

Double Trouble : Alcohol and Mental Illness

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Contents

- **Alcohol**: epidemiology, screening, withdrawal, intervention and psychopharmacology
- **Dual Diagnosis**: epidemiology, bipolar disorder, assessment and diagnosis, treatment issues

Male mean weekly consumption / percentage males consuming over 50 units of alcohol per week 1994-6

<u>Health Authority</u>	<u>Mean weekly units alcohol</u>	<u>% males consuming > 50 units/ week</u>
Manchester	24.1	14.5
Salford & Trafford	21.6	12.2
N Cheshire	15.9	5.2
England	17.4	7.1
Bury and Rochdale	22.4	11.0

Life expectancy and Alcohol

<u>Region</u>	<u>England Average</u>	<u>Manchester</u>	<u>Gap in life expectancy at birth</u>
Life expectancy Males years at birth (2001-03)	76.2 years	71.8 years	4.4 years
Females years at birth (2001-2003)	80.7 years	77.8 years	2.9 years

Contribution of alcohol deaths (in months) to the life expectancy gap for males – 4.63 (8% of total gap)

Contribution of alcohol deaths (in months) to the life expectancy gap for females – 2.42 (6% of total gap)

Mortality from chronic liver disease and cirrhosis

Standard Mortality ratio (SMR)

2001-2002

<u>Local Authority</u>	<u>Male</u>	<u>Female</u>	
Manchester	228	209	17.8 per 100,000
Liverpool	209	204	17.5 per 100,000
Macclesfield	57	93	9.0 per 100,000
Blackpool	312	234	19.8 per 100,000
North West	138.0	140.0	13.5 per 100,000
England	100.0	100.0	9.6 per 100.000

Comparative evidence base

Mesa Grande (Miller et al 1998, 2002)

UK Review of effectiveness (Raistrick and Heather 2005)

Swedish Health Technology report (Berglund 2003)

HTP Scotland (2004)

All studies

1 Brief Interventions

2 Motivational Enhancement therapy

3 GABA Agonists

4 Opiate Antagonist

5 Social Skills Training

Kindling 2

1 Severity of withdrawals correlates :

Amount alcohol consumed

Duration of consumption

Number of withdrawal episodes *

2 Withdrawal seizure correlate with
number previous withdrawals

3 Effects on GABA, Glutamate and
neuronal death

Kindling- clinical implications

- 1 Careful withdrawal history >5 may need inpatient treatment
- 2 To detox or not detox- maximise the chance of success
- 3 Limiting detoxifications
- 4 Kindling and relapse
- 5 Cognitive dysfunction and brain damage
- 6 Neuroprotective strategies -alternatives to benzodiazepines , acamprosate ?

Risk factors for DTs

Predisposing

various authors

Severe dependency,
High BAC when withdrawals occur
Drinking pattern
Abrupt cessation of intensive drink
Kindling processes eg prev DTs
Recent epileptic seizure
Concurrent medical problems
Metabolic abnormalities
Use of sedative-hypnotic drugs
Older age
Male sex

Positive predictors

Palmstierna T, 2001; Sweden

Infectious disease
Tachycardia at admission >120
Withdrawals with BAL $> 1\text{g/L} = 7$ units
History of epileptic seizures
History of delirious episodes

Lee J et al, 2004; Korea

History of delirium tremens
Tachycardia >100

- 20% dev DTs if no risk factors
- 46% dev DTs if one factor present
- 100% if both factors present

Medication

Benzodiazepines – drugs of choice

equally efficacious in prevention and treatment of DTs; McMicken D, 1990

chlordiazepoxide 30-100mg qds depending on clinical response, max 500mg/24hrs

diazepam – 5mg every 5min until calm; dose of 2640mg IV over 48 hrs in one case

lorazepam – shorter onset of effect, faster relief of agitation

midazolam – used on ICU. Limited experience

Changes to practice in the prevention of delirium tremens

1. Use of prediction rating scales to identify high risk individuals
2. Physical examination; tachycardia >120 whilst positive breathalyser reading >0.5 with severe withdrawals on CIWA-Ar
3. Active investigation of causes of confusion, pyrexia, raised WBC, CRP, MSU, sputum, ?CXR, Mg levels, BM, serum anticonvulsants (day 1 and 3)

Changes to practice in prevention of delirium tremens

4. If high risk group, commence CDZ 50mg qds + serial CIWA-Ar; if severe range give an additional 20mg PRN
5. Correct Magnesium levels with MgO or MgSO₄ and correct other electrolyte disturbance

