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----- 306 Minimization of Side Effects of Anti-Tuberculosis Drugs by Using Supplements Honey in the Region of Gorontalo City Health Center in 2016 Wenny Ischak a\* , Imelda Appulembang b , La banudi c a,b Health Polytechnic Gorontalo, Ministry of Health of the Republic of Indonesi c Health Polytechnic Kendari, Ministry of Health of the Republic of Indonesi a Email: wennyischak@gmail.com Abstract The world Health Organization (World Health Organization) recommends programs to cope with TB disease is by the method Strategy Directly Observed Therapy (DOT'S). Incidence of Adverse effects of Anti -Tuberculosis Drugs (OAT) is a problem that many complain ed of tuberculosis.

The purpose of this study see the effect of using honey supplement to the reduction of side effects of the drug on patients with tuberculosis in Puskesmas. The research type experimental study Randomized Clinical Trial (RCT) design with Randomized Pre-Post Test Control Group Design. Total sample used by 60 divided into intervention group 30 samples are given 30 ml Honey + OAT and a control group of 30 samples only OAT.

Data were analyzed by paired t test and unpaired t test. The results showed there was a difference a reduction in the average value of the side effects significantly in the intervention group compared to the group that is 14.1 dick that is only reduced 2.5 mean a side effect of the previous amount.

Supplementation of honey can be influential in the reduction of side effects in patients tuberculosis OAT. Keywords: Tuberculosis; honey; side effects.

----- \* Corresponding author. International Journal of Sciences: Basic and Applied Research (IJSBAR)(2017) Volume 31, No 2, pp 306-315 307 I.

**Introduction** Pulmonary tuberculosis is an infectious disease directly caused by TB bacteria (*Mycobacterium tuberculosis*) [1]. Globally, the disease is a public health problem in all countries [2]. According to WHO [3], the number of new cases of TB disease recorded 8.8 million cases and number of deaths due to TB is 1.4 million. Indonesia is one of the countries with a high prevalence of TB patients in the world [3].

Indonesia ranks fourth in the world's largest contributor of TB patients after India, China and South Africa. As for TB patients in Gorontalo recorded figures Case Notification Rate (CNR), namely 163 in 2013 and particularly in the city of Gorontalo to the highest CNR in Gorontalo province with the number 216 Success rate (SR), ie 99%. This figure is above the standards set by WHO that 85% [4].

Based on this, the WHO recommend the program to combat tuberculosis is Directly Observed Therapy Strategy (DOT'S). Implementation of the program, Indonesia is able to achieve the global targets for TB case detection and 73% treatment success of 85% in 2005 [4]. This is in line with the results of research which shows strategy DOT'S success in the treatment of TB.

Likewise research Kurniati [5], which says that the success of a high conversion rate will be followed by a high cure rate as well. However, along with the implementation of the program, cases of TB disease is still a burden for most countries, particularly developing countries including Indonesia Country. The prevalence of people diagnosed with pulmonary TB remains 0.4% 2007- 2013.

It shows that treatment with DOT'S strategy still requires further development efforts [4]. Results of research on treatment with DOT'S strategy shows that most patients feel no resistance to the OAT side effects experienced during treatment [6, 7]. According to the WHO in Sharma and his colleagues [8], side effects of drugs is harmful and unintended response to a drug, which occurs at doses normally used in humans for prophylaxis, diagnosis or treatment of disease or for modification of physiological function. It also occurs in patients with tuberculosis.

Research conducted in India by sinha and his colleagues [9], found that 69.01% of patients experienced side effects. According Hermayanti [2], that the Severity of effects experienced by patients will have an impact on patient treatment irregularity, the slow conversion of sputum smear and duration of treatment In addition, research conducted

by Sari and his colleagues [10], find that OATH side effects experienced by patients is one of the factors that affect patients experienced Drop Out (DO).

This is in line with research conducted by Rian [11], showed that patients who had complaints of side effects OAT 4.07 times the risk of default compared to patients who did not have a complaint OAT (OR = 4.07, 95% CI: 1, 64 to 10.07). Based on national data, the average conversion rate from 2000 to 2009 above 80% [12]. The conversion rate in Gorontalo City Health Department in 2013 was 99.7% and in 2014 by 104%. Additionally obtained 1 patient died in 2014.

Based on the research results and the fact that there is, indicates that the adverse effect of OAT is a risk factor that can be done so that intervention effects can be minimized (Rian, 2010). Based on this, the one which is a combination of TB treatment efforts herbal supplement with DOT'S program. Research conducted by George and Benny [13] showed that the use of herbs in the treatment has a good efficacy for treating the disease.

