On-Demand Clinical News

Managing Anxiety in EOL

Kristin Braschler, PharmD, BCPS

Anxiety is common in end-of-life. This symptom present in about 70% of medically ill patients, 50% of COPD patients, and 25% of cancer patients[1]. Anxiety as a symptom is different from an anxiety disorder, which can be debilitating and interfere with a patient's functioning and quality of life. The most common anxiety disorders in our population include PTSD, generalized anxiety disorder, and panic disorder[1]. Adjustment disorder with anxious features is also very common in our hospice population[1], particularly those moving into nursing homes and other facilities.

Benzodiazepine therapies such as lorazepam and alprazolam are very commonly used in hospice. However, more often than probably recognized, benzodiazepines can make anxiety or agitation worse. While their main effect is sedation, side effects commonly include but are not limited to hallucinations, confusion, delirium, and excitation (or paradoxical reaction)[1,2]. For this reason, they are not always the first-line therapy for anxiety treatment[1]. Whenever benzodiazepine therapy is initiated, patients should be monitored closely for possible worsened symptoms or untoward effects.

Anxiety is often a result of an underlying, primary cause (or several of them). It is important to evaluate for, and address, underlying causes of anxiety. These include but are not limited to nausea, pain, dyspnea, drugs and/or depression[1]. Of note, delirium is commonly mistaken for anxiety, as it often appears or presents similarly to anxiety. For example, patients may appear distracted, indecisive or restless[1]. However, delirium and anxiety often require different management.

Often, non-pharmacologic management and addressing possible underlying causes of anxiety can effectively reduce the patient's symptoms, and should always be considered before adding pharmacologic therapy.

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Complex Symptoms: Focus on Agitation

Excerpt from December Lunch & Learn

Meri Madison, PharmD, CGP

Agitation in hospice patients can be difficult to treat, however identifying strategies that individualizes patient care will allow for better management. Some strategies are: using routine and PRN orders, minimizing pill burden through selecting medications that treat multiple symptoms, and by planning ahead to make sure medications are on hand.

Agitation is a symptom that is present in most hospice patients and can be exacerbated by many different external causes.

Potential Causes of Agitation Include:

- ***Infection*** (encephalitis, meningitis, UTI, pneumonia)
- ***Medications*** (Opioids, steroids, anticholinergics, phenothiazines and/or benzodiazepines)
- ***Withdrawal*** (alcohol, nicotine, barbiturates, benzodiazepines, antidepressants)
- ***Metabolic disorder*** (electrolyte imbalance, hepatic or renal failure, hypothyroidism)
- ***CNS pathology*** (stroke, hemorrhage, tumor, seizure disorder, Parkinson's)
- ***Hypoxia*** (anemia, cardiac failure, pulmonary embolus)

In order to control and/or alleviate these symptoms a patient specific approach is necessary. The identification of possible contraindications in the current drug regimen is essential for success in treatment.

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Consider the following non-pharmacologic methods for management of anxiety[1]:

- Healing touch
- Reduce dose or discontinue stimulating medications such as oral steroids or stimulants (e.g., methyphenidate)
- Avoid caffeine and alcohol
- Massage therapy
- Aromatherapy
- Light therapy (for example, place patient near a window/sunlight, or place lamps nearby)
- Fresh air
- Cognitive behavioral therapy (CBT)
- Music therapy
- Relaxation skills
  - Guided imagery
  - Progressive muscle relaxation
  - Mantra

If pharmacologic treatment is warranted, consider the following therapies (Tables 1 and 2) for patients with anxiety. In end-of-life, treatment of anxiety with medications should be based on prognosis and severity of symptoms[1].

