DOI Number: 10.5958/0976-5506.2018.01906.X

Improving the Immune Response Il-10 and Secretory Immunoglobulin A in the Elderly after Getting Synbiotic

Rudy Hartono[1], Agustian Ipa[1], Aswita Amir[1], Bambang Wirjatmadi[2] , Ridho Pratama[1], Ronny Horax[3]

[1]Health Polytechnic of Ministry of Health in Makassar, Indonesia

[2]Professor of community nutrition, Public Health Faculty, Airlangga University, Indonesia

[3]Department of Food Science University of Arkansas, USA

ABSTRACT

Increasing age will reduce the body's resistance, so it needs functional foods that can maintain the body's immune system, especially the elderly. This research was conducted to see the synbiotics effect on IL-10 immune response and secretory immunoglobulin A (sIgA) which was done by intervening to the elderly using synbiotics. The results showed that after administration of IL-10 and sIgA ($p < 0.05$) there was an increase in the immune response of the two markers. Based on the results of this study can be recommended the use of synbiotics as an alternative to maintaining the immune system in the elderly.

Keyword: *Functional Foods, Synbiotic, Immune response, Immunoglobulin A*

INTRODUCTION

Elderly people grow very fast even faster than other age groups. Demographic implications that arise due to the growth of the elderly, namely the number of elderly population is increasing and according to WHO's projections Indonesia is a country with the number 8 elderly population in the world that is equal to 21,194,000 people or 8.2% of the total population in Indonesia. The other seven countries that have the highest number of the elderly population are China, India, USA, Japan, Russian Federation, Brazil and Germany [(17)].

This shows a very large amount, so if it is not done efforts to improve the welfare of the elderly from now on will cause problems and can become a time bomb in the future. The tendency of this problem to arise is also marked by the number of elderly dependents according to the 2008 BPS Susenas of 13.72%.

The population dependency rate will be high and felt by the population of productive age if it is coupled with the dependency of the population aged less than 15 years, where the current population of fewer than 15 years is 29.13% [(10)].

Provinces with a higher life expectancy also have more elderly population. A territorial is called old structure if the percentage of people older than 7%. There are 11 provinces in Indonesia with the elderly population more than 7%, namely Yogyakarta Special Region (13.4%), Central Java (11.8%), East Java (11.5%), Bali (10.3%) , North Sulawesi (9.7%), South Sulawesi (8.8%), West Sumatra (8.8%), West Java (8.1%), Lampung (7.8%), West Nusa Tenggara (7 , 7%), East Nusa Tenggara (7.5%)[(1)].

The obstacles faced in the effort to improve the health and welfare of the elderly are the lack of health service facilities and infrastructure that provide friendly health services and are easily accessible to the elderly. In addition, data on the elderly is inadequate and the most recent data on health problems in the elderly based on surveys and research related to the elderly are still very limited. Currently, the data in the new Ministry of Health contains 437 Elderly Community Health Centers and more than 69,500 elderly Posyandu in several districts/cities in Indonesia, but the program has not been maximized[(2)].

Corresponding Author:
Rudy Hartono
Health Polytechnic of Ministry of Health in Makassar, Indonesia Wijaya Kusuma Raya Street 56 Makassar, Indonesia, Email: dinomks70@gmail.com

The aging process also leads to a decrease in immune function (immunosenescence), which can increase hyporesponsiveness of vaccination and the tendency for infectious and non-infectious diseases[9].

Synbiotics are functional foods that the body needs. Sinbiotik is a combination of probiotics and prebiotics can be a food substrate that reaches the large intestine and can affect the composition and activity of bacteria present through fermentation capacity in the elderly. The metabolic products of intestinal bacteria can affect the immune system. Modulation of intestinal microflora by diet is the basis for the synbiotic concept. Various strains of bifidobacteria and lactobacillus as probiotics have also been shown to exert immunostimulatory properties[7].

In general, reports of research results in an increase in the amount of lactobacillus, bifidobacteria, or both and enterobacteria decrease after administration of FOS(20). The synbiotics function interacts with immune cells or receptors to improve the phagocytic function of white blood cells, increase IgA after contact with antigens, increase intraepithelial leukocyte proliferation, Th1 / Th2 cell regulation, induction of cytokine cytosis[17]. However, research has not fully determined its effect on the intestinal microflora of older people.