According Jabri in Sharma and his colleagues [4], Honey is one herbal product derived from bees are used in the treatment of various diseases in the world of medicine, including the treatment of TB disease. Consumption of honey can minimize the side effects of the drugs consumed. In addition, the high content of fruktosanya can, increase stamina and appetite for patients [14] .

Acetylcholine their substance in honey that play a role in stimulating gastrointestinal activity [15] . According Suranto [16], It is very useful to prevent and treat hypersensitivity reactions eg itching reaction and can prevent International Journal of Sciences: Basic and Applied Research (IJSBAR)(2017) Volume 31, No 2, pp 306-315 308 and relieve muscle pain in the joints of patients.

Research conducted in India by Sharma and his colleagues [4], shows that the highest percentage of OAT side effects experienced by the control group (OAT only) (69.88%), while in case group (OAT and honey) only (47.06%). 2. Methods and Materials Research conducted at the health center in the city of Gorontalo Province Gorontalo. The study was conducted during the two months up to the month of October 2016 Nofember.

This type of research is experimental research Randomized Clinical Trial (RCT) design with Randomized Pre -Post Test Control Group Design. The population in this study are all the visitors who came for t treatment at the health center of Gorontalo city with sputum examined. Samples were patients who were diagnosed as suffering from a new smear positive pulmonary tuberculosis were willing to participate in research.

Mechanical Sampling is done by systematic random sampling of 60 samples, which got the Anti -Tuberculosis Drug treatment (OAT) of the total, 30 samples are given (OAT + Honey 30 ml) and 30 samples without given honey. Minimum number of samples for experimental research is 15 samples in each group. [17] . Samples were selected based on inclusion criteria as follows: 1. The new patient who tested positive by sputum 2.

Following the OAT treatment program of health center 3. Patients who experience symptoms of adverse reactions OAT 4. Be willing and co-operative in the research process 5. Domiciled region puskesmas research sites The primary data collection using questionnaires and follow-up sheets honey supplement impact on side effects of drugs to the scale of values (numbers 0-10) to measure the severity of side effects from OAT.

Figure 2 To test the mean difference between the control group and the intervention group used test Independent Samples International Journal of Sciences: Basic and Applied Research (IJSBAR)(2017) Volume 31, No 2, pp 306-315 309 t-test. Meanwhile, to test the mean difference between before and after the intervention used Paired samples t - test Scheme lines of inquiry. 3.

Results and Discussion The characteristics of the respondent at the time of the initial data collection can be seen in Table 1, consisting of Gender, Age, Occupation and Education Recently respondents. Table 1: Characteristics of the sample by Treatment Group Variabel Group Total Intervention (n=30) Control (n=30) Sex (%) : Male Female 15 (50.0) 15 (50.0) 13 (43.3) 17 (56.7) 28 (46.7) 32 (53.3) Age (%) : Less 45 year =5 year 13 (43.3) 17 (56.7) 20 (66.7) 10 (33.3) 33 (55.0) 27 (45.0) Occupation (%) : Civil servant Business IRT Student Other 1 (3.3) 4 (13.3) 9 (30.0) 3 (10.0) 13 (43.3) 5 (16.7) 6 (20.0) 3 (10.0) 6 (20.0) 10 (33.3) 6 (10.0) 10 (16.7) 12 (20.0) 9 (15.0) 23 (38.3) Education (%) : Graduated senior H.S Not graduated Senior H. S 23 (76.7) 7 (23.3) 15 (50.0) 15 (50.0) 38 (63.3) 22 (36.7) Based on respondents' gender either the intervention group or the control group are mostly women 53.3% while 46.7% of men.

In terms of the age of the respondents in the intervention group or the control group mostly 55% International Journal of Sciences: Basic and Applied Research (IJSBAR)(2017) Volume 31, No 2, pp 306-315 310 aged less than 45 years. Based on the work of most of the respondents 38.3% were artisans and did not work. While education in most of the respondents (63.3%) completed high school.

Table 2: Distribution of respondents based Health Status Variables Group Total Intervention n=30 Control n=30 Smoking status (%) : Yes No 3 (10.0) 27 (90.0) 7 (23.3) 23 (76.7) 10 (16.7) 50 (83.3) Drug consumption (%) : Yes No 27 (90.0) 3 (10.0) 30 (100.0) 0 (0.0) 57

(95.0) 3 (5.0) Other Supplement (%) Yes No 1 (3.3) 29 (96.7) 0 (0.0) 30 (100.0) 1 (1,7) 59 (98.3) Allergy history (%) : Yes No 10 (33.3) 20 (66.7) 2 (6.7) 28 (9.3) 12 (20.0) 48 (80.0) Based on health status in table 2, according to smoking status either the control group or the intervention group the majority of respondents (83.3%) did not smoke.

