EFFECTS OF LOCAL ANASTESI USING LIDOCAIN OINTMENT ON WHITE RATS (RATTUS NORVEGICUS)

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ABSTRACT

This study aims to determine the effectiveness of drug administration, namely lidocaine ointment on male and female white rats (Rattus Norvegicus) as well as to see the comparison of water samples given to experimental animals and lidocaine ointment given to experimental animals and see the effects that occur when lidocaine ointment is given to the experimental animals. experimental animal.

The method used is a laboratory experimental method using 20 experimental male and female white rats which were divided into 2 groups, namely the male and female rats. cold, hot sensation of pain sensation and touch sensation in the observation period.

The results showed that lidocaine ointment smeared on the left arm on white rats had a smaller number of sensation responses than any given stimulus. This shows that lidocaine ointment has the effectiveness of local anesthesia while water does not have a local anesthetic effect because the nerves in the arm are still able to respond well to the stimuli given.

Keywords: local anesthetic, lidocaine ointment

INTRODUCTION

Anesthesia; comes from the Greek a means "no, without" and aesthētos means "perception, the ability to feel", generally means an act of relieving pain during surgery and various other procedures that cause pain in the body. A local anesthetic is a drug that produces a conduction block or a temporary blockade of sodium channels in the nerve wall against stimulation of transmission along the nerve, when used on the central or peripheral nerves.

A local anesthetic after discharge from the nerve is followed by a spontaneous and complete recovery of nerve conduction without any damage to the nerve structures. All new local anesthetic drugs are engineered old drugs which are considered to have shortcomings. Cocaine was the first anesthetic drug made from coca leaves and was first developed in 1884. Use of cocaine is safe only for topical anesthesia. Systemic use will cause side effects of toxicity to the nervous system, cardiocirculation system, so it is limited to making it only for topical eyes, nose and throat.

The term anesthesia comes from the Greek a which means not and aesthesis which means feeling. In general anesthesia means loss of feeling or sensation. Anesthesia is divided into two, namely, general anesthesia and local anesthesia. When it affects the whole body, the terms "general analgesia" or "general anesthesia" are used. When only a part of the body is affected, the term used is a local anesthetic. Local anesthesia is an anesthetic that is often used in tooth extraction.

Local anesthetics eliminate nerve conduction when applied locally to nerve

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tissue in appropriate concentrations. Works on a portion of the Central Nervous System (CNS) and every nerve fiber. The action of local anesthetics on sensory nerve endings is nonspecific. Only the sensitivity of the various structures that can be stimulated is different. Motor nerve fibers have a larger diameter than sensory fibers. Therefore, the effect of local anesthetics decreases as the diameter of the nerve fibers increases, the sensory nerve fibers are inhibited at first and only at larger doses the motor nerve fibers are inhibited.

Anesthesia means a condition with no pain. General anesthesia is a condition characterized by loss of perception of all sensations due to drug induction. In this case, apart from the loss of pain, consciousness is also lost. General anesthetic drugs consist of a heterogeneous class of chemical compounds, which depress CNS reversibly with almost the same spectrum and can be controlled. General anesthetic drugs can be given by inhalation and intravenously. The most important general anesthetic drugs given by inhalation (gas and volatile liquids) include N2O, halothane, enflurane, methoxiflurane, and isoflurane. General anesthetic drugs that are used intravenously, namely thiobarbiturates, narcotics-analgesics, other alkaloid compounds and similar molecules, and some special drugs such as ketamine [3].

Balanced anesthesia, a combination of drugs, is often used in general anesthesia [2]. Balanced anesthesia consists of:

1. Hypnosis was given the night before.
2. Premedication, such as narcotic analgesics or benzodiazepines (eg, midazolam and anticholinergics (eg, atropine) to reduce secretions are given approximately 1 hour before surgery.
3. Barbiturates with a short service life, such as sodium thiopental (Pentothal).
4. Inhalation gases, such as nitrous oxide and oxygen.
5. Muscle relaxant if needed.

Local Anesthesia

Local anesthetics or local numbing agents are drugs which in local use reversibly block the transmission of nerve impulses to the CNS and thereby relieve or reduce pain, itching, burning or cold. [4].