MATERIAL AND METHOD

This study aims to make recommendations to the elderly in order to improve the immune response (with parameters Il-10 and sIgA) so that the health status of the elderly can be maintained. This research was carried out for 3 months with the intervention using synbiotics that is in November 2015 to February 2016 in the elderly in the Mangasa Health Center in Makassar City.

The main tools used to make measurements were 1) ELISA (The enzyme-linked immunosorbent assay) to measure blood serum Il-10 and 2) the measurement was measured from the feces also using ELISA (21), 3) the study subjects were elderly, aged 60 - 70 years old, Makassar tribe, has no history of degenerative and infectious diseases with doctor's recommendations, free from probiotic and prebiotic intake and antibiotics, so the sample size is 12 people who get synbiotics.

Evidence of the effectiveness of this simple method implemented by several steps: 1) validation of synbiotics obtained from pharmacies with registration by the Republic of Indonesia Food and Drug Supervisory Agency 2) Synbiotics consisting of probiotics consisting of L. acidophilus 7.5 mg, L. casei subsp casei 0 , 25 mg, L. rhamnosus 10 mg, L. bulgaricus 12.5 mg, Bifidobacterium breve 5 mg, B. longum 5 mg, Streptococcus termophillus 9.75 mg and Fructooligosaccharide (FOS) as prebiotics 350 mg., 3) measure response immune IL-10 uses ELISA before and after getting synbiotics for 2 months using 3 cc of blood to get the serum and feces to measure the blood pressure taken at the Hasanuddin University Teaching Hospital Laboratory, 4) supplement control is carried out by enumerators conducted by supervision every day to the subject while the researcher every 3 days during the study, 4) compares the two measurement results to find out the improvement tan IL-10 and sIgA immune responses.

FINDING

Immune Response Measurement Parameters

Functional food is Indonesia's abundant natural resource including probiotics and prebiotics. The combination of probiotics and prebiotics is known as synbiotics. The usefulness of synbiotics is that it can increase immunoglobulin levels in the elderly, which will have a more positive effect on performance against disease [16].

In addition, Lactobacillus plantarum will reduce the Th1 / Th2 small intestine lamina propria (SILP) ratio. Lactobacillus lactis has an immunomodulating effect that regulates Th1 and Th2 balance, but it can also reduce GATA-3 & Tbet in SILP. Probiotics both Lactobacillus, Bifidobacterium and Streptococcus are promising strategies to prevent or overcome excessive intestinal inflammation and maintain immune homeostasis[14]. The importance of determining molecular biomarkers that are predictive of the immune system can give an indication that the elderly still remain productive, namely IL-10, and sIgA as a biomarker of immune response. The selection based on IL-10 is an anti-inflammatory function that balances Th1 and Th2 cells [8], and sIgA is an adaptive defense that functions as an antibody found on the mucosal surfaces of the mucous tractus digestivus, tractus urogenitalia, and respiratory tractus[12].

Effect of Sinbiotic Giving on IL-10 and sIgA immune responses

Based on the results of the descriptive study, there were 5 men (41.67%) and 7 (58.33%) men, 60-65 years

old, 10 (83.33%) and 2 66-70 years old women. people (16.67%), marital status shows that married 9 (75%) and divorced 3 (25%).

Table 1: Distribution of Immune Response of IL-10 and sIgA in the Elderly after Synbiotic Giving

Respon immune	before	after	p
IL-10 (ng/ml)	110,08±15,47	249,88±190,12	0,005
sIgA (µg/ml)	1,79±0,39	2,92±0,44	0,002

The average profile of IL-10 in group 2 before supplementation of synbiotics was 110.08 ng / ml with a variation of 15.47 ng / ml. After getting treatment, there was an increase of 140.70 ng / ml to an average of 249.88 ng / ml with a variation of 190.12 ng / ml. The results of statistical tests using Wilcoxon test obtained a value of 0.005 <0.05, meaning that there were significant differences in IL-10 profiles between before and after synbiotic supplementation.

The synbiotic supplementation group for sIgA also contained elevated levels of 1.79 ± 0.39 µg / ml to 2.92 ± 0.44 µg / ml, to see the effect of synbiotic supplementation using the Wilcoxon test had a p value of 0.002 <0.05 . This means that there is a significant change in the profile of the treatment group.

