International Journal of Current Science Research and Review
ISSN: 2581-8341
Volume 04 Issue 01 January 2021
DOI: 10.47191/ijcsrr/V4-i1-06, Impact Factor: 6.825
IJCSRR @ 2021
www.ijcsrr.org

The Effect of Nanogold-Nanosilver for Immune Enhancement of Drug Abuse Victims in Areas Affected by COVID-19

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ABSTRACT: The development of confirmed cases of COVID-19 in Indonesia is increasing, but until now there is no specific drug to prevent the virus. Therefore, it is necessary to do a research to produce a drug that can prevent this virus. Efforts to prevent the spread of COVID-19 and to avoid contracting the virus can be done by strengthening the immune system. Currently, the development of nanogold and nanosilver utilization occurs very rapidly, especially in the health sector due to its antibacterial and antioxidant properties. In this research, nanogold-nanosilver was presented in the form of drinking water that can be consumed directly. The purpose of this research was to find out the effect of nanogold-nanosilver health drinking water on immune enhacement in terms of anxiety level, stress level, and sleep quality. This research used one group pretest-posttest design. Data collection was conducted through observation and interviews with 75 victims of drug abuse who live in areas affected by COVID-19. Data were analyzed using one paired T-test on SPSS version 25. From the statistical test results obtained p-value 0.000 in all three aspects, it means that nanogold-nanosilver had an effect to boost the immune system.

KEYWORDS: COVID-19, drug abuse victims, immune enhancement, nanogold, nanosilver

1. INTRODUCTION

At the end of December 2019, the world was shocked by the outbreak of the coronavirus. This virus was reported and confirmed for the first time in Wuhan City, Hubei Province, China. There was initially a group of patients hospitalized with an initial diagnosis of pneumonia but of unknown etiology [1]. Epidemiologically, this group of patients has an association with a fish and wild animal market in Wuhan City [2]. An academic from the Chinese Academy of Engineering named Dr. Jianguo Xu declared that the spread of the virus was caused by a novel type of coronavirus, namely Sars-Cov-2. On February 11, 2020, this novel type of coronavirus termed by World Health Organization (WHO) as 2019-novel coronavirus (2019-nCov) [3]. The spread of Coronavirus Disease 2019 (COVID-19) is rapid and deadly. This virus can spread through direct physical contact and droplets such as coughing or sneezing from an infected person [4]. People most at risk of contracting this virus are those who have had close contact with COVID-19 patients, including those who treat these patients [5]. The most common symptoms of COVID-19 including fever, cough, and fatigue, while other symptoms include headache, hemoptysis, diarrhea, dyspnea, and lymphopenia. Time from COVID-19 symptom onset to death ranges from 6 to 41 days, depending on the patient's age and the patient's immune system [6].

Indonesia is one of the countries affected by COVID-19. The first positive case of COVID-19 in Indonesia was announced by the President of the Republic of Indonesia, Joko Widodo, on Monday, March 2, 2020. Furthermore, there has been a significant daily increase in COVID-19 cases. Various sources predict that COVID-19 cases in Indonesia will reach tens or even hundreds of thousands if the handling process is not optimal. Various efforts have been made by the government to break the chain of the spread of COVID-19. Based on guidelines for rapid medical and public health handling of COVID-19 in Indonesia, prevention at the individual level can be done by boosting the immune system and controlling comorbidity. Meanwhile, prevention at the community level can be done by limiting physical interactions (physical distancing) including maintaining a physical distance between people of at least 1 meter, avoid spending time in crowded places or in groups and implement working from home [7].

Surabaya is one of the cities in Indonesia that is affected by COVID-19. As of March 16, 2020, the virus began to spread in Surabaya [8]. Various agencies have implemented a work from home policy. However, several other places that mostly involving social activities certainly require residents to remain within the place. One of them is drug rehabilitation center which is very vulnerable to creating new clusters of COVID-19. The victims of drug abuse are very vulnerable in this pandemic condition [9]. This is because victims of drug abuse commonly have a background of experiencing physical and psychological disorders, such as lose enthusiasm and zest for life and mental-emotional exhaustion or devastation caused by the consumption of drugs (narcotics, psychotropics, and illegal

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drugs or other addictive drugs). Further, efforts of physical restriction and the condition of the news in the mass media regarding the development of the number of COVID-19 cases worldwide, especially in Indonesia, will make them even more worried and anxious, and therefore it will have an impact on their mental health. The rise of mental health problems dueto the COVID-19 pandemic can develop into serious and long-term health problems, such as depression, anxiety disorders, and post-traumatic stress disorder [10]. The disorder in such conditions is susceptible to causing the immune system to decline and the body is susceptible to viruses.