Management of established delirium tremens

- 1 Continued assessment
- 2 Fluid balance; daily U/E, Mg, bone profile
- 3 IV Pabrinex extended for further 3 days and reviewed
- 4 Maintain CDZ 50mg qds + PRN for at least 5 days/ delirium settles
- 5 Rapid tranquillisation policy
- 6 MHA
- 7 Criteria for transfer to the medics

Social Behaviour and Network Therapy

- Synthesis of social treatments Network Therapy, CRA, Relapse prevention, family therapy
- Includes those who cannot engage a network
- Developing and maintaining a network for positive change secondarily to minimize the influence of aspects of network supportive of drinking
- Family members and concerned others are central to the treatment process
- Therapist as an active agent of change a task orientated team leader

Topiramate

12 week PCT 150 subjects

Dose escalation Topiramate

Effectiveness over placebo at 200mg (week 6)

Self reported drinking (Drinks per day, % days heavy drinking, % days abstinent)

GGT assay

Craving (OCDS)

Effective in early and late onset alcohol dependence

Effective in those drinking at start of trial (with a goal of abstinence)

(Bankole-Johnson 2003)

Epidemiology

Psychiatric Disorder	Lifetime Rate SUD %	Odds Ratio
Any disorder	27%	1.9
ASPD	83.6%	29.6
Bipolar Disorder	60.7%	7.9
Schizophrenia	47%	4.6
Depression	27%	1.9
Anxiety	23.7%	1.7
General Population	14%	1.0

Why is Substance Misuse More Common in Bipolar Patients ?

- 1 Bipolar disorder initiates Substance Misuse.
- 2 Substance Misuse initiates Bipolar Disorder.
- 3 Bipolar disorder and Substance Misuse Share a Risk Factor.

Bipolar Disorder initiates Substance Use Disorder

Self-medication hypothesis (Khantzian 1997 Harvard Review Psychiatry)

Patients use sedatives to calm manic excitement

Patients use stimulants to relieve depression

96% bipolar patients said substance use helped mood
symptoms (Sonne et al 1994 J Ment Behav Dis)

Other studies do not support or show opposite e.g.

Increased stimulant use during mania (Weiss and Mirin 1987
Psych Med, Strakowski et al 1998 J Clin Psych)

Minimal support for hypothesis

Bipolar Disorder Initiates Substance Use Disorder

Substance Misuse a result of excitement,
impaired judgement, pleasure seeking.

25% increase consumption during manic episode

Rarely decrease use

70% no change

? Differential effect alcohol use more closely linked
to mood state c.f. cannabis (Strakowski et al 1998 J Clin Psych)

Primacy of Bipolar disorder

Study	Total No. Patients	No. with Substance Misuse antecedent (%)	No. with bipolar disorder antecedent (%)	Comment
Morrison et al 1975	18	8 (44)	10 (56)	Alcohol only
Winokur et al 1995	64	34 (53)	30 (47)	Alcohol only
Feinmann et al 1996	85	50 (59)	35 (41)	SUD
Strakowski et al 1996	42	32 (76)	10 (24)	First episode mania
Total	209	124 (59)	85 (41)	

Substance Misuse initiates Bipolar Disorder

Substance Use causing symptoms resembling bipolar disorder

Substance Use precipitates bipolar disorder in vulnerable individuals

Substance Disorder primacy

Bipolar disorder occur during substance misuse and not in sobriety

Patients with Substance Misuse who develop bipolar disorder lower familial rates of bipolar disorder

Substance Misuse initiates Bipolar Disorder

Primacy	No (%)
Mania developed after Substance Use	11 (61)
Mania with no primary substance use	3 (17)
Substance Misuse secondary to mania	1 (5)
Substance Misuse continued after resolution mania	3 (17)
Total	18 (100)

Familial studies

Few differences in rates of familial bipolar disorder in bipolar patients with or without alcohol misuse (Winokur et al 1995 Am J Psych)

Bipolar patients with primary SUD lower rates of affective disorder in relatives (DelBello et al 1999 J Affect Dis)

Shared risk Factor

Genetic- limited evidence (1990 Goodwin and Jamison)

Psychosocial stress- stress vulnerability model
(Brown et al 1995 J Stud Alc)