Table 1: anxiety therapy for prognosis ≤ 2 months

<table>
<tr><th colspan="4">PROGNOSIS ≤ 2 MONTHS</th></tr>
<tr><th colspan="2">Mild to Moderate Anxiety</th><th colspan="2">Severe Anxiety</th></tr>
<tr><td colspan="2">Trazodone PRN[1] or gabapentin PRN[1]
+/-
scheduled buspirone</td><td colspan="2">Lorazepam PRN[1]
+/-
scheduled clonazepam[1]
+/-
scheduled buspirone</td></tr>
<tr><td>TRAZODONE
DOSING/COMMENTS:

Trazodone 25mg PO Q2H PRN anxiety, not to exceed 3 doses without reevaluation[1]
• Monitor use with other serotonergic and QT prolonging medications, such as SSRIs
• Sedating (may be beneficial)</td><td>GABAPENTIN
DOSING/COMMENTS:

Gabapentin 100mg PO Q2H PRN anxiety, not to exceed 3 doses without reevaluation[1]
• Watch doses if patient with renal impairment.
• Sedating (may be beneficial)</td><td>LORAZEPAM (ATIVAN)
DOSING/COMMENTS:

Lorazepam 0.5-1mg PO Q4H PRN anxiety <u>OR</u>
Lorazepam 0.25mg PO Q2H PRN anxiety[1]
• Preferred over alprazolam (Xanax), which has two active metabolites
• Alprazolam (Xanax) also not preferred due to greater risk of euphoria, faster onset/offset and worse withdrawal reaction as compared with lorazepam[1]</td><td>CLONAZEPAM (KLONOPIN)
DOSING/COMMENTS:

Clonazepam 0.25-0.5mg PO QHS initial dose, may increase dose and/or frequency every 72 hours[2]
• Preferred long-acting benzodiazepine[1] over diazepam (Valium), which has active metabolites</td></tr>
<tr><td colspan="4">BUSPIRONE DOSING/COMMENTS[2]:
Buspirone 7.5mg PO BID initial dose; may increase every 2-3 days in increments of 2.5mg twice daily to a maximum of 30mg twice daily
• Particularly useful/effective in COPD patients
• Has low potential for cognitive or motor impairment
• Well tolerated in the elderly
• Monitor for signs of any dopamine-related movement disorders (eg, dystonia, akathisia, pseudo-parkinsonism)
• Use in severe hepatic or liver impairment not recommended
• Does not exhibit cross-tolerance with benzodiazepines or other sedative/hypnotic agents; if substituting buspirone for any of these agents, gradually withdraw the sedative/hypnotic prior to initiating buspirone</td></tr>
</table>

SSRI = selective serotonin reuptake inhibitor (examples: citalopram, escitalopram, fluoxetine, paroxetine, sertraline)

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Table 2: anxiety therapy for prognosis > 2 months

PROGNOSIS > 2 MONTHS	
Mild to Moderate Anxiety	**Severe Anxiety**
SSRI[1] +/- Trazodone PRN or gabapentin PRN[1] +/- scheduled buspirone	SSRI[1] +/- Benzodiazepines[1] +/- scheduled buspirone

SSRI* DOSING/COMMENTS[2]
(see Table 1 for dosing/comments on other recommended therapies):

Citalopram (Celexa) 20mg once daily; this is a therapeutic dose and an initial dose, even in the elderly

- avoid doses >20mg in patients 60 years and older due to increased risk of QT prolongation
- additional efficacy with doses >40mg daily has not been demonstrated in clinical trials

Escitalopram (Lexapro) 10mg once daily; dose may be increased to a maximum of 20mg once daily after at least 1 week

Fluoxetine (Prozac) 10mg/day; after 1 week, increase to 20mg/day; may increase after several weeks; maximum recommended dose 60mg/day

- give in the morning; can be activating

Paroxetine (Paxil) 20mg once daily, preferably in the morning (if dose is increased, adjust in increments of 10mg/day at 1-week intervals

- doses of 20-50mg/day were used in clinical trials; however, no greater benefit was seen with doses >20mg
- max dose in renal (CrCl<30) or severe liver impairment: 40mg/day (50mg/day if CR formulation)

Sertraline (Zoloft) 25mg once daily; increased after 1 week to 50mg once daily; maximum dose: 200mg daily

- Drug interactions (particularly with medications metabolized by CYP2D6), serotonin syndrome, and QT prolongation should be considered when initiating therapy with an SSRI

*SSRI = selective serotonin reuptake inhibitor; list is not all-inclusive

Remember that since SSRIs and other common antidepressants take several weeks for full effect, they also must be tapered off slowly (over several weeks) to prevent unpleasant withdrawal effects.

