Highlights from the Hospice & Palliative Care Literature

Opioid and Adjuvant Analgesics: Compared and Contrasted
Khan MIA, Walsh D, Brito-Dellan, N

An adjuvant (or co-analgesic) is a drug that in its pharmacological characteristic is not necessarily primarily identified as an analgesic in nature but that has been found in clinical practice to have either an independent analgesic effect or additive analgesic properties when used with opioids. The therapeutic role of adjuvant analgesics (AAs) is to increase the therapeutic index of opioids by a dose-sparing effect, add a unique analgesic action in opioid-resistant pain, or reduce opioid side effects. A notable difference between opioids and AAs is that unlike opioids some AAs are associated with permanent organ toxicity, for example, nonsteroidal anti-inflammatory drugs (NSAIDs) and renal failure. It is impossible to predict in advance in a given individual what opioid dose they may require to control cancer pain. Most AAs have a ceiling effect for their analgesic actions, but often with continued dose-related toxicities and side effects (with the exception of glucocorticoids). The blood levels of opioids (and their metabolites) can be measured with great precision and accuracy. There is sometimes a role for drug blood levels of certain AAs, like tricyclic antidepressants or anticonvulsants when used for neuropathic pain. Age affects metabolism of most opioids. The therapeutic window of opioids is wide, with no ceiling effect. Most AAs (except corticosteroids) have a narrow therapeutic window. Naloxone is a pure opioid antagonist that competes and displaces opioids from their receptor sites. All clinically useful opioids are mu opioid receptor agonists. Not all routes of administration are available to all opioids. Adjuvant analgesics lack the versatility in routes of administration that opioids possess. Dosing flexibility is a major advantage when treating cancer-related pain with opioids. Dose flexibility is much less with AAs than opioids. Unlike opioids, the analgesic response is usually observed within hours to days of attaining an adequate dose with most AAs (1-2 days). Rotation among opioids is a useful therapeutic strategy to improve analgesic response or minimize toxicity. Most AAs are unsuitable for rescue dosing because of their pharmacological characteristics. The mu agonist side effect profile is similar among the different opioid agents, regardless of the route of administration. The appropriate use of AAs will reduce opioid-related side effects. No apparent tolerance to analgesia develops with AAs. Abrupt discontinuation of an opioid after chronic repeated use for more than a few days will cause a withdrawal syndrome of variable severity. Adjuvant analgesics are an essential tool in cancer pain. Am J Hospice Palliat Care 2011;28(5):378-383

Home Care Clients in the Last Year of Life: Is Material Deprivation Associated with Service Characteristics?
Goodridge D, Buckley A, Marko J, Steeves M, Turner H, Whitehead S

Demographic, social, medical, and health care characteristics of home care clients in the last year of life by quintile of deprivation and examine associations between material deprivation and service characteristics were compared. This retrospective study used administrative data for 700 clients who died while receiving home care services. Outcome measures were the receipt of supportive or palliative home care. Associations were assessed using multiple logistic regression. Material deprivation was not associated with either the hours of home care received or the receipt of supportive home care services. Clients with dementia or stroke, those were older than...
Home Care Clients in the Last Year of Life: Is Material Deprivation Associated...cont’d

80 years and those who were single were less likely to receive palliative care services than other groups. Inequalities in allocation of home care services based on age, diagnosis, and marital status, but not material deprivation, suggest the need to carefully match service with need at the end of life. *J Aging Health* 2011;23(6):954-73

Guided Imagery for Musculoskeletal Pain: A Systematic Review
Posadzki P, Ernst E

The objective of this systematic review was to assess the effectiveness of guided imagery (GI) as a treatment option for musculoskeletal pain (MSP). Six databases were searched from their inception to May 2010. All controlled clinical trials were considered, if they investigated GI in patients with any MSP in any anatomic location and if they assessed pain as an outcome measure. Trials of motor imagery were excluded. The selection of studies, data extraction, and validation were performed independently by 2 reviewers. Nine randomized clinical trials (RCTs) met the inclusion criteria. Their methodologic quality ranged between 1 and 3 on the Jadad scale. Eight RCTs suggested that GI leads to a significant reduction of MSP. One RCT indicated no change in MSP in comparison with usual care. It is concluded that there are too few rigorous RCTs testing the effectiveness of GI in the management of MSP. Therefore, the evidence that GI alleviates MSP is encouraging but inconclusive. *Clin J Pain* 2011;27(7):648-53

