±2.6 cm, which is higher than the height and knee height of adult female patients, namely 150±6 cm and 46.3±2.3 cm. These results are in accordance with the study of Murbawani et al.[13] in elderly subjects, where men have higher knee heights than women.[13]

Chumlea Formula Validity

In this study, there was a strong correlation between the estimated height using the Chumlea formula and actual height. However, after analyzing the difference between the two measurements, the results were not significantly different only for the estimated height using Chumlea L1 and Chumlea L3 formulas. These two formulas have a difference of <1 cm from the actual stature, which is 0.97 cm in the Chumlea L1 formula and 0.13 cm in the Chumlea L3 formula. Meanwhile, in female subjects, although all formulas were strongly correlated with actual stature, there was a significant difference between actual height and estimated height using all formulas. So according to the results of this study, none of the Chumlea formulas can be used to estimate the height of adult female patients. This may be because the Chumlea formula was developed especially in the Caucasian race which has very different characteristics from the Indonesian race, especially women. The predictive equation that has been used so far using the Chumlea formula also does not include subjects with overweight and obesity[4], therefore in this study it does not exclude subjects with overweight or obesity.

Conclusions

From this study, we conclude that estimated height by Chumlea L1 formulation

(cm) = 64.14 + (2.02 × knee height [cm]) − (0.04 × age [y]) and estimated height by Chumlea L3 formulation (cm) = 73.42 + (1.79 × knee height [cm]) were valid fomulation for calculating the estimated body height in adult male patients in Dr. Cipto Mangunkusumo General Hospital. Meanwhile, there was no valid Chumlea's formulation for calculating the estimated body height in adult female patients.

Potentials for future research

Further studies are needed with larger number of participants to obtain a new calculation formula that can be used specifically for patients treated at the Dr. Cipto Mangunkusumo General Hospital. We suggest to provide a knee height measuring device to apply this estimated stature measurement for bed rest patients at the Dr. Cipto Mangunkusumo General Hospital.

Future studies are expected to test the validity of using other formulas with other measurement components such as fathom length, or half fathom length and the like to determine the estimated height of adult female.

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Conflict of Interest

Authors declared no conflict of interest regarding this article.

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