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MRCPsych General Adult Module

Bipolar Disorder- 3

Developing people
for health and
healthcare

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GA Module: Bipolar Disorder-3

Aims and Objectives

- The overall aim is for the trainee to gain an overview of treatment guidelines for BPAD

- By the end of the sessions, trainee should have:
  - Developed an understanding of NICE guidelines for management of BPAD.
  - Developed an understanding of role of psychological therapies for BPAD

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To achieve this

- Case Presentation
- Journal Club
- 555 Presentation
- Expert-Led Session
- MCQs

- Please sign the register and complete the feedback

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Expert Led Session

Bipolar Disorder

Biopsychosocial management

Overview

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- NICE guideline CG 185 highlights (2014)
- Notes on Lithium and valproate
- Psychological therapy in BPAD
- 7 MCQ’S

Treatment of Mania/hypomania

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- Consider stopping antidepressant
- In patients not already taking a mood stabiliser:
- First line options include Risperidone, Olanzapine, Quetiapine and Haloperidol
- Switch in first instance if ineffective or not tolerated

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Treatment of Mania/hypomania

- If switch is ineffective or partially effective add lithium, aiming for levels of 0.6-0.8mmol/L
- Augment with Valproate if lithium is unsuitable or ineffective (avoid valproate in women of child bearing age)
- If already on Lithium, optimise levels and consider adding an antipsychotic from previous list

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Treatment of Mania/hypomania

- Do not offer Lamotrigine – no convincing evidence for use in acute manic episodes

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Treatment of bipolar depression

- In the first instance/patient preference:
  - Offer evidence based, manualised psychological intervention tailored for bipolar affective disorder OR
  - High intensity Psychological intervention (CBT, IPT etc) as advised in NICE clinical guideline for depression
- Unmedicated patients:
  - Olanzapine-Fluoxetine combination
  - Quetiapine
  - Olanzapine OR lamotrigine

Treatment of bipolar depression

- On Lithium:
  - Optimise levels (0.8-0.1mmol/L)
  - Add Olanzapine-Fluoxetine combination
  - Or Olanzapine OR lamotrigine

- On Valproate:
  - Optimise levels (50-100mg/L)
  - Add Olanzapine-Fluoxetine combination
  - Or Olanzapine OR lamotrigine (CAUTION as valproate can double lamotrigine levels)

Prophylaxis

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– Offer evidence based, manualised psychological intervention tailored for bipolar affective disorder

OR

– High intensity Psychological intervention (CBT, IPT etc) as advised in NICE clinical guideline for depression

PLUS…

Prophylaxis

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- Lithium as first line prophylaxis (0.6-0.8mmol/L)
- Consider higher maintenance levels (0.8-1.0mmol/L) if a patient has relapsed on lithium previously or is currently symptomatic and functionally impaired

- If lithium is ineffective: add valproate
- If lithium is not tolerated: Switch to valproate or olanzapine
- Consider switch to quetiapine if it has been effective in the past

Tapering

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- Mood stabilisers should be tapered over at least 4 weeks
- Lithium should be tapered over 4-12 weeks to prevent rebound mania
- Patients should be monitored for 2 years after stopping mood stabilising medication

Advice for GPs

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- Primary care
  - Offer evidence based, manualised psychological intervention tailored for bipolar affective disorder OR
  - High intensity Psychological intervention (CBT, IPT etc) as advised in NICE clinical guideline for depression

- Guidelines advise against:
  - commencing lithium in naïve patients unless shared care arrangements with a specialist are in place
  - Commencing valproate in primary care for treatment of BPAD

Referring to secondary care

- Poor or partial treatment response
- Poor compliance with treatment
- Significant side effects leading to intolerance
- Significant decline in function
- Comorbid ETOH or substance misuse
- Patient wishes to taper mood stabilising medication after remaining well for a period of time
- Women with bipolar affective disorder who are planning pregnancy or who are already pregnant

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Exam notes on valproate

- GABA agonist (in reality complex, multiple mechanisms)
- Third line treatment in Bipolar affective disorder
- First line treatment of generalised seizures
- Hepatically metabolised (CYP 3A4 inhibitor)
- Half life 9-16h
- Trough level required (50-100mg/L)
- Serious SE's - hepatic failure, pancreatitis, hyperammonaemic encephalopathy
- Major teratogen

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Clinical notes on valproate

- Avoid in women of childbearing age:
- Associated with development of PCOS
- Significant risk of NTD's (reported rates vary between 2-10%)
- 30-40 percent of children show evidence of developmental disorders (delayed milestones, cognitive impairment)

- Risk:benefit counselling should take place, with emphasis on outlining risks, the need to use effective contraception and to consult asap if planning pregnancy/pregnancy occurs.
- DOCUMENT ALL THIS THOROUGHLY.

