Exploring and avoiding morphine-induced spinal masses

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Video Abstract

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Abstract

Harmful masses that accompany regular spinal or intrathecal infusions of opiates for pain management might one day be a concern of the past. Researchers have uncovered the cellular mechanisms behind these lesions, which occur with some opioids but not others. Their findings could help improve spinal pain therapy for patients without compromising their health or quality of life. Intrathecal opioids such as morphine are highly effective for managing pain. Direct access to opioid receptors in the spinal cord has made round-the-clock pain management possible, most notably through the use of so-called “pain pumps”. One concern, however, has been the possible formation of collagen-rich masses around the area of drug delivery. These masses, or granulomas, occur in about 8% of patients receiving spinal morphine infusions and have been linked, ironically, to increased pain and reduced neurological function. Once believed to be caused by the tubing that carries opioids to the spinal cord, these growths are now understood to be related to which opioid is delivered. Morphine, for example, leads to intrathecal masses, whereas fentanyl does not. Now, the research team, with members from the US, Canada, and Germany, has gone one step further. In their latest study, they propose a cascade of cellular mechanisms that give rise to these abnormal growths. The team looked at spinal cords from guinea pigs receiving morphine or one of two experimental opioids, PZM21 or DMT-DALDA. They found that in addition to activating opioid receptors in the spinal cord, morphine uniquely activates a non-opioid receptor that triggers the degranulation of mast cells and the growth of fibroblasts. These spindle-shaped cells form skin and other connective tissues, including the covering of the spinal cord, the dura. Here, fibroblasts are stimulated by morphine to release collagen, producing the masses observed in guinea pigs. These masses are thought to model the growths found in patients equipped with pain pumps. The experimental drugs, on the other hand, produced a different effect. Despite being opioids, they led to no growths when delivered at the concentrations required to produce an analgesic effect similar to that of morphine. PZM21 was observed not to trigger the mass-producing receptors in the spinal cord, while DMT-DALDA showed some effect, but only at concentrations well above those required for analgesia. ² These findings could be critical for the numerous patients seeking relief for chronic pain. By looking beyond morphine and other similar opioids, pain management could be made much safer and just as effective for patients.