“Palliative Care: Tricks of the Trade”

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Improvement in Symptoms for 2500 Mount Sinai Hospital Patients Followed by the Palliative Care Service (6/97-10/02)

Symptoms are improved by PC consultation or transfer at VCU-Massey

M-ESAS scale 0-3
30 pts with at least 2 consult days and symptoms >0
Khatcheressian J, et al. Oncology September 2005
PC service does provide better care than average, on most measures.

<table>
<thead>
<tr>
<th>Key Performance Measure</th>
<th>Median</th>
<th>VCU PC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain assessment within 48 hours of admission</td>
<td>98.5%</td>
<td>100%</td>
</tr>
<tr>
<td>Use of a numeric scale to assess pain</td>
<td>83.7%</td>
<td>82%</td>
</tr>
<tr>
<td>Pain relief or reduction within 48 hours of admission</td>
<td>78.3%</td>
<td>83%</td>
</tr>
<tr>
<td>Vital signs recorded with initial treatment order</td>
<td>89.1%</td>
<td>90%</td>
</tr>
<tr>
<td>Depress assessment within 48 hours of admission</td>
<td>95%</td>
<td>100%</td>
</tr>
<tr>
<td>Depression relief or reduction within 48 hours of admission</td>
<td>80%</td>
<td>82%</td>
</tr>
<tr>
<td>Document patient status within 48 hours of admission</td>
<td>15.6%</td>
<td>95%</td>
</tr>
<tr>
<td>Psychological assessment within 4 days of admission</td>
<td>17.8%</td>
<td>40%</td>
</tr>
<tr>
<td>Patient/family meeting within 1 week of admission (discussion must include planning and/or preferences for discharge)</td>
<td>40.5%</td>
<td>65%</td>
</tr>
<tr>
<td>Plan for discharge disposition documented within 6 days of admission</td>
<td>55%</td>
<td>90%</td>
</tr>
<tr>
<td>Discharge planner / social services arranged services required for death</td>
<td>75%</td>
<td>90%</td>
</tr>
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Prevalence of Symptoms Volunteered by Advanced Cancer Patients

4 Wks and 1 Wk Before Death (N=90)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>N(%) 4 Wks</th>
<th>N(%) 1 Wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>52(58)</td>
<td>47(52)</td>
</tr>
<tr>
<td>Pain</td>
<td>49(54)</td>
<td>31(34)</td>
</tr>
<tr>
<td>Generalized Weakness</td>
<td>30(33)</td>
<td>44(49)</td>
</tr>
<tr>
<td>Sleepiness</td>
<td>22(24)</td>
<td>51(57)</td>
</tr>
<tr>
<td>Mental Haziness/Confusion</td>
<td>22(24)</td>
<td>25(28)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>19(21)</td>
<td>16(18)</td>
</tr>
<tr>
<td>Weakness of Legs</td>
<td>16(18)</td>
<td>15(17)</td>
</tr>
<tr>
<td>Shortness of Breath</td>
<td>15(17)</td>
<td>25(28)</td>
</tr>
<tr>
<td>Nausea</td>
<td>11(12)</td>
<td>12(13)</td>
</tr>
<tr>
<td>Decreased Hearing</td>
<td>8(9)</td>
<td>5(6)</td>
</tr>
<tr>
<td>Depression</td>
<td>7(8)</td>
<td>4(4)</td>
</tr>
<tr>
<td>Loss of Appetite</td>
<td>7(8)</td>
<td>5(6)</td>
</tr>
<tr>
<td>Inability to Sleep</td>
<td>6(7)</td>
<td>5(6)</td>
</tr>
</tbody>
</table>
**Patient Risk Factors**

- Uninsured or underinsured
- No prescription plan or partial plan
- Not on disability
- Inmates of Correctional Facilities
- Homeless
- Very young or very old
- Undocumented
- No primary care physician
- Unable to communicate verbally
- Unable to speak English
- Unable to read and/or write
- Mental illness, including depression
- Caregiver for someone else
- No caregiver

**Caregiver Risk Factors**

- Elderly
- Disabled
- Unreliable
- Very young
- Employed (family leave act)

