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Pain Modulating Effects of Ketamine

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Abstract

Pain perception in the body is influenced when the upper sites of the central nervous system form two pathways that are descending, one which inhibits pain and the other which facilitates the pain. When these two pathways change the way they function or an imbalance is detected by the central nervous system someone will start to experience pain. Patients who experience chronic pains have pain receptors which are antagonists to Ketamine; these receptors are called the N-methyl-d-aspartate (NMDA). Ketamine makes chronic pain patients receive little or no pain because pain control is inhibited internally. There are two mechanisms in the body of chronic pain patients which are involved in descending the inhibitory nature of pain, one of the mechanisms is the Diffuse Noxious Inhibitory Control (DNIC) and the other mechanism is the Offset Analgesia (OA). Current studies are, therefore, carried out to investigate if Ketamine affects the responses Diffuse Noxious Inhibitory Control (DNIC) and Offset Analgesia (OA) as far as the control of pain in chronic pain patients is concerned. The studies are carried out using a paradigm called Conditioned Pain Modulation (CPM).

Keywords: Conditioned pain modulation (CPM); Diffuse noxious inhibitory control (DNIC); Offset analgesia (OA); Ketamine; Central nervous system.

1. Introduction

Normal pain in the human body of a patient occurs when pain signals are modulated in the central nervous system by the activation of internal mechanisms of relieving pain or the mechanisms that facilitate pain, for instance, analgesic and algesic mechanisms [1]. When these mechanisms are activated, the body functions occur at an optimal rate because the central nervous system is working on the normal pain [2]. When an individual experiences pain, pain facilitator mechanisms are activated and they put pressure on the part of the tissue that has been damaged and a patient, in this case, will tend to search for medical assistance or rest [2]. Chronic pain among patients has made scientists research on the internal modulation of pain.

The most part that the scientists have dwelled on is the Conditioned Pain Modulation (CPM). When chronic pains persist in patients it shows that the CPM is either impaired or it is lacking [3]. Other defects of the unavailability of CPM in the body of patients are that the descending inhibition cannot take place, the patients start to perceive the pain and in later stages, chronic pain develops [4]. The use of Ketamine in the treatment of chronic pain patients improves the response of CPM thereby reducing pain in the long-term [4]. This paper takes a close examination of how the body responds when chronic patients are administered using Ketamine.

2. Methodology

Before the research was carried out, approval was obtained from the Local Human Ethics Committee (LHEC). Ten chronic pain patients from referral hospitals in North America were selected for the study. The patients were required either of the following medical complications in legs or arms; Painful feet which worsened during the night, not normal legs or feet which cause chronic pain and central pain that was sensitized. The patients were required to be ages 18-80 with no history of an infectious disease; they later went medical examination to examine their physical damage. The average conditions that were to be taken into account during the experiment were that the temperature range between 0.1ºC and 0.3ºC. The patients were then treated with Ketamine with an average of 2.9mm to see the response of the central nervous system.

3. Results/ Findings

All the 10 patients completed the treatment 8 of them did not have any side effects but 2 of them experienced nausea after infusion of Ketamine and three of them showed no signs of origin of their pain. Before the patients were administered with ketamine, they showed no sign of CPM responses. After the treatment, CPM was detected and the chronic pain started to disappear. The patients were later released after the discomfort in their feet and hands had disappeared. Younger patients below age 40 relieved quickly after administration of Ketamine, older patients especially female recovered at a slower rate.

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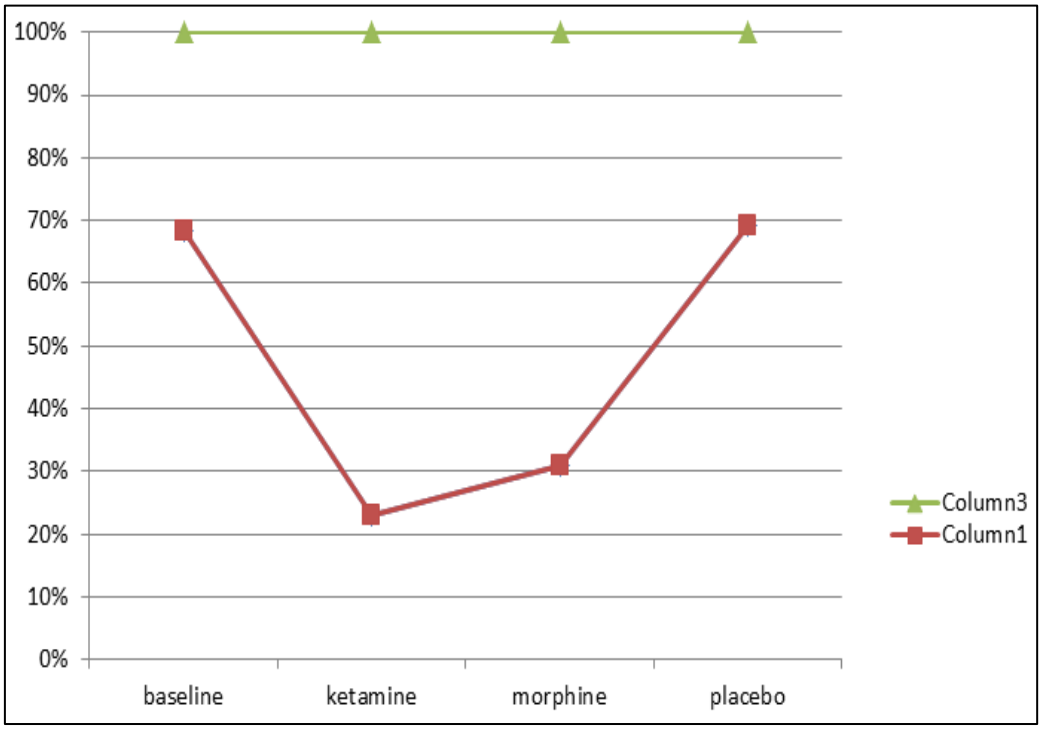
4. Discussion