One of the efforts that can be done by each individual so as not to be infected with COVID-19 is to boost the immune system. The immune system is responsible for recognizing and protecting the body from harmful substances, such as pathogens and free radicals that can cause disease in humans. Free radicals have very reactive and unstable properties because they have one or more lone pair of electrons in the outermost orbital, so to make these radicals non-reactive they must be stabilized. To obtain an electron pair, the free radical reacts with the compound around the radical which results in its stable form. The existence of free radical reactions that occur continuously may lead to many diseases. Therefore, free radicals must be quenched with compounds such as antioxidants [11].

In recent years, technological developments are not new to the public. Several countries in the world such as America, Japan, Australia, Korea, and China are intensively developing a technology that is currently popular, namely nanotechnology. Nanotechnology has been used in various fields of human life, one of which is the health sector. Nanogold and nanosilver are nanoparticles that are often used in the health sector. Nanogold can boost stamina, increase and balance hormone production which is useful for cell rejuvenation [12]. The in vitro and in vivo nanogold toxicity test results show that the nanogold is safe for the human body [13]. Nanosilver is believed to inhibit infection caused by viruses [14]. The combination of nanogold and nanosilver has been tested to have a positive effect on several diseases. Nanogold-nanosilver has a positive effect on improving the quality of life cancer patients [15]. A research on herpes simplex virus (HSV) showed the results of nanogold-nanosilver accelerate the recovery in herpes patients [16]. The addition of nanosilver to the antioxidant activity of nanogold has been tested and the result showed that the 10 ppm nanosilver concentration could support the reduction of free radicalsm namely 65.80% [17].

So far, confirmed COVID-19 cases have continued to increase but there is no specific drug to prevent the Sars-Cov-2. Therefore, it is necessary to do a research to produce a drug that can prevent this virus. Based on efficacy nanogold and nanosilver, namely as antibacterial, can reduce free radicals, and increase body immunity, both of which have the potential to have a positive effect to break the chain of COVID-19 transmission. With the presence of nanogold-nanosilver which has great potential to prevent various diseases because it can increase immune activity, this research aims to see how the effect of providing nanogold- nanosilver health water on the immune enhancement of drug abuse victims affected by COVID-19 in terms of several aspects which can affect the immune system, namely the level of anxiety, stress levels, and sleep quality.

2. RESEARCH METHOD

2.1 The Process of Making Health Water

The nanogold-nanosilver health water used in this research contained aquades, nanogold and nanosilver with a concentration or dose of 2 ppm. The dosage used is 1:10 for doses in many diseases and cosmetic products that have been developed previously. This dose was tested from July to November 2019 on volunteers with leprosy [18]. Nanogold is synthesized from HAuCl4 base material which is then reduced using sodium citrate. The synthesis product is immediately diluted with aquades to prevent the accumulation of thousands of reduced gold atoms. If it is not processed immediately, it will cause the formation of gold deposits that exceed the nano size. Nanosilver is synthesized from AgNO3 base material which is then reduced using sodium citrate. Similar to the procedure performed in the manufacture of nanogold, the synthesized nanosilver is immediately diluted to prevent the accumulation of thousands of reduced silver atoms. The ratio of nanogold and nanosilver used is 4:1.

Figure 1. Nanogold and nanosilver health water

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Figure 1 is nanogold-nanosilver health water that has been packaged in 1000 mL bottles. The outside of the bottle is given a sticker containing the benefits, ingredients and how to consume it. The recommendation to consume this water is 150-300 mL, one to three times a day.

2.2 Research Design

This research is quantitative using a pre-experimental design, namely one group pretest-posttest design. The pretest in this research is the level of anxiety, stress, and sleep quality of the victims of drug abuse before being given the nanogold-nanosilver health water intervention, while the posttest is the level of anxiety, stress, and sleep quality of the victims after being given the intervention.

2.3 Sampling Technique

The research was conducted from May to September 2020. The population in this research were the victims of drug abuse who were undergoing rehabilitation at Pondok Pesantren Inabah, which is located at Semampir Road number 43-47 Surabaya. The place is in an area affected by COVID-19. The sampling technique used a saturated sampling technique, namely all members of the population are used as samples. The number of samples in this research was 75 people.