**Family caregivers and the SUPPORT study**

*JAMA 1995;272:1839*

- Patient needed large amount of family caregiving: 34%
- Lost most family savings: 31%
- Lost major source of income: 29%
- Major life change in family: 20%
- Other family illness from stress: 12%
- At least one of the above: 55%
Living Conditions: Risk Factors

- Unsafe neighborhood: (hospice/home health unable to visit during night and/or day due to safety concerns)
- Drug diversion
- Patient lives in a nursing facility
- Stairs to bathroom or bedroom
- No running water
- No electricity
- No telephone
- No Food Stamps / Not enough food
- Rural location
- Unreliable or no transportation

Healthcare disparities:
Unequal access or utilization by minorities

- Medically underserved and minorities less likely to use hospice/palliative care
  - National hospice data -- about 50% expected utilization
  - VA Predictors of hospice use included older age, white race, married, better SES, less comorbidity (smith, under review)
- Much anecdotal experiences

Knowledge and Planning:
Risk Factors for Not Receiving Good Palliative/Hospice Care

- Limited understanding of disease and prognosis
- No living will/advance directive
- No knowledge about hospice/palliative care options
- Community/cultural suspiciousness, fear of discriminatory practices
Health Care Providers Risk Factors

- Don’t understand patient’s culture
- Attitudes/prejudices/behaviors because patient is underserved and/or in some way “different” from the HCP.
- May not understand risk factors, eg pt frequently a “no show” because transportation, child care, etc., a priority; NOT because he/she willingly misses appointments.

Deficiencies in medical education

Billings & Block JAMA 1997;278:733.

- 74% of residencies in U.S. offer no training in end of life care.
- 83% of residencies offer no hospice rotation.
- 41% of medical students never witnessed an attending talking with a dying person or his family, and 35% never discussed the care of a dying patient with a teaching attending.

Some useful hints

- Depression
  - “Are you depressed?” is 100% accurate (Chochinov H. JAMA 1997)
  - We recognize depression 17% of cases, anxiety 6% of cases (Newell S. Cancer 1998)
  - Treat like anyone else
  - Consider Ritalin

- Dyspnea
  - “Are you short of breath?” better than O2 sat
  - Treat with opiates and/or benzos
  - Nebulized fentanyl 25 mcg in 2 ml NS
Nebulized fentanyl for dyspnea

Patients said that it helped
- Improved 26/37 (79%)
- Unsure 3/37 (8%)
- None 4/37 (12%)

P=0.002
P=0.03

Noisy, moist breathing, occurs in 35-92% of patients in their last hours of death sometimes referred to as death rattles. In one study, median time from onset of “death rattle” to death was 23 hours. This can be a very distressing symptom to families

TREATMENTS
- Scopolamine, may be given Sub Q or IV (0.4mg) and/or as transdermal patch (patch may take 4-12 hours to work).
- Atropine causes less CNS depression, restlessness and delirium. However, the risk of tachycardia increases with doses >1.0mg.
- Glycopyrrolate - produces less sedation agitation and lasts longer than SQ scopolamine. However, not as effective as scopolamine.
TREATMENTS

Non-Pharmacological Treatments

• Re-positioning the patient

• Pharmacological methods are usually as effective as suctioning, therefore suctioning is not recommended. Suctioning is uncomfortable and may cause significant agitation and distress. In one study, only 3 of 81 patients required suctioning in the end of life.

Some useful hints

- Anorexia/cachexia
  - Assess goals of care
  - Common
  - Megace 200-400 mg/day trial
  - No evidence feeding helps unless disease reversible
  - "Not everyone needs to die with a PEG." - Don Kirby, MD

Some useful hints

- Agitation/Delirium
  - Common
  - Terrible for families
  - Reassure that it’s not mental illness
  - Use haloperidol, not benzo’s
There are two important types of delirium

- **Hypoactive**
  - distinguish from depression
  - distinguish from psychosis
  - or metabolic problems
  - 0.5 mg Haloperidol

- **Hyperactive**
  - or acting out
  - 1-5 mg Haloperidol

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**Agitation**

- Haloperidol 0.5 mg – 1.0 mg PO/SC in 4-8 hour intervals
- Continue same dose Haloperidol every 12 hours scheduled
- Evaluate to continue, taper or dc
- Titrate up by 1 mg every 1 hour until desired effect achieved (1mg, 2 mg, 3 mg, etc); MDD 30 mg
- Lorazepam 0.5 mg PO/IV/SQ
- Continue Lorazepam
- Evaluate regularly to taper or discontinue
- Physician/Nurse/Pharmacist consultation
- Relief no relief after MDD Haldol every 1 hour as needed (notify MD before initiating this step)
- MDD 12 mg

