Psychopharmacology at the End of Life

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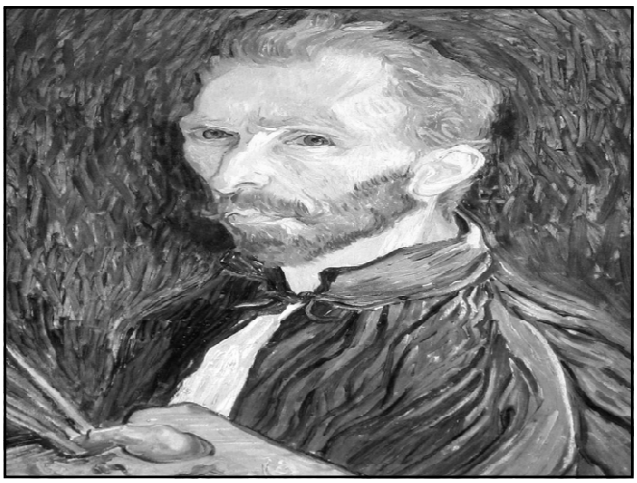
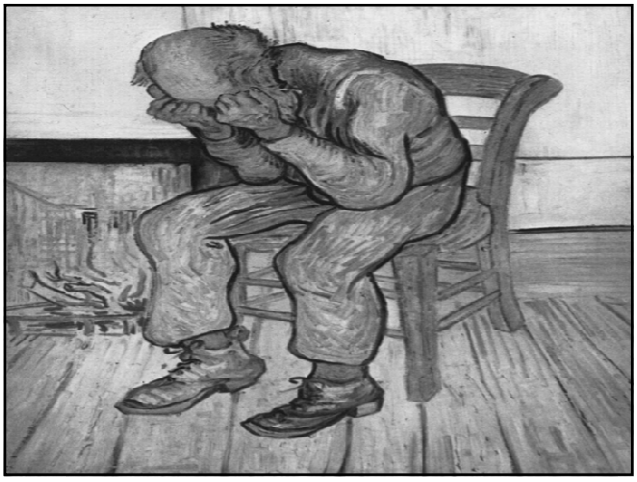


Objectives

- Describe 2 common psychiatric symptoms that can present at or near end of life.
- Review the differential diagnoses for end of life psychiatric symptoms.
- Discuss the pros and cons of 3 medications used in specific end of life symptoms



CASE #1: 79 yo man with metastatic pancreatic cancer

- Referral for: "sadness" and low energy
- Nonresectable tumor, attempting chemotherapy with gemcitabine, nausea
- Current symptoms: sadness, lack of enjoyment, hopeless, helpless, anxiety, poor energy, insomnia, no suicidal ideation, no psychosis
- Other medical conditions: hypertension, hypercholesterolemia, obesity, chronic back pain
- Current meds: oxycodone SR, oxycodone, prochlorperazine, lorazepam, ondansetron, atorvastatin, atenolol

Considerations?

- Previous history of psychiatric issues? Previous treatment?
- Time course of symptoms?
- Abusing narcotics? Abusing lorazepam?
- Psychosocial issues?
- Prognostic awareness?
- Poor pain control? Nausea control?

Differential diagnosis

- Adjustment disorder with depression
- Major depressive disorder
- Depression secondary to alcohol dependence
- Depression secondary to narcotic dependence
- Depression secondary to pain
- Bereavement

Case #1: Treatment Considerations

- ALWAYS make sure medical treatments are optimized
  - Pain control (consider longer acting options if addiction is concern)
  - Nausea control
- Traditional antidepressant options
- Atypical antipsychotic?
- Stimulant?
- Future possibilities?

