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Effect of Iodine Solution on Histopathology of Rats Kidney Induced by Lead Acetate

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Abstract*. Lead is a metal that is toxic to the environment and the human body. Lead can cause oxidative stress in body tissues and organs, including the kidneys. Iodine can function as an antioxidant because it can inhibit the increase in free radicals so that oxidative stress does not occur. This study aims to see the effect of giving iodine solution on the histopathological picture of lead acetate-induced rat kidney. This study was an experimental study using 18 Rattus novergicus rats which were divided into 3 groups, namely the negative control group which was only given standard feed, positive control which was given standard feed and lead acetate 10 mg/Kg BB, and the treatment group which was given standard feed. , 10 mg/Kg BB lead acetate, and 12.5 mg iodine solution for 19 day. The rat kidney damage scores were 4 for the positive group, 2 for the treatment group, and 1 for the negative group. The conclusion of this study is that there is an effect of giving iodine solution in preventing damage to the kidney cells of rats induced by lead acetate.*

Keywords*: Lead, Iodine, Kidney, Antioxidant*

1. INTRODUCTION

Lead is a type of heavy metal group IV A that can vaporize at temperatures of 550 - 600°C and form oxygen in the air to become lead oxide (Zarwin, 2020). Lead (Plumbum /Pb) is one of the most widespread heavy metals compared to most other toxic metals. This type of metal can pollute the environment, especially from motor vehicle exhaust gases (Arifuddin, 2016). Other sources of lead are industrial waste, coal combustion that contains lead. Natural sources of lead come from the evaporation of lava, rocks, soil and plants, but the levels of lead from these natural sources are very low compared to lead from motor vehicle exhaust (Ardillah, 2016).

Humans can be exposed to lead from the air, either by inhaling air or ingesting dust containing lead, but also through food or drinking water contaminated with lead. Based on research conducted by Putri in Sijantang Village, Talawi Subdistrict, Sawahlunto City on the concentration of lead in PDAM water in residents' homes, from a total of 50 samples, 31 homes or 62% of PDAM water samples contained lead, exceeding the Threshold Value (NAB) of 0.05 mg/L.

Research conducted by Carmen found that iodine can act as an antioxidant by competing with free radicals of lipid membranes, proteins and DNA, or by increasing the expression or activity of antioxidant enzymes to help stabilize cells, this antioxidant action

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can be used through oxidized iodine obtained from food or by local deiodination (Aceve, 2009).

There has been no research that explains the effect of iodine as an antioxidant on the histopathology of rat kidneys exposed to lead, so the authors are interested in examining the effect of iodine solution on the histopathology of rat kidneys exposed to lead.

Based on the above background, this study was conducted with the aim of knowing the effect of iodine solution on the histopathology of rat kidneys induced by lead acetate.

2. LITERATURE REVIEW

Lead is a type of heavy metal group IV A that can vaporize at temperatures of 550 - 600°C and form oxygen in the air to become lead oxide (Zarwin, 2020). Lead (Plumbum /Pb) is one of the most widespread heavy metals compared to most other toxic metals. Lead exposure is an environmental toxin that can cause renal, hematological, gastrointestinal, circulatory, and immunological disorders (Gayatri, 2017). Lead enters the body through the respiratory system and is absorbed directly by the skin. In the body, Pb affects enzymes related to heme synthesis, DNA transcription, and the release of neurotransmitters that regulate cell growth and memory (Fadila, 2018).

Lead in the body will be amplified in the liver and kidneys. Increased lead levels cause oxidative damage by increasing the production of reactive oxygen species (ROS) or free radicals, reducing the cell's antioxidant defense system, by decreasing glutathione (antioxidant) levels in the body (Suminta, 2020).

Organ damage caused by lead can induce the formation of free radicals and reduce the ability of the body's antioxidant system so that oxidative stress will occur (Zarwin, 2020). Oxidative stress can cause membrane and cytosolic lipid peroxidation which results in a series of fatty acid reductions that damage membrane organization and cell organelles. The occurrence of membrane lipid peroxidation will result in a complete loss of cell function, and if this continues it can lead to cell death and trigger degenerative diseases (Sari, 2014).

