Pain after total knee replacement

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The immediate management and investigation of an acute pain presentation in general practice is discussed in this article.

David is a 70-year-old retired accountant who presents to your general practice with severe right knee pain and difficulty mobilising seven days after having a right total knee replacement for osteoarthritis. He has been a patient at your practice for the past four years and his past medical history comprises depression, type 2 diabetes and hypertension, each of which is well controlled with a single first-line agent. He is overweight. Before having this operation he was requiring escalating doses of paracetamol and NSAIDS.

How would you assess David?

Answer: In Australia, where osteoarthritis is the most common musculoskeletal disorder and is the third largest contributor to disability,[1] scenarios similar to David's are increasingly being encountered by GPs. Total knee replacement (TKR) is one of the most cost-effective interventions for knee osteoarthritis to improve the quality of life of patients in Australia.[1,2] As a result, the TKR rate has increased from 133/100,000 population in 2005/06 to 172/100,000 population in 2014/15.[3] This is a pattern that is being replicated in the UK, the USA and most wealthy healthcare systems around the world.[4,5]

Enhanced recovery after surgery, or fast-track, programs are increasingly being adopted by healthcare services due to emerging evidence of improved recovery and reduced cost.[6] Consequently, more TKR patients are being discharged from hospital earlier, and many of these patients require more complex acute pain management.[7]

In a survey of Australian patients who had had a TKR, most reported that the first two weeks after discharge from hospital was the most painful period of their postoperative course, and most consulted their GP during this time because of pain.[8] Most of this cohort also reported their average pain as moderate to severe and were managing their pain with opioids despite significant side effects and without adequate nonpharmacological methods to manage pain.[8]

The causes of pain following TKR can be subclassified into intrinsic and extrinsic causes.[9,10] Pain associated with stiffness or instability is most likely due to intrinsic causes including infection, instability, malalignment, soft-tissue impingement, arthrofibrosis, osteolysis, prosthetic loosening or failure and patellofemoral problems.[9,10] Extrinsic causes include periprosthetic fracture, tendinopathy, bursitis, heterotopic ossification, vascular compromise, central or peripheral neuropathy, other musculoskeletal abnormality (hip, spine or ankle), psychosocial issues and inadequate analgesia.[9,10]

A thorough history for a patient such as David includes the indication for the operation, details of the operation and any early surgical complications, acute pain service strategies employed (regional anaesthesia

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techniques and analgesic regimens), a pain history regarding the current symptoms, a functional assessment including the patient's compliance with prescribed home exercises, constitutional symptoms, localising infective symptoms, past medical history, medication history (current and preoperative medications), and psychological and social history.[9,10]

Your physical examination of David includes gait, palpation of the knee, active and passive range of motion of the knee including patella mobility and tracking, examination of adjacent musculoskeletal structures including the hip, lumbar spine and ankle, a neurological and vascular examination of the limb and a general examination for signs of infection.[9,10]

David's early postoperative weight-bearing plain x-rays (AP, lateral skyline and long-leg alignment views) must be evaluated for alignment, component size and positioning, stress fracture, loosening, osteolysis, heterotopic ossification and unequal joint space.[9] Additional investigations should be considered if indicated. A serum C-reactive protein level with or without synovial fluid microscopy, culture and sensitivity is important if infection is suspected. CT scans are more sensitive for rotational malalignment and periprosthetic fractures, and bone scans are more sensitive for component loosening or infection.[9,10] At this time, consider referring the patient to their orthopaedic surgeon and any other specialist as appropriate.

David states that since his operation he has been experiencing the same severe mechanical, aching pain in his right knee with mild to moderate aching pain at rest. He is occasionally performing bed-based strengthening and active range-of-motion exercises but he is not mobilising regularly. In addition to regular doses of the same combined simple analgesics that he was prescribed before his operation, David was discharged from hospital with regular doses of oral sustained release (SR) oxycodone and oral immediate release (IR) oxycodone as needed (oral morphine equivalent daily dose of 90 mg). David states that he is about to run out of the medication he was provided with on discharge from hospital. He feels his right knee pain is poorly controlled and asks you for a prescription for further oxycodone medication at an increased dose. On further questioning you learn that David is experiencing constipation and is frequently falling asleep after taking doses of oxycodone.

