

# Management Review Part 6

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## Objectives

- Assess the effectiveness of an alfentanil and morphine mixture in the postanesthesia care unit.
- State the most effective method for diagnosis of sacroiliac dysfunction.
- Determine what proportion of patients will achieve pain relief and identify those patients most likely to benefit from systemic lidocaine.
- State the proposed relationship between pain-free external rotation range of motion and severity of daily pain.
- List two mechanisms whereby ketamine may effectively contribute to pain relief.
- Determine which antiepileptic drugs have the best analgesic potential for managing pain in patients suffering from painful diabetic neuropathy.
- Discuss the predictors of poor outcome in patients with neck pain treated by physical therapy.
- State a recent finding regarding the potential influence of pain expectation to nociceptive signal processing.
- State an important contrast between risperidone and haloperidol.
- Discuss greater trochanteric pain syndrome, its epidemiology and associated factors.

## **An audit of the safety and effectiveness of an alfentanil:morphine mixture in the postanesthesia care unit.**

*Alkharajy WK et al*

**Journal:** Acute Pain 9(1):13-19, 2007. 11 References

**Reprint:** Discipline of Anaesthesia and Intensive Care, School of Medicine, University of Adelaide, Frome Road, Adelaide, SA5005, Australia (Dr J Ong)

**Faculty Disclosure:** Abstracted by J. Joyce, who has nothing to disclose.

Providing rapid but safe management of postoperative pain is a vital goal in the immediate postsurgical period. However, despite the best efforts of anesthesiologists and nurses, many patients still experience moderate to severe pain in the postanesthesia care unit (PACU). Opioids remain the cornerstone of acute

pain treatment in this setting, in spite of adverse side effects. Yet an opioid with the desirable

pharmacokinetic characteristics of rapid onset and prolonged duration of effect is not clinically available. A mixture of opioids may allow for a more rapid onset of action, providing rapid relief of postoperative pain compared to morphine alone, while still maintaining a reasonable duration of effect. This study proposes using a mixture of alfentanil 55 mcg and morphine 0.75 mg per mL. Both morphine (M) and alfentanil-morphine (AM) were made freely available to anesthesiologists in the operating room suites.

The results of this study showed that administration of the AM mixture offered more rapid achievement of comfort than morphine alone. The dose volume to achieve comfort and the discharge time from the PACU were not statistically significantly different between the M group and the AM group.

The authors were unable to demonstrate any differences in the sedation or mean pain scores of the two groups. There were no differences in respiratory depression and oxygen saturation between the groups. From the pharmacokinetic perspective, use of an AM mixture should be advantageous, based on the previous determination of the optimal ratio of the two drugs that gave an apparent time-course of CNS concentrations with an earlier time to the peak CNS concentration and onset of analgesia, but relatively long duration of action.

With different opioids, the concentration-effect relationship is elusive because analgesia lags behind plasma concentration to varying degrees, the extent of hysteresis is dependent upon the physiochemical characteristics of the drug. In the case of alfentanil, the hysteresis is minimal due to its rapid CNS penetration, while with morphine the hysteresis is most marked because of its slow CNS equilibration. The slower cerebral uptake and low lipophilicity of morphine contributes to its prolonged relative duration with little delay in relative onset.

### **The role of intraarticular injection in diagnosis and treatment of sacroiliac joint dysfunction.**

*Çakit BD et al*

**Journal:** J Musculoskel Pain 15(3):57-63, 2007. 26 References

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**Faculty Disclosure:** Abstracted by J. Joyce, who has nothing to disclose.

Sacroiliac joint (SIJ) pathology is a frequently overlooked component of the differential diagnosis of low back pain (LBP) and sciatalgia. The most common dysfunction type of the SIJ is the unilateral anterior rotations of the innominates. In sacroiliac dysfunction (SID), the SIJ is fixed at the side of restricted sacral movement, ipsilateral innominate is displaced laterally, and the iliac crest is shifted upwards. This fixation leads to an obliquity in the pelvis if the dysfunction is unilateral.

Diagnostic injection is an invasive procedure. Therefore, it must be administered to patients with severe SIJ

pain who do not respond to aggressive functional restoration and have reached a plateau in the therapeutic procedure. The main function of the SIJ is to attenuate and transmit the body weight to the lower limbs. The mechanical pain concept of the SIJ has not been fully understood in differential diagnosis of LBP. There is weak correlation between history and diagnosis of SID.

