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Sustained-Release Opiate Therapy Following Surgery: A Cautionary Tale: A Case Report and Systematic Literature Review

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Abstract

We describe the case of a lady who suffered catastrophic injury likely attributable to the use of high doses of sustained-release (SR) opioid analgesia following routine surgery. This serves as a timely reminder of the need to balance good post-operative analgesia in optimising functional recovery against the well-known consequences of opioid therapy. In particular, the life-changing morbidity from iatrogenic drug prescribing is often underappreciated when emergent readmission occurs. We believe the routine use of sustained-release opioids should be discouraged following surgical procedures. A brief review summarising the risks of SR opioid prescription in the post-operative phase follows.

Abbreviations: IR = immediate-release; SR = sustained-release; OR = odds ratio; SCI = spinal cord injury

Introduction

We describe the case of a lady who suffered a catastrophic injury likely directly attributable to the use of high doses of sustained-release (SR) opioid analgesia following routine shoulder arthroscopy. The patient and her family provided written consent for writing and submitting this case report.

Case Report

A 66-year-old previously independent lady received an elective shoulder arthroscopic rotator cuff repair with biceps tenotomy. She had prior chronic neck, shoulder, and knee degenerative arthritis for which she took intermittent Oxycodone immediate-release and paracetamol. Her medical history was significant for previous C6-7 cervical discectomy and fusion, left total knee replacement, and hypertension. Her perioperative recovery was uncomplicated. She was cleared for discharge the next day following allied health assessments and sent home with a course of SR Oxycodone/Naloxone 20/10mg twice daily but suffered a fall down five steps while getting into her unit the same day.

She was readmitted to a different hospital with incomplete quadriplegia. A trauma survey diagnosed a C4 spinal cord injury (SCI). Unstable C4 and C5 vertebral fractures with retrolisthesis of C5-on-C6 on imaging required emergent C4-C7 decompression and fusion. After five days, she was discharged from the intensive care unit, eventually regaining just enough upper limb function to use a self-propelled electric wheelchair. Her stay was complicated by significant at-level and below-level spinal pain, reinjury of her shoulder rotator cuff bilaterally, postoperative delirium, spinal dysreflexia, and severe psychological distress requiring regular mental health liaison. Development of opiate tolerance necessitated opiate rotations and pregabalin, nortriptyline, and duloxetine.

Her inpatient stays in a tertiary spinal rehabilitation center totalled nine months and was compounded by her family's reluctance to come to terms with her increased care requirements and significant distress on how her care had been managed following her last admission. Their collective experiences would likely be detrimental in all future healthcare encounters.

Discussion

Post-surgical opioid prescription is often unavoidable, even with optimal perioperative management, including the use of regional anesthesia. However, continued use is linked with increased medium- and long-term harm risks. Cognitive impairment and injurious falls are often forgotten additional considerations, especially in older adults with paraplegia from vertebral fractures, with SCI amongst the most catastrophic outcomes on nearly all measured indicators.**[1]** Falls are among the most common types of accidents occurring in hospital inpatients and those recently discharged, often resulting in increased morbidity, extended hospital stays, and higher

costs.**[2]** Use of high-risk medications within 24 hours prior is one of the most critical risk factors for falls.**[3,4]** One study conducted in an urban academic hospital found that 62 % of inpatient falls occurred within 24 hours of administration of high-risk medications, with opioids being the most frequently implicated high-risk medication (32 %), with over 50 % being prescribed in higher than generally recommended doses in near opioid-naïve individuals.**[5]**

Compounding the issue is the widespread acceptance of using slow-release opioids for acute pain in addition to immediate-release (IR) formulations. This strategy has its underpinnings in cancer pain management, where the cause of pain is often an identifiable lesion sustaining pain through direct tissue destruction or inflammation.**[6]** Here, a strategy of time-scheduled administration and rescue dosing for breakthrough pain is necessary to provide adequate analgesia. Unfortunately, an overtly liberalized prescribing approach is partly responsible for an almost four-fold increase in total opioid usage between 1990 and 2014 and a 17-fold increase in dispensing of long-acting opioids between 1990 and 2000 in Australia, with per-capita use significantly higher in the US and Canada.**[7]** Research by the Centers for Disease Control and Prevention lists explicitly the commonplace use of SR opioids as contributing to the country's opioid epidemic.**[8]**