How will you respond to David's request?

Answer: Given the potential risk of opioid medication to both patients and the community, 'universal precautions' for opioid prescription, which have been adapted in the local Faculty of Pain Medicine guidelines (www.fpm.anzca.edu.au/documents), should always be applied.[11,12] Before an opioid therapy trial is considered, a comprehensive biopsychosocial assessment and opioid misuse assessment must be performed, with subsequent optimisation of a multimodal plan toward active self-management.[11,12]

The assessment referred to above is consistent with a biopsychosocial assessment, but a more detailed description written by local experts is available.[13] The Opioid Risk Tool is a quick, easy and well-validated tool that is most useful in an acute care setting as it provides excellent discrimination between patients with low and high risk of opioid misuse.[7,14,15]

A multimodal plan toward active self-management includes nonmedication therapies, multimodal analgesics (both nonopioid and opioid analgesics) and interventional therapies (if indicated).[12] Evidence-based nonmedication strategies include education, pacing activity (including using the painful body part), graded exercise, sleep hygiene and psychological therapies, many of which may require the input of allied health providers.[12] Optimisation of such a comprehensive approach requires time and the co-ordination of a multidisciplinary team.

If an opioid therapy trial is considered appropriate, it is recommended that this involve a mutual agreement between the prescriber and the patient regarding clear goals (both symptomatic and functional) of the trial within an agreed time frame, regular assessment of the five As (analgesia [pain], activity [function], adverse effects, affect and aberrant behaviours) and a clear plan to appropriately wean opioid therapy should the goals not be achieved.[11,12]

At his current dose of oxycodone, David is experiencing inadequate desired effects with significant side effects. This would suggest that oxycodone is not the best opioid for him. It is important for all opioid prescribers to appreciate that there is a significant variability in individual patient responsiveness to each of the actions (analgesia, side effects and toxicities) of each opioid.[16] This primarily relates to individual genetic factors and opioid receptor polymorphism.[17] Also, it is important to appreciate that, on a population basis, there is little evidence to suggest any major differences in efficacy or adverse effects between any of the pure agonist opioids.[7,18] Thus, optimal opioid therapy for each patient is only achieved after evaluating different pure agonist opioids until one is identified that provides the ideal balance of desired effects with minimal or no side effects.

Opioid rotation, a change in opioid drug with the goal of improving outcomes, is indicated for David but caution is required.[19] There is strong evidence that opioid rotation practices (which generally accounted for incomplete cross tolerance by reducing an equianalgesic dose by 25%) may be an important contributor to the increasing incidence of opioid-related fatalities.[17] Revised consensus guidelines attempt to account for both interindividual variability in responsiveness and incomplete cross tolerance.[19] The recommended steps for opioid rotation (which apply for all strong opioids with the exception of methadone or transbuccal fentanyl) are shown in Box 1.

Extra caution should be applied when considering prescribing codeine and tramadol preparations, as pharmacogenetic variations in CYP2D6 are associated with significant risk of adverse effects, including death.[7]

As well as rotating to a different opioid agent, David may benefit from an ongoing prescription that comprises just an IR opioid preparation to be taken as needed. There is moderate evidence that pain-contingent dosing with oral IR opioids, when compared to time-contingent dosing with a combination of oral SR and oral IR opioids, results in significantly lower average daily opioid doses (97 mg versus 37 mg average daily dose oral morphine equivalent) and significantly lowers levels of opioid control concerns with no significant difference in analgesia.[20] Also, transdermal opioid preparations are unsuitable for acute pain management due to their slow onset and

