EDITORIAL

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Feedback control systems could revolutionize the administration of prescription opioids

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ABSTRACT

Opioids pose significant risks of addiction due to the cyclical nature of serum opiate concentration associated with traditional dosing methods. Emerging technologies, including closed-loop feedback control systems, offer a promising solution by enabling dynamic, real-time microdosing that minimizes fluctuations in drug levels and reduces the risk of dependency. Drawing on advancements in biosensors and feedback systems used in other medical applications, these innovations could revolutionize pain management, potentially reducing opioid addiction rates by up to 87 percent compared to current oral administration methods.

Key words: pain management, feedback control, feedback control in medicine, medical devices, opioid pain pumps

Opioids are some of the most prevalent pain medications for both acute and chronic pain, with over 125 million prescriptions being dispensed in 2023 alone.[1] However, opioids have also become known for their addictive properties. Estimates indicate that opioid use disorder affects 16 million people globally and between 2.1 and 6.1 million in the United States.[2,3] These numbers are likely underestimated, as reporting is inconsistent throughout various jurisdictions.[4]

A significant factor contributing to the addictive nature of opioid pain medications is the cycle of highs and lows associated with taking a pill or injection. When a patient ingests a pill or receives a dose of medication, the concentration of that medication will increase. As their body metabolizes the medication for use, the concentration of that medication will fall. It is this cycle of highs and lows with each dose that leads many opioid users to develop a dependency or craving for the euphoric feeling that is associated with the high point in the cycle.

Examining the various methods of administering opioid pain medications, there are some notable differences in the rate of addiction among patient populations, considering variations on the aforementioned cyclical dosing cycle. Traditional pills (oral route) for opioids lead to addiction in 3 percent to 19 percent of patients, with misuse rates up to three times higher.[5] Injections and intravenous (IV) opioids tend to have a higher rate of addiction and misuse, owing to the faster route of metabolization, and a greater sense of patient control over the timing of dosages. This combination of rapid pain relief and euphoria in the case of some patients represents a pavlovian response. With this route of administration, misuse peaks as high as 81 percent in particularly vulnerable patient populations.[6] Even with implanted intrathecal pain pumps and other devices that utilize a bolus rate, there is still a risk of addiction, albeit lower than through oral administration.[7]

Due to the pervasive nature of this problem in the medical field, several new technologies are starting to arise that could change the landscape of pain management in the coming years. Among the most promising is the use of feedback control systems within medical devices for dynamic dosing in accordance with individual patient needs. Feedback control systems have become widely used to revolutionize other industries, and have recently been implemented in certain medical devices to greatly improve the efficacy of treatment.

A feedback control system is a system that maintains a relationship of one variable to another by collecting data from one of those variables and using the difference as a means of controlling the

other variable.[8] These systems are sometimes referred to as "closed loop systems," because they incorporate the feedback from measuring the output into the control algorithm, thus "looping" the output back into the calculations. Such systems typically utilize a desired setpoint about which to control the output variable. For example, a modern air conditioning system utilizes a feedback control system to maintain a setpoint temperature by measuring the current temperature, comparing that data to the desired setpoint, and using that difference to control the flowrate of chilled air into the space in order to achieve and maintain the desired temperature setpoint. Other examples of feedback control systems that are fundamental in engineering disciplines include automotive cruise control and aircraft autopilot, which each revolutionized their respective fields.

The medical field has begun to incorporate feedback control-based devices to improve the quality of medical care. One of the most notable examples is the use of pacemakers to regulate heart rhythms. These devices utilize a closed-loop feedback control system to adjust the output of electrical signals to optimize patient heart rhythms.[9] Certain insulin pumps are already using feedback control systems to control the administration of synthetic insulin and help patients maintain a desired setpoint or range of blood sugar. The Medtronic MiniMed and Omnipod Horizon are two such examples.[10]

New microfluidic biosensors are in development at a variety of companies to make it possible to take opioid measurements in real time.[11,12] Furthermore, mathematical models have recently been developed to measure the concentration of opioid pain medication in a patient's interstitial fluid.[13] When such technologies reach the market, closed-loop feedback control are likely only a step behind, leading to smaller, more frequent doses of opioid pain medication administered automatically. This method of microdosing causes a smaller amplitude in fluctuation of the concentration of pain medication in a patient's system, preventing that patient from experiencing the significant highs and lows associated with ingesting opioids pain medications through contemporary methods.

While it is impossible to predict how such technology will manifest itself into a physical device, this has the potential to minimize the addictive potential of opioid pain medications, as it could combine the benefits of smart pumps and intrathecal pain pumps with a bolus rate. Current literature indicates a 17 percent reduction in opioid addiction among patients who utilize smart pumps to administer their medications, and up to a 70 percent reduction in addition with a bolus rate of pain medication, as such dosing nearly eliminates the cyclical highs and lows in serum opioid concentration.[14,15] Closed loop feedback control systems could combine the operational benefits of both of these innovations, suggesting that the use of feedback control for administering opioid pain medications could reduce the likelihood of a patient developing an addiction by up to 87 percent, compared to contemporary oral administration of the same medications.

Just as autopilot was revolutionary for the aerospace industry, and cruise control was revolutionary for the automotive industry, so too could feedback control systems revolutionize the medical field. In fact, we already see the early stages of this revolution with the FDA clearance of closed loop insulin pumps and next generation pacemakers. With recent advancements in the pain management space, as well as emerging biosensor technologies, it is only a matter of time before closed-loop feedback control is commonplace in the field of pain management, as well.

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