2.4 Data Collection Techniques

Data collection techniques were conducted through observation and interviews using the questionnaire instrument of Depression Anxiety and Stress Scale 42 (DASS 42). The instrument contains 42 questions that measure the level of anxiety, stress, and depression. In this study only measured levels of anxiety and stress, so questions to measure the level of depression were not used. Interpretation of the DASS score for the scale of anxiety at the normal level is 0-7, the mild level is 8-9, the moderate level is 10-14, the severe level is 15-19, and the extreme level is >20, while the stress scale at the normal level is 0-14, the mild level is 15- 18, the moderate level is 19-25, the severe level is 26-33, and the extreme level is >20 [19]. The sleep quality of respondents was measured using instruments adopted from previous researchers and their validity and reliability had been tested. Based on these instruments, for poor sleep quality it has a value of 1-7, while for good sleep quality is 8-15 [20]. At the beginning of the research, a pretest was carried out, then direct counseling was conducted regarding nanogold-nanosilver health drink products as well as interviews with respondents regarding the initial conditions before consuming these products and monitoring the respondent's physical and psychological health conditions at the end of the research. At the end of the research, the researcher conducted the interview using the questionnaires with the respondents.

2.5 Data Analysis

The results of the interview were analyzed using paired sample T-test in SPSS version 25 to find out whether there was a significant effect of nanogold-nanosilver health drinking water on several aspects that affect the body's immune system activity, namely anxiety level, stress level, and sleep quality.

3. RESULT AND DISCUSSIONS

The purpose of this research was to find out the effect of nanogold-nanosilver health drinking water to increase the immune system of drug abuse victims in Pondok Pesantren Inabah in terms of 3 aspects, namely anxiety level, stress level, and sleep quality. The following are the results of the research:

Table 1. Characteristics of respondents

Characteristics	Frequency(n)	Percentage (%)
Male	65	86.7
Female	10	13.3

Table 1 shows that most of the respondents were male by 86.7%, while female respondents were 13.3%. Table 2 shows the comparison of the respondents' anxiety level, stress level, and sleep quality before and after consuming nanogold-nanosilver health drinking water from May to September 2020.

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Table 2. Comparison of respondents' anxiety levels, stress levels, and sleep quality before and after consuming nanogold- nanosilver health drinking water

Variable	Pretest		Posttest	
	n	%	n	%
Anxiety Level				
Normal	2	2.7	70	93.3
Mild	4	5.3	5	6.7
Moderate	60	80	0	0
Severe	9	12	0	0
Extreme	0	0	0	0
Stress Levels				
Normal	2	2.7	70	93.3
Mild	13	17.3	5	6.7
Moderate	55	73.3	0	0
Severe	5	6.7	0	0
Extreme	0	0	0	0
Sleep Quality				
Good	2	27	75	100
Poor	73	97.3	0	0

Based on the level of anxiety, before consuming nanogold-nanosilver health drinking water, most of the respondents had mild anxiety levels. However, after regularly consuming nanogold-nanosilver health drinking water, the anxiety felt by the respondents gradually improved and normal. Before consuming, the most respondents' anxiety level was at moderate level, namely 60 people, at the severe stress level there were 9 people, at the mild stress level there were 4 people, and only 2 people had normal anxiety levels. After consuming, the respondents' anxiety level is reduced and normal. Respondents with a mild anxiety level were only 5 people, and the highest is shown at the normal level of anxiety, which is 75 people. In terms of stress levels, before consuming nanogold-nanosilver health drinking water, most respondents had mild stress and after consuming nanogold-nanosilver health drinking water, the number of respondents experiencing normal stress increased from 2% to 93.3%. In terms of sleep quality, before consuming nanogold-nanosilver health drinking water, most respondents had poor sleep quality, as many as 73 out of 75 people. Of 73 respondents experienced sleep disturbances such as insomnia which was caused by anxiety and extreme anxiety, this resulted in morning fatigue (waking up tired and the body feels very weak) and lack of enthusiasm in doing activities. After consuming the healthy drinking water regularly, the sleep quality of all respondents gradually improved. Feelings of anxiety and restlessness are greatly reduced and the respondents do not have difficulty sleeping so that when they wake up, the body becomes fit, and they feel excited to carry out activities. The quality of sleep that is getting better is in line with the changes in the level of anxiety and stress of the respondents who are getting better or normal.

