Prescribing for substance misuse: Alcohol detoxification

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Terminology and definitions

Previously:
- Sensible
- Hazardous
- Harmful
- Dependence

Current:
- Lower Risk
- Increasing Risk
- Higher Risk

Risk levels

<table>
<thead>
<tr>
<th>Risk</th>
<th>Men</th>
<th>Women</th>
<th>Common Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Risk</td>
<td>No more than 3-4 units per day on a</td>
<td>No more than 2-3 units per day on a</td>
<td>Increased relaxation, Sociability, Reduced risk of heart disease (for men over 40 and post menopausal women)</td>
</tr>
</tbody>
</table>

Risk levels

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<tr>
<td>Increasing Risk</td>
<td>More than 3-4 units per day on a regular basis</td>
<td>More than 2-3 units per day on a regular basis</td>
<td>Progressively increasing risk of: Memory loss, Low energy, Relationship problems, Depression, Insomnia, Impotence, Injury, Alcohol dependence, High blood pressure, Liver disease, Cancer</td>
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</table>
### Risk levels

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<td>Higher Risk</td>
<td>More than 8 units per day on a regular basis or more than 50 units per week</td>
<td>More than 6 units per day on a regular basis or more than 35 units per week</td>
<td>Same as common effects for Increasing Risk above</td>
</tr>
</tbody>
</table>

### Alcohol Use Disorders

- **Hazardous use of alcohol:**
  - 24% population
  - 33% Men
  - 16% Women

- **Alcohol Dependent:**
  - 4% (1.6 million)
    - 2% F: 6% M
    - Severe AD

### Alcohol-related harms

- **Acute:**
  - Homicide
  - Suicide
  - Other intentional injuries (i.e., interpersonal violence)
  - Domestic violence
  - Sexual assault
  - Unprotected sex
  - Motor vehicle accidents
  - Other accidents
  - Drowning
  - Burns
  - Public disorder

- **Chronic:**
  - Liver cirrhosis and other forms of alcohol-related liver disease
  - Hypertension and haemorrhagic stroke, CV disease
  - Cancers of the mouth, larynx, pharynx, and oesophagus
  - Colorectal cancer and breast cancer
  - Foetal alcohol syndrome (FAS) and foetal alcohol effects
  - Mental illness
  - Alcohol dependence syndrome

### Treatment gap in alcohol dependence

- Treatment gap = difference between number of people needing treatment for mental illness and number of people receiving treatment
- Alcohol abuse and dependence have the widest treatment gap among all mental disorders
- Less than 10% of patients with alcohol abuse and dependence are treated

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2010 Drugs Strategy for England
Kohn et al. Bull World Health Organ 2004;82:858–866*
Prevalence UK

Psychiatric patients
- CMHT (London) - 44% harmful alcohol use or recent substance use (Weaver 2003)
- Psychiatric IP (SW London) - 49% harmful alcohol use (1/12) and 27% drug use (1/12) (Barnaby 2003)
- Psychiatric IP (Oxfordshire) - 50% men and 29% women harmful alcohol use (1/12) (Sinclair 2008)

Primary care:
- AUDs 41.7% (95% CI: 23.0–61.7), but, alcohol problems were recorded correctly in only 27.3% (95% CI: 16.9–39.1) (www.warc.soton.ac.uk)

Hospital staff:
- AUDs 52.4% (95% CI: 35.9–68.7) of cases, and made correct notations in 37.2% (95% CI: 28.4–46.4) of case notes

Mental health professionals:
- AUDs 54.7% (95% CI: 16.8–89.6) of cases (www.warc.soton.ac.uk)

Identification of AUDs (39 studies)

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Mental health professionals:
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NICE CG115

Staff working in services provided and funded by the NHS who care for people who potentially misuse alcohol should be competent to identify harmful drinking and alcohol dependence. They should be competent to initially assess the need for an intervention or, if they are not competent, they should refer people who misuse alcohol to a service that can provide an assessment of need (KPI)

www.warc.soton.ac.uk
Wessex Alcohol Research Collaborative

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Recommendation 9:
"Conduct alcohol screening as part of routine NHS practice. If universal screening is not feasible focus on those..."
• with relevant physical or mental health conditions
• who have been assaulted
• at risk of self-harm ......
What is alcohol dependence?