The formation of ROS mainly occurs in mitochondria and partly in phagocytic cells. The composition of ROS includes superoxide anion, hydrogen peroxide and hydrogen radicals. The physiological function of ROS in small amounts is for example as a defense mechanism against pathogens. However, excess ROS will cause cellular damage through biomolecular interactions resulting in negative effects on function and structure such as in chronic kidney disease (Perdhana, 2019).

Kidneys intoxicated by Pb acetate in the acute state will cause damage, such as proximal tubular malfunction, manifestations of glycosuria, hematuria with hypophosphatemia, amino acids in the urine, increased sodium, and decreased uric acid excretion. In chronic exposure, renal function is impaired with characteristic nitrogen deficiency, progressive interstitial fibrosis, and decreased glomerular filtration rate (LFG). This will negatively affect the work of receptors, enzymes, membrane transport, and cellular DNA as the main targets of oxidation (Papanikolaou, 2005). Lead-induced toxicity can occur due to increased oxidative stress. Oxidative stress can occur if there is an imbalance between ROS production and antioxidant capacity (Buser, 2020).

The microscopic picture of the kidney experiencing oxidative stress can be in the form of swollen proximal tubule epithelial cells with granular cytoplasm due to the shift of extracellular water into the cell. This fluid shift occurs due to the presence of toxins that cause changes in the electrical charge on the surface of the tubule epithelial cells, changes in the active transport of ions and organic acids, and the ability to concentrate from the kidneys which ultimately results in damaged tubules, decreased flow. This picture of cell swelling is called albuminous degeneration or parenchymatous degeneration or cloudy swelling, which is the mildest form of degeneration and is reversible. This may cause the lumen of the proximal tubule to narrow and close.

Many ways have been used to fulfill the body's antioxidant needs to prevent oxidative stress, including by consuming foods that contain antioxidants. One of these antioxidants is iodine. The human body needs approximately 150-300 µg of iodine per day. This need can be fulfilled by consuming iodine-rich foods such as fish and dairy products. In addition, iodine solution, namely lugol's solution, is a source of iodine that is widely used in meeting iodine needs (Aprilianti, 2020).

Iodine is one of the micronutrients that is very easy to find and is widely contained in foods consumed daily, but the role of iodine that is widely known and researched to date is only as a raw material for the formation of thyroid hormones, while the role of iodine as an external body antioxidant is not too widely known and discussed and there are still few studies on it (Kumar, 2013).

Iodine is an important substance for the body, which is useful as an ingredient in the manufacture of thyroid hormones in the thyroid gland. In addition to working on the thyroid, iodine also provides extrathyroidal effects that are also important for the body, namely iodine can be an antioxidant as well as antiproliferative and differentiation that helps maintain the integrity of several organs with the ability to take iodine (Aceves, 2013).

3. RESEARCH METHOD(S)

This type of research is a true experimental with the design of the posttest only control group design using white rat animals (Rattus norvegicus) which are divided into 3 groups, namely the negative control group, positive control group, and treatment group.

The sample size to be used for each group is 5 rats. The sample size to be used for each group is 5 rats. In order to prevent dropouts in the middle of the study due to dead or sick rats, it is necessary to correct the sample size and obtain a total of 18 rats used.

This study used kidney preparations of Rattus norvegicus mice that were given iodine solution which was previously induced by lead acetate.

The data obtained in the form of kidney damage scores were previously given 3 different treatments. Based on tubular cells that degenerate and necrosis, the average kidney damage is calculated and converted into a kidney damage score.

The ethical review permit number in this study is 869/UN.16.2/KEP-FK/2022, and the institution that issued the ethical review permit number is the Faculty of Medicine, University of Andalas.

