CO-MORBID PSYCHIATRIC DISORDERS

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Declaration of Potential Conflict of Interest

The content of this presentation is non-commercial and I have no conflict of interest to disclose

Overview

- Definitions
- Epidemiology
- Diagnostic considerations
- Treatment considerations
- Case studies

Co morbidity

Two or more illnesses in the same person at the same time, e.g.., bipolar illness and alcoholism

One may affect the course or response to treatment of the other

Psychiatric Disorders

Mood - depression, anxiety, bipolar

Cognitive - autism, ADHD, dementia

Psychotic - schizophrenia, delusional d/o

Somatoform - conversion, somatization d/o

Substance use disorders = abuse or dependence

Substance use = *non- problematic* use

Substance misuse = use in a manner not intended

Substance abuse = *recurrent;*
*life problems, role function affected

*interpersonal, legal problems

*use in situations that are physically hazardous to the user

4 C's of Addiction

Control attempts
Compulsive use
Continued use despite consequences
Craving when the drug is stopped

Addictive disease is obsession + compulsion +/- physiologic withdrawal symptoms

Drug dependence is physiologic adaptation and withdrawal on stopping the drug

Mental Health and Treatment settings 1980's and 1990's

substance abuse programs reported co- occuring mental disorders in 50 to 75%

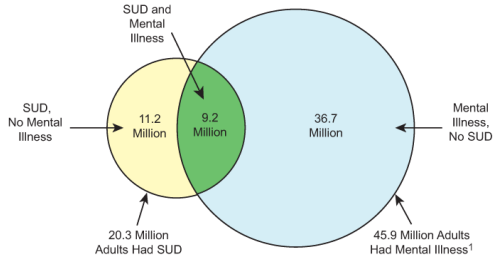
Mental health programs reported co-occurring substance use disorders in 20 and 50%

CSAT, SAMHSA (TIP) Series 42. DHHS Publication No. (SMA) 05-3992. 2005, Rockville, MD

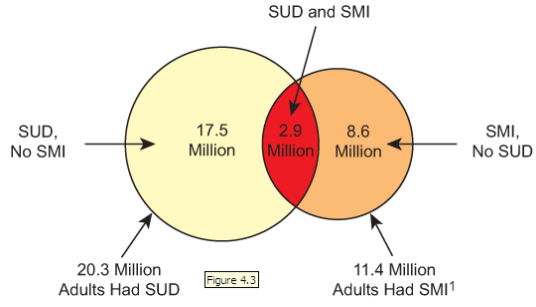
21.3% with serious mental illness had a SUD in the past year

National Epidemiologic Survey on Alcohol and Related Conditions, 2004

Past Year Substance Dependence or Abuse and Mental Illness among Adults Aged 18 or Older: 2010

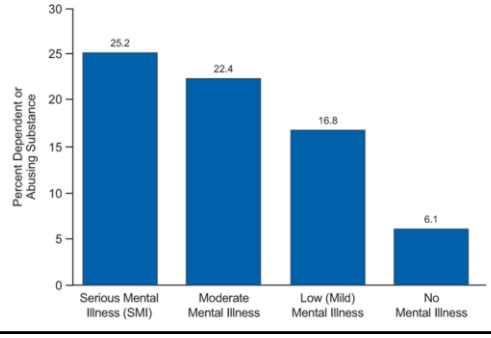


2010 NSDUH : Summary of National Findings

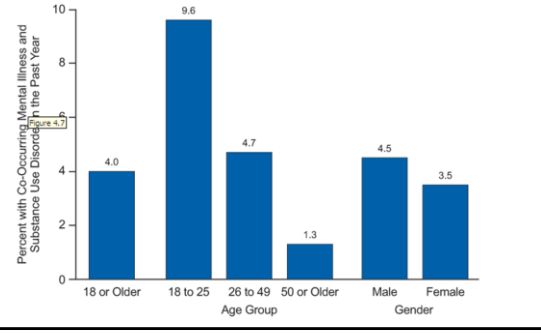


Past Year Substance Dependence or Abuse and Serious Mental Illness among Adults Aged 18 or Older: 2010
2010 NSDUH : Summary of National Findings

Past Year Substance Dependence or Abuse among Adults Aged 18 or Older, by Level of Mental Illness: 2010
2010 NSDUH : Summary of National Findings



Co-Occurring Mental Illness and Substance Use Disorder in the Past Year among Adults Aged 18 or Older, by Age and Gender: 2010
2010 NSDUH : Summary of National Findings



Why do drugs affect mood ?