Mirtazapine (Remeron)

- Alpha-2 antagonist; disinhibits serotonin and norepinephrine release
- FDA Indications: Major depressive disorder
- Dosage: 15-45 mg qhs
- Blocks H1→weight gain, sedation, drowsiness
- Blocks several serotonin receptors
  - 5HT1A→anxiolytic, antidepressant
  - 5HT2A→anxioltyic, antidepressant, no sexual dysfunction
  - 5HT2C→anxiolytic, weight gain
  - 5HT3→no GI problems, no nausea

Olanzapine (Zyprexa)

- Serotonin/Dopamine Antagonist
- FDA Indications: schizophrenia, bipolar disorder, major depressive disorder, tx resistant
- Off label: mood symptoms, agitation, delirium, nausea
- Dosage: 2.5-30 mg po qhs
- Less extrapyramidal symptoms
- Antiemetic properties (5HT3)
- Weight gain (5HT2C, H1)

Methylphenidate (Ritalin)

- Release dopamine from presynaptic terminals
- FDA Indications: ADHD, narcolepsy
- Off label: narcotic induced confusion, chemotherapy induced fatigue
- Dosage: 5-15 mg bid-tid
- Improve concentration, apathy, mood and energy
- Benefits: fast acting for energy, mood if effective
- Side effects: jitteriness, appetite suppression, psychosis (rare)

Ketamine

- NMDA receptor antagonist
- FDA Indications: general anesthesia induction and maintenance
- Off label: May possibly rapidly improve mood in palliative care patients with single oral dosage
- Dosage:
- Side effects: delirium, hallucinations, dissociation

Case #2: 55 yo woman with stage IV lung cancer

- Referral for "anxiety"
- Primary lung lesion with known metastases to brain, not currently on chemotherapy, on observation but no referral to hospice yet
- Current symptoms: restless, agitation, pacing, intermittent confusion, mood lability, jerking movements in extremities
- Other medical conditions: atrial fibrillation, hypothyroidism, COPD, fibromyalgia
- Current meds: fentanyl, oxycodone, lorazepam, levothyroxine, digoxin, duloxetine, amiltriptyline

Considerations?

- Thyroid status?
- Digoxin level?
- Pain control?
- Psychiatric history?
- Pattern of benzodiazepine usage? Narcotic usage?
- Serotonin syndrome?

Differential diagnosis

- DELIRIUM!
- Drugs e.g. alcohol, opiates, anticonvulsants, recreational, post-general anesthetic
- Electrolyte imbalance e.g. hypoglycemia, uremia, liver failure, hypo/hypernatremia
- Lacking medication/drugs e.g. alcohol withdrawal, benzodiazepine withdrawal
- Infections e.g. encephalitis, meningitis
- Reduced sensory input e.g. lack of sleep
- Intracranial e.g. trauma, strokes
- Urinary/fecal retention
- Myocardial (MI) or pulmonary (pneumonia)

Serotonin syndrome

- Symptoms: Agitation or restlessness, confusion, rapid heart rate, high blood pressure, twitching muscles, heavy sweating, diarrhea, dilated pupils, headache, shivering, goose bumps
- If severe: irregular heart rate, high fever, seizures, unconsciousness
- Rule out: alcohol withdrawal, thyroid conditions, anticholinergic syndrome (amitriptyline level), neuroleptic malignant syndrome, amphetamine usage
- Treatment: stop serotonergic medications, supportive care, cyproheptadine

Cyproheptadine (Periactin)

- Antagonizes central and peripheral histamine H1 receptors, serotonin receptor antagonist
- FDA Indications: allergic rhinitis, urticaria, anorexia nervosa
- Off label: serotonin syndrome
- Dosage: 4-8 mg bid

Case #2: Treatment considerations

- Treat medical conditions first!
- Minimize sedating medications
- Opioid rotation if concern for opioid induced neurotoxicity
- If concern for serotonin syndrome stop all serotonergic medications
- If no medical etiology found consider treating delirium with antipsychotics

Haloperidol (Haldol)

- Conventional antipsychotic blocks D2 and alpha 1
- FDA Indications: psychosis, tourette syndrome, acute agitation
- Dosage: 2 mg po q6h with 2 mg po q1h prn or 1mg IV q6h and 1mg IV q1h prn
- Lacks potent antimuscarinic and antihistaminic activity
- Side effects: decreased blood pressure, dizziness, drowsiness, QTc prolongation (check baseline EKG)

Bottom Line

- Medically complex
- Polypharmacy issues are the norm; try to simplify if at possible and use medications with multiple actions
- Team approach (oncologist, palliative medicine, primary care, psychiatrist, pharmacist) and communication is key

References

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