CONCLUSIONS AND RECOMMENDATIONS

The results showed that a significant increase in IL-10 and sIgA immune responses in all samples increased with time, although the increase was not too high but still showed a balanced state (homeostasis) to maintain the health of the elderly. It is recommended to provide synbiotics to the main elderly who are in an unhealthy condition to improve the immune response to be healthy.

DISCUSSION

Symbiotic are probiotics and prebiotics that are combined in food products. Probiotics are non-pathogenic microorganisms that live as digestive microflora that can have a positive influence on human health, while prebiotics are substrates or food ingredients for probiotic bacteria, where these substrates will help increase the growth and liveliness of one or more probiotic bacteria that are in one colon, so that physiological and metabolic conditions can be obtained which can provide protection to the health of the digestive tract. A good combination of prebiotics and probiotics can increase the number of good bacteria (probiotics) that can survive in the digestive tract by fermenting the substrates[5][3].

The synbiotic composition has each function, namely, B. breve maintains normal intestinal flora, inhibits E. coli, reduces the growth of Candida albicans. B. longum is preventing colon cancer, allergies, crohn colitis, and high cholesterol with the effects of increased IL-10 and IL-12 [19]. L. bulgaris as a natural antibiotic that works with a broad spectrum also increases immune, anti-tumor or cancer. L. caseisubsp. casei has the effect of increasing NK cell activation [15], inducing differentiation of regulatory T cells[14]. L. rhamnosus has the effect of increasing the capacity of pagocytosis[4]. L. acidophilus increases stimulation of IgA production and capacity for phagocytosis[20][13]. S. thermophiles serve to suppress lymphocyte proliferation by inducing apoptosis[6].

Based on the synbiotic composition used as supplementation material, it reflects pro-inflammatory cytokines by producing IFN-γ because they are bactericidal, suppress chronic colitis, increase commensal bacteria, increase sIgA and increase phagocytosis[4]. The synbiotic composition also directs / potentially increases the immune balance by producing high IL-10 by B. longum and L. casei subp casei so that even on the other hand IFN-γ is produced high but IL-10 is also produced to suppress IFN-γ production. The other side of the synbiotic composition FOS serves to suppress by blocking the growth of pathogens[14]. This is evidenced by the increase in IL-10 after the administration of symbiotic increased significantly.

CONCLUSION

This study recommends functional food ingredients in this case synbiotics that can maintain the health of the elderly while maintaining IL-10 and sIgA while

increasing according to the state of homeostasis. This finding is expected to provide a positive contribution to improve the quality of the elderly immune response and can be developed in other studies in other vulnerable groups such as pregnant women, toddlers, and young women.

Conflict-of-Interest Statement: In this study between researchers and research, subjects did not have a conflict of interest, because subjects did not have personal or informal relationships with researchers.

Source of Funding : The source of funds in this study came from the Research of Health Workforce Development of the Ministry of Health of the Republic of Indonesia in 2016.

Ethical Clearance: The ethics of this study were obtained from the Ethics Commission for Health Research, Public Health Faculty, Airlangga University, Surabaya, Indonesia.