The action of local anesthetics on sensory nerve endings is nonspecific. Only the sensitivity of the various structures that can be stimulated is different. For example, motor function does not stop with common doses of local anesthetics mainly because motor nerve fibers have a larger diameter than sensory fibers. Therefore, the effect of local anesthetics decreases with an increase in nerve fiber diameter, so sensory nerve fibers are inhibited at first and only at larger doses motor nerve fibers are inhibited [4].

Surface anesthesia, used on the mucosa/wound surface. From there it diffuses to the sensory end organs and to the nerve terminal branches. In the intact (unharmed) epidermis, local anesthetics are almost ineffective because local anesthetics barely penetrate the lining of the horns.

1. Infiltration anesthesia, injected into the tissue, as well as filling into the tissue. Thus in addition to the sensory end organs, small nerve trunks are also inhibited.
2. Conduction anesthesia, it is injected around a specific nerve to which it is directed and the stimulant delivery at this site is severed. Example: spinal anesthesia, peridural anesthesia, paravertebral anesthesia.
3. Intravenous regional anesthesia in the area of the limb, the flow of blood in and out is stopped by binding with the aid of a blood pressure meter and then the injected local anesthetic diffuses

out of the vein and into the surrounding tissue and within 10-15 minutes creates anesthesia. Blood emptying should be maintained for a minimum of 20-30 minutes to avoid the outflow of large quantities of penetrating local anesthetics that have not yet penetrated the tissues. At the end of blood emptying, the local anesthetic effect decreases within a few minutes.

Requirements anesthesia Local

There are several criteria that must be met for a type of drug used as a local anesthetic, including:

1. Does not stimulate tissue,
2. Does not cause permanent damage to the nervous system,
3. Low systemic toxicity,
4. Effective by injection or local use on mucous membranes,
5. Start work as short as possible, but last quite a long time,
6. Can dissolve in water and produce a stable solution, also to heating (sterilization).
7. Classification anesthesia Local [4].

The basic structure of local anesthetics generally consists of three parts, namely a hydrophilic amino group (secondary or tertiary) connected by an ester (alcohol) or amide bond with a lipophil aromatic group. The longer the alcohol group, the greater the action of the anesthetic, but the toxicity also increases.

Local anesthetics can be classified chemically into the following groups:

1. Esters: cocaine and PABA-esters (benzocaine, procaine, oxybuprocaine, tetracaine).
2. Amides: lidocaine and prilocaine, mepivacaine, bupivacaine, and cinchocaine.
3. Others: phenol, benzylalkohol and ethyl chloride. All the drugs mentioned above are synthetic, except natural cocaine.

Experimental Animal Classification

Rats are mammals that are often used in various scientific studies because they have good adaptability. The mice that are widely used in research are white rats (Rattus Norvegicus). The advantages of white mice include their small body so they are easy to handle and maintain, healthy and clean, high reproductive ability with a short gestation period.

The classification of white rats (Rattus Norvegicus) is as follows:

Kingdom: Animalia
Phylum: Chordata
Class: Mammals
Order: Rodentia
Family: Muridae
Genus: Rattus
Species: Rattus Norvegicus.

Mechanism of action

Local anesthetics cause loss of taste in several ways. For example, by temporarily avoiding the formation and transmission of impulses through nerve cells and their endings. The center of its mechanism of action is located in the cell membrane. Like alcohol and barbital, local anesthetics inhibit impulse transmission by decreasing the permeability of the nerve cell membrane to sodium ions, which is necessary for proper nerve function. This is due to competition with calcium ions which are adjacent to the sodium channels in the neuron membrane. At the same time, as a result of a decrease in the rate of depolarization, the threshold of sensitivity to electrical stimulation gradually increases, resulting in a reversible loss of local flavor.

It is thought that in the membrane stabilization process, calcium-ion plays an important role, that is, the large lipophil molecule of local anesthetics may force some of the calcium-ion in the cell membrane without taking over its function. Thus the cell membrane becomes denser and more stable, and can

better resist any changes regarding its permeability.

Inhibition of impulse transmission can also be achieved by strong cooling (ethylchloride) or by poisoning the protoplasm of cells (phenol) [6].

