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11:30 a.m. to 12:15 p.m.

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"Bipolar Depression"

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Presentation Objectives:

1) Define Bipolar Depression (BD).
2) Discuss epidemiology of Bipolar Depression.
3) Clinical presentation.
4) Evaluation.
5) Acute treatment options.
6) Maintenance treatment options.

BIPOLAR DEPRESSION

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DEFINITION

Bipolar Disorder (formerly called manic depressive illness or manic depression) is a mental disorder that causes unusual shifts in mood, energy, activity levels, concentration, and the ability to carry out day to day tasks.[1]

CATEGORIES

BIPOLAR I

BIPOLAR II

CYCLOTHYMIA

MIXED FEATURES

CATEGORIES

BIPOLAR I

defined by manic episodes that last at least 7 days, or by manic symptoms that are so severe that the person needs immediate hospital care. Usually, depressive episodes occur as well, typically lasting at least 2 weeks[1].

CATEGORIES

BIPOLAR II

defined by a pattern of depressive episodes and hypomanic episodes, but not the full blown manic episodes that are typical of Bipolar I disorder[1].

CATEGORIES

CYCLOTHYMIA

defined by periods of hypomanic symptoms as well as periods of depressive symptoms lasting for at least 2 years (1 year in children and adolescents). However, the symptoms do not meet the diagnostic requirements for a hypomanic episode and a depressive episode.[1]

EPIDEMIOLOGY

- Affects more than 1% of the world's population
- Has no predilection for race, gender, ethnicity, or socioeconomic status
- Bipolar I has a higher lifetime incidence (0.6%)
- Bipolar II has a slightly lower incidence (0.4%)[2]

EPIDEMIOLOGY

- Mean age of onset is 18 for Bipolar I
- Mean age of onset is 22 for Bipolar II
- One-fourth of patients presenting with depression or anxiety in the primary care setting have been diagnosed with a bipolar disorder.[2]

ETIOLOGY

- There is a general consensus that there is a genetic component associated with Bipolar Disorder but the numbers range from 4 to 15% all the way up to 70-90% heritability[1,3].

ETIOLOGY

- Other theories include the ‘kindling’ hypothesis which states that bipolar disorder is triggered by a life stressing event and can be reactivated by subsequent stressors.[3]
- These stressors may include:
  - Adverse childhood events (ACE’s) or traumas[4]
  - Suicide of a family member
  - Disruptions of sleep cycle[1]

ETIOLOGY

- Progressive changes to brain structure are hypothesized to occur over time
- Aberrations in the hypothalamic-pituitary-adrenal axis are thought to play a role as well[2]
- Other factors that may contribute include Type 2 DM, use of psychoactive substances, smoking, or sedentary lifestyle

CLINICAL PRESENTATION

- Bipolar patients typically present with DEPRESSION
  - This can be misleading, though, and could lead to inappropriate choices of medication.
  - If they have failed on multiple SSRI's in the past, keep Bipolar disorder in mind.

CLINICAL PRESENTATION

- It is important to be purposeful in asking about signs/symptoms of mania or hypomania

- Periods of time where they don't require sleep
- Excessive risk taking
- Hypersexuality
- Spending sprees
- Multiple jobs
- Grandiose thoughts and goal setting
- Attempted suicide
- Substance abuse
- Irritability, irrationality
- Multiple divorces
- Legal troubles[2]

EVALUATION

- History and Physical
  - A thorough history, in particular, is crucial
- CBC (rule out pernicious anemia)
- CMP (rule out liver, kidney, or electrolyte abnormalities)
- TSH
- Prolactin level (+/-)
- Ammonia Level
- Pregnancy test

EVALUATION

- Urine Drug Screen
- Urinalysis
- EKG
- Others: heavy metal screen, urine porphyrins, Hepatitis C screen, and RPR[2]
- MRI or EEG may be indicated in certain cases if seizures or intracranial pathology is suspected[5]

