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Effect of Symbiotic Supplementation to the Immune Response Ifn-Γ and Il-2 on Elderly

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Abstract

Along with the increasing age it will have an impact on the emergence of a variety of life issues such as: social, economic, cultural, educational, health primarily because of the function of organs will decrease either due to natural or due to illness. The result will be an increase in the number of elderly people that is one indicator of the success of development as well as challenges in development. If it is not anticipated at this time, it is probable that the development process will encounter a variety of obstacles. Nutritional factors play an important role of the immune response in healthy elderly. One factor is the nutritional functional foods in this case is symbiotic. The purpose of this study was to analyze the effect of supplementation on the immune response symbiotic with marker IFN-γ and IL-2 in elderly patients. This research is a study pre-experiment in the treatment group were given supplementation symbiotic. We then measured IFN-γ and IL-2 in this group. Analysis of normality and homogeneity test for determining the parametric or non-parametric statistics with the Shapiro-Wilk test. Furthermore, if eligible, the parametric analysis used in this research is to use before after t test to see the effects of the intervention.

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The results showed that supplementation symbiotic effect on the increase in the levels of IL-2, but not significantly to the increase in IFN-γ. Based on the results of the study are advised to consume as food symbiotic functional in order to maintain the immune system of the elderly.

Keywords: Elderly; symbiotic; IFN-γ and IL-2.

1. Introduction

The elderly population is growing very fast even the fastest compared to other age groups. The implications of demographic arising from the growth of the elderly are the elderly population is increasing and according to projections of the WHO in 1995 that by 2050 compared to 1990 there has been growth of the elderly Indonesia with the largest growth in Asia, which amounted to 414%, Thailand 337%, India 242%, and China 220%. Indonesia number of elderly people, according to Central Bureau of Statistics (BPS) that in 2004 amounted to 16,522,311, of 2006 amounted to 17,478,282, and in 2008 amounted to 19,502,355 (8.55% of the total population of 228 018 900), whereas in 2020 the estimated number of about 28 million elderly people. It is indeed a very large number so that if there is no effort to improve the welfare of elderly from now would cause problems and could be a time bomb in the future. The tendency of these types of problems is also marked with numbers corresponding Susenas elderly dependency BPS 2008 amounted to 13.72%. Figures dependency high and the population will be felt by the population of productive age when coupled with the number dependence of population aged less than 15 years, where the current population of less than 15 years amounted to 29.13% [1].

Meanwhile, life expectancy (UHH) increasing human Indonesia where the National Medium Term Development Plan (RPJMN) MoH in 2014 is expected to occur in life expectancy of 70.6 years in 2010 to 72 in 2014 which will lead to changes in the age structure of the population, According to projections Bappenas number of senior citizens 60 years and older will increase from 18.1 million in 2010 to double to 36 million people in 2025 CBS, 2010). Based on the aspect of quality of life, the elderly also suffer from health problems. In 2003 the morbidity rate of 29.53 urban elderly, rural elderly at 27.46 and elderly towns and villages at 28.48. Morbidity in 2005 showed that elderly urban areas it was 27.83, 31.32 for the rural elderly and elderly towns and villages at 29.98. Furthermore, according to the Basic Health Research RISKESDAS showed that elderly urban shows morbidity of 27.42, 33.35 for the rural elderly and morbidity rate amounted to 31.11 towns and villages. From these data indicate a trend in morbidity in the elderly has increased from year to year. Diseases in the elderly suffer the most was followed by a joint disorders hypertension, cataracts, stroke, emotional mental disorders, heart disease and diabetes mellitus. In addition it is the cause of death at the age of 65 years in men are stroke (20.6%), chronic lower respiratory disease (10.5%), Tuberculosis (TB) (8.9%), hypertension (7.7%), NEC (7.0%), ischemic heart disease (6.9%), other heart diseases (5.9%), diabetes mellitus (4.9%), liver disease (4, 4%) and pneumonia (3.8%). While the women's cause of death was stroke (24.4%), hypertension (11.2%), NEC (9.6%), chronic lower respiratory diseases (6.6%), diabetes mellitus (6.0%), ischemic heart disease (6.0%), other heart diseases (5.9%), TB (5.6%), pneumonia (3.0%) and liver disease (2.2%) [2]. This condition should certainly get the attention of various parties. Elderly ailing would be a

burden for the family, the community and even the government, so it would be a burden in development [3].

