

Opiate Treatment and Benzodiazepines: Treatment Options.

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Introduction

- This presentation explores the use of benzodiazepines (bzd's) in the context of opiate maintenance treatment.
- It explores the interaction between bzd's with opiates; the importance of dosing issues; safety issues; and detoxification issues.

Alcohol or Bzd Dependence: Definition

- Alcohol dependence is defined according to 7 criteria.
 - ◆ Alcohol is important, central, or plays a major role in the individuals life
 - ◆ Alcohol has caused harm in that persons life. This is assessed in 3 areas:
 - ★ Harm in their primary relationship
 - ★ Harm in the primary occupation
 - ★ Harm in their broader social and occupational role

Definition.

- The individual generally drinks more than they want to when they have a drink.
- The individual has keep on drinking, despite believing there was a problem with alcohol.
- They may have a strong urge to drink

Definition.

- The individual shows sign of physical addiction to alcohol:
 - ◆ They have withdrawal symptoms or signs such as anxiety, shakes, sweats, nausea, or agitation on stopping alcohol
 - ◆ They have increased or altered tolerance to alcohol over the years.
- A total of 3 out of 7 criteria makes the definition of alcohol dependence.

What is the profile of Bzd abuse in the non-opiate dependent population?

- High rate of bzd users become dependent.
- In a general GP population, 40% of users become dependent.
- In a self help population, 97% of users become dependent.
- In a psychiatric out-patient population, 60-75% of users become dependent.

– Kan et al., Acta Psych Scand 1997 96: 85-93

Psychiatric diagnoses of patients with severe Bzd dependence.

- Current:
 - ◆ Drug/alcohol dependence – 83%
 - ◆ Panic disorder – 13%
 - ◆ Generalised anxiety – 20%

- Lifetime:
 - ◆ Major depression – 40%
 - ◆ Drug/alcohol dependence – 100%
 - ◆ Panic disorder – 30%
 - ◆ Personality disorder –
 - ★ Anti-social - 42%
 - ★ Avoidant – 25%
 - ★ Borderline – 17%

Busto et al., J Clin Pshchopharmacol 1996, 16: 51-57

Interactions between Bzd's and opiates

- These medications work at different receptors.
- Opiates work at opiate receptors, methadone predominantly works at the mu receptor, with some delta activity.
- Bzd's work at the bzd receptor, stimulating the GABAergic system.

Interactions between Bzd's and opiates

- Both cause sedation and respiratory depression.
- There is a synergistic interaction between the systems: the combination may cause increased side effects over those of each one alone.
- Both medication types are highly addictive.

Opiate and Bzd dependence

- Most opiate abusers make opiate dependence criteria.
- Most bzd abusers will not make bzd dependence criteria, whether they abuse opiates or not.
- Thus a high index of suspicion is required when prescribing bzd's in this population, even if they do not make bzd dependence criteria.

What is the profile of the Bzd abuser?

- Prevalence of bzd dependence in opiate dependent population in Dublin is 34%.
- Those who were co-dependent were:
 - ★ Older
 - ★ More likely to be on a MMP
 - ★ Using heroin longer
 - ★ Using bzd's longer, at increased doses than non bzd dependent population
 - ★ Used more drugs in general
 - ★ Past history of depression
 - ★ Past history of deliberate self harm

– Rooney et al., IJMed Sci 1999 168: 36-41

Israeli Bzd abuse in MTP study

- Prevalence and course of bzd abuse in existing MMTP using urine and self report data.
- Lifetime prevalence of bzd abuse 66%, current incidence 51%
- 44.6% of patients who abused during the first month ceased after 1 year.
- 27.4% who had not abused did so after 1 year.
- Overall reduction by 12% over the course of the year.
- Flunitrazepam (93%)> diazepam (54%)> Oxazepam (39%).
- 93% oral ingestion, 43% smoked/snorted, 8% IV.
- Mainly “self-medication”

