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REVIEW ARTICLE

EFFECTIVITY OF HERBAL MEDICINE TO DECREASE SEROPOSITIVE IgG ANTI-TORCH (*Toxoplasmosis, Rubella, Cytomegalovirus, Herpes Simplex Virus*) IN A COMMUNITY-BASED SAMPLE

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ABSTRACT

Objectives: To determine the effect of herbal medicine therapy on decreasing of IgG anti-TORCH and comparison of the effectiveness of herbal therapy based on IgG titer group.
Design: Experimental Study with Pre-Post Study Design
Setting: The study was conducted at the Clinic of Aquatreat Therapy Indonesia Yogyakarta.
Procedure: 255 subjects diagnosed with TORCH infection, were divided into three groups, each group was given with same treatment method using herbal medicine which Curcuma mango (White Turmeric), Catharanthus roseus (Rose Periwinkle), Phaleria macrocopra (Gods Crown), Curcuma longa (Turmeric), and Morinda sp. (Noni).
Result: The result showed that there was significant in Cytomegalovirus (CMV) groups of pre and post test to decreases of IgG titers in patients with CMV with the value of asymp. Sig (2-tailed) <0.00.
Conclusion: Herbal medicine therapy at Klinik Aquatreat Therapy Indonesia was effective to reduce the titer of IgG of TORCH patients within 3 months. The results of this research show the best effectiveness are CMV and Toxoplasmosis groups.

INTRODUCTION

Infectious disease is very crucial public health problem in Indonesia and becomes one of the causes of death for mothers and children, the infectious disease itself has many various types, one of them is TORCH infection. TORCH (*Toxoplasmosis, Rubella, Cytomegalovirus, Herpes Simplex Virus*) as an infectious disease can infect the central nervous system in infants and children so that causes congenital defects in all organ tissues. TORCH infection consists of parasites and viruses. It provides almost the same clinical manifestation syndrome in every patient (Sofoewan, 1997). Approximately 60-70% of adults who live in developed countries with the good socioeconomic condition, show seropositive for TORCH infection, meanwhile, 80-90% of people are infected in poor economic conditions or developing countries (Griffiths and Emery, 2002). The prevalence of TORCH infection in developing countries is high and commonly attacks the group with productive ages. In Indonesia, the prevalence of seropositive Toxoplasmosis among healthy people be at variance. The second highest number of prevalence TORCH in Indonesia located in Yogyakarta with 51%, whereas the other Provinces in Java Island with 20-63% (Sofoewan, 1997).

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"Klinik Aquatreat Therapy" is one of the health clinics for the prevention and healing of TORCH Infection with an alternative method. Clinic as an alternative therapy using standardized herbal medicine as a medicinal preparation made from natural ingredients such as liquid extract of *Curcuma mango* (White Turmeric), *Catharanthus roseus* (Rose Periwinkle), *Phaleria macrocopra* (Gods Crown), *Curcuma longa* (Turmeric), and *Morinda sp.* (Noni). These ingredients are generally natural medicines that contain antioxidants and serve as immunomodulators. At this clinic, the time required for therapy depends on IgG level of patient interpreted from laboratory analysis. Therapy in this clinic is stopped regularly after 3 months. After consuming for 3 months, the patient carries on for laboratory test (ImmunoassayTest) to evaluate the result of treatment. If the resulting test is seronegative, then therapy can be stopped. However, if the resulting test is still seropositive, the therapy should be continued for the next 3 months.

Objectives

To determine the effect of herbal medicine therapy on the decreasing of IgG anti-TORCH and comparison of the effectiveness of herbal therapy based on IgG titer group.

MATERIALS AND METHODS

The study was conducted from 20 August to 22 October 2010 at the Klinik Aquatreat Therapy Indonesia Yogyakarta.