Table 3. Results of analysis of the effect of nanogold-nanosilver health drinking water on respondents' anxiety levels, stress levels, and sleep quality

Analysis	n	Mean	p-value
Anxiety Levels			
Pretest		12.64	0.000
Posttest		5.57	
Stress Levels			
Pretest	75	21.09	0.000
Posttest		8.11	
Sleep Quality			
Pretest		5.55	0.000
Posttest		12.43	

Table 3 is the result of the analysis of the effect of nanogold-nanosilver health drinking water on the respondents' level of anxiety, stress

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levels, and sleep quality. Based on the results of the analysis using the paired sample statistical test T-test using SPSS version 25, after consuming the nanogold-nanosilver health water the mean value of the respondent's anxiety and stress level decreased, while the mean value of the respondent's sleep quality increased. In all three aspects, the p-value is 0.000. Thus, it means that there is an effect of nanogold-nanosilver health drinking water on the level of anxiety, stress levels, and sleep quality of respondents. Nanogold-nanosilver health water has an effect on increasing the immunity of drug abuse victims.

In this research, all respondents were victims of drug abuse. This means that they have a background of mental health problems due to consuming illegal drugs. Based on the results of interviews with respondents, some of the reasons they used drugs were overcoming insomnia, running away from problems, eliminating anxiety, fear, and feeling of restlessness in life. They directly feel the impact of drug use, one of which is drug dependence. One respondent even gave information that his negative actions led to the murder of one of his parents. This happens because parents force them to stop using drugs, but because they are very dependent, these conditions eventually support them for committing the evil act. When they first undergo the rehabilitation process, their psychological condition is poor because their bodies are forced to withdraw from their old habit of using drugs. Drug withdrawal symptoms cause psychological shocks and even affects the victims of drug abuse physically. At first, they feel stress, irritability with others, which causes fights and harms one another, until eventually the body's health becomes unstable.

Since the beginning of the emergence of Sars-Cov-2, which until now is known as the COVID-19 pandemic, many countries have announced that there has been a health crisis due to this pandemic. Various media continuously broadcast the number of victims and deaths, economic and social problems such as mass layoffs, many companies go bankrupt, and so on. Based on the results of the interview, this had a huge impact on their psychological condition. With a background as victims of drug abuse, in this pandemic condition, they become anxious, afraid, and feel restless to think about what if they suddenly contracted this virus because they are still recovering from the effects of drug use psychologically and physically. This causes them to have sleeping difficulty and when they wake up, they feel morning fatigue (waking up tired and the body feels very weak) due to not sleeping soundly. Anxiety disorders, stress, and sleeping difficulty experienced by respondents during the COVID-19 pandemic are the same as the conditions in America. The demand for anti-anxiety drugs in America has increased by 34% from mid-February to March 2020. It happened to overcome the stress and anxiety among people amid the COVID-19 pandemic [21]. The anxiety amid the COVID-19 pandemic has known as coronaphobia and is strongly associated with increased depression or stress [22].

During the COVID-19 pandemic, these victims of drug abuse continue to carry out rehabilitation programs as usual to recover their conditions. They continue to fight to recover until they fully recovered and hope that they will not repeat using drugs again, as well as trying not to be infected with COVID-19. Based on the results of interviews with respondents, nanogold-nanosilver health drinking water helps maximize their efforts to recover psychological problems that have been experienced so far. A recovered psychological condition indicates that their body is working properly. The good quality of sleep makes them fitter in the morning, more enthusiastic about doing activities, and not feel easily tired and sick. These conditions show an improvement in their immune system so that the immune system will provide maximum protection during this pandemic and in the aftermath.

3.1 The Relationship between Anxiety, Stress, and Sleep Quality on the Immune System

The immunological process is regulated during sleep. The levels of cortisol, epinephrine, and norepinephrine hormones decrease during sleep, but the levels of growth hormone, leptin, and prolactin increase [23]. These three hormones are related when the body experiences anxiety and stress. During sleep, these and other hormones support the activation, proliferation, and differentiation of the body's immune cells, and produce pro-inflammatory cytokines such as IL-1, IL-12, TNF-α, and IFN-γ [23]. Cytokines are proteins involved in the activation and communication of the immune system which is mostly secreted by immune cells and various cells in them [24]. In the first stage of sleep, there is a process of releasing GH (Growth Hormone) and prolactin, while the cortisol and catecholamine hormones are at the lowest levels. This condition supports not only a shift in the balance of Th1 or Th2 cytokines towards Th1 but also allows an increase in the production of IL-12 by antigen-carrying cells. It is an important process to activate and increase the proliferation of helper T cells. Some of these things make sleep extremely important for the formation and maintenance of the immune system [25]. In the late stages of sleep, Th2 activity predominates [26]. The main function of Th1 cells is as a defense against infection, especially by intracellular microbes, the mechanism occurs through the activation of macrophages, B cells, and neutrophil cells [27]. Meanwhile, in this case, Th2 is a mediator for allergic reactions and defense of infection against bacteria or parasites [26]. Sleep deprivation reduces monocyte production of IL-12 and cytokines that support the Th1 response [28]. A decrease in the quality of sleep can coexist with stress or depression [29]. Sleep disturbances or insomnia is caused by stress and anxiety [30]. This situation has an impact on hormones that are

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responsible for controlling stress which in turn will also affect the immune coordination function in the body.