Based on the consumption of drugs given by the doctor, the majority of respondents (95%) regularly taking the drug. According supplements most respondents (98.3%) did not consume other supplements. While a history of allergy majority of respondents (80%) did not have a history of allergy in the family. Based on the type of side effects experienced by patients with TB before the intervention can be seen in Table 3, where the majority of patients in the intervention group experienced side effects such as Urine red with a mean of  $7.2 \pm 2,7SD$ , following hives mean  $4.2 \pm 3, 1SD$ .

International Journal of Sciences: Basic and Applied Research (IJSBAR)(2017) Volume 31, No 2, pp 306-315 311 Similarly in the control group most common side effects experienced by patients is Urine red with a mean of  $7.53 \pm 1,71SD$ , hereinafter Itching  $3,18SD \pm 3.23$  and  $3.2 \pm 2,75SD$  Nausea. Table 3: The difference in the average type of side effects experienced by TB patients before the intervention

Variable	Group	Intervensi (n=30)	Kontrol (n=30)	Mean	SD	Mean	SD
Less appetite		1.8	2.6	2.33	2.82		
Nausea		2.0	2.8			3.2	2.75
Stomach ache		0.2	0.8	0.33	1.26		
Joint pain		0.7	2.0	0.2	1.09		
Dizzy		1.3	2.2	1.66	2.55		
Needles		0.5					

1.7 0.83 1.89 Sight disturbance 0.2 0.8 0.53 1.67 Red urine 7.2 2.7 7.53 1.71 Itches and other 4.3 3.1 3.23 3.18 Table 4: A comparison of the side effects before intervention by the first week after intervention

Group	Intervention	P1	Delta	Mean	P2	Before	After	Mean ± SD	Mean ± SD	Intervention	(n =30)	20,1±8,5	14,7±6,3	0,00	0 - 5,4	0,000
Control						22,0±7,5	20,8±7,3	0,00	2 - 1,1							

Table 5: Table comparing the mean side effects before the intervention and after the intervention the second week

Group	Intervention	P1	Delta	Mean	P2	Before	After	Mean ± SD	Mean ± SD	Intervention	(n =30)	20,1±8,5	10,2 ±4,7	0,00	0 - 9, 9	0,000
Control						22,0±7,5	20,1 ±6,9	0,000	- 1,8							

International Journal of Sciences: Basic and Applied Research (IJSBAR)(2017) Volume 31, No 2, pp 306-315 312 An average ratio of the side effects before and after the intervention of the first week can be seen in Table 4.

Where between treatment groups before intervention mean ( $20.1 \pm 8.5$ ) to ( $14.7 \pm 6.3$ ) with  $P = 0.000$  means that there are significant differences between before and after the intervention. While on average the control group ( $22.0 \pm 7.5$ ) to ( $20.8 \pm 7.3$ ) with  $P = 0.002$ .

An average ratio of the side effects before and after the intervention the second week

can be seen in Table 5 where between treatment groups before intervention mean ( $20.1 \pm 8.5$ ) to ( $10.2 \pm 4.7$ ) with  $P = 0.000$ , which means **there are significant differences** between before and **and after the intervention**. While on average the control group ( $22.0 \pm 7.5$ ) to ( $20.1 \pm 6.9$ ) with  $P = 0.000$ .

Table 6: Table comparing the mean side effects before the intervention and after the intervention of the third week

Group	Mean $\pm$ SD Before	Mean $\pm$ SD After	P-value
Intervention (n=30)	$20.1 \pm 8.5$	$6.2 \pm 3.6$	0.000
Control (n=30)	$22.0 \pm 7.5$	$20.5 \pm 7.3$	0.000

In Table 6 shows a comparison of the mean **side effects before and after the intervention** of the third week, where there is a difference between treatment groups before intervention mean ( $20.1 \pm 8.5$ ) to ( $6.2 \pm 3.6$ ) with  $P = 0.000$  means that **there are significant differences** between before and after the intervention. While on average the control group ( $22.0 \pm 7.4$ ) to ( $20.5 \pm 7.3$ ) with  $P = 0.000$ . Both groups **showed a significant difference** ( $0.000$ ) to changes in side effects after the intervention.