The number of samples in this study was 89 Patients of Toxoplasmosis, 73 Patients Rubella, and 93 Patients CMV. The inclusion criteria were (1) Age, the age range of patients used in this study was age 5-73 years. (2) Types of Infection; the patient was infected with a single infection. (3) Patient with chronic and chronic sub-infections based on the type of antibody (Immunoglobulin-G) that recognizes TORCH infection. (4) Treatment time; herbal therapy is done within 3 months. The ingredients used in treatment therapy at "Klinik Aquatreat Therapy" were juices containing *Curcuma mango* (White Turmeric), *Catharanthus roseus* (Rose Periwinkle), *Phaleria macrocopra* (Gods Crown), *Curcuma longa* (Turmeric), and *Morinda sp.* (Noni). The dose of use for each type of medicinal plant was unknown because it was confidential. The evaluation of laboratory analysis was conducted at Multi Lab as a diagnostic laboratory in collaboration with "Klinik Aquatreat Therapy". The uantitative method which is used in this research is a non-parametric statistical test. There are several benefits to using a non-parametric test. First, assumptions on nonparametric tests are relatively looser. Since the data doesn't meet the classical assumption, then the non-parametric statistical test is more appropriate to use. Second, nonparametric statistical efficiency is higher than parametric methods for a small number of samples. Third, the calculations can be done quickly and easily.

This research use Wilcoxon Test that compares two paired groups, pre-test and post-test, within 3 months. The null hypothesis for this test is that the medians of two samples are equal. Otherwise, Kruskal Wallis and Dunn test are also used for measuring which group is more effective to reduce the IgG of anti-TORCH patients. The Kruskal-Wallis Test is a rank-based nonparametric test that can be used to determine if there are statistically significant differences between three groups (Toxoplasmosis, Rubella, and CMV) of an independent variable on the ordinal dependent variable. Then, the post-hoc test is needed to determine whether infected group IgG's value is statistically significant difference between Group A (patients infected by Toxoplasmosis and Rubella), Group B (patients infected by Toxoplasmosis and CMV) and Group C (patients infected by Rubella and CMV).

Exclusion Criteria: Patient with *Herpes Simple Virus* 1-2 (invalid data) and the patient who did not complete herbal medicine in "Klinik Aquetreat Therapy".

Ethical considerations: Does not use ethics committees because the data in this study uses secondary data and has been authorized by the clinics of the study sites.

Statistical Method: Was done by Microsoft Excel program and data were analyzed using SPSS 15 software.

RESULTS

The infection with the highest prevalence is CMV. The patient data at "Klinik Aquatreat Therapy" was recorded with 89 Patients of Toxoplasmosis, 73 Patients Rubella, and 93 Patients CMV. These data of patients is only those who are doing herbal therapy treatments at "Klinik Aquatreat Therapy". The TORCH prevalence rate in Yogyakarta for the last 5 years is unknown because the data in the Department of Health is incomplete for this type of infection.

DISCUSSION

The results of this research show the best effectiveness based on willcoxon test are CMV and Toxoplasmosis. The antibody titers in CMV and Toxoplasmosis infection are linearly decreased for all groups of IgG titers. Toxoplasmosis titers are more easily lowered because Toxoplasmosis is a parasitic infection.

Table 1. Characteristic of Patient with seropositive IgG anti-TORCH

Characteristics	Toxoplasmosis		Rubella		Cytomegalovirus	
	Pre Test	Post Test	Pre Test	Post Test	Pre Test	Post Test
Mean	4.94	1.17	4.93	1.12	4.62	1.2
Minimum	4.03	0.69	3.93	1.1	3.91	1.1
Maximum	5.7	1.79	5.71	1.39	5.71	1.79
n	89	89	73	73	93	93

Table 2. Descriptive Statistics of Data

Characteristics		Toxoplasmosis	Rubella	Cytomegalovirus
Age	Min	15	15	5
	Max	73	61	68
	Mode	26	27	32
Sex	Female	78	58	84
	Male	11	15	9

Table 3. Statistic Test for pre-post study of infections TORCH

Test		Asymp. Sig (2-tailed)	|Ri - Rj|	Z
Wilcoxon Test	Toxoplasmosis	0.00	-	-
	Rubella	0.00	-	-
	Cytomegalovirus	0.00	-	-
Kruskal Wallis Test		0.002	-	-
Dunn Test	Toxo-Rubella	-	3.99	25.27041
	Toxo-CMV	-	18.87	25.27041
	Rubella-CMV	-	22.86	25.27041