The treatment of Ketamine stimulated the response of CPU which activated the internal inhibitory receptors that relieved the pain of the patients. The rate of how CPU responded was determined by the magnitude at which pain was relieved as well as the time taken to relieve the pain. The higher parts of the central nervous system such as the prefrontal cortex, rostral Anterior Cingulate Cortex (rACC) and Insula activate the two mechanisms for controlling pain in the damaged tissues, for instance, the inhibitory and facilitator mechanism pathways [5]. When inhibitory pathways mechanism is activated, the nociceptor is deactivated so that there is no trafficking in this neuron [3]. The trafficking is later sent to the upper parts of the spinal cord which process and perceives the pain [1]. When a patient is induced with Ketamine it balances between the inhibitory pathways and the facilitatory pathways to reduce pain in chronic pain patients. Patients who are below age 40 have a higher response in CPM when administered with Ketamine; this makes their central nervous system release inhibitory pathways, thus recovering from pain at a faster rate [6]. The case is different in older patients because they seem to have a low response of CPM which makes them relieve their pain slowly.

When ketamine is administered to patients that are in acute pain, their central nervous systems respond at a faster rate to initiate inhibitory pathways that make the CPM respond reducing the pain within 30 minutes. Acute patients have a low response to CPU because pain receptor neurons in the central nervous system are less activated. Ketamine blunts central sensitization which makes postoperative patients feel less pain. Ketamine plays a crucial role in making the NMDA receptor less sensitive, thus reducing pain in patients. Ketamine binds on the NMDA receptors and later modify these receptors by changing their response to physical injury or pain [7].

Ketamine is also used in IV sedation, this means that this drug is used by physicians to make sure that the patients are comfortable during surgical operations or when being diagnosed for possible medical conditions [8]. Ketamine relaxes these kinds of patients and sometimes makes them fall asleep. In serious cases, for example when cancer patients are being diagnosed for possible throat cancer or colon cancer, ketamine is placed in their veins to help reduce pain and make them feel comfortable during the diagnosis. Ketamine also prevents pain by developing a mechanism of tolerating Opioid substances in the body [9]. Ketamine is the mostly used drug in all areas of relieving pain because of its efficiency in relieving pain faster. The graph below shows the performance of various drugs (morphine, ketamine, morphine, and placebo) when used by physicians to relieve the pain of patients with chronic pain. Column 3 shows that the patient has chronic pain and when he is administered with the four drugs, the level of the graph varies (column 1). The percentage levels correspond to the extent of pain in patients. The level is lower when administered with ketamine than the other drugs. This shows that ketamine relieves pain faster than morphine, baseline, and placebo. Concerning our topic, it shows that ketamine is efficient in stimulating pain inhibitory pathways to send signals to CPM.



Opioid substances in the body activate pain receptors that increase the effectiveness of glutamate synapse by transmitting neurons to the NMDA receptors. Ketamine responds by making the receptors not to transmit signals by neutralizing them. When Ketamine interacts with the brain it causes a central effect in reducing pain by interacting with the NMDA making it less sensitive to pain [10]. The presence of Ketamine in the veins of the human body changes brain connectivity in areas where internal pain regulation is required. This is possible because ketamine reduces the connection of the brain to areas where pain can be processed and sensed. When ketamine is administered in low doses it desensitizes the inhibitory pathways and the facilitatory pathways making the CPM response low, consequently, it modifies the opioid receptors [11].

5. Conclusion

Initially ketamine was used as a drug to patients who had acute pains but recent developments have seen Ketamine being used in advanced stages like postoperative management of relieving pain. Most of the studies carried out have seen ketamine having numerous effects as far as pain modulation is concerned. They include; effectiveness in controlling or modulating pain after a patient is operated and reducing the level required for opioids. Currently, ketamine is widely used in various areas of surgery, for example, orthopedic surgery, surgery of the spinal cord, abdominal surgery and otolaryngology kind of surgery. Scientists have rarely agreed on all the mechanisms of Ketamine but they have widely accepted that Ketamine has an antagonistic role in the NMDA receptors. ketamine desensitizes the NMDA receptors making a chronic pain patient relieve the pain. Patients who have undergone postoperative are encouraged to infuse ketamine in harmfully or painful procedures in a 48h time frame so that the risk of developing pain after surgical operation is reduced in the future. The response of CPM is faster in young age people than old age making old people have an extended period in relieving pain. When administering Ketamine to help in relieving pain there are certain side effects experienced for example nausea as seen in the experiments during this research. When the two pathways mechanisms in the upper part of the central nervous system show some state of imbalance pain are not relieved because the CPM will not receive signals to respond.

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