EVALUATION

- USPSTF recommends screening for depression in all patients 12 and older
- Patient Health Questionnaire (PHQ-9) is a well established tool
- Mood Disorder Questionnaire (MDQ) can be useful for excluding bipolar disorder but is not sufficient to confirm the diagnosis[2]
  - It is the most specific (0.90)
  - It has a sensitivity of (0.73)
- Ultimately, the criteria in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) is used to help diagnose patients with Bipolar Disorder[2]

TREATMENT

ACUTE MANIA

- Mood Stabilizers
    - Lithium (especially for patients with euphoria)
    - Valproic Acid
    - Antipsychotics
        1. Often used with Lithium to help with sleep and other acute issues while the Lithium is taking effect (up to 5 days for steady state)[2]

TREATMENT

MIXED FEATURES

- Both depressive and manic/hypomanic symptoms present at the same time
- **Single agent therapy with antidepressants alone is contraindicated**
- Atypical Antipsychotics
  - Aripiprazole, Olanzapine, Risperidone, Ziprasidone
  - Asenapine, Cariprazine also helpful but cost can be an issue
- Carbamazepine
- Lithium not helpful

TREATMENT

ACUTE DEPRESSION

- **Always screen for Suicidal or Homicidal thoughts**
  - Quetiapine, Cariprazine, and Lurasidone in combination with Lithium or Valproic acid appear to be the most fast acting options
    - Side Effects such as weight gain, diabetes, and extrapyramidal effects must be considered[2]
  - Electroconvulsive therapy (ECT) also is an option

TREATMENT

ACUTE DEPRESSION

- If mood stabilizers are not sufficient, adding in an Selective Serotonin Reuptake Inhibitor (SSRI) or Buproprion is a reasonable choice
- Medications such as tricyclic antidepressants (TCA's), monoamine oxidase inhibitors (MAOI's), venlafaxine, and trazodone should be avoided because they are more likely to induce manic or hypomanic symptoms.[2]

MAINTENANCE THERAPY

Current guidelines recommend the following for maintenance therapy:

- Lithium
- Lamotrigene
- Quetiapine
- Quetiapine along with lithium or valproic acid
- Aripiprazole
- Olanzapine[2]
- Meta-analyses show that these medications may also be effective in reducing long term morbidity in juvenile bipolar disorder, but the study number, quality, and effect magnitude were limited so further studies are recommended[6]

SUMMARY

- DEPRESSION is the most common presenting symptom of Bipolar Disorder
  - Bipolar patients make up approximately 25% of the depressed patients that present to your office
- HISTORY can help make the diagnosis
- STABILIZE ACUTE MANIA
  - with lithium, valproic acid, and/or antipsychotics
- TREAT ACUTE DEPRESSION
  - with quetiapine, cariprazine, or lurasidone in combination with lithium or valproic acid for fastest results
- AVOID SSRI's in patients with MIXED FEATURES
- MAINTENANCE THERAPY includes lithium, valproic acid, and/or atypical antipsychotics

QUESTIONS?

BIBLIOGRAPHY

1. Bipolar Disorder. https://www.nimh.nih.gov/health/topics/bipolar-disorder/index.shtml
2. Bipolar Disorders: Evaluation and Treatment. Marzani MD, Gabrielle. Neff MD, Amy Price. American Family Physician. 2021 Feb 15; 103(4) : 227-239.
3. Bipolar Disorder. Carvalho MD, Ph.D, Andre F. Firth Ph.D, Joseph. Vieta MD, Ph.D, Eduard. N Engl J Med 2020; 383: 58-66
4. Environmental Risk Factors for Bipolar Disorders and High-Risk States in Adolescence: A Systematic Review. Menculini, Balducci, Attademo, et al. *medicina*. Dec 11, 2020
5. Bipolar Disorder (Quick Lesson). Avital, Schub. Cinahl Information Systems, Glendale, CA. Dec 14, 2018.
6. Maintenance Pharmacological Treatment of Juvenile Bipolar Disorder: Review and Meta-Analyses. Yee, Hawken, Baldessarini, Vazquez. International Journal of Neuropsychopharmacology (2019) 22(8): 531-540