- After 1 year on MMTP, Bzd abusers relative to non Bzd abusers:
 - ◆ More time in prison
 - ◆ Unemployed
 - ◆ Greater degree of parental drug abuse or mental illness problems.
 - ◆ Used heroin earlier
 - ◆ Used more heroin, cocaine and cannabis
 - ◆ More psychopathology and depression.
 - ◆ More Hep c, more HIV risk behavior

Follow on study

- Trial of of clonazepam maintenance treatment (CMT)
 - ◆ 20 subjects in open label trial
 - ◆ Daily dose 6mg gradual taper to maintenance dose.
 - ◆ Maintenance dose: patient satisfied, no cravings, no overdose.
 - ◆ Successful in 75% of patients over 6 months.
 - Bleich et al., Isr J Psychiatry 2002, 39: 104-112

Outpatient Bzd Detox in MMTP patients.

- Slow taper of whatever bzd medication the patient was taking.
- 4/22 refused the taper.
- 12 patients completed detoxification, on average 8 weeks later.
- No long term follow up available.
 - McDuff et al., J SAT 1993, 10: 297-302

Contingency reinforcement post detoxification.

- 14 patients on an MMTP with chronic bzd abuse admitted for inpatient detoxification from bzd's.
- 7-day detoxification.
- Contingency Management (CM): \$25 or take home dose of meth for drug free urine sample submitted (up to 3/week) versus Standary Care (SC).
- More drug free urines in CM group relative to baseline, no difference in SC group relative to baseline.

- Chutuape et al., Drug Alcohol Depend 1999, 54: 69-81

Clinical predictors of outcome in long term treatment.

- 82 patients with alcohol or bzd dependence treated over 6 months in outpatient setting.
- Both groups decreased bzd use over that time.
- Bzd dependent patients reported decreases in level of anxiety in follow up period despite lower bzd use.
- Bzd dependent patients had
 - ◆ Lower abstinence rates
 - ◆ More frequent drug use
 - Charney et al., JClin Psych 2000, 61: 190-195

Bzd prescription practices in opiate dependent population: recommendations

- Use caution
- Bzd's should be prescribed in as low dose as possible
- Short term only, not longer than 8 weeks
- Beware of diversion, multiple prescription seeking

Bzd withdrawal: syndromes

- High dose withdrawal: begins 1-2 days after a short acting bzd is stopped, 3-8 days after a long acting bzd is stopped.
- Characterized by: anxiety, insomnia, nightmares, seizures, psychosis, hyperpyrexia, death.
- Treated with hypnotic dose of bzd.

Bzd withdrawal: syndromes

- Protracted low dose withdrawal: 1-2 days after short acting bzd is stopped/reduced, 3-8 days after a long acting bzd is stopped/reduced, lasts 7-14 days.
- Anxiety, agitation, tachycardia, palpitations, anorexia, blurred vision, cramps, insomnia, nightmares, confusion, spasms, startle, paraesthesia.
- Vague symptoms may last for a number of months.

Bzd treatment strategies

- Do nothing, leave on current bzd's.
- Gradually taper current bzd of choice over weeks, to patients level of tolerance, or to nil.
- Inpatient admission for detox followed by opd follow up.
- Switch to long acting bzd e.g. diazepam, and commence taper.
- Taper lasts 8 weeks on average, may take longer.

- Encourage re benefits, mood and anxiety levels.
- Contingency reinforcement to maintain abstinence.
- A significant reduction of bzd's is safer, decreases psychopathology, and leads to overall increase in well being than doing nothing.
- Abstinence from bzd's is ideal.

Bzd equivalents

- Dose equivalents:

◆ Alprazolam	(Xanax)	1
◆ Chlorodiazepoxide	(Librium)	25
◆ Clonazepam	(Klonopin)	2
◆ Diazepam	(Valium)	10
◆ Flurazepam	(Dalmane)	15
◆ Lorazepam	(Ativan)	2
◆ Temazepam	(Normison)	15
◆ Triazolam	(Halcion)	0.25