The process of population aging will have an impact on the emergence of a variety of life issues such as: social, economic, cultural, educational, health mainly due to the increasing age of the organ function will decrease either due to natural or due to illness. As a result of this, the rising numbers of elderly people in addition to being one of the indicators of the success of development as well as challenges in development. If it is not anticipated at this time, it is probable that the development process will encounter a variety of obstacles. Therefore, the problem of the elderly should be the concern of all parties, not only the government, public institutions and society itself. The mindset that had been there that the elderly population is a vulnerable community to be borne by the family, society and the state, to be changed. Elderly should be an opportunity nation must continue to be empowered. To be elderly healthy, productive and independent, must be at the start with a healthy lifestyle and preparing for elderly times better [2].

The obstacles faced in efforts to improve the health and welfare of the elderly is still the lack of facilities and infrastructure of health services that provide health services that are friendly and easily accessible by the elderly. In addition, insufficient data on the elderly and the most recent data about the health problems of the elderly is based on surveys and studies related to the elderly is still very limited. Currently, the data in the new Health Ministry there are 437 health centers Santun Seniors and over 69 500 elderly Posyandu scattered in several districts / cities in Indonesia, but the programs have not been up [4].

Numerous studies show that the prevalence of malnutrition among the elderly is very high and often only realized when the elderly had to be hospitalized. A study in Jakarta showed that about two-thirds of the elderly suffer from a deficiency of thiamin. Immune function also decreases with age, resulting in increased incidence of infections and malignancy (cancer). Research on immune function in the elderly introduced the idea that the immune system in the elderly have specific characteristics, the immune system not only decreases with increasing age, but the regulation of immune system disorders will be progressive throughout his life. Early changes occur in the immune system humoral than cellular, the evolution of the immune system associated with reduced function of the thymus. Nutritional factors play an important role of the immune response in healthy elderly [4].

The aging process also leads to a decrease in immune function (immunosenescence), which can increase the tendency to hypo responsiveness vaccination and infectious diseases and non-communicable. Immunosenescence characterized by a decrease in the number of circulating CD3 T cells, increased production of interleukin-6 (IL-6), IL-1 and tumor necrosis factor-α (TNF-α) by peripheral blood mononuclear cells, cell activity decreased as both phagocytosis and natural killer (NK).Substrate food reaches the large intestine can affect the composition and activity of bacteria present by fermentation capacity of the elderly. The products of metabolism of gut bacteria can affect the immune system. Modulation of intestinal microflora through diet is the basis for the concept of probiotics [5].

Furthermore, oral administration lipopolysaccharide (LPS) from Escherichia coli in the rat would increase the inflammatory response that release TGF-β and IL-10, and eventually also will increase the concentration of Ig A, Ig M, IgE and IgG in the intestinal mucosa , Giving Lactobacillus salvarium the elderly would induce CD4 + and CD8 + T cells (T helper and T cytotoxic), while Lactobacillus plantarum more WCFSI induce Fenotype regulator. Besides, Lactobacillus plantarum would reduce the ratio of Th1 / Th2 small intestine lamina propria (SILP). Lactobacillus lactis has immunomodulating effects on regulating the balance of Th1 and Th2, and also it can reduce GATA-3 & Tbet on SILP. The good probiotic Lactobacillus, Bifidobacterium and Streptococcus is a promising strategy to prevent or treat excessive intestinal inflammation and maintain immune homeostasis [5].

Problems in the elderly is the importance of enhancing the role of the levels of IFN-γ and IL-2 as a biomarker of immune response, the study will focus on "The Effects of Supplementation Sinbiotik the Immune Response Marker Seniors with IFN-γ and IL-2".

2. Materials and Methods

2.1 Study Design

This type of research is the study of pre experimented with symbiotic supplements. We then measured IFN-γ and IL-2 to see the effect of supplementation on the expression of immune symbiotic elderly.

2.2 Location and Time Research

Location Symbiotic supplementation studies on the immune response of elderly will be conducted in Posyandu Elderly in Puskesmas Mangasa in Makassar. Symbiotic supplementation on samples carried out for 3 months starting in November 2015 through to February 2016, with weight control and nutrition of the elderly.