1. Recommended steps for opioid rotation[19]

- Calculate the current daily opioid dose then, using an opioid conversion tool, calculate the equianalgesic dose in an appropriate alternative opioid. A recommended free local resource is the Faculty of Pain Medicine opioid calculator app (available online at www.fpm.anzca.edu.au/front-page-news/free-opioid-calculator-app).
- Apply an automatic dose reduction of 25 to 50% (apply the greater reduction if the current regimen involves high doses or elderly, medically frail and noncaucasian patients).
- Based on assessment of the patient's pain severity and medical or psychological comorbidities, apply an additional dose increase or reduction of 15 to 30%.
- Frequently reassess the new opioid regimen (as recommended above).

offset as well as evidence of a high incidence of respiratory depression.[18]

Finally, consideration should be made to refer David to a local physiotherapist. There is strong evidence that, compared with the home exercise programs provided to patients in hospital (isometric strengthening exercises, exercises to regain active range of motion, gait training and stretches), additional outpatient exercise sessions based on functional activities with a subsequent home exercise program result in a significant small to moderate improvement in function for up to four months.[21]

Weight-bearing plain x-rays taken on the first day after David's operation were normal and your assessment does not reveal anything suspicious other than inadequate analgesia. To reassure both yourself and David, you call his orthopaedic surgeon and they kindly arrange for a review the following week. With no risk factors for opioid-related aberrant behaviours other than depression and an alcoholic father, David's opioid risk tool score is in the moderate risk category. You decide to rotate David to a regimen of oral IR morphine as needed (maximum daily dose of 60 mg) by applying a 35% dose reduction given his age and current severe pain. Before providing a prescription, you negotiate a trial agreement with David. The agreed goal is to reduce his knee pain so as to facilitate a gradual increase in his functional activity including walking, as guided by the physiotherapist to whom you arrange a referral. David also agrees to weekly reassessments and the aim to ultimately wean then cease this medication.

David returns to your practice four months later requesting another prescription for IR oral morphine. Unfortunately he was lost to follow up and has not attended either of the appointments with the physiotherapist or orthopaedic surgeon. He confides that he has increased the daily dose of morphine to 120 mg, having been provided with prescriptions by a local emergency department and a number of after-hours GPs, each of which he consulted in a pain crisis. Despite the increased opioid dose, his right knee pain, walking and functional capacity remain the same as when you saw him last.

What options do you have for managing David's opioid use?

Answer: Presenting to emergency departments, obtaining opioids from multiple prescribers and self-initiated dose escalation are all behaviours suggesting prescription opioid abuse.[22] Other suggestive behaviours include frequent early appointments to a GP, recurrent lost prescriptions, frequently running out of medication early, refusal to pursue nonopioid treatments and focusing mainly on opioid issues during consultations.[22] These are the aberrant behaviours that should be evaluated as part of the regular five As assessment that is recommended for use by all opioid prescribers.[12]

As a result of increased opioid prescribing, prescription opioid abuse with resultant fatalities is currently a global epidemic.[23] In the USA from 1996 to 2011 medical use of prescription opioids increased by 1448% and prescription opioid abuse increased by 4680%. From 1999 to 2010 prescription opioid overdose deaths increased by 313%.[23,24] In Australia the problem is not as large but the trend is similar: opioid dispensing increased 15-fold from 1992 to 2002, opioid-related hospitalisation increased 2.4-fold from 1998 to 2009 and death from accidental poisoning (from prescription opioids and illicit drugs) increased 1.7-fold from 2002 to 2011.[25]

2. Risk factors for persistent postsurgical pain after total knee replacement

- Preoperative high pain intensity[38,39]
- Preoperative greater duration pain (more than 12 months)[40]
- Preoperative greater facilitated temporal summation and reduced preoperative pressure pain detection thresholds on quantitative sensory testing (a proxy for central sensitisation)[39,41]
- Preoperative greater symptomatic arthritis-affected joints (more than four)[42]
- Preoperative greater number of other pain sites[38,43,44]
- Preoperative greater cytokine levels in synovial fluid[45]
- Preoperative depression[38]
- Female sex[35,40]
- Fibromyalgia[46]
- Pain catastrophising and poor coping strategies[38,44,47]
- Postoperative early moderate to intolerable pain[40]
- Postoperative major depression[43]
- Revision surgery[48]