Herbs produced by the "Klinik Aquatreat Therapy" of five types of medicinal plants have a role to control the infection of Toxoplasmosis, Rubella, and CMV in the body. In the composition of the herb, there are 3 types of medicinal plants containing alkaloids as anti-parasite *Phaleria macrocarpa, Cantharantus roseus,* and *Morinda sp*. meanwhile *Curcuma longa* and *Curcuma mango* contain curcumin as antimicrobial. Curcumin is the most widely studied molecule for biological activity. The main focus on anti-inflammatory, antimicrobial, hepato and nephroprotective and anticancer activities of *C. longa* has been using natural and synthetic curcuminoid derivatives. In addition, many studies show compelling evidence that curcumin activity is synergistically enhanced with other antioxidants such as dehydrozingerone, flavonoids, vitamin A, E, coumarin, and chromanol (Afzal *et al.,* 2013). Other studies have shown curcumin is highly capable of interacting with many molecular targets involved in inflammation.

Curcumin modulates an inflammatory response by decreasing the activity of cyclooxygenase-2 enzyme (COX-2), lipoxygenase, and inducible nitric oxide (iNOS) enzymes; inhibit the production of alpha-factor-alpha necrotizing cytokine proteins (TNF-a), interleukins (IL) -1, -2, -6, -8, and -12, mono-chemotherapy protein (MCP), and migration inhibitory proteins; and decrease-regulate mitogen-activated and Janus kinase (Jurenka, 2009). Curcumin in some other studies is classified as anti-cancer, antioxidant, anti-angiogenic, anti-proliferative, pro-apoptosis, and others. Curcumin is one of the most studied compounds for its immunomodulatory properties. Curcumin reduces the inflammatory response by inhibiting the production of NO, cyclooxygenase-2 (COX-2), nuclear factor-kappa B (NKKB), inducible nitric oxide synthase (iNOS), and lipoxygenase in NK and IFN-γ cells, or TNF-α activated macrophages (Jantan *et al.,* 2016). Curcumin can induce apoptosis and inhibit the proliferation of malignant cells. The mechanisms underlying the activity shown by curcumin are complex, and involve regulating the combined signaling pathways at various levels by acting on different targets (Pan *et al.,* 2012).

In *C. roseus* plants commonly associated with a faster wound healing process can be a function of individual effects. In one study it has been demonstrated that the tannin phytoconstituent content in *C. roseus* has a positive effect on wound healing. Wound healing is a complex and dynamic process for restoring cellular structures and tissue layers in damaged tissues to the maximum extent possible under normal circumstances. It has 3 phases; inflammatory, proliferative and mature and depend on the type and extent of damage, the general state of host health and the ability of the tissue to repair. The inflammatory phase is characterized by hemostasis and swelling, followed by epithelial, angiogenesis, and collagen deposition in the proliferative phase. In the maturation phase, the final phase of wound healing contracts to produce a smaller amount of scarring. The content of *C. roseus* is known to support the wound healing process caused by viral and parasite infections (Nayak and Pereira, 2006). Catharanthus is a tropical medicinal plant that produces more than 130 different terpenoid terpene alkaloid (TIAs), some of which exhibit strong and important pharmacological activity. In fact, vinblastine and vincristine are commercial TIAs used in anticancer chemotherapy, and together with a number of related semi-synthetic compounds, collectively named Vinca alkaloids. Vinflunine, a fluorinated vinorelin analogue, has been approved in Europe.

Vincristine and vinblastine also show strong antimicrobial activity (Almagro *et al.,* 2012). Treatment using *Morinda sp* can regulate the production of IL-4 and increase the production of IFN α which is known to be involved in the activation of macrophages and modulate the immune system. Hirazumi's research in 1996 reported that *Morinda sp.* can show antitumor effects and act as immunomodulators (Palu *et al.,* 2008). An important key role for plant medicines in protozoa and viruses infections is immunomodulation. Such natural medicines have been reported to serve as biological response modifiers by activating, increasing and restoring the reactivity of immunological effector mechanisms. A variety of herbal medicines and plant compounds directly stimulate this innate immune response (Tavakoli *et al.,* 2012). Many beverages, foods, and supplements consumed by human contain alkaloids. Molecules such as adrenaline (epinephrine) and 5-hydroxytryptamine (serotonin) fit the structural definition of alkaloids. Several alkaloids have documented or purported immunomodulatory effects (Senchina *et al.,* 2014). Alkaloids in medicinal plants have alkaline properties. It relates to parasites that do not like the state of alkaline (Roerder *et al.,* 2015). In this study, Toxoplasmosis infection is effectively derived using herbal therapy because some of the ingredients in medicinal plants can suppress the amount of tachyzoite *T. gondii* in the body. Immune responses that occur in the body can affect symptomatic symptoms in patients with Toxoplasmosis.