4. FINDINGS

Observations of kidney preparations were made in five different fields of view at a magnification of 400. Images of kidney preparations were taken using a light microscope with an Olympus BX5 camera connected to the software, DP2-BSW.

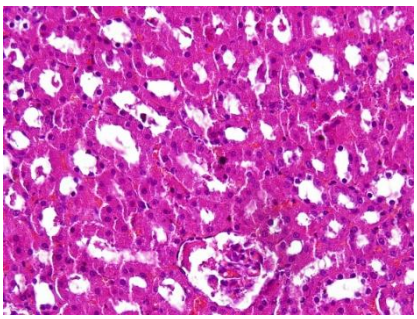

Figure 1. Histopathologic features of the kidneys of rats in the negative control group

The picture above shows a histopathological picture of the rat kidney which is a negative control group seen with a magnification of 400 HE staining. The histopathology picture of the rat kidney of the negative control group (K-) has a score of 1, namely the

kidney cells look like there are some samples that have degenerated cells in a very small amount.

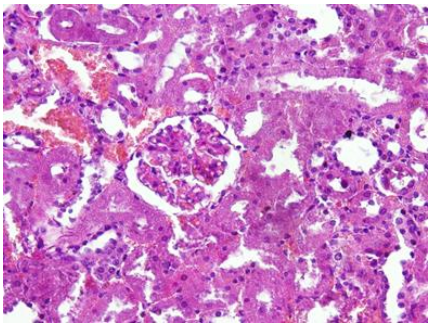

Figure 2. Histopathologic features of the kidneys of rats in the positive control group

Histopathologic features of the kidneys of the negative control group rats. The positive control group (K+) had scores ranging from 3 to 4. The histopathological picture of the rat kidney of the negative control group shows normal kidney cells. While the histopathology picture of the rat kidney of the positive control group shows a picture of damaged cells in the form of cell degeneration and necrosis.

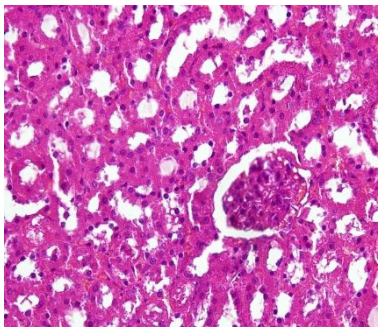

Figure 3. Shows the histopathology picture of the rat kidney which is the treatment group viewed with a magnification of 400 HE staining.

The treatment group showed a varied picture, but fewer kidney cells were damaged compared to the positive control group. The treatment group (KP) had a damage score of 2.

Tabel 1. Kelompok kerusakan sel pada ginjal

Kelompok	Kerusakan Sel Ginjal						
	1	2	3	4	5	Mean	P value
K-	1	1	1	1	1	1	P<0,001
K+	3	4	4	4	4	3,8	P<0,001

P	2	2	2	2	2	2	P<0,001

The table shows the difference in the degree of kidney damage between groups. The highest kidney damage score was found in the positive control group (K+), while the lowest kidney damage was found in the negative control group (K-).

5. DISCUSSION

The results of this study showed damage to kidney cells characterized by an increase in kidney damage scores and the discovery of degeneration and necrosis in cells. The mean score of kidney damage in the positive control group was higher than the negative control and treatment groups.

Research conducted by Aprilianti et al on the effect of administration of red fruit oil (pandanus conoideus Lam.) on the degeneration of kidney cells of mice exposed to plumbum showed that the administration of lead to the kidneys can cause disruption of the excretion process, causing degeneration of kidney cells. Fathur's research16 also showed that lead acetate exposure caused damage to the histology of white rat kidney (rattus norvegicus). Both researchers concluded that the negative effects of lead occur due to oxidative stress produced by lead (Aprilianti., 2020).