The clinical appearance of SID varies considerably and may coexist with other musculoskeletal disorders. If the radiation areas of back pain include the sacral sulcus and provocative tests are positive, SID must be considered in the differential diagnosis. Multiple positive provocative tests strongly indicate SID in the differential diagnosis of LBP. Previously reported pain referral sites for SID include posterior superior iliac spine and the surrounding area, lower lumbar region, buttock, groin, greater trochanter, medial and posterior thigh, lower abdomen, lower leg, calf, and foot. Computed tomography has a limited diagnostic value for SID because of low sensitivity and specificity. The most effective method in the diagnosis of SID is intraarticular SIJ injection. Magnetic resonance imaging is shown to be the best modality in the visualization of sacroiliitis in the spondyloarthropathies, but it is ineffective in the diagnosis of SID.

The drawbacks of this study are the small sample size and the absence of a control group to assess the placebo effect. The rich innervation of the SIJ causes multiple patterns of pain radiation and frequently mimics radicular pain. It should be noticed that the painful pathologies of SIJ consist of not only spondyloarthropathies, infections, malignancies, and trauma, but also mechanical causes such as SID.

**Multivariate analysis of chronic pain patients undergoing lidocaine infusions: increasing pain severity and advancing age predict likelihood of clinically meaningful analgesia.**

*Carroll I et al*

**Journal:** Clin J Pain 23(8):702-706, 2007. 20 References

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**Faculty Disclosure:** Abstracted by J. Joyce, who has nothing to disclose.

Neuropathic pain, pain caused by an injury to nerves, afflicts an astounding 5.5 million Americans. Patients with neuropathic pain are at high risk of being undertreated. Lidocaine can be safely and effectively administered intravenously to treat neuropathic pain. Nonetheless, little has been published to clarify the degree of relief that can be expected, and the proportion of patients who will achieve relief. Furthermore, little has been done to identify the patients most likely to benefit from systemic lidocaine. There remains a paucity of data on how patients respond to systemic lidocaine and which clinical characteristics determine the degree of analgesic efficacy in patients given IV lidocaine. The authors hypothesized that the analgesic response to IV lidocaine would be bimodal with clear responders and clear nonresponders. They also hypothesized that more refractory patients would be less likely to respond to IV lidocaine. The goals were

to clarify what proportion of patients will achieve relief, what degree of relief can be expected, and identify the patients most likely to benefit from systemic lidocaine.

This study reports the largest cohort of patients undergoing lidocaine infusion subjected to statistical analysis to date in the literature. The analgesic response to lidocaine is not normally distributed. However, the distribution of analgesic responders did not demonstrate self-evident responders and nonresponders. These results contrast with those of other recent work, suggesting that lidocaine reduces mechanical allodynia but not spontaneous pain. The magnitude of pain relief seen in this large cohort is consistent with earlier work. Lidocaine may not be helpful in other types of pain, and inclusion of patients with non-neuropathic pain in the meta-analysis would reduce mean pain score reductions in response to lidocaine.

Age and pain severity influenced the likelihood of responding to IV lidocaine. Each decade of advancing age increases the odds of being a lidocaine responder by 36%. The finding that analgesia is predicted by baseline pain severity is consistent with previous studies of IV lidocaine, which have suggested that analgesia is predicted by the severity of mechanical allodynia. Thus, formal testing of mechanical allodynia may not be needed to identify such patients. Simply assessing baseline Numerical Rating Score (NRS) in patients with neuropathic pain may be sufficient. In contrast, indexes of pain refractoriness, such as duration of pain and number of failed medications, did not predict response to lidocaine.

### **Poststroke shoulder pain: its relationship to motor impairment, activity limitation, and quality of life.**

*Chae J et al*

**Journal:** Arch Phys Med Rehabil 88(3):298-301, 2007. 32 References

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**Faculty Disclosure:** Abstracted by J. Joyce, who has nothing to disclose.

Shoulder pain is a common complication of hemiplegia; its reported prevalence ranges from 5% to 84%. Numerous studies have reported a relationship between poststroke shoulder pain and limited shoulder external rotation range of motion (ROM), sensory impairment, adhesive capsulitis, impingement, subluxation, spasticity, and complex regional pain syndrome (CRPS). Its relationship to motor impairment and activity limitation is less clear.

The objective of this study was to test the hypothesis that poststroke shoulder pain, motor impairment, activity limitation, and pain-related quality of life (QOL) are statistically related. Poststroke shoulder pain was associated with reduced QOL related to pain. This study failed to demonstrate a statistical relationship between poststroke shoulder pain and motor impairment and activity limitation. QOL is generally referred to as a multidimensional construct involving the physical, emotional, functional, and social domains, which allows us to view the impact of disability, illness, or pain on a person as a whole. To interfere with specific

tasks does not necessarily mean that shoulder pain prevents the completion of the tasks. The pain may simply make the tasks more difficult by requiring greater investment of emotional and volitional effort.