The use of SR formulations in acute pain is fraught with the well-described risks of respiratory depression resulting in accidental overdose and death.**[9]** Data from population-level studies suggest risk gradations associated with duration and dose. In one cohort study involving the initiation of opioid therapy in approximately 840,000 opioid naïve patients over 10 years, unintentional overdose in the first two weeks were five times more likely in patients receiving SR opioid formulations compared with those taking IR opioids.**[10]** Another study utilizing US Medicare data and state pharmacy benefit programs found that patients with a new opioid prescription had a fivefold higher risk of hip or upper extremity fracture than those receiving an anti-inflammatory prescription.**[11]** A Swedish regional population-based nested case-control study in Scania (n=203,607) found the use of psychotropic drugs (including opioids, antidepressants, and hypnotic-sedatives) within 3 months before a fall was associated with more than a doubling of odds for a falling accident among both men (odds ratio(OR)=2.14; 95 % CI 2.64-2.44) and women(OR=2.21; 95 % CI 2.04-2.39), with even higher odds for falling accidents with psychotropic drug (including opioid) use during the week before a falling accident in men (OR=6.07; 95 % CI 2.64-13.99) and women (OR=5.16; 95 % CI 3.11-8.56) in than exposure during a more extended period.**[12]** In another retrospective multicentre cohort trial of 57,929 patients using registry data, those who had filled an opioid prescription two weeks preceding a fall were 2.4 times more likely to sustain a fall-related injury than non-fallers. These patients were also at an increased risk of death (OR=1.58; 95 % CI 1.34-1.86). Finally, another nationwide registry-based analysis examining fracture and other fall-related injuries among all Swedish adults found the strongest association in the first week of opioid therapy dispensation (OR=5.14; 95 % CI 4.76-5.55), with risk decreasing every 7 days after that (OR=1.23; 95 % CI 1.10-1.38 by the fourth week).**[13]** What was surprising was that the falls-related injury risks in newly prescribed opioids were most pronounced among younger adults aged 18–29 years (OR=7.17; 95 % CI 5.04-10.2), possibly attributable to the increased early exposure to dangerous situations among younger adults who may return to a broader range of daily activities than older adults.

Recognizing this alarming trend, the Faculty of Pain Medicine and the Australian and New Zealand College of Anaesthetists (ANZCA) recently released a joint position statement recommending against the use of slow-release opioid preparations in acute pain.**[14]** This recommendation aligns with international guidelines and statements by regulatory bodies and government agencies. They are also in line with the approved indications for slow-release opioids issued by regulatory authorities, including the Therapeutic Goods Administration in Australia (TGA), the New Zealand Medicines and Medical Devices Safety Authority (MedSafe), and the US Food and Drug Administration (FDA). These indications, listed in the Product Information sheets for both SR oral and transdermal opioids, include the "management of moderate-to-severe chronic pain unresponsive to non-narcotic analgesia," "treatment of opioid-responsive, chronic severe pain," "treatment of moderate-to-severe chronic pain" and "prolonged relief of opioid responsive severe and intractable pain in adults." Therefore, using SR formulations in managing acute pain is not an approved indication.

Finally, it should also be noted that even long-term chronic opioid use can be problematic. A recent meta-analysis and systematic review of 30 studies conducted by Seppala and colleagues among older patients found that after adjustment for confounders, opioid therapies (28 studies in long-term opioid therapy) were associated with an increased risk of falling (pooled OR=1.60; 95 % CI: 1.35-1.91) based on best available adjusted data.**[15]**

This case is a sober reminder of the need to balance good analgesia and its anticipated benefits with the attendant neurocognitive impacts, injurious potential, and other unintended consequences of continued opioid use. We believe that for the vast majority of post-surgical care where an oral opioid-based regime is recommended as part of multimodal care that the most appropriate initial treatment of acute pain use is instituted by titration of immediate-release opioids on an as-needed basis by the guidelines mentioned above.

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B. Teo – This author provided 90 % contribution to draft manuscript of case report and literature review.

K. Khor – This author 10 % contribution to draft manuscript, provided initial ideas for contribution, identified contemporary gaps in current clinical practice, requested points for clarification, advice on simplification, flow of ideas, and final review.

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