Lead exposed to rats orally is absorbed in the digestive tract, then enters the bloodstream and is circulated throughout the body, especially soft tissues such as the liver, kidneys, testes and will accumulate in these organs continuously. Lead accumulated in the kidney at the cellular stage will increase the susceptibility and change the integrity of the cell membrane so that the quality and function of the kidney cell membrane components decrease. Lead damages the cell membrane by increasing the number of fatty acid double bonds in the cell membrane, which increases the concentration of MDA, a marker of oxidative stress and makes the cell membrane susceptible to lipid peroxidation. In addition, lead can induce the formation of ROS by ALA which will trigger oxidative reactions and change the chemical structure of DNA and cause it to mutate (Ercal, 2001).

Lead is toxic to cells in several ways. First, by causing cellular damage by covalently binding to parts of cell macromolecules, such as DNA, RNA and cell proteins. The effect of cellular damage will be more quickly seen if the reactive xenobiotic binds to macromolecules that are essential for the continuity of cell function (oxidative phosphorylation or regulation of membrane permeability). Secondly, the reactive species of a xenobiotic can bind to cell proteins, altering their antigenicity and turning into a hapten. The hapten will trigger the formation of body antibodies that then damage the cell through

immunological mechanisms. Third, reactive species can act as indirect carcinogens due to their reaction with body enzymes such as monooxygenase and other enzymes that will make xenobiotics into carcinogenic substances that cause mutations to DNA without undergoing cell chemical processes (Murray, 2018)

Cells can adjust their structure and function to adapt to changes and extra-cellular stress, in the sense that cells can adapt to their environment. Changes in the cell environment can be caused by various chemicals such as lead which is a xenobiotic substance and acts as a free radical to cells. Hyperplasia is one example of a cell adaptation mechanism to environmental changes caused by these compounds. If the adaptation mechanism is carried out excessively, cellular damage will occur (Kumar, 2007).

This study found that the administration of iodine solution at a dose of 12.5mg which was carried out simultaneously with the administration of lead acetate at a dose of 10 mg/KgBB for 19 days of treatment could reduce the average percentage of kidney cell damage in the microscopic picture. Giving iodine solution to the sample showed a lighter cell damage picture compared to the sample that was only given lead acetate alone. This shows that iodine solution can act as an antioxidant that can reduce damage to kidney muscle cells due to lead exposure.

This study is similar to the results of Rudolf Winkler's case study which found that iodine has a role as an external antioxidant of the body as well as a role in neutralizing ROS (Winkler, 2015). The results of this study are in line with the study of Aceves et al found that iodine as an antioxidant, antiproliferative, and immune modulator (Aceves, 2013). Iodine in form I can act as an antioxidant by acting as an electron donor. Iodine radicals that appear are immediately converted into molecular iodine ($2I^- \rightarrow I_2$) and can convert the body's free radicals that have dangerous unpaired free electrons into more stable ones. Iodine can also play a role in the reduction of hydrogen peroxide ($H_2O_2 + 2I^- \rightarrow H_2O + I_2$) and in lipid peroxidation ($LOOH + 2H^+ + 2I^- \rightarrow LOH + H_2O + I_2$). The antioxidant effect of iodine can be seen through its role as the body's external antioxidant and also helps to improve the body's internal antioxidant status such as catalase and GPx enzymes so that the amount of MDA and the body's oxidative stress load decreases (Winkler, 2015).

Iodine as an antioxidant binds to free radicals in lipid membranes, proteins, and DNA, increases the activity of type II antioxidant enzymes so that SOD and catalase enzymes increase, and also helps inactivate pro-inflammatory cell pathways in the body (Aceves, 2013).

Based on the results of the study and the explanation above, it can be seen that iodine solution can protect kidney cell damage by preventing the accumulation of ROS and preventing oxidative stress in the body.

Based on the results of this study, it can be said that there is indeed an effect of iodine solution administration on the histopathological picture of rat kidney induced with lead acetate.

CONCLUSION AND RECOMMENDATION

Based on the results of the study of differences in rat kidney histopathology in the administration of iodine solution induced by lead acetate, it can be concluded that there is an effect of iodine solution administration on the histopathological picture of rat kidneys induced by lead acetate.

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