Pain-free external rotation ROM likely overestimates the severity of daily pain. The pain experience is increased when a shortened muscle is stretched or if soft tissue is impinged between the humeral head and the acromion process in movement. Thus, pain-free external rotation ROM introduces artificial constraints that may not be relevant to participants' routine daily activities. It is possible that the presence of pain is more important than its degree in predicting motor impairment and activity limitation. Second, with regard to Functional Independence Measure (FIM) self scores, the lack of a relationship to Brief Pain Inventory (BPI) 12 may be because compensatory strategies were allowed.

### **Ketamine for pain relief in acute pancreatitis.**

*Chaudhari M et al*

**Journal:** Acute Pain 9(1):83-86, 2007. 11 References

**Reprint:** University Hospitals Coventry and Warwickshire, Clifford Bridge Road, Coventry CV2 2DX, UK (Dr M Chaudhari)

**Faculty Disclosure:** Abstracted by J. Joyce, who has nothing to disclose.

The authors report the case of a 56-year-old, 70 kg female with a confirmed diagnosis of pancreatitis. In the course of her treatment, the acute pain team was consulted with regard to refractory abdominal pain. The prescription of a morphine PCA, with local anesthetic epidural infusion relieved the pain for only a brief period of time. The acute pain team then suggested using an intravenous ketamine infusion along with epidural bupivacaine and IV morphine infusion. This regimen improved the patient's visual analog score (VAS) dramatically within 2 to 3 hours and sustained the relief for 2 days. After 2 days, the ketamine rate was increased from 10 mg/hr to 20 mg/hr with pain relief that continued onward from the 3<sup>rd</sup> day of admission.

The severe refractory abdominal pain associated with pancreatitis was treated with ketamine infusion in combination with opioids and epidural analgesia. Ketamine has been used as adjuvant analgesic by subcutaneous, IV, epidural, and intrathecal routes. It is known to be effective in reducing the opioid requirements and related side effects. Ketamine is a potent analgesic at sub-anesthetic doses by virtue of its action on NMDA receptors. Additionally, ketamine also can reverse opioid tolerance and thereby increase the effectiveness of opioids. The blockade of NMDA receptors reduces or reverses opioid tolerance at the spinal level. There is an increasing body of evidence that suggests that NMDA receptors are also present in peripheral afferent nerves.

Use of ketamine, with epidural bupivacaine and morphine infusion, improved pain relief dramatically within a few hours. This could have been due to two mechanisms. First, ketamine itself is a strong analgesic, and second, it could be due to reversal of opioid tolerance, thereby increasing the effectiveness

of morphine.

### **Antiepileptic drugs in treatment of pain caused by diabetic neuropathy.**

*Gutierrez-Alvarez AM et al*

**Journal:** J Pain Symptom Manage 34(2):201-208, 2007. 44 References

**Reprint:** Universidad del Rosario, Research Office, School of Medicine, Calle 63D No. 24-31, Bogotá, Columbia (AM Gutierrez-Alvarez, MD)

**Faculty Disclosure:** Abstracted by J. Joyce, who has nothing to disclose.

Pain is one of diabetic neuropathy's most common and incapacitating symptoms; its pharmacological control is difficult. Neuropathy is one of the most frequent complications of diabetes. It is a heterogeneous disorder that may affect sensory, motor, and autonomic nerves. The commonest type is a symmetric distal sensorimotor polyneuropathy, in which pain is a predominant symptom. Given the appearance of new antiepileptic drugs on the market, systemic and rigorous evaluation of their effectiveness in managing painful diabetic neuropathy has become necessary when making evidence-based clinical recommendations.

To clarify the evidence, a meta-analysis was performed to determine which antiepileptic drugs have the best analgesic potential for managing pain in patients suffering from painful diabetic neuropathy. Tricyclic antidepressants have generally been proposed for treating neuropathic pain as first-line medications and antiepileptic drugs have been considered to be second-line medications due to their ability to suppress neuronal hyperexcitability. Around 30% of patients suffering from neuropathic pain do not respond suitably to monotherapy. Combined therapy must, therefore, be provided in such cases. Antiepileptic drugs are frequently used in the specific case of diabetic neuropathy.

Two different meta-analyses were performed for interpreting the results of this study. The first one included all studies fulfilling the selection criteria. It was found that the studies were very heterogeneous. There are few differences between the studied drugs. Accordingly, to select the final analgesic treatment, the side effects of all these drugs must be considered. The most common side effects are somnolence or drowsiness, nausea or vomiting, and dizziness. Meta-analysis concerning the analgesic effect of antiepileptic drugs in patients suffering from diabetic neuropathy had two limitations. The first was a lack of consensus in classifying diabetic neuropathy. The second lay in the difficulty in precisely and objectively evaluating pain. Even though the visual analog scale is generally used for evaluating its intensity, there is still discussion about the clinical interpretation of this scale and other similar ones.

