Depression and Comorbidities: Common Diseases and Conditions Effected by Depression

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Objectives

Discuss the prevalence of depression in certain medical conditions

Explore factors with each comorbidity that would predispose one to depression

Propose current treatment strategies for medical conditions complicated by depression
General Information

Many chronic medical conditions are accompanied by depression

Increases the burden of illness

- More complicated course
- Worse outcomes
- Greater expense
- Lessens quality of life
General Information

Diagnosis hard to make

- Many symptoms overlap
  - Fatigue
  - Lack of appetite
  - Poor sleep
  - Anhedonia
  - Cognitive changes
Cardiovascular
Cardiovascular

Acute cardiovascular disease 15-22%
- 65% report some symptoms of depression

By diagnosis
- CHF 24-42%
- CABG 20%
- MI 40%

Concerning
- Only 25% depressed heart patients diagnosed
- Of those diagnosed only about half treated
Congestive Heart Failure (CHF)

Depression five times more common than in the general population

- Depressed CHF patients over 50yo
  - Mild 35%
  - Moderate 33.5%
  - Severe 9%

- Types of depression
  - 13.9% age 18 or older had MDD
  - Over 35% had significant subsyndromal depression
CHF

Outcomes

- Reduced function
- Higher readmission rates
- Higher mortality risk
- Greater severity and decline after 6 months
  - Holding for co-morbid medical conditions, clinical severity, baseline function, demographic factors
- Twice as likely to be readmitted or die
Coronary Artery Bypass Graft (CABG)

20% will develop depression
- Most have no history of depression

Will affect recovery from the surgery
- Worsens fatigue
- Leads to more withdrawal post-op
- Makes pain more intense
- Increases risk of morbidity and mortality following surgery
Myocardial Infarction (MI)

Two years later (Van Melle, et al., 2004)
- If depressed, mortality risk was twice as high as non-depressed post-MI patients

Depressed a week after MI (Frasure-Smith, et al., 1993)
- 3-4 times more likely to die in 6 months

Beck Depression Scale score on admit (Lesperance, et al., 2002)
- The higher score the greater the 5-year mortality rate
Increased risk of CV disease

Depression

- Four times the risk of an MI
  - Increases relative risk 1.64
- Independent risk factor for heart disease
- Exacerbates classic symptoms of heart disease
  - Smoking, diabetes, obesity, inactivity
- Hospitalized depression
  - Triples the risk for heart disease
Do cardiac drugs cause depression?

Beta-blockers

- No increase risk of depression symptoms
- Small increased risk of fatigue, sexual dysfunction

Statins

- Suspected of leading to depression, suicide
- Not found in follow-up studies
- Long-term use actually associated with feelings of well-being
Plausible Mechanisms

**Autonomic imbalance**
- Too much sympathetic, too little parasympathetic
  - Lack of variability in heart rate
  - Ventricular arrhythmia and sudden cardiac death

**Platelet activation, endothelial dysfunction**
- Exaggerated platelet reactivity
- Impaired flow mediated dilation
  - Endothelial dysfunction
  - Not in cardiac vessels, however
Plausible Mechanisms

Hypothalamic-pituitary-adrenergocortical and sympatheic adrenal medullary activation

- High cortisol levels with HPA activation
  - Hypertension, atherosclerosis
  - Endothelial injury

- Sympathoadrenal activation
  - High levels of catecholamines
    - Vasoconstriction
    - Rapid HR
    - Platelet activation
Plausible Mechanisms

Inflammatory cytokines

- Atherosclerosis
  - Cytokines etiologic factor
- CRP
  - Induced by cytokines
- Damage to endothelium
  - Release of IL-1, IL-6, TNF-alpha
- Depressed
  - Higher levels of these markers
Plausible Mechanisms

Anticholinergic inflammatory pathway

- Vagal tone inhibits the release of cytokines
- Stimulate the vagus nerve
  - Exercise
  - Biofeedback
  - Meditation
Plausible Mechanisms

Polymorphism in the serotonin transport promoter region gene (Otte, 2007)

- Two alleles
- Long and short
- Short one promotes depression

MI patients

- More likely to have another event if they had a short gene allele
Treatment

Psychotherapy

- No efficacy
  - MHART (Montreal Heart Attack Readjustment Trial, 1999-2005)
    - Phone calls and home visits
  - ENRICHD (Enhancing recovery in Coronary Heart Disease, 1998-2001)
    - CBT
  - CREATE (Candesartan trial in Japan, early 2000s)
    - Interpersonal therapy
Treatment