2.3 Population, Sample and Sampling

The population studied is the entire elderly in Puskesmas Mangasa Makassar.
The samples are aged between the ages of 60 -70 years and become active participants in Puskesmas Posyandu Elderly Mangasa Makassar. The sample size is the number of members of the population to be sampled. The sample size of each treatment group was calculated using the following formula [6]: n = (((Z_ (1-α) + Z_ (1-β)). ^ 2 σ ^ 2) / Δ ^ 2)

Where: n = number of samples

Z = the value of z

α = 0.05 "

$\beta = 0.1$

σ 2 = variant of IL-2 (assumed to be) the same on each - each group with 3.24

Δ = difference differences between the mean increase in IL-2 (assumed) every month between treatment groups zinc and probiotic treatment was 1.8.

Based on the sample size formula above, then obtained the required number of samples each is 9 person. To avoid the drop out of the sample, then use the formula Higgins = 1 / (1-f) where f is 20% of the total sample. Furthermore, the sample size was n = 1 / (1 to 0.2) x 9 = 11,25≈12. With the addition of the total sample now 12 people.

2.4 Data Collection

Primary data that IFN-γ and IL-2 will be collected before and after intervention ie in November2015 to February 2016. Secondary data are the characteristics of the samples collected at the same time.

2.4.1 Data Analysis

Analysis of normality and homogeneity test for determining the parametric or non-parametric statistics with the Shapiro-Wilk test. Furthermore, if eligible, the parametric analysis used in this research is to use before after t test to see the effects of each intervention group.

2.4.2 Presentation of Data

Data are presented in tabular form accompanied by narration.

3. Results

3.1 Characteristics of Respondents

This study uses 12 elderly people who came from the tribe Makassar, Muslims, residing in the territory of Makassar Puskesmas Mangasa RW 2 and RW 5, aged between 60 -70 years old. The entire elderly Muslim, gender elderly person is 3 males and 9 females. Activity elderly generally worship at the mosque or help care for grandchildren. Of the 12 elderly were given Symbiotic supplements obtained from one of the pharmacies in the city of Makassar. Characteristics of respondents (sample) can be seen in table 1.

The results showed that the average weight for 3 months of intervention 57.25 kg and average protein intake of 29.42 g. This suggests that this indicates that the weight factor and protein intake is not a factor that affected the results because it fits the needs of the elderly ($p > 0.05$).

Table 1: Characteristics of Respondents (sample) Elderly

	Symbiotic	p
Body weight	57,25±13,09 kg	0,771
Protein intake	29,42±15,07 g	0,898

3.2 Effect on Immune Response Sinbiotik IFN-γ

Based on the results showed that the average levels of IFN-γ before getting Sinbiotik and after getting Sinbiotik increased but is still in a state of homeostasis. Analysis of the data concluded that Symbiotic not affect the immune response to the cytokine IFN-γ. There are differences in the average increase before and after the intervention but not significantly. Data can be seen in the table below:

Table 2: Effect on Immune Response Symbiotic IFN-γ

	Symbiotic supplementation		**p**
	Before	After	
Average IFN- γ	85,46±12,43	184,99±166,36	0,055

3.3 Effect on Immune Response Sinbiotik IL-2

Based on Table 3 shows that an increase in the average levels of IL-2 before and after the intervention. According to the data analysis can be concluded that there is significant influence Symbiotic supplementation on levels of IL-2 to increase, but still being dynamic.

Table 3: Effect on Immune Response of Symbiotic IL-2

	Symbiotic supplementation		**p**
	Before	After	
Average IL-2	101,77±7,12	724,87±313,51	0,000

4. Discussion

4.1 Effect on Immune Response of Symbiotic IFN-γ

Cellular response to IFNγ activated through interaction with the heterodimeric receptor consisting of interferon gamma receptor 1 (IFNGR1) and interferon gamma receptor 2 (IFNAR2). IFNγ receptor binding activates the JAK-STAT pathway. IFNγ also bind to heparan sulfate glycosaminoglycan (HS) on the cell surface. However, in contrast

to many other proteins bind to heparan sulfate, which binds promote biological activity, the binding of IFNγ to inhibit the biological activity of HS [7].

Full length IFNγ is 143 amino acids long, the model 126 amino acids long. Affinity for heparan sulphate are solely the deleted sequence of 17 amino acids. In this sequence of amino acids 17 to lie two basic groups of amino acids called D1 and D2, respectively. Heparan sulfate interacts with both groups. In the absence of heparan sulfate sequence D1 attendance rates increase. The interaction between the cluster and the amino acid D1 receptor is probably where IFNγ-receptor complex shapes. be the first step in the formation of the complex. By binding to D1 HS can compete with the receptor and preventing the formation of an active receptor complexes [8] .

