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Mini Review

OPIOID RECEPTOR EXPRESSION IN IMMUNE SYSTEM CELLS

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ABSTRACT

Researchers began to think about the possibility of opioid receptors (OR) being present in immune system cells after they became aware of opioids' ability to modulate the immune system. Numerous studies have been conducted to examine the expression of OR subtypes in human and animal immune cells. While some of them failed to find the receptor mRNA, others confirmed OR expression on both the mRNA and protein levels. Despite the fact that this issue is still up for debate, new research is constantly being published. Recent research suggested that the expression level of OR in human peripheral blood lymphocytes could be used as a biomarker to diagnose chronic pain or assess the efficacy of methadone maintenance therapy in ex-opioid addicts. However, additional research is required to confirm these findings' applicability to clinical practice. Opioids, both natural and synthetic, are powerful pain relievers that are frequently used to treat acute, chronic, and inflammatory pain. All other opioid agonists are measured against morphine, the standard. Long-term, high-dose analgesic therapy is necessary for many patients, particularly those with chronic pain. However, opioids are also misused by healthy individuals for their additional properties a positive emotional effect and even euphoria leading to addiction or even intoxication. Unwanted side effects, such as analgesic tolerance, physical dependence (addiction), respiratory depression, constipation, and severe withdrawal symptoms following drug discontinuation, limit the clinical utility of morphine and other opioids.

Keywords: Bioavailability; Gastrointestinal fluid; Metabolism

INTRODUCTION

New drugs have been developed and synthesized to replace the traditional opioids in the treatment of pain while avoiding their undesirable side effects. These included peptidomimetic enkephalin and endorphin analogues and several morphine derivatives. Although many of these substances were used as analgesics in clinical settings only methadone and buprenorphine have been used to treat addictive disorders. Methadone is an opioid analgesic that is used for the detoxification and substitution treatment of opioid addiction, to reduce cravings and normalize physiological homeostasis. It is a synthetic derivative of diphenyl heptane that was made in the 1960s. Methadone is taken orally, and unlike morphine, tolerance to it and physical dependence on it develop more slowly. Methadone withdrawal symptoms are milder but last for a longer period of time than morphine withdrawal symptoms Methadone substitution therapy continues to be the most effective

treatment option for opioid addiction worldwide.

Expectations that the issues of opioid tolerance, addiction, and side effects will be addressed have not been met. As a result, a more secure medical treatment for addiction and withdrawal symptoms, as well as, most importantly, the prevention of relapse, are required. A definition of the appropriate biomarkers for opioid drug addiction is desirable due to the fact that the majority of medical treatments that have been approved show only moderate effects over time.

DISCUSSION

Twofold downregulation of trimeric G subunits was found in plasma membranes isolated from the forebrain cortex of morphine-treated rats after proteomic analysis. In addition, the functionally related upregulation of proteins associated with oxidative stress and apoptosis was observed. A subsequent study revealed that chronic morphine altered 28 (MALDI-TOF MS/MS) or 113 (MaxLFQ) proteins, depending on the method used for protein detection and quantification. Importantly, the number of altered proteins decreased to 14 (MALDI-TOF MS/MS) and 19 (MaxLFQ) in rats sacrificed 20 days after the last dose of morphine. We interpreted these findings as evidence of a living organism's capacity to combat the morphine-induced change in the protein composition of the target tissue and elicit a partial return to normal physiological conditions following drug withdrawal [1,2].

Although the effects of chronic opioid drug administration on tolerance, dependence, and withdrawal have been extensively studied, determining the neurobiological mechanisms that lead to addiction remains a significant challenge. Human neurobiological adaptations cannot be examined directly, unlike animals. As a result, there is a tendency to discover some peripheral markers that may assist in assessing the health status of human subjects who have been exposed to opioid drugs for an extended period of time. The studies focused on analyzing the expression and function of OR in immune system cells represent one area of research in this context. The optimistic expectations regarding the resolution of opioid tolerance, addiction, and side effects remain unfulfilled. As a result, safer medical treatment for addiction and withdrawal symptoms, as well as, most importantly, prevention of relapse, are required. The identification of the appropriate biomarkers for opioid drug addiction is desirable due to the fact that the majority of medical treatments that have been approved have only mild effects over the long term [3,4].

Human neurobiological adaptations cannot be examined directly. As a result, it is necessary to discover some peripheral markers that could assist in assessing the health status of human subjects who have been exposed to opioid drugs for an extended period of time. The study of OR's expression and functional state in immune system cells is one potential area of investigation in this setting. Evidence that long-term opioid drug exposure alters the expression of OR in immune system cells was found in the analysis of peripheral blood cells from methadone-treated drug addicts. However, there were both increased and decreased expression levels of OR, so the findings were contradictory. Recent research lends credence to the hypothesis that, in addition to being immunosuppressive, OR ligands have more complex effects on immune system cells. The current body of knowledge regarding the treatment of trauma, cancer, and acute and chronic pain suggests that immunosuppression and immunostimulation are the most common approaches [5,6].

CONCLUSION

Pathological pain conditions like rheumatoid arthritis, osteoarthritis, or fibromyalgia were also

found to alter OR expression in human immune cells. Because the receptor expression levels were inversely correlated with both the intensity of the pain and the severity of the symptoms, this case's results were more consistent. Overall, research on OR in immune system cells suggested that OR in human immune cells could be useful as a diagnostic tool for defining chronic pain states or as potential biomarkers of opioid drug addiction in the periphery. To better understand the specific roles and responsibilities of the various OR subtypes in these pathological situations, as well as to verify and define the applicability of these findings to clinical practice, additional research is required.

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