Medications

- Tricyclics
  - Avoid in cardiac patients
- SSRIs
  - Reduce cardiac morbidity
  - SADHART (Sertraline Anti-Depressant Heart Attack Trial, early 2000s)
    - Death and non-fatal MI 20% lower
    - Sertraline
  - ENRICHD
    - Death and non-fatal MI 42% lower
    - Sertraline
Treatment

Medication

- Depression
  - SADHART and CREATE
    - Effective use of sertraline and citalopram in treating depression
  - MIND-IT (Myocardial Infarction and Depression-Intervention Trial, 1999-2002)
    - Mirtazapine
    - No efficacy in cardiac patients
Treatment

Medications

- SSRIs
  - Less risk of MI than other anti-depressants
    - Lower ischemia
    - Higher bleeding rates

CABG

- Preop SSRIs
- More death, rehospitalization
  - Marker of depression pre-operatively more than the effect of the SSRI
Treatment

Sertraline, citalopram recommended

- Acute phase 1-3 months
  - Sertraline 50-150mg
  - Citalopram 10-40mg

- Continuation phase 4-9 months

- Then, slowly taper the medication

- Other classes
  - TCAs not recommended
  - SNRIs, bupropion, mirtazapine all used
Stroke
Stroke

500,000/year

- 70-80% survive
- Up to 50% may have depression

Most diagnosed within 1-2 months

- 17-52% develop depression
- Major Depressive Disorder 50%
- Minor Depression 50%

10-20% not diagnosed until 6-12mos later
- Only a few develop symptoms after 1 year
Stroke

Various settings

- Rehabilitation
  - 27-55%
- Outpatient clinic
  - 40%
- Community
  - 62%
Stroke

Severity

- The more severe the stroke the greater the risk of depression
  - 66% in those most impaired

History of pre-morbid depression

- Only 1 in 5 depressed stroke victims had a history of mood problems that predate the stroke
Stroke

Significant effect upon recovery

- 21/55 of depressed patients whose mood improved had a more significant recovery than those who remained depressed
- Affects ability to participate in therapy
  - Less interest
  - Less effort
  - More easily frustrated
  - More fatalistic
Stroke

Why do they get depressed?

- Physiology v. psychosocial debate
  - The effect of the stroke on areas of the brain that control mood, emotion
    - Frontal and temporal lobes
    - Neurotransmitters

- Inflammatory
  - Cytokines

- Genetic
  - 5-HTTLP
    - Serotonin transporter polymorphism
Stroke

Why do they get depressed?

Physiologic v. psychosocial debate

Response to change

- Self image
  - Lack physical robustness
  - See self as damaged

- Activity
  - No longer able to hobbies, occupations
  - Less enjoyment or purpose

- Independence
  - Dependent upon others now
  - Transportation, finances, ADLs, decision-making
Stroke

Treatment

- Psychotherapy
  - CBT
    - Mainly positive
    - Over several months in moderate and severe post-stroke depression

  Problem-solving therapy
    - Teaching skills to deal with everyday problems
    - Limited, but positive data
Stroke

Treatment

Medications

Some indication of efficacy

- Nortriptyline
  - Limited by side effects
- SSRIs
  - No one choice
    - Serotonin, then citalopram
- Venlafaxine
- Mirtazapine
  - Open-label trial to prevent PSD
COPD
COPD

Higher incidence of depression than the general population

- 6-42% historically
  - 42-57% most recent numbers
- Most have never had depression
  - High risk of first depressive episode
- More likely to experience recurrent depression
- More likely as age
- More likely in moderate to severe disease states
- Often untreated
COPD

Disease course
- More exacerbations
- More hospitalizations

Pulmonary rehabilitation (Jennings, 2009)
- 16.5% had depressive symptoms
- Depressed rehab patients had almost 3 times the rate of illness exacerbation in a year
- Had their first exacerbation earlier in time
COPD

What causes this?

- Physiologic v. psychosocial
  - Breathing
    - Established link
      - Rapid breathing and anxiety
      - Hypoventilation and depression
      - Effort, posture in depressed patients
  - Oxygenation
    - Brain consumes 40% oxygen
    - COPDers often have a 50% reduction in oxygen
    - Hypoxia leads to cognitive impairment and depression
What causes this?

- Physiologic v. psychosocial
  - Nicotine
    - Smokers rate of depression high
      - More depressed, smoke more
    - Depressed adolescents are more likely to begin and continue smoking

Are there possible genetic links between smoking and depression?

- Brain MRIs of depression and smokers look alike
- Long-term nicotine exposure to neurobiological systems implicated in depression
  - Noradrenaline and dopamine
COPD

What causes this?

