



Karim Ladha at the University of Toronto, Canada, prepares a multidrug treatment before surgery.

SURGERY

Operating without opioids

The opioid crisis is driving a rethink of pain relief in surgery.

BY BIANCA NOGRADY

Around a decade ago, Edouard Trabulsi, a urologist at Thomas Jefferson University in Philadelphia, Pennsylvania, was approached by a colleague who suggested that he try an alternative way to manage pain in people recovering from surgery. The regimen dispensed with the usual opioid drugs, and instead combined pregabalin (an anti-epilepsy drug that also treats nerve pain) with paracetamol (acetaminophen) and the non-steroidal anti-inflammatory drug celecoxib.

Opioids were available if patients requested them or doctors felt that they were necessary.

At the time, opioid consumption rates in the United States were soaring, as were concerns about their misuse and overdose. So Trabulsi decided to test the regimen in people who were undergoing robotic-assisted keyhole surgery to remove the prostate, to see whether it might reduce the use of opioids during recovery.

Almost immediately, he found that his patients asked for extra pain relief less frequently. When Trabulsi and his colleagues examined opioid use in patients after the

regimen's introduction, they discovered that the mean amount of opioids used following surgery had more than halved¹. Opioid use during surgery had also decreased considerably.

"I certainly became a believer," says Trabulsi. "We call it our 'TLC' cocktail — Tylenol [paracetamol], Lyrica [pregabalin] and Celebrex [celecoxib] — and that's become our care path for basically every surgery I do robotically, even open surgeries."

The cocktail is given to patients two hours before their operations, and also after surgery. Although it doesn't eliminate the use of opioids entirely, Trabulsi says that now half of his prostate-surgery patients don't ask for opioids at all after surgery, and many never use the opioid prescription that is automatically given to them on discharge. Thanks to his willingness to test alternatives to opioids, and the success he has had doing so, he is often contacted by people who have had problems in the past with addiction and who want to limit exposure to opioids during surgery.

DO LESS HARM

Long-term, or chronic, opioid use often follows surgery. A 2019 study estimated that each year in Australia, around 13,000 people who have not previously used opioids will become chronic users after undergoing elective surgery². Around 4% of those who take opioids for the first time after major elective surgery will still be taking them 90 days later². And people who undergo low-risk surgery are 44% more likely to become long-term opioid users in the year that follows if they are given a prescription for such drugs within a week of their surgery³. Given this reality, it is no wonder that there is such interest in reducing the amount of opioid pain relief that is used during and after surgery.

"The perioperative period is this unique time because, on the one hand, you're inducing a lot of pain in somebody, but on the other hand, you have this public-health concern of the opioid crisis," says Karim Ladha, who investigates the health outcomes of anaesthesia at the University of Toronto in Canada.

The balancing act that is required to do no harm became clear to Ladha when he started to notice that an increasing number of people who were coming in for surgery were chronic opioid users. He undertook a study to compare such patients' risk of opioid overdose after surgery with that of people undergoing surgery who hadn't previously received opioids, and found that it was more than 50 times greater⁴. Ladha realized that this presented both an opportunity and a challenge. The surgery offered an opportunity to wean patients off opioids during the postoperative period, and the challenge was how to do it.

One of Ladha's colleagues proposed that they establish a programme to deal specifically with chronic opioid users who needed to undergo surgery, using a multidrug, multidisciplinary approach to pain management. The strategy aims to wean people off the opioids that

they already use, and then manage their pain through a combination of non-opioid drugs (such as the neuropathic pain medication gabapentin and tricyclic antidepressants), psychological therapies and non-pharmacological and alternative therapies such as physiotherapy, acupuncture and yoga. The programme began at Toronto General Hospital in 2014, and is now being tested at five sites in the Canadian province of Ontario as part of the RECOUP clinical trial.

Often it becomes clear during the programme that people who are chronic users of opioids do not require them to deal with pain. “The craziest thing I’ve seen as a clinician is taking someone who’s on 500-milligram equivalents of morphine, and getting them off completely and seeing that their pain didn’t change,” he says. “They actually feel a lot better.”

Whether people are chronic users or new to opioids, it is crucial that those who undergo surgery use opioids for the shortest possible time, says Gabriel Brat, a trauma surgeon at Beth Israel Deaconess Medical Center in Boston, Massachusetts. “It’s really important to take into account the element of time.” Brat and his colleagues looked at opioid prescribing patterns in more than one million opioid-naïve people undergoing surgery, and found that each additional week of opioid use was associated with a 44% increase in the rate of opioid dependence, abuse or overdose⁵.

“That extended exposure is really a significant risk factor, and one that we should use clearly to identify patients who are going to be at risk of long-term misuse,” he says.