Pharmacokinetics

1. Absorption, all local anesthetics are poorly absorbed in the gastrointestinal tract after oral administration, except for cocaine. Nearly all local anesthetics have a first-pass effect on the liver so that the drug is metabolized into inactive metabolites. Local anesthetics are absorbed at different rates on different mucous membranes. In the tracheal mucosa, absorption occurs almost the same as intravenous administration. In the pharyngeal mucosa, absorption is slower and in the esophageal and bladder mucosa, absorption is slower than topical application of the pharynx. Meanwhile, the rate of absorption of local anesthetics on parenteral administration depends on the vascularization of the injection site and the vasoactivity of the drug.
2. Distribution, when local anesthetics enter the bloodstream, they are distributed throughout the body tissues.
3. Metabolism, toxicity depends on the balance of absorption with metabolism. The ester compounds hydrolyze in plasma with the help of the pseudocholinesterase enzyme. The faster the hydrolysis speed, the smaller it ispotential for local anesthetic toxicity. The biotransformation of amide local anesthetics is more complex than the ester group. The metabolic organs of lidocaine, ethidocaine, bupivacaine are in the liver while prilocaine is metabolized in the liver and lungs.
4. Excretion, the main organ of the excretory process is the kidneys. Healthy kidney function is a factor that plays an important role in the excretion process. A large number of esters are metabolized so that only a small amount remains unchanged. While amide compounds because they are more complex, their original form can be found larger in the urine [6].

Pharmacodynamics

Effects of local anesthetics:

1. Restlessness and tremors,
2. Seizures,
3. Affects the transmission of muscle nerve connections,
4. Cardiovascular collapse,
5. Allergy

Drug Interactions

The center of its mechanism of action is located in the cell membrane. Like alcohol and barbital, local anesthetics inhibit impulse transmission by decreasing the permeability of the nerve cell membrane to sodium ions, which is necessary for proper nerve function. This is due to competition with calcium ions which are adjacent to the sodium channels in the nerve cell membrane. At the same time, due to a decrease in the depolarization rate, the threshold of sensitivity to slow electrical stimulation increases, so that eventually there is a reversible loss of local flavor [12]

Lidocaine

Lidocaine, an amino amide type local anesthetic, was first developed by Nils Lofgren and Bengt Lundqvist in 1943 and first marketed in 1948 [7].

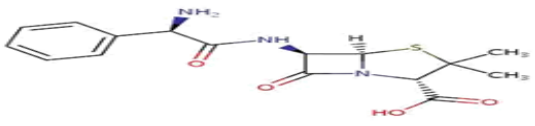

Figure 1. Chemical structure of lidocaine

Pharmacokinetics of Lidocaine

Lidocaine has a faster onset and longer duration than amino ester-type local anesthetics such as procaine. Lidocaine is metabolized in the liver in close to 90% [7]. The onset of local anesthetics is determined by the pKa, which is the pH at which the concentration between the ionic and non-ionic forms is the same. The nerve cell membrane will be easily passed by the uncharged ion form so that the onset of the drug is related to the base form of the local anesthetic drug.

The percentage of local anesthetics in the alkaline form at pH 7.4 is inversely related to the pK of the drug. For example, mepivacaine, lidocaine and procaine have a pKa of nearly 7.7 so they have a fast onset while bupivacaine has a slow onset. When the drug is injected at a pH of 7.4 then 65% of the drug is in the ionic form while 35% is in the alkaline form (non-ionic). Meanwhile, amethocaine has a pKa of 8.6 and only 5% is in the non-ionic form. Bupivacaine has a pKa of 8.1 which means only 15% is in the non-ionic form. Local anesthetics after extravascular injection will undergo absorption, distribution and elimination stages. In addition to these stages, the a-glycoprotein level factor will affect the level of lidocaine concentration in the blood [1].

The elimination half-life of lidocaine approaches 1.5-2 hours in most patients. This could be prolonged in patients with fatty liver (mean 343 minutes) or congestive heart failure (approx. 136 minutes). Lidocaine is readily absorbed from the injection site and can cross the blood brain barrier. [11]

Pharmacodynamics of lidocaine

Lidocaine changes the depolarization of nerves by blocking sodium channels in the cell membrane. With sufficient blockade, the membrane will not depolarize and thus send no action potentials [7].

Indication

Lidocaine is used for topical anesthesia, infiltration anesthesia, nerve blockade, epidural anesthesia, intrathecal anesthesia and IV regional anesthesia [7]. Lidocaine can reduce cardiac irritability so it is used as an anti-arrhythmic. Lidocaine is classified as a class 1b anti-arrhythmic agent, blocking sodium channels at cardiac action potential, which is automatically decreased by reducing the phase 0 depolarization slope with little effect on the PR interval, QRS complex and QT interval [7].

lidocaine contraindication

Contraindications for lidocaine include:

1. Heart block, grade 2 or 3 (without a pacemaker)
2. Great sinoatrial blockade (no pacemaker)
3. There is an adverse reaction when using lidocaine or the local anesthetic amides.
4. Concomitant treatment with quinidine, flecainide, disopyramide and procainamide (class I anti-arrhythmic agents) [7].