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**Neuroleptics**

- **Indications**
  - Continuous neuropathic pain, nausea, anxiety, insomnia, agitation, restlessness, delirium, dementia, psychosis, tenesmus, hiccuphs
- **Toxicities**
  - Sedation, orthostatic hypotension, confusion, extrapyramidal reactions, tardive dyskinesia, jaundice
- **Drugs**
  - Haloperidol, prochlorperazine, chlorpromazine, promethazine, methotrimeprazine, fluphenazine
Some useful hints

- **Fatigue**
  - 70% of patients report it
  - Exercise helps
  - Ritalin 5 mg tabs every 2-3 hours helps

Why compound?

- Fills a need for unique medications that industry does not provide.
- Often industry will not pursue or introduce certain medications due to high costs associated with FDA approval as well as development costs and risks.
- Drugs being used off label may be obtained.
- Drugs in short supply may be formulated.

(Coyne 06)

Why compound? (continued)

- Compounding individual medications can modify ingredients to prevent allergies.
- Prepare medications using alternate delivery system such as suppository, ointments.
- Compounded drugs may be created to treat rare diseases when other treatments don’t exist.
Reasons for concerns

- Physicians and pharmacists currently are not required to obtain training or certification in compounding.
- Individuals have died from contaminated medications.
- One case example of this industry issues were related poor inspection, were in North Carolina there were a contaminated compounded steroid was produced and distributed. N.C has 6 inspectors to evaluate 2000 pharmacies. The take home message is there is limited oversight, and it varies state to state.

Evaluating Compounded Drugs

- Doctors & nurses as well as others need to understand how bioavailability, absorption, sterility, safety, efficacy and stability can cause impact all medications.
- However often with compounded medications information and research are lacking.

Safety and Efficacy

- Most compounded medications have not been clinically tested to determine their efficacy or adverse effects.
- Through an informal internet search, 5 random compounding pharmacies were selected, they listed medications available, only 3 of 18 medications listed had some research basis for treatment of the indication.
Safety and Efficacy (CONT)

- Lack of a standardized system makes tracking adverse effects difficult.
- Lack of standardization of compounding makes efficacy difficult to determine, as different pharmacist use different agents and carriers.
- In 2001 the FDA examined the potency, quality and purity of compounded medications obtained over the Internet. The study demonstrated 34% failed 1 or more standard quality test. Note this was a small sample.

End of Story

- Compounding medications offer great opportunities to improve comfort as well as other benefits.
- Much is unknown about compounded medications therefore increased risks may be present.
- If a large pharmaceutical company hasn’t produced a compounded medication of a frequently used drug questions should be raised.

Figure 1.1: Effect of interventions on pain control

<table>
<thead>
<tr>
<th>Months</th>
<th>Pain VAS Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
</tr>
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Dupre S, et al JCO 2000
Smith T, et al JCO 2002
Questions Regarding Pain Control...

- What about the 20% who do not get relief from the WHO ladder or the 46% of those whose families stated we failed? (Tolle, 2001)
  - Have the opioids been titrated aggressively?
  - Is the pain neuropathic?
  - Has a true pain assessment been accomplished?
  - Have invasive techniques been employed?
  - Have you examined the patient?
  - Is the patient receiving their medication?
  - Is the medication schedule and route appropriate?

Today’s Issues

- PAIN MANAGEMENT

- Over 50% of patients will require a new route of analgesia in the last two weeks of life (Coyle, 1990).

- Over a third of patients will require 25% or more opioids in the last month of life.

- 40% of oncologists surveyed thought there is a ceiling effect dose to morphine. However, oncologists knowledge of pain overall is very good to excellent. Their major weakness is in assessment (Levin, 1998).

Today’s Issues (cont’d)

- Over 50% of patients with advanced cancer have 7 or more sites of pain.

