Viewpoint

# Perioperative opioids: Reclaiming Lost Ground

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Opium (poppy tears) has been in use since 3400 BCE, with historical writings recording its sedative, euphoric and analgesic properties, but it was not until the 19th century that morphine was isolated, paving the way for its therapeutic use. The 20th century witnessed advances in pharmacology and molecular biology leading to the development of many different types of opioids and the recognition and classification of opioid receptors.

Analgesia is fundamental to recovery from surgery, and whilst opioids continue to be the cornerstone of perioperative analgesia, overreliance on these agents and their many side effects have led to a re-evaluation of their role in modern perioperative practice. Persistent postoperative opioid use (PPOU), with addiction at the extreme end of the spectrum, and opioid-induced ventilatory impairment (OIVI) have led to a global opioid crisis that has resulted in more than 100,000 deaths per annum worldwide, and rising yearly.[1] PPOU and OIVI are exacerbated by other factors such as non-medical opioid use and opioid diversion. Whilst the numbers of deaths are clearly not on the scale of the current Covid-19 pandemic, regrettably there are few signs of measures that will force it to recede in the near future. In addition, the financial costs for increased healthcare and substance abuse treatment costs, lost productivity and criminal justice ran in to US$ 150 billion (in the US alone) in 2015.[1] Whilst the opioid epidemic may have originated in the US, it has spread to other areas of the world, with Europe having more than 1.3 million high-risk opioid users.[1] Besides the modifiable risk factors (**Table 1**),[2] indiscriminate use of opioids has also been fuelled by aggressive marketing strategies by pharmaceutical companies and the erroneous impression that consumption of opioids for pain does not lead to addiction.[3]

Many patients receive opioid analgesia following major surgery. Given that nearly 15% of patients prescribed opioids for the first time became long-term users within a year[4] it is

logical to see why clinical practice should be changed.[2] For nearly 30 years, the concept of opioid sparing, multimodal analgesia to reduce over-reliance on opioids has been widely practiced. Whilst a key area, this is limited to the intraoperative and immediate postoperative periods; hence, a broader focus on the entire patient pathway is required.

The advent of patient pathways, from the decision to operate until normal physiological function has been restored provides the ideal opportunity and infrastructure to tackle many aspects of opioid stewardship.[5] Perhaps the most well-known are Enhanced Recovery After Surgery (ERAS) pathways, which have for been at the forefront of this concept globally for well over fifteen years and have a proven place in the evidenced-based delivery of perioperative care and ongoing research and audit.[6] Moreover, the multidisciplinary approach of ERAS is unique, so that healthcare professionals as well as managers and the national institutions responsible for purchasing and managing healthcare work together.[6]

The major areas for opioid stewardship are summarized in **Table 1** and represent the way in which opioid use can be appropriately targeted within the patient pathway.[2] Many patients are on opioids preoperatively, often inappropriately for the management of chronic pain. The concept of prehabilitation is well established within ERAS and can be applied to optimizing preoperative opioid usage as well the identification of patients who may have unrealistic expectations for pain control.[5] Education of patients and their carers about the dangers of opioids, including addiction, and realistic management of expectations regarding postoperative pain (e.g. some pain is inevitable) can help.[2] Patients should receive input during preassessment from pain clinicians, psychologists or psychiatrists as appropriate. Opioid tapering is a complex and slow process, yet evidence is accumulating that if it is achieved, quality of life is improved and perioperative risk is reduced. Finally, the

prescription and proposed deprescription of opioids and their attendant risks should be discussed with patients and their carers at this stage.

Perhaps the area of greatest progress to date has been intraoperative analgesia, as anesthesiologists seek to reduce intraoperative opioid usage, with alternatives such as non-opioid systemic analgesics and/or the use of regional anesthesia. The promotion of opioid-free anesthesia (with or without regional anesthetic blocks) is also topical but with little high-quality evidence to support its widespread use.

It is in the postoperative period that the greatest changes are required. Opioid prescribing is often seen as routine with patient counselling being rare.[7] Administration of opioids to address self-reported severe pain scores is commonplace. The use of modified-release opioids and/or compound opioids, rather than the recommended immediate-release preparations, is not uncommon for severe pain.[2,7] In addition, monitoring for OIVI and appropriate dose adjustments for age are also required.[2] Finally, it is crucial to discuss deprescribing at this stage. Many of these areas can be addressed with multidisciplinary input postoperatively from medical, nursing and pharmacy teams. In addition, prescribing opioids without even seeing the patient and/or automated refill prescriptions must cease.[2]

Appropriate discharge planning is fundamental, with short prescription duration (typically only a few days) of immediate-release opioids. Patients should be advised to lock opioids away securely and ensure that unused opioids are returned or destroyed safely. The patient and their carers must be aware of the danger of sedation, with the need for prompt action (including the use of opioid antagonists).

Future technologies and research may also help mitigate the opioid crisis. These include remote monitoring of patients at risk, and the use of genomics to identify those at risk of both severe postoperative pain and development of chronic pain. In addition, as intraoperative analgesia (e.g. by remifentanil or local anesthetic blocks) does not necessarily translate into reduced opioid use postoperatively when the effects wear off, studies are required on how to best manage pain in this setting. Further data are needed on the known risks of opioid-induced immunosuppression and adverse effects on endocrine function (and presumed deleterious effects on surgical outcome).[8] Finally, perhaps, a checklist similar to the World Health Organization surgery checklist will drive better practice in opioid stewardship.

In the UK, the Medicines and Healthcare products Regulatory Agency has recommended that before prescribing opioids, clinicians must discuss the risks and features of tolerance, dependence and addiction with patients, and jointly agree a treatment strategy and plan for discontinuation of treatment.[9] Similar directives from regulatory bodies in other countries, including low- and middle-income countries, will help reclaim lost ground and prevent the spread of the epidemic. Opioids have played a key role in delivering analgesia for many years, but we must strive to ensure that we control opioids and not *vice versa*.

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This viewpoint is linked to an ERAS Society hosted webinar where the topic is addressed in greater detail: https://erassociety.org/perioperative-opioids-and-eras/

Table 1: Modifiable Risk Factors to Improve Perioperative Opioid Stewardship[a]

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| **Preoperative care**<br>Medication optimization for patients taking long-term opioids and other sedative analgesics<br>Referrals to pain team<br>Psychological input<br>Management of patient expectations (eg, pain will be controlled but not eliminated) |
| **Intraoperative care**<br>Multimodal analgesia (nonopioid and nonpharmacological)<br>Nerve blocks |
| **Postoperative care**<br>Functional pain scores instead of unidimensional scores<br>Immediate-release opioids, not modified-release opioids<br>Avoidance of compound opioids<br>Better monitoring of sedation for opioid-induced ventilatory impairment<br>Education of patients and caregivers<br>Opioid dosage based on age |
| **Postdischarge care**<br>Limited supply of opioids<br>Safe storage, disposal, and return of unused opioids<br>Formal deprescribing<br>Avoidance of reliance on opioids<br>Education about the risks of sedation and how to treat it |

[a]Modified from Levy et al.[2]