Lidocaine overdose

In general, symptoms of overdose are rare and are usually caused by negligent intravascular injection, excessive dosing or rapid absorption that leads to high blood concentrations. Symptoms of xxi overdose can also be caused by hypersensitivity or a patient's lack of tolerance [7]. Symptoms of a lidocaine overdose are usually related to its effect on the CNS, eg drowsiness, dizziness, paresthesis, mental disorders, coma and seizures. Excessive doses of lidocaine can cause death due to ventricular fibrillation or cardiac arrest [11].

RESEARCH METHODS

This research was conducted in the laboratory of the University of Bina Mandiri Gorontalo. The method used is a

laboratory experimental method using 20 experimental animal's male and female rats divided into 2 groups, namely groups of male rats and female rats. Then, in each experimental animal, white mice and female rats were marked on each mouse in the left ventricle and right ventricle. Lidocaine ointment was smeared on the right ventricle area and water was applied to the left bladder area. Then provide stimulation in the form of a touch sensation, namely, in the form of a hot sensation on the blunt end of a pin soaked in hot water, a cold sensation and a painful sensation.

Tools and materials

The tools and materials used in this study were the tools used, namely bristles and pins, the materials used in this study were lidocaine, warm water, cold water, 20 male and female white rats (Rattus Norvegicus).

RESEARCH RESULT

This research was conducted in the laboratory of the University of Bina Mandiri Gorontalo using experimental animal samples of white rats *(Rattus Norvegicus)* Male and female rats were divided into 2 groups, namely male and female rats.

Table 1. The results of observations on the treatment of male white rats

Treatment	Minute							
	1	2	3	4	5	6	7	8
Hot sensation	√	√	√	√	√	√	√	√
Cool sensation	√	√	√	√	√	√	√	√
Pain sensation	√	√	√	√	√	√	√	√
Touch sensation	√	√	√	√	√	√	√	√

Source: Practicum Report

In the results of table 1 using water samples, the results obtained in the treatment of male white rats (Rattus Norvegicus), namely at 1-8 minutes give the effect of a sensation of heat, cold, pain and touch.

Table 2. The results of observations on the treatment of female rats

Treatment	Minute							
	1	2	3	4	5	6	7	8
Hot sensation	-	-	-	-	-	-	√	√
Cool sensation	-	-	-	-	-	√	√	√
Pain sensation	-	-	-	-	√	√	√	√
Touch sensation	-	-	-	-	-	-	√	√

Source: Practicum Report

In the results of table 2 using a sample of lidocaine ointment, the results obtained in the treatment of female white rats (Rattus Norvegicus) are at 1-6 minutes they do not feel a hot sensation, while at 7 and 8 minutes the female rats feel a hot sensation. In the results of table 2 for the cold sensation treatment, the results obtained are that at 1-5 minutes you don't get a cold sensation, while at 6-8 minutes you get a cold sensation. In the results of table 2 for the treatment of pain sensations, the results obtained are that at 1-4 minutes there is no pain sensation, while at 5-8 minutes you feel a pain sensation. In the results of table 2 for the treatment of touch sensations, the results obtained are that at 1-6 minutes they do not feel the touch sensation, while at 7-8 minutes the samples of female white rats feel the touch sensation.

DISCUSSION

Local anesthetics or local numbing agents are drugs which in local use reversibly block the transmission of nerve impulses to the CNS and thereby relieve or reduce pain, itching, feeling of heat or cold. Local anesthetic drugs prevent transmission of nerve impulses (conduction block) by means of inhibits the delivery of sodium ions through selective sodium ion gates on the nerve membrane.

Local anesthesia/local anesthetics or what is often called numbing is a drug that blocks nerve delivery when applied locally to the nerves with sufficient levels of this drug to work on each part of the nervous system. For example, if a local anesthetic is applied to the motor cortex

the implant draining from the area stops, and when it is injected into the skin sensory transmission is inhibited. Local anesthesia aims to determine how it works and the administration of anesthesia locally and the factors that affect the workability of local anesthetics [12]. In this study, the experimental animals used were male and female white rats (Rattus Norvegicus) which were divided into 2 groups and given 4 treatments on male and female white rats.

