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Cover story

Automatic antidote delivery device for opioid overdose

The opioid crisis in the United States is reaching uncharted territory with recent waves of overdose deaths associated with various opioids. From 1999 to 2018, almost 500,000 people died due to some form of opioid overdose [1]. To reduce opioid abuse, various abuse-deterrent formulations have been developed, but to no avail. Easy availability of nonprescription opioids has made the current opioid epidemic out of control. In addition to further research on abuse-deterrent formulations, a greater emphasis needs to be placed on developing drug delivery systems and devices for treating addiction and preventing overdose deaths [2]. One of the current approaches to preventing death by overdose of ultrafast-acting synthetic opioids is to deliver naloxone, an opioid antidote. Despite its wide availability, however, the number of opioid-related overdose deaths remains unacceptably high. In this issue, Professor Hyowon Lee and his collaborators from Purdue University present a simple and minimally invasive automatic antidote delivery device (A2D2) to address overdose related deaths [3]. They propose to use respiration rate as a biomarker for detection of opioid overdose to trigger a release of a large dose of naloxone from a subcutaneously placed drug delivery capsule. The idea of using an implantable drug delivery device is not new, but the Lee team presents a unique closed-loop triggered naloxone delivery system to address the opioid overdose epidemic.

The implantable drug delivery capsule chosen by the Lee team consists of a high-density polyethylene tube, a polytetrafluoroethylene seal, a stainless steel heating element, and a phase-change material as the drug releasing valve. The size of A2D2 is approximately 3 mm in diameter and 8 mm in length, which can be placed percutaneously using a trocar. The drug release occurs when a portable magnetic field generator applies a burst of high frequency magnetic field for approximately 10 s from 1 cm away, just above the skin, to heat and open the valve. They even used a portable induction heater circuit and a portable battery to demonstrate fast drug release using a wearable prototype. As designed, the A2D2 can carry up to 12 mg of powder or 20 μL of liquid payload, which is necessary to reverse the effects of severe respiratory depression.

Translation of this simple idea to a real impact in curtailing the opioid epidemic requires overcoming many challenges, such as ensuring reproducibility and reliability. First, the stability of the implanted drug and the packaging needs to be better characterized to ensure proper release at the time of use. Although Professor Lee and his colleagues have demonstrated that the device has minimal leakage, it is unknown how long the drug will remain viable once implanted. Second, the proof-of-concept in measuring respiration and delivering the drug separately demands further engineering work to ensure immediate naloxone release after detection. The risk and the severity of any type of device failure in time of need could have a detrimental impact for the user of this device. Thus, it may be necessary to provide a multi-chamber or a multi-use device as a fail-safe mechanism. This, in turn, makes the simple prototype more complicated. Finally, and perhaps most importantly, the Lee team will need to consider the acceptability of this approach from the patient's perspective. It is unclear how likely patients will opt to have an implantable drug delivery device as a safety net for accidental overdose.

This study by the Lee team highlights the urgency of the opioid epidemic, and it also represents a timely effort by scientists and engineers to address this critical national emergency. It is time to collect all ideas from the researchers in diverse disciplines and develop/test different approaches to find one that works. The current opioid crisis is not someone else's problem, but ours. Having a potential solution alone is not enough [2]. We all need to work together to bring what might be a potential solution to what will be used clinically.

References

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