Given the risk that David's behaviour presents to both himself and the community, it is important to safely contain his prescription opioid use. An ongoing regular therapeutic relationship is fundamental to this aim, so empathy and maintenance of rapport are essential. This situation should prompt another detailed biopsychosocial assessment, as outlined above, to attempt to identify any precipitating and/or perpetuating factors contributing to this situation. This would include assessments by the orthopaedic surgeon and physiotherapist. Should such factors exist, addressing them may assist in managing David's opioid use.

Regardless of whether such factors are identified, education and certain containment measures are advisable. First, David should be educated that there is no strong evidence for efficacy of long-term opioid therapy for chronic noncancer pain but there is good to fair

quality evidence of harm, including opioid abuse and dependence, overdose, fractures, myocardial infarction and sexual dysfunction.[26,27] Second, a revised opioid agreement should be reached with David that includes interval dispensing at short intervals as a condition and, ideally, physician-guided tapering as the goal. Finally, any future opioid prescriptions for David require an authority. Individual state and territory laws differ slightly, but in general in Australia an authority is required to prescribe Schedule 8 drugs if the duration exceeds two months or if the patient is suspected of being or known to be drug dependent.[28]

Your assessment identifies that David has unrealistic expectations of the outcomes of TKR as well as features consistent with catastrophic thinking. David is prepared to comply with an opioid agreement that involves an authority prescription of his current daily dose of oral IR morphine with second-daily dispensing from a local pharmacy. He is aware that this is conditional on attending appointments with his orthopaedic surgeon, a psychologist and a physiotherapist as well as participation in graded functional exercise. David asks you why it is that the pain in his right knee is worse after TKR.

What is persistent postsurgical pain (PPSP) and what are the risk factors for its development?

Answer: Most patients who have a TKR for osteoarthritis experience a significant and sustained improvement in both knee pain and physical function, but there are a substantial number of patients who experience little or no benefit from the operation.[29] You reassure David that, although he is currently in the latter group, there is potential to make functional gains while gradually reducing his opioid dose if he actively engages with the multidisciplinary team that you have brought together to manage his problem. If he struggles in achieving this goal, referral to a pain management clinic is recommended.

PPSP is defined as pain in the area of surgery that began after a surgical procedure and exists beyond the normal time for healing or the process of repair and is present at least three to six months after this initial event.[30,31] There is strong evidence that the prevalence of PPSP after TKR is about 20% with an overall range in the studies of 10 to 39%.[32-35] This figure is remarkably similar to the consistent 18% dissatisfaction rate after TKR identified in registry studies in Europe and North America.[36]

The mechanism of PPSP is complex and poorly understood but many models often involve central sensitisation.[31] This is consistent with evidence that almost half of patients with PPSP after TKR have features of neuropathic pain.[33]

PPSP after TKR is associated with reduced function, increased rates of mood disorders and reduced quality of life.[37] TKR is an elective procedure aimed at symptomatic and functional improvement, yet, clearly, it can make some patients worse. Unfortunately, there is limited evidence of any effective preventive treatments for PPSP after TKR, only conflicting evidence that perioperative gabapentinoids reduce neuropathic symptoms.[35] To date, the focus of most research is on identifying risk factors for PPSP after TKR (Box 2).[38-48]

It is theorised that preoperative screening and targeted strategies aimed at treating modifiable risk factors might reduce the incidence of PPSP after TKR. An alternative theory is that preoperative screening might improve selection of patients for whom surgical intervention might be reconsidered. **PMT**

References

A list of references is included in the online version of this article (www.painmanagementtoday.com.au).

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