- Recognizable pattern of signs and symptoms
- Secondary effects on body functioning
- Associated social impairment

ICD-10 Criteria for Alcohol Dependence Syndrome

- Three or more of the following manifestations should have occurred together for at least one month or, if persisting for periods of less than one month, should have occurred together repeatedly within a 12-month period:

ICD-10 Criteria for the Alcohol Dependence Syndrome (1)

- a strong desire or sense of compulsion to consume alcohol
- impaired capacity to control drinking in terms of its onset, termination, or levels of use, as evidenced by
  - alcohol being often taken in larger amounts or over a longer period than intended; or
  - by a persistent desire to or unsuccessful efforts to reduce or control alcohol use
- a physiological withdrawal state when alcohol is reduced or ceased, as evidenced by
  - the characteristic withdrawal syndrome for alcohol, or
  - by use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms;

ICD-10 Criteria for the Alcohol Dependence Syndrome (2)

- evidence of tolerance to the effects of alcohol, such that:
  - there is a need for significantly increased amounts of alcohol to achieve intoxication or
  - the desired effect, or a markedly diminished effect with continued use of the same amount of alcohol
- preoccupation with alcohol, as manifested by:
  - important alternative pleasures or interests being given up or reduced because of drinking; or
  - a great deal of time being spent in activities necessary to obtain, take, or recover from the effects of alcohol
- persistent alcohol use despite clear evidence of harmful consequences, as evidenced by continued use when the individual is actually aware, or may be expected to be aware, of the nature and extent of harm.
To summarise

Alcohol dependence
- Compulsion
- Lack of control
- Withdrawal state
- Tolerance
- Primacy of drinking
- Narrowing of repertoire
- Re-instatement
- Harm

Associated problems
- Long term heavy use
- Psychiatric problems
- Binge drinking
- Blackouts / fits / cirrhosis
- Cognitive disturbance
- Social problems

...not of themselves sufficient for a diagnosis

Withdrawal states
- Clear evidence of recent cessation or reduction of alcohol after repeated/ prolonged/ high dose use
- Symptoms fit withdrawal pattern and are not better accounted for by another disorder
- 3 or more of the following are present:

What is alcohol withdrawal?
- Tremor of the tongue, eyelids or hands
- Sweating
- Nausea, retching or vomiting
- Tachycardia or hypotension
- Psychomotor agitation
- Headache
- Insomnia
- Malaise or weakness
- Transient visual, tactile or auditory hallucinations or illusions
- Grand mal convulsions

What are the associated conditions?
- Delirium tremens (DTs)
  - characterised by increasing severity of withdrawal symptoms
  - Clouding of consciousness (disorientated with either excessive agitation or stupor)
  - Agitation, irritability
  - Hallucinations (visual hallucinations such as seeing things that are not present are most common)
  - Sensory hyperacuity (highly sensitive to light, sound, touch)
  - Grandmal seizures
  - Untreated DTs have a mortality of 10-20%
Mortality in 10%

Hallucinations, delusions

Psychotic
Marked over arousal
Fear, low mood, agitation
Emotional

+ altered consciousness
fits in 10%

Tremor, nausea, sleep disturbed, cramps, ↑ HR, (fits)
Somatic

Onset (duration)
1-2 days (1-3 days)
2-5 days (3-12 days)

Detoxification from alcohol

Aim
Prevent alcohol withdrawal effects (↓ GABA, ↑ Glutamate)
Reduce neurotoxicity and micronutrient imbalance

Pharmacotherapies
- Benzodiazepines
- Anticonvulsants
- B vitamin complex
- (Baclofen)
- (Topiramate)

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<td>Psychotic</td>
<td></td>
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<tr>
<td>Illusions, fleeting hallucinations</td>
<td>Hallucinations, delusions</td>
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<tr>
<td>Prognosis</td>
<td></td>
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<tr>
<td>Full</td>
<td>Mortality in 10%</td>
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Benzodiazepines
- Current ‘gold standard’
- Cross tolerance with alcohol
- Diazepam / Chlordiazepoxide (oxazepam in severe liver disease)
- Reduces risk of de novo seizures and second seizure in same episode
- Prevention of delirium
- No benefit for combined use with anti-convulsants

But:
- Addictive potential
- Safety aspects
- Potential ‘priming’ for future drinking
- Risk of relapse to other substances in high risk patients

Anticonvulsants

Carbamazepine
- Carbamazepine has also been shown to be efficacious and can be chosen as an alternative to benzodiazepines for alcohol withdrawal and seizure prevention

Mechanism
- Inhibit ‘kindling’ phenomena
- Improve sleep, anxiety and instability post detox
- Non addictive
- Interactions (especially in liver disease)

Lingford-Hughes et al. 2012
Longo et al. 2002; Malcolm et al 2002
Ait-Daoud et al. 2004
What are the associated conditions?