- 70% of physicians (and nurses) in one study could not convert opioids using an equianalgesic comparably. This is extremely important if new routes are sought.
Equianalgesic conversions

- morphine PO = oxycodone PO
- 1 mg morphine IV = 3 mg PO morphine
- 1 mg IV morphine/hr = 25 mcg IV fentanyl
- 1 mg IV morphine = 10 mcg IV fentanyl
- 5 mg morphine = 1 mg dilaudid (PO and IV)
- 10 mg PO morphine = 1 mg PO methadone
- 200 mcg Fentanyl lozenge = 2 mg IV morphine
- 2 mg PO Methadone = 1 mg IV Methadone

Methadone

- Acute pain: methadone = morphine (1:1)
- Chronic pain: ratio depends upon previous opioid dose (methadone:morphine)
  - < 90 mg (1:5)
  - 91-299 mg (1:10)
  - >300 mg (1:12 or 20)
- Torsade de Pointes, EKG needed for most, qt over 450 millisecond

Methadone

- May be more effective in neuropathic pain syndromes than other opioids
- More potent than previously reported
- Patient may require significantly lower doses resulting in less side effects
- $ - Inexpensive  (Mannino 07)
What does work for cancer neuropathy

Tramadol (Ultram) vs. Placebo


Adult Acute Pain Management

At 24 hours, calculate the total morphine equivalent (PCA and bolus) used and convert to long acting if basal needed

Continue PCA dosing, reassessment and dose adjustment as needed
Role of Invasive Procedures...

- Intractable pain
- Intractable side effects

Intrathecal/Epidural Titration Guidelines

Massey Cancer Pain Center at Virginia Commonwealth University

Use epidural trial dose to obtain initial opioid dose (always preservative free).

Intrathecal dose = 10% of epidural dose.

Morphine is typically the opioid of choice due to its hydrophylic nature; however, hydromorphone may also be utilized (of note preservative free morphine is the only opioid approved by the FDA).

Consider changing to or adding clonidine.

The local anesthetic should be stopped if no relief was achieved.

Clonidine initial starting dose 50mcg/day. When titrating intrathecal pump with clonidine monitor for hypotension. May increase by 15% by q24 hours as outpatient, may increase by 15% q 12 hours as inpatient.

If the dose of clonidine reaches 850mcg/day intrathecally without relief, another medication should be considered, such as:

- Droperidal 25-250mcg/d
- Ketamine 25-1000mcg/d
- Baclofen 10-1000mcg/d
- Midazolam 50-2000mcg/d
- Ziconotide

Cancer pain, acute pain service or palliative care consult highly recommended.

Dilaudid or morphine may increase by up to 20% every 12 hours as inpatient prn. Monitor level of sedation, pain assessment scores, functional level and side effects.

If titrating above 25mg/day of MS04 or 6mg/day of Dilaudid intrathecally without relief consider initiating bupivacaine.

Dilaudid or morphine may increase by up to 20% q24 hours as outpatient prn. Monitor level of sedation, pain assessment and scores, functional level and side effects.

Starting dose of bupivacaine intrathecally is about 3 mg/day. When titrating with local anesthetic may increase by 15% q12º as inpatient, q24 hours as outpatient prn.

Monitor for level of sedation, pain assessment and scores, functional level and side effects, leg weakness, dermatome (sensory) level, and urinary retention.

Systemic Local Anesthetics

- Indications
  - Neuropathic pain

- Toxicities
  - Dizziness, nausea, tremor, nervousness, incoordination, headaches, paresthesias

- Drugs
  - Lidocaine, mexiletine

Note – If patients require frequent refills, consult pharmacy to determine if higher concentrations are available.
Intravenous Lidocaine
100 mg IVPB, 30 min

- Some studies demonstrate long-lasting pain relief even after drug has been stopped
- More effective in neuropathic pain but can be used for all pain syndromes. Starting dose 0.5mg-2 mg/kg per hr IV or SC. (Ferrini, Paice, 2004)

Ketamine

- N-methyl-D-aspartate receptor antagonist (NMDA)
- Used as an anesthetic for years
- Case reports show effectiveness when traditional and invasive techniques fail
- Starting dose 150mg qd (0.1-0.2mg/kg) with reduction of opioid achieved
- Appears to have a synergistic effect with opioids

Other Ideas

- Cocaine, nerve blocks, sedation