Most drugs of abuse influence production of dopamine and serotonin

Depression is most common symptom during any substance withdrawal followed by anxiety and irritable mood.

Withdrawal related mood symptoms may last weeks to many months depending on the substance.

Why is diagnosis difficult?

Alcohol/drugs can cause psychiatric symptoms in anyone (acute toxicity)

Prolonged A/D use can cause short or long-term psychiatric illness

A/D use can escalate in episodes of psychiatric illness

Psychiatric symptoms and A/D use can occur in other psychiatric disorders

Marc A. Schuckit: Am. J Psychiatry, 143:2 p. 141 – modified

Substance-induced mood disorder DSM IV

Prominent/persistent mood disturbance

Develops within 1 month of intoxication or withdrawal *or* medication use is causative

Not better accounted for by other axis I d/o

Sx not exclusively during delirium

Sx cause significant distress or impairment

Substance induced depression?

191 male alcoholics, none with prior major psychiatric Hx.

42% had significant Sx (Ham D > 19) **within 48 hrs. of admission**

At 2 weeks, 12% with Ham D score >19

At 4 weeks, 6% with Ham D score > 19

Rapid decline in Sx intensity over first 4 weeks of Tx., largest reduction at 2 weeks

Recommended: defer antidepressant Rx prior to first 4 weeks of abstinence*

(Brown and Schuckit, 1988.)

Chicken or Egg?

25-year longitudinal study, 635 boys, 630 girls, birth cohort, general community sample in New Zealand

found that:

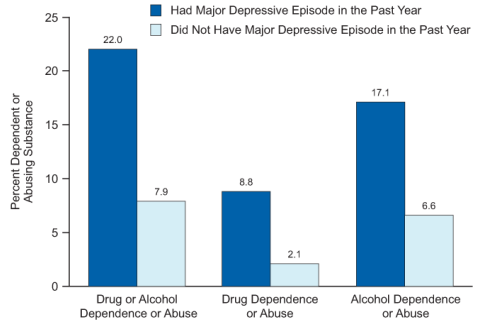
problems with alcohol led to increased risk of Major Depression

as opposed to:

a self-medication model in which Major Depression led to increased risk of AAD.

Fergusson, Boden, et al, Arch Gen Psychiatry. 2009 Mar;66(3):260-6

Past Year Substance Dependence or Abuse among Adults Aged 18 or Older, by Major Depressive Episode in the Past Year: 2010
2010 NSDUH : Summary of National Findings



What's the difference?

Post-Acute Withdrawal
Depression
Anxiety
Mood Lability
* normal in early abstinence
resolves with time
Responds to behavioral measures
responds to 12-Steps

Psychiatric Disorder
Major Depression
Anxiety/Panic Disorder
Bipolar Disorder
*not normal
won't resolve without Tx
12-Steps won't hurt

Early phase psychosis w/ co-morbid substance use vs. substance induced psychosis ?

N=386, 44% sub induced psychosis, 56% primary psychosis

Predictors of substance-induced Sx:

parental substance abuse (odds ratio [OR], 1.69; 95% confidence interval [CI], 1.00-2.85)

diagnosis of dependence on any drug (OR, 9.41; 95% CI, 5.26-16.85),

visual hallucinations

Caton et al, Arch Gen Psychiatry. 2005;62:137-145.