Subgroup of patients PTSD, Bipolar Disorder
and SUD

Childhood sexual abuse

General Reasons for Substance Use

Availability

Main recreational activity, life style

Entry into social group, peer pressure

Pleasure, euphoria, craving

Empowering

Coping with stress

Poor social skills, low self esteem

Lack of structure, Boredom

Diagnostic Issues

1 Substance Induced Mood Disorder

Develop within 4 weeks of Intoxication or withdrawal

Less likely if:

Persist for > 4 weeks (mania if persists > few days)

Previous history of non substance related affective episode

Family History of Affective Disorder

Affective symptoms excessive given amount/ type of substance used

Associated with Alcohol, cannabis, amphetamines, cocaine,
opiates

Diagnostic Issues

2 Affective symptoms in intoxication

Reversible substance specific mood change

eg Alcohol initial euphoric effect and severe intoxication can mimic manic/ hypomanic symptoms -

Alcohol/ opiate use can lead to increasing depression, anxiety and suicidal ideation/ self harm

Also associated with stimulants, cannabis, hallucinogens, inhalants and sedatives

Diagnostic Issues

3 Affective symptoms in withdrawal

Common symptoms anxiety and depression may persist for several weeks

Ratio of symptoms to syndromes

Brown and Schuckit 1988 J Stud Alc

42% depressed on HADS on day 2

6% depressed on HADS at week 4

Ideally wait 4 weeks before excluding this diagnosis

Assessment

False attribution individual/ assessor e.g. erroneous interpretation of neurovegetative symptoms

False attribution of worsening symptoms

Use of rating scales AUDIT, FAST, DAST, BDI, YMRS etc

Physical sequela of Substance Misuse

Markers of Substance Misuse- Drug Screening, LFT, GGT, MCV, CDT

Exclude physical causes of Affective disorder eg Anaemia, Iron and B12, Hypo/ hyperthyroidism

Assessment

Chronological Assessment involving a variety of sources. Time line follow back method.

Collateral history

Sequential Assessment

Observe symptom pattern after adequate period of abstinence

Effect on Course

- Suicide rates (Weiss and Hufford 1999)
 - Violence / Aggression
 - Early Onset, early hospitalization
 - Prolonged course more frequent admissions
 - Treatment non compliance (Keck et al 1998 AmJPsych)
 - Poor clinical outcome – bipolar disorder and SUD (Tohen et al 1998 Harvard Review of Psychiatry)
- Bipolar patients with SUD more likely to have mixed manic/ rapid cycling (Sonne et al 1994 J Nerv Ment Dis)
- Secondary alcohol problem more likely to stop drinking or episodic drinking
 - Increasing physical/ social problems

Pharmacotherapy

Bipolar Disorder

Poor outcome with Lithium predicted by SUD

Limited data 4 studies, 49 patients

Lithium results equivocal

Adolescent population better function and increased negative drug screen (Geller et al 1998)

Valproate reduced alcohol consumption in bipolar with alcohol dependence (Salloum et al 2005 Arch Gen Psych)

Lamotrigine in cocaine abusing bipolar patients (Brown et al 2003)

? Quetiapine and Olanzapine

Pharmacotherapy

Drug interactions alcohol/ drug of abuse

Alcohol induced liver metabolism

CBZ induced metabolism methadone (not with valproate)

Fluoxetine increases level methadone

Hepatotoxicity with anticonvulsants and alcohol

Some psychotropic drug effects similar to drug of abuse e.g stimulant AD, procyclidine

Compliance Valproate > Lithium (Sonne and Brady 2002)

Pharmacotherapy

Depression

Antidepressants may improve mood but not alcohol behaviour in depressed alcoholics (BAP 2004, Nunes and Levin 2004)

One RCT demonstrated improved drinking outcomes and depression in severely depressed alcoholics (Cornelius et al 1997, 2000)

Anxiety

RCT Paroxetine improved outcome anxiety in socially phobic alcoholics (Randall et al 2001)

Pharmacotherapy

Schizophrenia and SUD

Avoid typical antipsychotics (Siris 1990)

Olanzapine associated with decreased substance use

Schizophrenia with SUD less likely to respond to

Olanzapine and Haloperidol (Green et al 2004)

Clozapine reduces substance misuse in psychotic patients strongest evidence base (Drake et al 2000)

85% reduction in substance use in comorbid patients with Clozapine (BAP 2004)

SUD Pharmacotherapy

Methadone mood stabiliser/ antipsychotic

Naltrexone effective depressed alcoholics

(Salloum et al 1998)

Acamprosate

Valproate/ carbamazepine

Topiramate (Bankole-Johnson 2003 Lancet)

Disulfiram

A Network Model