Efficacy of Small Doses of Ketamine with Morphine to Decrease Procedural Pain Responses during Wound Care

Objective: The purpose of this study was to evaluate differences in pain intensity, pain quality, physiological measures, and adverse effects when patients received morphine with saline (MS) compared with morphine and a small dose of ketamine (MK) before an open wound care procedure (WCP). Methods: A randomized, cross-over design was used to determine whether the addition of a small dose of ketamine would potentiate morphine's analgesic effects and decrease WCP pain intensity. Patients were randomized to receive either 0.1 mg/kg of morphine (8 mg maximum) plus saline intravenously (IV) or 0.05 mg/kg of morphine (4 mg maximum) plus ketamine 0.25 mg/kg IV before the WCP. Patients were crossed-over to receive the alternate treatment during the next WCP. Results: Eleven male patients participated in the study. Mean rank of pain intensity during WCP-MK was significantly less than during WCP-MS (*P*=0.005). Mean±standard error of mean pain intensity during the WCP-MK was 3.09±0.99, whereas it was 6.82±0.92 during the WCP-MS. However, 91% of the patients had adverse effects (eg, strange sensations, hallucinations, blurred vision) with MK versus 0% with MS. Diastolic blood pressure was significantly higher during the WCP-MK. Discussion: Ketamine with morphine significantly reduced procedural wound pain intensity during WCP. Adverse effects and higher diastolic BP occurred with MK. Further research is warranted to determine the optimal analgesic dose of ketamine or if the addition of a benzodiazepine would mitigate the psychotomimetic effects of ketamine. *Clin J Pain* 2011;27(7):561-566
Pain in the Elderly: Validity of Facial Expression Components of Observational Measures
Sheu E, Versloot J, Nader R, Kerr D, Craig KD

Objectives: Assessing pain in elderly persons, who have diminished capacity to communicate verbally, requires use of observational scales that focus upon nonverbal behavior. Facial expression has been recognized as providing the most specific and sensitive nonverbal cues for pain. This study examined the validity of facial expression components of 6 widely used pain assessment scales developed for elders with dementia. Descriptions of the facial expression of pain vary widely on these scales. Methods: The detailed, anatomically based, objectively coded, and validated Facial Action Coding System was used as a criterion index to provide a definitive description of the facial expression of pain. Thirty elderly inpatients with clinically significant pain in the back or hip, the majority of whom had cognitive impairments, provided videotaped reactions to physical activities. Participants' facial expressions were videotaped during 4 randomly ordered physical activities and coded by a qualified Facial Action Coding System coder. Three 6-second clips indicative of mild, moderate, and severe pain intensities were selected for study for each participant. The 90 clips were coded by 5 raters using the facial expression components of the following observational scales: Dolopulus-2, Mahoney, Abbey, pain assessment checklist for seniors with limited ability to communicate, noncommunicative patient’s Pain Assessment Instrument, and Pain Assessment in Advanced Dementia. Results: Overall, scales that provided specific descriptions using the empirically displayed facial actions associated with pain yielded greater sensitivity, interjudge reliability, and validity as indices of pain. Discussion: Facial expression items on observational scales for assessing pain in the elderly benefit from adherence to empirically derived descriptions. Those using the scales should receive specific direction concerning cues to be assessed. Observational scales that provide descriptors that correspond to how people actually display facial expressions of pain perform better at differentiating intensities of pain. Clin J Pain 2011;27(7):593-601

Prevalence of Life-Threatening Conditions in Children
Randall V, Cervenka J, Arday D, Hooper T, Hanson J

We estimated the prevalence of children with life-threatening conditions (LTC) cared for in the military health system (MHS) in response to a Congressional inquiry and to inform program planning. Methods: We developed a case definition of LTC, using the concept “death trajectory”1,2 to define our cases. We conducted an unduplicated count of children with LTC in the MHS database during FY 2001/FY 2002 using selected ICD-9 codes based on our case definition. We then surveyed the literature for reported prevalence of LTC among children with similar case definitions. The concept of “death trajectory” describes non-categorical life-threatening conditions of four types: progressive decline to death (e.g., spinal muscular atrophy); intermittent periods of intensive care to maintain quality-of-life (e.g., cystic fibrosis); curative treatment is possible but may fail (e.g., childhood cancers); and severe but non-progressive disability with extreme health vulnerability (e.g., spastic quadriplegia with tracheotomy). Results: There were 3,976 children identified with LTC in a population of 2.6 million children, for a prevalence of 0.15%. Conclusion: A prevalence of 0.15% for children with LTC in the MHS population agrees closely with that derived for similar case definitions by other authors among populations of children in other single-payer health care systems (i.e., United Kingdom). The method used here may apply to similar health care systems with ICD 9 codes in a searchable database. Am J Hospice Palliat Care 2011;28(5):310-315

Please Note: This newsletter includes news briefs and abstracts of the current literature related to hospice and palliative care. Because abstracts are not always accurate reflections of the content of the article, please refer to the complete journal article before making changes to practice or patient care based on the information contained in this update.