Future studies concerning this topic should consider administering the medication over more prolonged periods of time and objectively evaluating their effects on quality of life in dimensions such as sleep, effects on work, social life, and state of mind.

### **Predictors of poor outcome in patients with neck pain treated by physical therapy.**

Hill JC et al

**Journal:** Clin J Pain 23(8):683-690, 2007. 33 References

**Reprint:** Primary Care Musculoskeletal Research Centre, Keele University, Keele, Staffordshire, ST5 5BG; UK (JC Hill, MSc)

**Faculty Disclosure:** Abstracted by J. Joyce, who has nothing to disclose.

Neck pain is a common musculoskeletal symptom with approximately a fifth of adults reporting a new episode over the course of a year and around two-thirds experiencing neck pain over the course of their lifetime. Because of limited healthcare resources, early identification of patients who are at risk of a poor prognosis is needed to enable effective, early targeting of important prognostic indicators. A systematic summary of the literature concerning the clinical course and prognosis of nonspecific neck pain concluded that little was known about potential risk factors and that the methodological quality of existing studies was low.

Recent high-quality studies have further identified prognostic indicators for neck pain chronicity, including comorbid back pain, older age, patient expectations of treatment, previous neck pain, and psychological risk factors. The aim of this study was first to evaluate the predictors of minimal clinically important difference (MCID) for patients with neck pain and to compare these predictors to those identified using measures of patient perceived improvement. Second, this study sought to compare these empirical findings with physical therapists' subjective perceptions about which potential indicators have the greatest prognostic value.

Significant independent predictors of short-term (6 wk) outcomes for global change and MCID-NPQ (Northwick Park Neck Pain Questionnaire) were patient's social class, expectations of treatment success, and severity of neck pain. Independent predictors of longer-term (6 mo) outcomes included a single item question relating to catastrophizing, as well as anxiety and depression, patient treatment expectations, severity of baseline neck pain/disability, presence of comorbid back pain, and older age. There was a marked difference in the explained variance of the multivariable models, with baseline variables better predicting longer-term outcome for patient perceived global change than clinically important differences in patient's pain/disability.

The main clinical implications of the study findings concern the fact that patients with significant psychosocial factors and low treatment expectations are at risk of a poor treatment outcome and may require an alternative or more targeted approach than routine physical therapy. It seems that, using baseline characteristics studied, it is much harder to predict short-term, than long-term outcomes and to predict improvement in pain/disability (MCID-NPQ) compared with patient perceived global change.

**Changes in pain perception and descending inhibitory controls start at middle age in healthy adults.**

*Larivière M et al*



**Journal:** Clin J Pain 23(8):506-510, 2007. 24 References

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**Faculty Disclosure:** Abstracted by J. Joyce, who has nothing to disclose.

Until recently, only 1% of pain studies addressed the issue of pain in the elderly. Pain is a complex phenomenon, resulting from the integration of excitatory and inhibitory influences. Among inhibitory mechanisms, one of the best known is the bulbospinal endogenous pain control mechanism, also called diffuse noxious inhibitory controls (DNICs). The mechanisms underlying the phenomenon of DNIC are partly opioid-mediated, however, psychologic parameters can also shape the DNIC response. It is possible that older adults' apparent change in DNIC strength reflects nothing more than an age-related change in expected pain relief, which is plausible because older adults usually expect higher levels of pain than younger adults.

The goal of this study was to expand the scope of research regarding pain and aging by adding a middle-aged group to the habitual intergroup contrast composed of young adults and elderly adults. Specifically, the desire is to: 1) assess the strength of DNIC across the adult lifespan and 2) measure the relationship between expectations, analgesic responses, and age.

This study showed that the strength of DNIC declines progressively across the adult lifespan and that this decline is not explained by an age-related change in expected pain relief. These authors' results also showed that for older adults the analgesic response recorded during the conditioning stimulus was either weak or absent.

As elderly adults are generally thought to expect higher levels of pain, the authors also tested the possibility that expectations of pain explain part of the age-related change in DNIC strength. The results presented failed to support that hypothesis. It is interesting that, regardless of age, expectations predicted part of the variance in DNIC strength, suggesting that endogenous inhibitory control is subject to top-down modulation. Thus, expectations of pain relief can potentially affect nociceptive signal processing at the earliest stages of the central nervous system. This observation is consistent with recent neuroimaging studies which show that expectations of analgesia, or placebo analgesia, produce changes in cortical activity that are mirrored by changes in the activity of descending inhibitory circuits and pain perception.