- Physiologic v. psychosocial
  - Reduced activity
    - More fatigued
    - Physical pursuits may be given up
  - Body-image change, embarrassment
    - Dragging around oxygen
- Dependency
  - Cannot go anywhere without oxygen
- Anger about self destruction
  - Why did I smoke?
COPD

Medications

- Few adequate trials
  - Best trial is rather dated
    - Nortriptyline (Boorson, et al., 1992)
  - Paroxetine
    - Several studies
    - Positive, but not significant
    - Fluoxetine trial n=137 (Yohannes, 2001)
      - 72% refused treatment
      - 4/7 responded

- Bupropion, nortriptyline
  - Used in smoking cessation
COPD

Psychotherapy

- Few adequate trials
- Efficacy for CBT
  - Relaxation exercises
  - Exposure and desensitization
  - Identify automatic thoughts

Pulmonary rehabilitation

- Exercise
- Training about lung function
- Psycho-education
Diabetes
Diabetes

Prevalence

- 11% have Major Depressive Disorder
  - 31% have clinically-relevant depression (Anderson, et al., 2001)
- Up to 45% of diabetes patients may have undiagnosed depression (Li, et al., 2008)
- Depression rate with diabetes 17.6%
  - Without diabetes 9.8% (Ali, et al., 2006)
    - Women 23.8%
    - Men 12.8%
Diabetes

Bi-directional relationship

- Depression and type II diabetes
  - Consequence of diabetes
  - Risk factor for diabetes (Knol, et al., 2006)
- Depression associated with a 60% increase in diabetes
- Diabetes associated with a 15% increase in risk for depression (Mezuk, et al., 2008)
Diabetes

Two hypotheses

- Depression increases risk of diabetes
  - Poorly understood
    - Increased counter-regulatory hormone action
    - Alterations in glucose transport
    - Increased immunoinflammatory activation

- Lead to
  - Insulin resistance
  - Beta islet cell dysfunction
Diabetes

Two hypotheses

- Diabetes leads to depression
  - Chronic psychosocial stress
    - Having a chronic medical condition
- National Health and Nutrition Examination Survey Epidemiologic Follow-up Survey (NHANES) (Saydah, et al., 2003)
  - 9000 subjects; follow-up 9 years
  - Higher rate of depression in diabetics
- Rancho Bernardo study (Palinkas, et al., 1991)
  - 1560 older patients
  - 3.7x increased risk for depression in diabetics
Diabetes

Glycemic control

- Poor control blood glucose in Type I and II (Lustman, et al., 2000)
- Higher HbA1c over 4 years (Richardson, et al., 2008)

Self care

- Depressive symptoms predict poor self-care (Gonzalez, et al., 2008)
  - Less adherence to diet, exercise, and medications
Diabetes

Complications of diabetes

- Medical complications
  - Increases risk
    - Diabetic retinopathy, nephropathy, peripheral neuropathy, microvascular complications, sexual dysfunction (de Groot, et al., 2001)

- Social, societal costs
  - Increases risk of disability (Egede, et al. 2004)
  - Decreases work productivity (Egede, et al., 2004)
  - Decreases quality of life (Eren, et al., 2008)
Diabetes

Higher healthcare costs

- Higher costs than diabetes alone (Le, et al., 2006)
  - Diabetes-related...$3264/ $1297
  - Total....$19,298/$4819

Mortality rates

- Medicare (Katon, et a., 2008)
  - 36-38% increased risk of death
- NHANES (Zhang, et al., 2005)
  - Diabetics with depression 54% higher risk of mortality than diabetes alone
Diabetes

Treatment

- Three drug trials
  - Nortriptyline (Lustman, et al., 2000)
  - Fluoxetine (Lustman, et al., 2000)
  - Variety of antidepressants with CBT (Williams, et al, 2004)
  - Improved mood but not glycemic control

- Psychotherapy
  - Again help with mood (Wang, et al., 2008)
    - Not necessarily glycemic control
Diabetes

Medication

- **Appetite enhancing**
  - Paxil (paroxetine), Remeron (mirtazapine), Pamelor (nortriptyline)

- **Middle of the road**
  - Prozac (fluoxetine), Zoloft (sertraline)

- **Weight neutral**
  - Celexa (citalopram), Lexapro (escitalopram)
  - Effexor/Pristiq (venlafaxine/desvenlafaxine), Cymbalta (duloxetine)
  - Wellbutrin (bupropion)
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Propose current treatment strategies for medical conditions complicated by depression
Questions?