Quick differential: Psychosis

Visual Hallucinations:
-hallucinogens, alcohol withdrawal, organic i.e, Lewy body dementia, delirium (uncommon with 1º psychosis)
-vague (shadows, etc.) with Axis II

Auditory Hallucinations:
-Schizophrenic or schizoaffective d/o (less common with substances)
-vague sounds (mumbling, name called, etc.) with Axis II

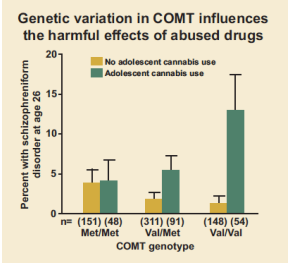
Paranoia:
-substances: cocaine, psych stimulants, occ. THC and ETOH withdrawal
-Axis I: mania, schizophrenia/schizoaffective
-Axis II: paranoid personality disorder (rare)

Mania: simultaneously activated behavior, mood and thinking

**medical causes to be considered include thyrotoxicosis, temporal lobe epilepsy

- Bipolar, schizoaffective, psychosis, anxiety disorders
- Methamphetamine/Cocaine
- Ecstasy (MDMA)
- Hallucinogens
- Alcohol/Benzodiazepine withdrawal?
- Medication induced (i.e. corticosteroids)

Schizophrenia and Marijuana



Up to 2x >risk of developing schizophrenia
Moore, et al, Lancet 2007; 370: 319–28

Caspi et al., Biol Psychiatry, May 2005

Meier et al. Persistent cannabis users show neuropsychological decline from childhood to midlife
Proc Nat Acad Sci, October 2, 2012 vol. 109 no. 40 E2657 – E2664

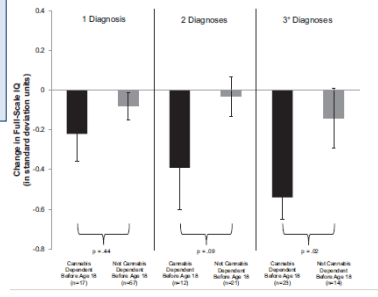


Fig. 2. Adolescent vulnerability. Change in full scale IQ (SD units) from childhood to adult. Adolescent onset (black bar) had >IQ decline vs. adult onset. IQ ↓ approximately -0.55 units (8 IQ points) with 3+ diagnosis over time

Adolescents and marijuana use

- have higher levels of anxiety (Dorard et al., 2008), depressive symptoms (Medina et al., 2007), suicidality (Pedersen 2008) and externalizing behavior (Monshouwer et al., 2006)
- neurocognitive deficits, including intentional, learning, memory, and intellectual functioning decrements (Fried et al., 2002; Di Forti et al., 2007; Harvey et al., 2007; Brook et al., 2008)
- poorer sleep (Bolla et al., 2008), respiratory problems (Aldington et al., 2007; Brook et al., 2008), cancer (Berthiller et al., 2008)

Personality disorders and substance use

Antisocial PD - highest likelihood of co-morbid substance use (may facilitate further behavioral or emotional excursions)

Borderline PD – predictable clinical worsening (increased externalizing, impulsivity)

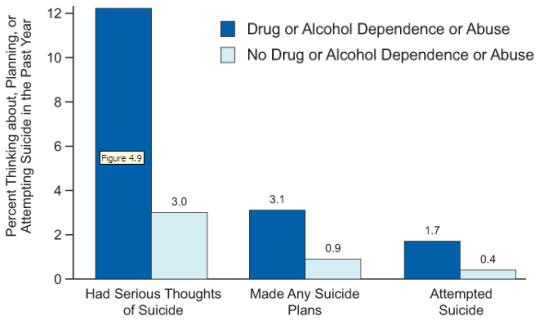
Hard to diagnose in presence of early onset and/or active substance use

What is the most fatal mental disorder?

Risk Factor		Odds Of Attempting Suicide
Cocaine use	→	62 times more likely
Major Depression	→	41 times more likely
Alcohol use	→	8 times more likely
Separation or Divorce	→	11 times more likely

NIMH/NID

Suicide Thoughts, Plans, and Attempts in the Past Year among Adults Aged 18 or Older, by Substance Dependence or Abuse: 2010
2010 NSDUH : Summary of National Findings



Eating disorders and substance use

- 50% of persons with an eating disorder also have problematic drug or alcohol use, (compared with 9% of the general population)
- 35% of females with a substance use disorder report having an eating disorder (compared with 1–3% of the general population)

Root, et al, Int J Eat Disord March 2009; (online pub.)