IFNγ secreted by helper T cells (specifically, the Th1 cells), cytotoxic T cells (TC cells) and NK cells alone. IFNγ is the only type II interferons and it is serologically distinct from Type I interferon; it is acid-labile, while type-I variant is stable. IFNγ acid has antiviral, immuno regulatory, and anti-tumor properties. This change in the transcription of 30 genes that produce a variety of physiological and cellular responses. The results showed that Symbiotic not affect IFN-γ caused by increasing the activity of NK cells, increases antigen presentation and activity lysosomes of macrophages, activate inducible Nitric Oxide Syntheses iNOS, induces the production of IgG2a and IgG3 of the B cell plasma active, promote Th1 differentiation by upregulating transcription factors T-bet, eventually causing cellular immune cytotoxic CD8 + T-cells and the activity of macrophages - while suppressing differentiation of Th2, which will cause antibody response humoral, causing normal cells to increase the expression of molecular classes of MHC and MHC class II antigens of cell specifically, through the induction of genes antigen processing, including a subunit of the immunoproteasome (MECL1, LMP2, LMP7), as well as TAP and ERAAP other than perhaps to upregulation directly MHC heavy chain and B2-microglobulin itself, promotes adhesion and binding required for leukocyte migration, induces expression of defense intrinsic factor [9] .

IFNγ is the main cytokine that defines the Th1 cells: Th1 cells secrete IFNγ, which in turn leads to more differentiated CD4 + cells (Th0 cells) to differentiate into Th1 cells, which represent positive feedback loop while suppressing Th2 cell differentiation. Defining cytokines Equivalent to other cells, including IL-4 for Th2 cells and IL-17 for Th17 cells. NK cells and CD8 + cytotoxic T cells also produce IFN-γ. IFN-γ suppresses the formation of osteoclasts by rapidly lowering the RANK adapter protein TRAF6 in the RANK-RANKL signaling pathway, which otherwise stimulates the production of NF-kB [10] . Some research indicates that IFN-γ regulated by elements pseudoknokted 5'UTR (Ben et al, 2002), but it is also regulated by micro RNAs: miR29, also the expression of IFN-γ is also maintained through GAPDH on T cells [11] . This interaction occurs in the 3'UTR, which will prevent the binding of GAPDH mRNA translation sequence [12].

4.2 Effect of Symbiotic on the immune response of IL-2

Previous research indicates that there are some major changes in the immune function of elderly people is their response changes proliferative lymphocytes, such as reduced Il-2, which is reflected in the breakdown process of the

signal in the elderly, poor levels of Ca in the body, and changes in the membrane of lymphocytes, thus affecting the immune function. The decline in the elderly Ca affect the displacement signal that the failure to stimulate the enzyme and inhibit the production of sitokin. One of the Il-2 cytokines are produced and secreted by T cells to induce cell proliferation. T cells with age, the capacity of T cells to produce IL-2 decreased. If exposed to the antigen, the T cells will divide into more against the antigen. If the production of Il-2 bit or the T cells cannot respond to the Il-2, then the function of T cells damaged [13]. Il-2 is a cytokine called leukositotropik hormone, acts as a stimulant in the proliferation of B cells and T cells Il-2 has similar functionality to the Il-15. Il-2 plays a role in apoptois activated T cells rather than by antigen, whereas IL-15 plays a role in the maintenance of memory T cells [10]. According to the research, the treatment given that symbiotic supplementation significantly affect the Il-2. Thus phagocytosis that occurs in innate immunity are also the most active. Consequently cytokine that arises from signaling or antigen antibody reaction will increase rapidly. Phagocytosis that occurs in innate immunity play active role in giving Symbiotic.

5. Conclusion

Symbiotic has no significant influence on the increased levels of IFN-γ in the healthy elderly. Symbiotic affect significantly to increased levels of IL-2 healthy elderly.

6. Suggestions

To maintain the immune system of elderly, it is advisable to consume symbiotic every day. Need to be replicated in the elderly by gender in the region were closed eg nursing homes.

Conflict of Interest

Authors declare no conflict of interest within this research

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