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Clinical notes on lithium

- Most effective long term therapy for BPAD
  - Antimanic, antidepressant, anti-suicide

- Drawbacks classically described as:
  - Need for recurrent monitoring, including blood tests
  - Narrow therapeutic index and associated risk of serious toxicity
  - Side effect profile
  - Teratogenicity

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Exam notes on lithium

- Complex, multiple mechanisms of action
- First line prophylaxis in Bipolar affective disorder
- Renally excreted (unchanged)
- Half life 18-36h (peak 1-2h SR, 4-5h MR forms)
- 12h post dose levels required
- Narrow therapeutic window - toxicity risk
- Serious SE’s - hyperparathyroidism, hypothyroidism, nephrogenic diabetes insipidus
- Teratogenic – Ebsteins anomaly (tricuspid valve defect)

Clinical notes on lithium

- Recent meta analysis in the Lancet (Knight et al 2012) highlights:
  - Weight gain (less than Olz)
  - Hyperparathyroidism and associated rise in Ca (10%)
  - Hypothyroidism (OR = 6.05)
  - Reduced urinary concentrating ability (15% lower)

  - Evidence questionable for skin disorders, alopecia, clinically significant drop in GFR over short term
  - Teratogenicity also called into question but studies possibly underpowered

Psychological therapy in BPAD

- Growing RCT evidence base for psychotherapy as an adjunct to medication in BPAD:
  - CBT
  - Interpersonal Therapy
  - Social Rhythm Therapy (stabilizing patients' social and sleep routines and at improving the quality of their interpersonal relationships and their performance of key social roles.)
  - Psychoeducation

Psychotherapy in BPAD

- The course of bipolar disorder *can* be modified by interventions targeted at the social and environmental context.

- Foci include:

- Stressful events
- Interpersonal conflict
- Social and circadian rhythm disruption
- Medication non adherence

Further reading

- Cuijpers P, Geraedts AS, van Oppen P , et al. Interpersonal psychotherapy for depression a meta-analysis. Am J Psychiatry. 2011;168:581–92.
- Cuijpers P, Andersson G, Donker T, van Straten A. Psychological treatment of depression results of a series of meta-analyses. Nord J Psychiatry. 2011;65:354–64.
- Driessen E, Cuijpers P, de Maat SC , et al. The efficacy of short-term psychodynamic psychotherapy for depression a meta-analysis. Clin Psychol Rev. 2010;30:25–36.
- Cuijpers P, Smit F, Bohlmeijer E , et al. Efficacy of cognitive-behavioural therapy and other psychological treatments for adult depression meta-analytic study of publication bias. Br J Psychiatry. 2010;196:173–8.
- Cuijpers P, van Straten A, Bohlmeijer E , et al. The effects of psychotherapy for adult depression are overestimated a meta-analysis of study quality and effect size. Psychol Med.2010;40:211–23.
- Picardi A, Gaetano P. Psychotherapy of mood disorders. Clin Pract Epidemiol Ment Health. 2014; 10: 140–158.

MCQs

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1. Sodium valproate:

A - is mostly renally metabolised

B - commonly causes hypertrichosis

C - reduces lamotrigine levels

D - is licensed for prophylaxis of BPAD

E - is a first line choice in acute mania

1. Sodium valproate:

A - is mostly HEPATICALLY metabolised

B - commonly causes ALOPECIA

C - can DOUBLE lamotrigine levels

D - is licensed for prophylaxis of BPAD

E - is NOT a first line choice in acute mania (atypical antipsychotics or haloperidol)

2. Which of the following commonly causes hypercalcaemia:

A - Lithium

B - Valproate

C - Risperidone

D - Quetiapine

E - Clozapine

2. Which of the following commonly causes hypercalcaemia:

A - Lithium - up to 10%

B - Valproate

C - Risperidone

D - Quetiapine

E - Clozapine

3. Match the following to a drug from the list below:

1. Spina Bifida
2. Tricuspid valve defect
3. Cleft palate
4. Microcephaly

A - Lithium
B - Benzodiazepines
C - Valproate
D - None of the above

3. Match the following to a drug from the list below:

1. Spina Bifida (C Valproate and CBZ)
2. Tricuspid valve defect (A Ebsteins – Lithium)
3. Cleft palate (B Benzodiazepines)
4. Microcephaly (D none of these – ETOH as part of foetal alcohol syndrome or cocaine)

A - Lithium
B - Benzodiazepines
C - Valproate
D - None of the above

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4. The risk of Ebstein's anomaly in babies born to woman taking lithium is:

A – 1:50

B – 1:100

C – 1:500

D – 1:1000

E – 1:5000

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4. The risk of Ebstein's anomaly in babies born to woman taking lithium is:

A – 1:50

B – 1:100

C – 1:500

D – 1:1000 but consider new data from Knight's meta analysis in clinical practice

E – 1:5000

5. Lithium levels in once daily nocte dosing should be taken:

A - 4 hours post dose

B - 12 hours post dose

C - 6 hours post dose

D - immediately before the next dose

E - 8 hours post dose

5. Lithium levels in once daily nocte dosing should be taken:

A - 4 hours post dose

B - 12 hours post dose (0.6-0.8mmol/L prophylaxis, 0.8-1.0mmol/L in acute episodes)

C - 6 hours post dose

D - immediately before the next dose

E - 8 hours post dose

6. Which of the following drugs has a high therapeutic index:

A - Lithium

B - Carbamazepine

C - Phenytoin

D - Warfarin

E - Gabapentin

6. Which of the following drugs has a high therapeutic index:

A - Lithium

B - Carbamazepine

C - Phenytoin

D - Warfarin

E – Gabapentin

7. Match the following mood stabilisers to their chemical structure:

1. Haloperidol
2. Risperidone
3. Olanzapine
4. Quetiapine

A. Benzizoxazole
B. Dibenzothiazepine
C. Thienobenzodiazepine
D. Butyrophenone

7. Match the following mood stabilisers to their chemical structure:

1. Haloperidol D
2. Risperidone A
3. Olanzapine C
4. Quetiapine B

A. Benzizoxazole
B. Dibenzothiazepine
C. Thienobenzodiazepine
D. Butyrophenone

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