Figure 1. Experimental animal handling and labeling of experimental animals.

In Figure 1. before the experimental animal is given treatment, the experimental animal is first given an experimental animal handler so that the experimental animal does not experience stress before being given the treatment. After being given the treatment of male and female rats, they were given treatment by giving a sign using a red marker on the left arm and right arm of the male and female white rats.

Figure 2. The treatment of white rats using blunt pins and brush bristles (Rattus Norvegicus).

In Figure 2. above the treatment carried out namely giving treatment to the right arm which aims to be a control so that it can be compared with the left arm which is given lidocaine ointment with a stimulus in the form of a touch sensation using bristles, a hot sensation using a blunt part a pin that has been soaked using hot water, a cold sensation using the blunt part of a pin that has been soaked in cold water and a painful sensation using the sharp part of a pin. This treatment was carried out before being given lidocaine ointment to experimental animals.

Figure 3. Treatment of white rats (Rattus Norvegicus) using lidocaine ointment

In Figure 3. the treatment given is the application of lidocaine ointment on the left arm in white rats. From the picture above, lidocaine ointment in male and female samples of white mice (Rattus Norvegicus) has a smaller number of sensation responses from each given stimulus, compared to the right arm which is only smeared with water. This shows that lidocaine ointment has local anesthetic activity while water samples do not have a local anesthetic effect.

From the observational data, it was found that the number of sensations felt in the right arm for each given stimulus was the first minute to the eighth minute of the observation time. This shows that water does not have a local anesthetic effect because the nerves in the right arm can still respond well to the stimuli given. Meanwhile, the left arm smeared with lidocaine decreased the number of sensations, including pain, heat, and cold. This suggests that lidocaine has a local anesthetic effect due to reduced response to given stimuli. Then there has been

surface anesthesia because local anesthetics are applied to the surface of the skin and reach the sensory nerve endings.

Obtained from the observed results of lidocaine ointment, for the sensation of touch using brush bristles and the sensation of pain using a pin. In the first minute to the fifth minute the effect of lidocaine was still reacting, and at the sixth minute it had begun to return to normal. It was seen from the stimulus that had been felt by the white mice. After that, the pins are heated using hot water on top of the hot plate and the other pins are cooled using ice cubes. Then the second treatment was carried out by smearing lidocaine back on the right and left thighs of the white rat, seeing the sensation of heat and cold sensation by using these pins. In the first and fifth minutes, the white mouse stimulus has not been felt, at the sixth minute a cold sensation begins to be felt and the seventh minute a hot sensation is felt, at the eighth minute the white mouse stimulus has returned to normal.

The working nature of lidocaine is faster, stronger, longer and more extensive. Side effects of lidocaine are usually related to its effects on the CNS such as drowsiness, dizziness, paraesthesia, mental disorders, coma, and seizures [11].

This shows that lidocaine has a local anesthetic effect because there is a reduced response to the stimuli given while water does not give the slightest anesthetic effect to reduce the stimulus given, then for lidocaine surface anesthesia has also occurred because local anesthetic is used on the skin surface and reaches the tip. sensory nerves thereby inhibiting the delivery of pain implants to nerve fibers.

CONCLUSION

Drugs that block nerve delivery when applied locally to nerve tissue with sufficient levels of drugs are often called numbing agents are drugs that block nerve delivery when applied locally to nerve tissue with sufficient levels of this drug acting on each part of the nervous system called numbing/drug local anesthetic/local anesthetic. Lidocaine is a local anesthetic drug from the amide class.

From the research results, it was found that the water sample used did not have the effect of local anesthesia because the nerves in the right arm were still able to respond well as well as the stimuli given. Meanwhile, the left arm smeared with lidocaine decreased the number of sensations, including pain, heat, and cold. This suggests that lidocaine ointment has a local anesthetic effect due to reduced response to given stimuli.

Then there has been surface anesthesia because local anesthetics are applied to the surface of the skin and reach the sensory nerve endings. In this study, a topical local anesthetic effect was tested. When local anesthesia is applied to the motor cortex the implant draining from the area stops,

The suggestions for this practicum are for the practitioner to be even better at conducting each experiment and always be careful in every treatment of rats so that unwanted things do not happen.

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