**Wernicke’s Encephalopathy (WE)**

- Classical triad of ataxia, oculary signs and confusion only present in 10% (Harper *et al.* 1986)
  - 23% present with ataxia only
  - 29% oculary signs
  - 82% confusion
- **Residual Korsakoff Psychosis**
  - Impaired short term memory
  - Confabulation

**Wernicke Encephalopathy - management**

1. **Prevention is better than cure**
2. Have a high index of suspicion (50% likely to have malnutrition)
3. On admission review nutritional status
   - Iv/im Parentovite (Pabrinex)
   - Oral balance complete multivit/min (Santogen Gold)

(Must ensure thiamin (and other B vitamins) replete before providing any additional iv glucose or feeding to prevent precipitating WE)

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**Micronutrient imbalance and WKS**

- Priority of alcohol over eating balanced diet
- Vomiting and diarrhoea prevent absorption
- Beer and wine contain carbohydrate which need thiamine for its metabolism
- Liver damage \( \downarrow \) capacity to store vitamins and metabolic demand (Seymour and Whelan 1999)
- Effects of malnourishment and alcohol appear to be additive:
  - Alcohol (p.o or i.m) reduces thiamine absorption
  - \( \downarrow \) absorption by 30-98% in malnourished alcoholics.
  - Absorption returned to normal after 6-52 high protein-high vitamin diet.

**Serum thiamine levels following i.m. and i.v. administration**

- Serum thiamine levels fall to 20% of peak values within 2 hours (Thomson, 1969)
- At high blood cone, thiamine is transported by passive diffusion.
- i.v. admin. Needed for rapid correction of brain thiamine levels.
Prevention of WKS
Thiamine should be given in doses toward the upper end of the 'British national formulary' range.
Offer prophylactic parenteral thiamine followed by oral thiamine to harmful or dependent drinkers:
− if they are malnourished or at risk of malnourishment or
− if they have decompensated liver disease
and in addition
− attend an emergency department or
− are admitted to hospital with an acute illness or injury.

Prevention & Treatment of WKS
Offer parenteral thiamine to people with suspected WE.
Maintain a high level of suspicion for the possibility of WE, particularly if the person is intoxicated.
Parenteral thiamine should be given for a minimum of 5 days, unless Wernicke's encephalopathy is excluded.
Oral thiamine should follow parenteral therapy.

After detox – what next?
Relapse Prevention:
Psycho social
Pharmacological

Psychological interventions are an important component of treatment
• Psychological interventions may be used alone or in combination with pharmacological treatments
Maintenance of abstinence / Control of drinking

- Disulfiram
- Acamprosate
- Oral naltrexone

NICE review
Acamprosate vs placebo
- 19 RCTs (N=4629)
- DSM or ICD diagnosis of AD
- Baseline mean 145 units alcohol/week
- Rx: 8-52 weeks
- FU: 12-24 months
- “High quality” evidence

Astinence (RR=0.83, 95%CI 0.77-0.88)

NICE review
Naltrexone vs placebo
- 27 RCTs (N=4296)
- DSM or ICD diagnosis of AD
- Baseline mean 99 units alcohol/week
- Rx: 12-24 weeks
- FU: 6-12 months
- “High quality” evidence

Return to heavy drinking (RR=0.83, 95%CI 0.75-0.91)

CG115
- After a successful withdrawal for people with moderate and severe alcohol dependence, consider offering acamprosate or naltrexone in combination with a psychological intervention to service users
CG115

- After a successful withdrawal for people with moderate and severe alcohol dependence, consider offering disulfiram in combination with a psychological intervention to service users who:
  - have a goal of abstinence but for whom acamprosate and oral naltrexone are not suitable, or
  - prefer disulfiram and understand the relative risks of taking the drug (see 1.3.6.12).

Disulfiram

- Acetylaldehyde dehydrogenase (ALDH) inhibitor
- Results in accumulation of acetylaldehyde
- ‘psychological threat’ and aversive mechanism of action
- Possible additional mechanism of brain dopamine increase (Gaval-Cruz & Weinshenker, 2009).

Summary

- AUDs are common in patients known to mental health services
- AUDs are often poorly recognised and treated
- Detoxification in necessary in patients with severe alcohol dependency
- Need to prevent DTs, WKS and seizures
- Detoxification is only one part of the process and relapse prevention needs to be integrated into the care plan
- AUDs need to be addressed if outcomes for mental health patients are to be improved