3.2 Relationship between Nanogold-Nanosilver on Immune Enhancement

Nanoparticles have unique characteristics such as small size, large surface area, mass unity, have surface charge, and the ability to exist in various stable geometric shapes [31]. Since the middle of the century, nanogold can be used in almost all medical applications such as diagnostics, therapy, and prevention. The various benefits shown by this nanogold are based on their unique physical and chemical properties [32]. In a review article, several studies reveal that metal in the form of colloids can strongly recognize antigens which in turn stimulate antibody formation. The formation of these antibodies was shown in a test on rabbits, 5 mL of nanogold was inserted intravenously and after 2 hours it was noted that the leukocyte content in 1 mL of blood increased rapidly. In this case, the nanogold serves as an antigen carrier which has been shown to stimulate the phagocytic activity of macrophages and affect the performance of lymphocytes which are responsible for the immune modulation effect. The effect of nanogold on lymphocyte performance is shown by a ten-fold increase in proliferation. It is also shown that nanogold acts directly in the destruction of pathogens [13]. In the process, the nanogold will be conjugated with peptides and then enter the macrophage cytoplasm. After that, the conjugate interacts with the TLR-4 receptor and the nanogold penetrates into the cell accompanied by secretion of inflammatory cytokines-TNF, IL-1β, IL-6, and increased TNF [33].

During a COVID-19 pandemic like this, maintaining a healthy body is extremely important so that people are not easily infected by a bacteria or virus. A study revealed that nanosilver has antibacterial properties [34]. Nanosilver can inhibit bacterial growth by releasing silver ions which then inhibit enzymatic activity and then destroy the protein structure in the bacterial cell membrane [35]. Due to its antibacterial properties, until now nanosilver is used predominantly in various consumer and medical products [36], [37]. The nano silver antibacterial mechanism starts with the particles that will stick to the surface of the bacteria and then change the properties of the membrane. Furthermore, nanosilver in bacterial cells can cause DNA damage, which is then followed by dissolving the nanosilver, releasing antimicrobial silver ions which can interact with protein groups containing thiols in the cell wall and at that time will also affect its function [38]. Nanosilver that attack membranes can also disrupt the respiratory system and inhibit energy production in bacteria [39]. Until recently, nanosilver was used as an antiviral, antibacterial, anti- inflammatory, antifungal, and anticancer agent due to its unique physicochemical properties and amazing biological functions [40].

Combining two nanoparticle elements, namely nanogold and nanosilver into one material can show a synergistic effect. The two nanoparticles can inhibit viral replication and prevent the release of viral particles to enter the host cell. In this case, these nanoparticles play a role in inhibiting the neuraminidase enzyme which separates the attachment between hemagglutinin in the progeny virus and the sialic acid receptors found in host cells [41]. In association with the Coronavirus, the two nanoparticles can inhibit the binding of the virus to the surface receptors of the host cell. In this case, ACE2 is a receptor that plays an important role for Coronavirus to enter into host cells. Therefore, this inhibition can reduce ACE2 levels so that it can help fight infection and develop antibodies to fight ACE2 [42].

4. CONCLUSION

Based on the research that has been conducted, it shows that there is a significant effect after consuming nanogold-nanosilver health drinking water on the three aspects that can affect immune systems including anxiety level, stress level, and sleep quality. After five months of consuming healthy drinking water, the respondent's anxiety and stress are reduced and become normal. This condition also supports the respondent to have better sleep quality and the respondent's immune system will increase so that it can fight any infections caused by bacteria or viruses, especially COVID-19.

ACKNOWLEDGEMENTS

The writer would like to say thank you to the Ministry of Research, Technology, and Higher Education, and also the Ministry of Education and Culture for funding research and development research schemes with contract numbers 193/SP2H/LT/DRPM/2019 and B/21831/UN38.9/LK.04.00/2019.

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Cite this Article: ***Titik Taufikurohmah, Tia Ayu Novitasari, Djodjok Soepardjo (2021). The Effect of Nanogold-Nanosilver for Immune Enhancement of Drug Abuse Victims in Areas Affected by COVID-19. International Journal of Current Science Research and Review, 4(01), 32-39***