REFERENCES

1. Indonesian Ministry of Health. Elderly Situation in Indonesia May 29 – National Elderly Day. Jakarta: data and information Center; 2016.
2. Ministry of Health of Republic of Indonesia, Services and Improvement of Old Age Health. Center for Public Communication Secretariat General of the Ministry of Health of the Republic of Indonesia, Jakarta. 2015. Available from URL: http://www.depkes.go.id Accesed December 12, 2016.
3. Bogden JD and Louria DB. Diet and human immune function Edited by: Hughes
4. DA, Darlington LG, Bendich A. Humana Press Inc., Totowa, NJ; 2004:79-101.
5. Braat H, Rottiers P, Hommes DW, Huyghebaert N, Remaut E, Remon JP, van Deventer
6. SJ, Neirynck S, Peppelenbosch MP, Steidler L, A phase I trial with transgenic bacteria expressing interleukin-10 in Crohn's disease. Clin. Gastroenterol. Hepatol. 2006;4 (6): 754–9. doi:10.1016/j.cgh.2006.03.028. PMID 16716759.
7. Caglar, E., Kargul B., & Tanboga I. BacterioTherapy and Probiotics Role on Oral
8. HealTh, Review Article Blackwell Munksgaard, 11. Pp. 2005; 131-136.
9. Carmen del Silvina , Alejandra de Moreno de LeBlanc, Rebeca Martin, Florian Chain,
10. Philippe Langella, Luis G. Bermúdez-Humarán, and Jean Guy LeBlanc. Genetically Engineered Immunomodulatory Streptococcus thermophilus Strains Producing Antioxidant Enzymes Exhibit Enhanced Anti-Inflammatory Activities. Appl Environ Microbiol, PMC; 2014.
11. Cedgard L dan Widell A. The Intestinal Microflora, The Immune System and Probiotics. 2011; Available from URL: http://www.wasamedicals.com/pdf/ref_smj_eng.pdf . Accessed 9 November 2013.
12. Emmerich J, Mumm JB, Chan IH, LaFace D, Truong H, McClanahan T, Gorman DM,
13. Oft M. IL-10 directly activates and expands tumor-resident CD8(+) T cells without de novo infiltration from secondary lymphoid organs". Cancer Research 2012; 72 (14): 3570–81. doi:10.1158/0008-5472.CAN-12-0721. PMID 22581824.
14. Kane Robert & Joseph Ouslander. Essentials of Clinical Geriatrics. McGraw-Hill
15. Medical, China; 2013
16. Martono, Heru. Elderly and Systemic Impacts in the Life Cycle. 2010. Available from URL: www.komnaslansia.go.id. Accessed November 19, 2013.
17. Mantis Nicholas J. , Nicolas Rol and Blaise Corthésy. Secretory IgA's Complex
18. Roles in Immunity and Mucosal Homeostasis in the Gut. Mucosal Immunology NCBI, PMC. 2013.
19. Ramachandran L., Shah NP. Effect of addition of Versagel on microbial, chemical,
20. and physical properties of low-fat yogurt. J Food Sci. Pubmed; 2008.
21. Smelt, Maaike J., Bart J. de Haan, Peter A. Bron, Iris van Swam, Marjolein Meijerink,
22. Jerry M. Wells, Marijke M. Faas, Paul de Vos et al. L. plantarum, L. salivarius,and L. lactis Attenuate Th2 Responses and Increase Treg Frequencies in HealThy Mice in a Strain Dependent Manner. Plosone 2012; 7(10).
23. Ogawa T., Y Asai, R Tamai, Y Makimura, H Sakamoto, S Hashikawa, and K Yasuda. Natural killer cell activities of synbiotic Lactobacillus casei ssp. casei in conjunction with dextran. Clin Exp Immuno, PMC, NCBI; 2006.

24. Tadesse Solomon. Probiotics, Prebiotics and Synbiotics as Functional Food Ingredients: Production, Health Benefits and Safety. Journal of Biologically Active Products from Nature; 2013.
25. Toma, M.M., & Pokrotnieks. Probiotics as Functional Food : Microbiological and
26. Medical Aspects. Acta Universitatis Latviensis vol. 710 Biology; 2006.
27. United Nations. World Population Ageing 2015. Department of Economic and
28. Social Affairs Population Division, New York, USA ST/ESA/SER.A/390; 2015.
29. Vidal Emili Barba, Lorena Castillejos, Paola López-Colom, Montserrat Rivero Urgell,
30. José A. Moreno Muñoz, and Susana M. Martín-Orúe. Evaluation of the Probiotic Strain Bifidobacterium longum subsp. Infantis CECT 7210 Capacities to Improve Health Status and Fight Digestive Pathogens in a Piglet Model. Front Microbiol. PMC, NCBI; 2017.
31. Vulevic Jelena, Alexandra Drakoularakou, Parveen Yaqoob, George Tzortzis, and Glenn
32. R Gibson. Modulation of the fecal microflora profile and immune function by a novel trans-galactooligosaccharide mixture (B-GOS) in healthy elderly volunteers. The American Journal of Clinical Nutrition; 2010.
33. Ng EW, Yeung M, Tong PS. Effects of yogurt starter cultures on the survival of Lactobacillus acidophilus. NCBI, Pubmed; 2013.
34. Rockland. antibodies & assays,Enzyme-Linked Immunosorbent Assay (ELISA), https://rockland-inc.com/elisa.aspx. Accessed December 2, 2017.