### **A retrospective chart review of the antiemetic effectiveness of risperidone in refractory opioid-induced nausea and vomiting in advanced cancer patients.**

*Okamoto Y et al*

**Journal:** J Pain Symptom Manage 34(2):217-222, 2007. 33 References

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**Faculty Disclosure:** Abstracted by J. Joyce, who has nothing to disclose.

Nausea and vomiting commonly occur and are distressing symptoms in advanced cancer patients. Nausea and vomiting may be induced by cancer or its treatment, or a comorbid process. The causes are often multifactorial. Emesis is mediated centrally by the brainstem's chemoreceptor trigger zone (CTZ) and central pattern generator (CPG). Risperidone is an atypical antipsychotic drug that blocks dopaminergic (D2) and serotonergic (5-HT<sub>2</sub>) receptors. Risperidone exerts an antiemetic effect in animals, but there has been no clinical report on its antiemetic activity. These authors examined the effectiveness of risperidone in the treatment of opioid-induced nausea and vomiting in advanced cancer patients. The findings from the study were that risperidone was generally effective in treating refractory opioid-induced nausea and vomiting in advanced-cancer patients and produced no serious adverse effects.

Currently, haloperidol, a conventional antipsychotic agent used for management of various symptoms, including delirium, in the field of palliative care, is a first-line drug for opioid-induced nausea and vomiting. D<sub>2</sub> receptor stimulation by opioids is considered the principal cause of opioid-induced nausea and vomiting. Risperidone acts as a serotonin-dopamine antagonist, and its affinity to D<sub>2</sub> receptor stimulation is equivalent to that of haloperidol, but its extrapyramidal side effects are dose dependent and less frequent than those of haloperidol. In addition, it is reported that the severity of extrapyramidal side effects of haloperidol is higher than that for risperidone. Risperidone is also reported to be superior to haloperidol in assessment using the Extrapyramidal Symptom Rating Scale. Because concomitant administration of antiparkinsonian drugs is unnecessary with risperidone, the risk of tardive dyskinesia can be avoided with it.

Concerning pharmacokinetics and dosage, CYP2D6 in the liver plays a principal role in the metabolism to its main metabolite, and it is reported that in poor metabolizers, treatment tends to be discontinued due to adverse reactions. It has also been reported that drugs that induce or inhibit CYP2D6 influence the pharmacokinetics of risperidone. Drug metabolism appears to be an important factor in use of risperidone. In the present study, risperidone at 1 mg/day was effective for opioid-induced nausea and vomiting in most patients. Further study is required with increased numbers of cases to determine the appropriate dosage of risperidone, although attention should be paid to individual differences in metabolism of risperidone and drug interaction.

**Greater trochanteric pain syndrome: epidemiology and associated factors.**

*Segal NA et al*

**Journal:** Arch Phys Med Rehabil 88(8):988-992, 2007. 24 References

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**Faculty Disclosure:** Abstracted by J. Joyce, who has nothing to disclose.

Greater trochanteric pain syndrome (GTPS) is defined as tenderness to palpation over the greater trochanter with the patient in the side-lying position. Referring to this entity as GTPS is preferable to previous references for two reasons: 1) pain in this region frequently is not associated with signs of inflammation, and 2) the etiology is not fully known and may relate to myofascial pain rather than inflammation. For providers of musculoskeletal care, it is important to understand factors associated with GTPS to minimize significant decline of physical function and quality of life.

This study assessed the prevalence of GTPS in a community-based population complaining of lower limb pain and whether GTPS was associated with 4 purported risk factors: 1) ipsilateral iliotibial band (ITB) pain, 2) knee osteoarthritis (OA), 3) obesity, and 4) low back pain (LBP). A secondary aim was to determine whether hip internal rotation ROM or levels of physical activity and physical performance are limited in adults with GTPS.

This study was useful in both identifying the prevalence of GTPS in a non-clinic-based population as well as assessing the validity of common teachings regarding GTPS. The GTPS prevalence of 17.6% in this community-based sample of older adults at high risk of knee OA contrasts with the 20% to 35% reported for spine clinic patients presenting with LBP. These authors found that the following were associated with GTPS: female sex, ITB tenderness, knee OA or knee pain, and LBP. In addition to pain, people with GTPS appear to have a slowed gait and ability to rise from a chair. The contrast between differences in function, but not in activity score, may relate to subjects with GTPS limiting their activities to the reduced activity level in obese patients.