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Adverse Experiences with Implantable Defibrillators in Oregon Hospices
Fromme EK, Stewart TL, Jeppesen M, Tolle SW

Implantable cardioverter-defibrillators (ICDs) improve survival in patients at risk for recurrent, sustained ventricular tachycardia or fibrillation. Unless deactivated, ICDs may deliver unwanted shocks to terminally ill patients near the time of death. This study sought to determine the frequency and nature of adverse experiences with ICDs in hospice programs and what preventative measures the programs had taken. Method: A mailed survey to all 50 Oregon Hospice Programs in August 2008. Results: 42 (84%) of 50 programs participated. In all 36 (86%) of 42 programs reported having taken care of a patient with an ICD in the preceding 4 years. The average number of patients with ICDs per program increased from 2.2 (SD 2.5) in 2005 and 2006 to 3.6 (SD 3.7) in 2007 and 2008. Of the 36 programs who had cared for a patient with an ICD, 31 (86%) reported having some kind of adverse experience. These ranged from unwanted shocks delivered (64%), patient/family distress related to the decision to deactivate the ICD (47%), and time delay in ICD deactivation (42%). Only 16 (38%) programs had policies for managing ICDs and only 19 (43%) routinely screened new patients for ICDs. Discussion: As patients near the end of their lives, receiving defibrillating shocks may no longer be consistent with their goals of care. Based on the high frequencies of potentially preventable adverse outcomes documented by this study, we propose that hospices routinely screen patients for ICDs and proactively adopt policies to manage them, rather than in response to an adverse event. Am J Hospice Palliat Care 2011;28(5):304-309

Sertraline or Mirtazapine for Depression in Dementia (HTA-SADD): A Randomized, Multicenter, Double-blind, Placebo-controlled Trial

Depression is common in dementia but the evidence base for appropriate drug treatment is sparse and equivocal. We aimed to assess efficacy and safety of two of the most commonly prescribed drugs, sertraline and mirtazapine, compared with placebo. We undertook the parallel-group, double-blind, placebo-controlled, Health Technology Assessment Study of the Use of Antidepressants for Depression in Dementia (HTA-SADD) trial in participants from old-age psychiatry services in nine centres in England. Participants were eligible if they had probable or possible Alzheimer’s disease, depression (lasting ≥4 weeks), and a Cornell scale for depression in dementia (CSDD) score of 8 or more. Participants were ineligible if they were clinically critical (eg, suicide risk), contraindicated to study drugs, on antidepressants, in another trial, or had no carer. Participants were to receive sertraline (target dose 150 mg per day), mirtazapine (45 mg), or placebo (control group), all with standard care. The primary outcome was reduction in depression (CSDD score) at 13 weeks (outcomes to 39 weeks were also assessed), assessed with a mixed linear-regression model adjusted for baseline CSDD, time, and treatment centre. Decreases in depression scores at 13 weeks did not differ between 111 controls and 107 participants allocated to receive sertraline or mirtazapine, or between participants in the mirtazapine and sertraline groups. These findings persisted to 39 weeks. Fewer controls had adverse reactions (26%) than did participants in the sertraline group (43%) or mirtazapine group (41%), and fewer serious adverse events rated as severe. Five patients in every group died by week 39. Because of the absence of benefit compared with placebo and increased risk of adverse events, the present practice of use of these antidepressants, with usual care, for first-line treatment of depression in Alzheimer’s disease should be reconsidered. Lancet 2011;378(9789):403-411
Promoting Excellence in End of Life Care: Lessons Learned from a Cohort of Nursing Home Residents with Advanced Huntington’s Disease
Dellefield ME, Ferrini R