These symptoms are difficult to sleep, decreased appetite, heart function disorders, and muscle contraction disorders. These symptoms appear to be closely related to the number of tryptophan levels in the body. Toxoplasmosis patients with chronic infection in the body there have a lot of *T. gondii* tachyzoite. *T. gondii* requires a tryptophan amino acid as a food source, therefore tryptophan levels in the body of low Toxoplasmosis patients (Christopher *et al.,* 2012). A very important component of an initial immune response to T.*gondii* infection is IFN-α. Acute or chronic infections can be controlled by controlling IFN-α which acts as a cytokine. IFN-α serves to inhibit parasite growth by stimulating macrophage function and induces indoleamine 2.3 dioxygenase (IDO) and decreases tryptophan levels so that parasites do not get their food source (Mc Leod and Dowell, 2000). Increased levels of IFN-α will stimulate the IDO causing the body to lack tryptophan resulting in *T.gondii* growth blockage. This occurs because of growth and replication tachyzoite required amino acid tryptophan (Adeyemi *et al.,* 2017). Rose Periwinkle that became one of the ingredients in the herb contains various active chemicals. Compounds with indole or dihydro indolic structures in Rose Periwinkle plants can decrease tryptophan levels in the body so that parasites lack nutrients to survive and multiply (Canto-Canché *et al*., 2005).

In addition to tryptophan, Nitrogen Oxide (NO) has the ability to kill tachyzoite and stimulate the production of Heat Shock Protein (HSP) which is a specific protein produced by cells as a result of stress, such as infection, intoxication, response to physiological stimuli and energy metabolism (Miller , 1999). High levels of tryptophan as a food source *T. gondii* are associated with serotonin that is naturally produced by the pineal gland. Serotonin is an active neurotransmitter during sleep. Serotonin plays an important role in the control of appetite, sleep, memory, temperature regulation, behavior, heart function, muscle contraction, regulation of endocrine hormones, and prevent depression.

Serotonin is associated with tryptophan, because this essential amino acid is a precursor of serotonin formation. Tryptophan will be converted into serotonin in the body with the help of vitamin B6 and C (Rancillac, 2016). The high levels of tryptophan in the body are very good for the body because as a precursor of serotonin formation, but in the case of Toxoplasmosis patients the amino acid tryptophan in the body is used as a food source by *T. gondii,* so the body lacks serotonin. Therefore, the initial symptoms of Toxoplasmosis sufferers according to Strickland in 1991 were 89% experienced clinical symptoms of fever, 84% headache and lymph gland enlargement, 60% muscle pain, 54% stiff neck and no appetite, 20% red patches of skin, 24% pain of disedify and 11% with liver inflammation (Strickland, 1991 in Juanda, 2007). In Toxoplasmosis patients need some way to accelerate the change of parasitic form as an indicator that determines the presence of antigen, because the antigen is detected in tachyzoite stage. The change in parasitic shape is influenced by several things, such as (1) the high acidity of the parasite environment, (2) the ambient temperature of the parasite below normal, (3) the low nitrogen oxide content, because if the nitrogen oxide content is high, then *T.gondii* is virulent and generally form cysts in certain organs (Darcy, 1994). This is the first known report of the effects of herbal medicine to decrease seropositive IgG anti-TORCH in a community-based sample. The effectiveness of herbal therapy is expected to be an alternative treatment torch patients in Indonesia. Further research is necessary to support these findings and review the differentiated effectiveness of different types of patient groups that can be investigated.

