Update on Pharmacotherapy for PTSD in military personnel and veterans

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Scope

- Case study
- Clinical Practice Guidelines for PTSD
- Pharmacotherapy for:
  - Insomnia and nightmares
  - Anger and aggression
  - Agitation and arousal/anxiety
Case

• 35 yo male SF operator with 10 deployments to AFG, extensive combat experience, 2+ mTBI, witnessed death and wounding of a number of mates

• 4 year history of depressed mood, panic attacks, angry episodes, insomnia and nightmares, social withdrawal, intrusive disturbing memories, guilty rumination, poor concentration, increased startle and vigilance with increasing alcohol intake

• Self-referred for treatment six months previously

• Initially reluctant to accept Dx and Rx for PTSD and MDD

• Eventually had 6 x 90 minute sessions of Prolonged Exposure Therapy from clinical psychologist with good PTSD symptom reduction

JC
Case (ctd)

• Three months later symptoms of PTSD are worsening as he prepares to discharge and move to the country
  – Insomnia and nightmares
  – Explosive anger and aggression
  – Agitation and arousal
  – Impaired concentration and memory

Three potential target disorders:
• PTSD
• MDD
• mTBI/PPCS
Australian PTSD Guidelines

- Developed in consultation with experts and people affected by PTSD
- Supported by the Australian Government and approved by peak health research body
- Endorsed by professional associations

Available from www.phoenixaustralia.org
Indications for Pharmacotherapy for PTSD

- Drug treatments for PTSD should **not** be used as routine first-line treatment in preference to trauma-focused psychotherapy (B)
- When medication is considered, the class of SSRIs should be considered the first choice (C)
- Significant sleep disturbance after non-pharmacological interventions - hypnotics, if used, for no more than one month continuous use (GPP)
- Partial response to AD → increase dose, switch AD, adjunctive Prazosin, Risperidone, or Olanzapine (GPP)

First Line Monotherapy ‘Recommendations’

Selective Serotonin Reuptake Inhibitors (SSRIs)
- Sertraline
- Fluoxetine
- Paroxetine

Second Line Monotherapy ‘Suggestions’

Serotonin-Noradrenaline Reuptake Inhibitors (SNRIs)
- Venlafaxine

- Imipramine
- Phenelzine

Augmentation

• Cites strong evidence to recommend against augmentation with:
  – Atypical Antipsychotics
  – Benzodiazepines
  – Sodium Valproate
  (Low quality/absent evidence & association with known adverse effects.)

• Cites insufficient evidence to recommend Prazosin as monotherapy or augmentation
PTSD Pharmacotherapy Crisis

• Only two drugs approved by US FDA for PTSD
  – Sertraline and Paroxetine
• Their limited efficacy has necessitated poly-pharmacy and off-label prescribing
• Research and development of new drugs has stalled
• Called for new research on different agents, using different trial designs and development of a psychopharmacology clinical trials workforce and infrastructure.
Practical prescribing – beyond the evidence

- Dosages
- Duration
- Partial response
- Side-effects
- When to change
- When to augment
- Symptom priority – what to target first
- PBS/RPBS, TGA
- Controversial prescribing...
Insomnia and Nightmares

- Prazosin
- Mirtazapine
- Atypical antipsychotics
- Benzodiazepines/minor tranquillizers
- Melatonin
Adjunctive medications:

Prazosin

[Raskind et al. 2013]

- Several RCTs found it effective in reducing nightmares in PTSD [Boehnlein & Kinzie (2007); Calohan et al (2010); Raskind et al 2013]]. **Dose range 0.5 – 25 mg daily**

- Raskind et al 2018- large, multi-site, placebo controlled RCT of Prazosin in US veterans over 26 weeks found **no improvement** in sleep or distressing dreams on CAPS, Sleep Quality Index and CGI.

  - Possible reasons for lack of response included
    - Participants had to be clinically and psychosocially stable
    - High threshold for nightmare frequency and intensity may have selected treatment resistant cases
Adjunctive medications: Quetiapine

- Can reduce symptoms such as insomnia, nightmares, dissociation, hypervigilance and anger
- Dose range of 12.5 - 300 mg nocte for these purposes
- Need for Metabolic Monitoring
- Potential for misuse
- Problems with patient acceptability
Anger and Aggression

• Atypical antipsychotics
  – Quetiapine +/- Metformin 1000 mg daily with metabolic monitoring and lifestyle & nutritional advice to prevent weight gain [Newall et al 2012]
  – Aripiprazole 2-30 mg per day [Britnell et al 2017]

• Anticonvulsants
  – Sodium Valproate +/- Metformin
  – Lamotrigine
Agitation and Arousal

- Benzodiazepines
- Atypical antipsychotics

Both of these classes of medication require thorough risk-benefit appraisal and informed consent when used to treat PTSD-related symptoms.
Questions?