Eating disorders and substance use

Alcohol and drug abuse or dependence
more common in: *mixed binge/purge
*purging only eating behaviors

than in: **restrictive only eating behaviors**

Treatment outcomes poor unless both conditions addressed

Root, et al, Int J Eat Disord March 2009; (online pub.)

Red Flags
for co-occurring psychiatric illness include:

Family history of psychiatric illness

Onset of psychiatric symptoms before the onset of substance use disorder

Psychiatric symptoms during lengthy periods of abstinence in the past

The longer from last use and acute withdrawal, more likely to be seeing a co-morbid process

Implications for treatment

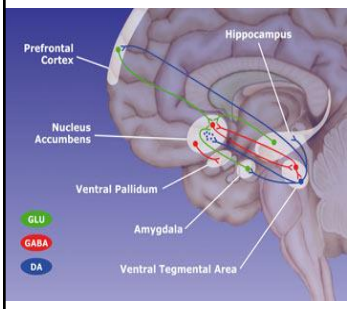
addictive disease is predictive

Exposure kindles "a new biological drive" to use the drug (success in meeting basic drives decreases anxiety i.e., not getting fed)

Encouraging self confidence, empowerment as goals not always desirable

Heritability ranges from 40 – 60%

Drugs of abuse act on:



Amphetamine and **cocaine** elevate DA in NAS

Nicotine acts on cholinergic receptors at cell bodies and terminals of mesolimbic system, increasing DA in NAS

PCP blocks NMDA (GLU) increasing DA in NAS.

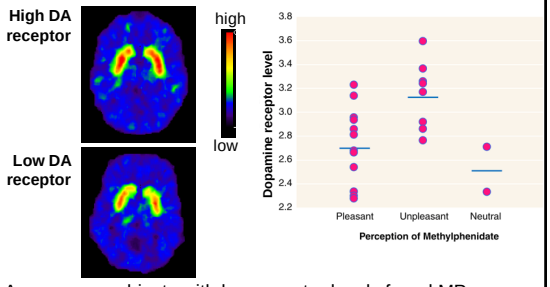
Opiates inhibit the GABAergic cells that normally inhibit the mesolimbic system increasing dopamine in NAS

Barbiturates and **benzo's** do the same at some GABAergic level

Ethanol and **marijuana** end with the same results in NAS through unknown mechanisms

Caffeine doesn't involve the same circuit.

DA Receptors and the Response to Methylphenidate (MP)



As a group, subjects with low receptor levels found MP pleasant while those with high levels found MP unpleasant

Adapted from Volkow et al., Am. J. Psychiatry, 1999.

Treatment: generally avoid cross-dependency producing drugs

Benzodiazepines **Ativan, Xanax, Klonopin, Valium, Librium, Restoril, Tranxene, Versed**

Benzodiazepine analogs **Ambien, Sonata, Lunesta**

Other Sedative-Hypnotics **Soma, meprobamate, chloral hydrate, etc.**

Barbiturates **Fiorinal, Fioricet, phenobarbital**

Psychostimulants **Adderall, Ritalin, etc.**

Opioids **codeine, Ultram, Vicodin, methadone, heroin, etc.**

How to address sleep and anxiety problems?

Thorough history, +/- medical evaluation if needed

Optimize self care * recovery program
*** sleep**
*** diet, caffeine use**
*** exercise**

Psychiatric referral if necessary

Medical procedures and pain management in recovering persons:

Generally, **avoid elective procedures** **in 1st year** of recovery

Co-ordination of care is essential (PCP, surgeon, dentist, etc.)