Figure 1: Mean changes in **side effects before and after the intervention** of **the first week, second** and third.

Time Point	Intervention Group Mean	Control Group Mean
SEBELUM INTERVENSI	20.1	22.0
INTERVENSI KE-1	14.7	20.5
INTERVENSI KE-2	10.2	20.8
INTERVENSI KE-3	6.2	20.1

The mean of side effect change before and after week 1, 2 and 3 Intervensi Kontrol **International Journal of Sciences: Basic and Applied Research (IJSBAR)(2017) Volume 31, No 2, pp 306-315** 313 This study shows that **supplementation of honey can reduce or minimize the side effects** of OAT **in patients with tuberculosis**.

In the control group the side effects with the highest rates experienced by the control group of 20.5, or a decline of only 2.5 from the previous average of 6.2, while the intervention group, or a decline of 14.1 from the previous average. **These results are consistent with** research conducted by **Sharma and his colleagues** [4], that the highest percentage of **OAT side effects experienced by** the control by 69.88% compared to 47.06% for the intervention group. This is because honey has properties that are very beneficial to patients with tuberculosis.

These **results are consistent with the** statement that honey is a supplement that contains various nutrient components that are needed by the body and especially for people with tuberculosis. The types of side effects that may be experienced by patients such as nausea, lack of appetite, joint pain, itching, dizziness, nausea, abdominal pain, joint pain, impaired vision, numbness and pee red.

The emergence of drug side -effects such as nausea, vomiting and abdominal pain caused by the slow process of absorption of the drug causing high drug concentrations

in the gastrointestinal tract. Their sodium content results in honey plays a role in accelerating the absorption of the drug. Thus, honey has properties as a laxative and detoxification function to aid digestion. In the digestive tract, the necessary enzyme [14]

Honey contains enzymes that, among other things invertase, diastase, catalase, oxidase, proksidase and protease. The existence of this enzyme is important in the digestive process in the body and especially gastrointestinal drugs [16]. The sugar content in honey serves as an energizer. This is because the largest composition of honey is sugar, fructose and glucose (85- 95%).

Besides Honey is a source of energy required by the smooth muscle cells of the stomach to do an activity that helps improve gastric motility. It makes honey with a high content of fruktosanya so as to increase energy, improve stamina and appetite for patients [16]. The emergence of itchy reaction on the body caused by interference on one of the histamine receptor through a process degranulase on mast cells from the reaction sensititas causing histamine expenditure. Uncontrolled spending histamine causes blood poisoning that resulted in patients experiencing hypersensitivit y.

Honey has a substance called acetyl choline. Acetyl choline can inhibit nociceptor activation and release of histamine that have anti-inflammatory effects [18]. Thus, the presence of substances acetyl choline can improve the circulation of histamine in the body that causes a reaction of itching due to consumption of OAT. The emergence of joint pain caused by the concentration of excessive acid in the body, causing poisoning.

Thus, consumption of honey can neutralize the acid concentration in the body, especially the stomach acid and are antinflamasi so as to reduce the pain experienced by patients with tuberculosis. This is because honey contains vitamins B1. The existence of these vitamins function of stimulating the formation of erythrocytes and plays a n important role in the regulation of the heart rhythm and the functioning of the nervous system properly so as to reduce pain in the nerves.

In addition, the emergence of numbness caused by lack (deficiency) of vitamin B, especially B6 in the body. Vitamin B6 play a role as a bastion of balance hormones and regulate immune function. 4. Conclusion There are differences in the mean reduction in side effects OAT before and after supplementation of honey in International Journal of Sciences: Basic and Applied Research (IJSBAR)(2017) Volume 31, No 2, pp 306-315 314 the intervention group from a mean of 20.1 to 6.2 after the intervention.

OAT mean a decrease in adverse effects on preliminary data the mean average of 22 to

20.5 at the end of the study. Differences in mean reduction in the amount of side effects in the control group only 2.5 from the previous average of 14.1, while the intervention group than the previous average.

The use of honey supplementation can be recommended to minimize the side effects of OAT by any dipelayanan health policy makers. References [1] Erawatyningsih P. & Heru S. E. (2012). Faktor -Faktor yang Mempengaruhi Ketidakpatuhan Berobat pada Penderita Tuberkulosis Paru. Jurnal Berita Kedokteran Masyarakat(BKM), 25, 117. [2] Hermayanti D. (2010). Studi Kaus Drop Out Pengobatan Tubekulosa di Puskesmas KodyaMalang. Jurnal universitas Muhammadiyah Malang [3] WHO.(2011).

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