Huntington disease (HD) is a genetic neurodegenerative disorder that progresses over decades and is ultimately terminal. As HD advances, patients are frequently placed in institutional care settings, including nursing homes and hospices where family, nursing staff, and interdisciplinary team members are challenged to help patients live to their highest potential and die with dignity. Edgemoor, a distinct part of the San Diego County Psychiatric Hospital, is a regional referral facility for patients with HD. Over the past 8 years, we have cared for 53 patients with advanced HD and describe our experiences by presenting their demographic characteristics and the lessons we have learned in caring for them. Ultimately, we found that the Robert Wood Johnson Foundation’s Promoting Excellence in End-of-Life Care Initiative provided a meaningful framework for setting clinical priorities. This framework is used to summarize the clinical lessons that nursing staff and interdisciplinary team members learned about caring well for institutionalized individuals with advanced HD. *J Neurosci Nurs* 2011;43(4):186-192

Urinary Incontinence Nursing Considerations at the End of Life
Baker B, Ward-Smith P

Urinary incontinence occurs at the end of life either as a consequence of treatment(s) for a urologic health condition or as the result of disease progression. End-of-life urinary incontinence conditions include bladder abnormalities (urge, emptying, hesitancy), infection, and/or the need for diversional methods. Alterations in skin integrity may be the result of previous treatment(s) to the urinary system and lower abdomen, or from urinary incontinence. Treated urinary incontinence at the end of life provides dignity and will maintain quality of life. This article describes the urinary care needs and options for individuals receiving end-of-life care. *Urol Nurs* 2011;31(3):169-72

General Principles of Antimicrobial Therapy
Leekha S, Terrell CL, Edson RS

Antimicrobial agents are some of the most widely, and often indiscriminately, used therapeutic drugs worldwide. Important considerations when prescribing antimicrobial therapy include obtaining an accurate diagnosis of infection; understanding the difference between empiric and definitive therapy; identifying opportunities to switch to narrow-spectrum, cost-effective oral agents for the shortest duration necessary; understanding drug characteristics that are peculiar to antimicrobial agents (such as pharmacodynamics and efficacy at the site of infection); accounting for host characteristics that influence antimicrobial activity; and in turn, recognizing the adverse effects of antimicrobial agents on the host. It is also important to understand the importance of antimicrobial stewardship, to know when to consult infectious disease specialists for guidance, and to be able to identify situations when antimicrobial therapy is not needed. By following these general principles, all practicing physicians should be able to use antimicrobial agents in a responsible manner that benefits both the individual patient and the community. *Mayo Clinic Proc* 2011;86(2):156-167

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Clinically Significant Drug Interactions at the End of Life
Herndon CM

Potential drug interactions encountered at the end of life may be cumbersome to predict and have significant impact on the palliation of symptoms. Recent advances in identifying metabolic pathways and metabolites of frequently used medications allow clinicians to consider the fate and pharmacodynamic effects of drugs prescribed. Numerous medications used in the palliative care population undergo hepatic and extrahepatic metabolism to active and inactive metabolites. Hepatic reactions rendering medications prepared for excretion or removal from the system are complex, but may be summarised for medications frequently used in end-of-life care as Phase 1 oxidation, hydroxylation, and reduction reactions, and Phase 2 glucuronidation reactions. Both general types of drug metabolism pathways may be altered by medications, disease states, and normal ageing processes. Specific to end-of-life care, Phase 1 reactions may become less robust, while Phase 2 reactions are typically preserved. Benzodiazepines, opioids, non-opioid analgesics, and hypnotics may all exhibit additive or reduced efficacy when given concurrently with medications which inhibit or induce these pathways. Unexpected dose-related toxicity or adverse effects may also manifest. In summary, understanding and anticipating potential drug interactions in end of life and palliative care is paramount for the health professional. Prog Palliat Care 2010;18(3):147-156

Role of the Pharmacist in Palliative Care
Walker KA

Pharmacists are uniquely positioned to provide expert medication advice and education, thus creating a specialised role within the team providing end-of-life care dedicated to rational medication use. The role of pharmacists varies among different palliative care practice settings; however, all pharmacists participate in providing pharmaceutical care. Countries vary greatly in the accepted definitions to describe pharmaceutical care and in the scope of pharmacy practice. Activities of pharmacists can include detecting and resolving drug-related problems, advising providers on appropriate medication use, medication reconciliation, creating medication guidelines, education and many more. Pharmacy organisations support pharmacists as key members of interdisciplinary care, and there is growing recognition of the value of their contribution. This review will explore the role of the pharmacist and available literature supporting outcomes associated with pharmacy involvement in palliative care. Pharmacists provide valuable patient care, contribute to a growing literature base of medication knowledge, and participate in the education of patients, families and fellow professionals. Prog Palliat Care 2010;18(3):132-139