Consult a ProCare clinical pharmacist to guide therapy selection, to avoid or manage anticipated drug interactions or side effects, recommend a starting dose, check dose adjustments for liver/renal function, or titrate up or taper off doses.

References:

1. Hirst, Jeremy. "Mental Illness at the End of Life: Improving the Practice of Interdisciplinary Team Members". NHCPO webinar online. November 13, 2014.
2. Lexi-Comp Online™ , Lexi-Drugs Online™, Hudson, Ohio: Lexi-Comp, Inc.; March 2015

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Metformin Use in Hospice Patients

Sheri Irvine, PharmD

The use of metformin in hospice patients is typically not recommended due to increased risks of negative side effects like GI discomfort and hypoglycemia. Metformin is not necessary for palliation of pain and/or symptom management. With declining renal function, use of metformin may also lead to risk of lactic acidosis.

Metformin is currently contraindicated in patients with a serum creatinine ≥1.5mg/dL in males or ≥1.4mg/dL due to increased risk of lactic acidosis. However, recent studies indicate the lactic acidosis is extremely rare with approximately 3 cases per 100,000 of patients per year. While many organizations, including the American Diabetes Association, are looking to relax the prescribing practices, metformin is still not recommended in patients with unstable or severe renal dysfunction.

Table 1. Recommended Prescribing Practices Based Of Estimated GRF

eGFR (ml/min)	Maximum Daily Dose	Renal Function Monitoring
>60	2550 mg	Annually
45-59	2000 mg	Every 3 to 6 months
30-44	1000 mg	Every 3 month. Do not initiate therapy, but may continue if patient taking
<30	Do not use	N/A

References

1. Lexi-Comp Online™ , Lexi-Drugs Online™, Hudson, Ohio: Lexi-Comp, Inc.; March 2015
2. PL Detail-Document, Clinical Use of Metformin in Special Populations. Pharmacist's Letter/Prescriber's Letter. March 2015.

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The identification of possible contraindications in the current drug regimen is essential for success in treatment. For example, the use of haloperidol is contraindicated in Parkinson's disease as it can exacerbate symptoms. Are the doses adequate or causing toxicity? We can avoid side effects by appropriately titrating up to a tolerable dose that adequately controls agitation.

Table 1. Agitation Medication Therapies

1st Line for Agitation	Alternatives for Agitation
• Haloperidol (Haldol) 0.5-5mg PO Q2-6H ATC & PRN • Chlorpromazine (Thorazine) 25mg PO Q8H & Q2H PRN	• Ativan 0.5-1mg PO/SL Q4H PRN anxiety/restlessness • Trazodone 25mg PO Q4H PRN agitation • Phenobarbital 30mg PO/SL/PR BID • Quetiapine 25-50mg PO BID

Creating an individualized plan is crucial in controlling refractory agitation. The assessment of a patient based on current medications, comorbidities, and potential causes will allow for proper medication selection and control of refractory symptoms. The utilization of medications that will treat multiple symptoms will also increase compliance. Using a team approach to manage a hospice patient during end of life care will make the patient and family members more comfortable.

References

1. Symptom Management at End of Life. Care Search Palliative Care Knowledge Network. Online Available from: http://www.caresearch.com.au/caresearch/ClinicalPractice/Physical/EndofLifeCare/SymptomManagementattheEndofLife/tabid/741/Default.aspx
2. Palliative Pharmacy Care. JM Strickland. Agitation and Delirium. Pgs. 77-89. American Society of Health-System Pharmacists. Bethesda, MD. 2009.
3. Lexicomp Drug Database. Available by subscription only from: online.lexi.com.

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