PARED-DOWN PRESCRIPTIONS

Such awareness is driving a change in how opioids are prescribed to people when they are discharged from hospital after surgery.

In 2018, a study examined the effect of implementing a restrictive postsurgical opioid prescribing protocol at Roswell Park Comprehensive Cancer Center in Buffalo, New York⁶. Patients who were undergoing gynaecological surgery for cancer were prescribed opioids when discharged from hospital only if they had needed five or more doses of opioids while in hospital. The researchers found that under the new protocol, few women took opioids home: the mean number of opioid tablets given to women who had keyhole or robotic surgery fell from 38.4 tablets to just 1.3 tablets.

They also found no increase in the proportion of patients who requested a refill of their opioid prescription, or in patients’ post-operative pain scores or complication rates⁶. This is unsurprising, because it is becoming clear that people often do not need the opioids that they have been prescribed. A study of 313 people who underwent thyroid surgery⁷ showed that although these patients were discharged with a median of 30 oral morphine-equivalent doses — and as many as 120 — 83% took fewer than 10 doses, and 93% took fewer than 20. “What really needs to happen is that



Acupuncture is used to manage pain.

an opioid prescription should only be given if it’s appropriate for that surgical intervention,” says Greta Palmer, a paediatric anaesthetist and pain specialist at the Royal Children’s Hospital in Melbourne, Australia.

It’s a change from the days when patients were automatically discharged with a standard prescription for opioids, whether or not it was needed. But that doesn’t mean that restrictive prescribing is a one-size-fits-all solution; Palmer says that the challenge is identifying those at high risk, whose pain management needs are likely to be greater and more complex.

People with anxiety and who have a high pain catastrophizing score — which means that they tend to exaggerate descriptions of their pain, as well as dwell on and feel helpless about it — seem at greater risk of becoming a chronic user of opioids, Palmer says. Although they use an opioid initially to help their pain, “it helps their anxiety at the same time, and then they stay on it to help their anxiety”.

There are some red flags that indicate that a person who has undergone surgery is more likely to progress to chronic opioid use. Brat

“Right now, the reliance is simply on opioids and nothing else.”

and his colleagues’ research has highlighted factors such as depression, tobacco-use disorder and existing chronic pain, but the team also found that having weight-loss surgery is associated with a higher probability of developing chronic opioid use⁵. Brat suggests that a subset of people who undergo weight-loss surgery might have a history of psychiatric conditions that could put them at higher risk of opioid misuse.

People with these risk factors are those for whom alternative or multidisciplinary approaches to pain relief are probably going to be most important. At the Royal Children’s Hospital, Palmer uses an ‘analgesic ladder’ to manage surgical pain. The idea is to make best use of non-opioid analgesics during surgery, including intravenous paracetamol, intravenous non-steroidal anti-inflammatory drugs or a dose of the analgesic ketamine. In addition to the TLC regimen, Trabulsi and

his colleagues at Thomas Jefferson University inject keyhole surgery incision and tool-insertion sites with the anaesthetic lidocaine, which seems to ease post-operative pain.

However, there is still nothing as good as opioids at relieving pain, says Ladha. At pain conferences, there is much talk about developing opioids that have a lower risk of triggering dependence, or that are selective for particular cell-surface receptors (see page S4). But Ladha is not convinced that this is the right approach. “There’s no amazing drug that’s going to be better than opioids, but we’re simply not using what we have often enough,” he says. “Right now, the reliance is simply on opioids and nothing else, and slowly that’s changing, but there’s a long way to go.”

FINDING MIDDLE GROUND

Neurosurgeon and pain specialist Andrew Zacest at the Royal Adelaide Hospital says that the message being given to surgeons in Australia is to be wary of using opioids before and after operations, to avoid patients developing or experiencing a worsening of problems with such drugs. But he says that there is a risk of the anti-opioid push going too far.

“We need to be a little bit cautious not to swing the other way, because patients will go into withdrawal, and we’ll see a whole bunch of other complications from this if we are too aggressive,” he says. “We need a middle ground.”

He also raises the issue that although it is helpful to combine pharmaceutical pain management with other approaches such as psychological therapies, not all patients and general practitioners will have access to them.

Ladha found that out when he described the multidisciplinary approach being taken at Toronto General Hospital to physicians working elsewhere. The consensus among those doctors, he says, was that it sounded amazing but could never be implemented in their centres because of the cost of such an intensive programme. Ladha hopes the RECOUP trial will show that the approach makes economic as well as medical sense. But he is also wary of the backlash against opioids, and of the mindset that opioids are so pernicious that they should not be prescribed at all.

“Is it possible to treat someone’s acute pain without opioids?” he asks. “Yes — but is that necessarily the best thing for their pain? We don’t really know yet.” ■

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