Conclusion

Herbal medicine therapy in Klinik Aquatreat Therapy Indonesia is effective to reduce the titer of IgG of TORCH patients within 3 months. The results of this research show the best effectiveness are CMV and Toxoplasmosis groups.

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REFERENCES

Adeyemi, O.S., Murata, Y., Sugi, T., Han, Y. and Katoa K. 2017. Modulation of host HIF-1α activity and the tryptophan pathway contributes to the anti-Toxoplasma gondii potential of nanoparticles. *Biochem Biophys Rep*. 11: 84–92.

Afzal, A., Oriqat, G., Khan, M.A., Jose, J. and Afzal, M. 2013. Chemistry and Biochemistry of Terpenoids from Curcuma and Related Species. *Journal of Biologically Active Products from Nature*. 3(1); 1-55

Almagro, L., Fernandez-Perez, F. and Pedreno, M.A. 2015. Review Indole Alkaloids from Catharanthus roseus: Bioproduction and Their Effect on Human Health. *Molecules.* 20: 2973-3000;

Christopher, D.D., David, A.C. and Christopher, A.H. 2012. Immune response and immunopathology during toxoplasmosis. *Semin Immunopathol*. 34(6): 793–813.

Griffiths, P.D. and Emery, V.C. 2002. Cytomegalovirus. In: *Clinical Virology* Richman DD, Whitley R.J, Hayden F.G (eds). Washington: ASM Press.

Jantan, I., Ahmad, W. and Bukhari, S.N.A. 2015. Plant-derived immunomodulators :an insigh to their preclinical evaluation and clinical trials. Frontiersin Plant Science. 6:1.

Juanda, H.A. 2007. *Solusi tepat Bagi Penderita TORCH*. PT wangsa Jatra Lestari.Solo. Hal : 1-7, 13-14,19-21.

Jurenka, J.S. 2009. Anti-inflammatory Properties of Curcumin, a Major Constituent of Curcuma longa: A Review of Preclinical and Clinical Research. *Alternative Medicine Review*. 14 : 2.

McLeod, R. and Dowell, M. 2000. *Basic Immunology : The Fetus and The Newborn.* Cambridge, Spinger-Verlag.

Miller, C.M., Smith, N.C. and Johnson AM. 1999. Cytokines, Nitric Oxide, Heat shock Proteins and Virulence in Toxoplasma. *Parasitology Today* : 15 :418-422.

Nayak, B.S. and Pereira, L.M.P. 2006. Catharanthus roseus flower extract has wound-healing activity in Sprague Dawley rats. *BMC Complement Altern Med*. 6: 41.

Palu, A.K., Kim, A.H., West, B.J., Deng, S., Jensen, J. and White, L. 2008. *The effects of Morinda citrifolia L. (noni) on the immune system: Its molecular mechanisms of action. Journal of Ethnopharmacology*. 115: 502–506

Pan, L., Chai, H.B. and Kinghorn. A.D. 2012. Discovery of new anticancer agents from higher plants. *Front Biosci*. 4: 142–156.

Rancillac, A. 2016. Serotonin and sleep-promoting neurons. *Oncotarget.* 7(48): 78222–78223.

Roeder, E., Wiedenfeld, H., Edgar, J.A. 2015. Pyrrolizidine alkaloids in medicinal plants from North America. *Pharmazie.* 70(6):357-67.

Senchina, D.S., Hallam, J.E., Kohut, M.L., Nguyen, N.A., Ann M. and Perera, N. 2014. Alkaloids and athlete immune function: Caffeine, theophylline, gingerol, ephedrine, and their congeners. *Alkaloids and athlete immune function*. 20: 1.

Sofoewan, H.M.S. 1997. *TORCH Infection in Pregnancy*. Yogyakarta: Department Obstetrics & Gynecology Faculty of Medicine Gadjah Mada University/dr. Sardjito General Hospital.

Tavakoli, J., Miar, S., Zadehzare, M.M. and Akbari, H. 2012. Evaluation of Effectiveness of Herbal Medication in Cancer Care: A Review Study. *Iran J Cancer Prev*. 5(3): 144–156.

Thyller, 1981. Pharmacognosy, 8th edition. Lea and Febiger. Philadelphia.

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