Avoid practice outside of specialty (prescribing for conditions you don't have experience with, can't evaluate or follow)

Consider non-opioid measures such as long- lasting local anesthesia (i.e, bupivicaine), NSAIDS, acetaminophen, anti-convulsants for neuropathic pain, topical analgesics, physical therapy

ADHD in Recovering Persons

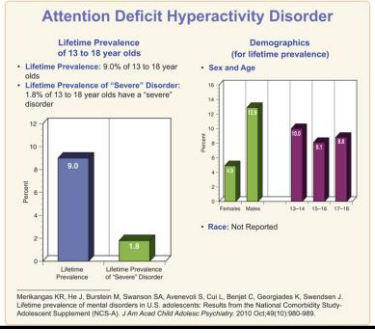
Consider non-stimulants agent first (Strattera®)

Controlled release (i.e. **Adderall®**, **Concerta®**) or pro-drugs (**Vyvanse®**) have less abuse potential, harder to get high peak effect by IV or snorting

All activate mesolimbic and mesocortical areas of the brain involved in addictive disease, kindle craving, obsession and compulsion, and all have been abused

Of persons having true ADHD diagnosis in childhood, only 30% will carry functional symptoms into adulthood

ADHD in Recovering Persons



General points on pharmacotherapy for co-occurring disorders

Avoid the trap of reacting to symptoms with polypharmacy

Many substance-use patients like taking drugs, *any drugs*

Decision to medicate should always be with clear rationale and consideration of alternatives including psychosocial and behavioral interventions.

Always weigh risk versus benefit

Persons with persistent anxiety, apathy, irritability or social withdrawal are describing barriers to engagement in recovery process

Successful adaptation to the substance-free state for most means:

Abstinence plus engagement in a psychosocial process which can facilitate a transfer of dependency needs to sources of supply which are:

1. *non-destructive
2. *intrinsically rewarding
3. *inexhaustible

Meta analysis of literature on AA effectiveness found:

Katsukis, 2009 , Addict Dis. 2009;28(2):145-57.

(1) magnitude of effect: rates of abstinence about 2x higher

(2) dose response effect: > attendance associated with > rates of abstinence

(3) consistent effect: these relationships are found for different samples and follow-up periods

(4) temporally accurate effects: prior AA attendance predictive of subsequent abstinence

(5) specific effects: evidence establishing the specificity of an effect for AA or Twelve Step Facilitation/TSF is mixed

*(2 trials+, 1 trial -, 1 trial no effect)

(6) plausibility: mechanisms of action predicted by theories of behavior change are present in AA

AA and Doctors, Medications

- **"In the doctor's (Karl Jung) opinion, he was utterly hopeless"**
- **"Try to remember that though God has wrought miracles among us, never belittle a good doctor or psychiatrist, their services can be indispensible…" p.133**
- **"No AA member should "play doctor", all medical advice and treatment should come from a qualified physician" The AA member – medications and other drugs"**

AA world services, Inc., ©1984, 2011

Depressive Sx in 20 y.o. male

Past Psych Hx: None beyond HPI

Psych Sx review: Non-contributory

PMH: Non-contributory

FHx: *Mother: problematic ETOH use,
*Father -depression ? Dx or Tx.
*P. cousin (distant), suicide when patient age 9

Depressive Sx in 20 y.o. male

- **Substance Hx:**

*ETOH, 1st at age 14, daily use 6-10 beers for 9 mos prior to 11/06 then MIP, tether

*Marijuana: 1-8 "bong hits" daily for past 2.5 yrs

*Oxycontin®, first at age 18, 4-5 occ./week, 80-120mg/occ. ("snorting") X 6 mos.

Depressive Sx in 20 y.o. male

Social Hx:

*Only child, parents divorced when patient age 15, raised by mother.

*Never married, no long term relationships.

*H.S. grad, "barely"

*On probation for DUI 12/06 (BAC 0.23%), 3 prior MIP's

Depressive Sx in 20 y.o. male, Diagnosis:

AXIS I: ETOH dep., cannabis dep., opioid dep., all in early full remission
Substance-induced depressive disorder by HX

AXIS II: deferred

AXIS III: no active medical problems

AXIS IV: mod. to severe inc. legal, social, occupational, family, financial

AXIS V: 58

Depressive Sx in 20 y.o. male, Considerations

- Stable/improving mood, engaging in program
- No prior psychiatric history before onset of substance use
- No self perceived need for medication or investment in having a psychiatric diagnosis
- Recommendation:
  1. Taper off Celexa® over 2-4 weeks
  2. Stop trazodone
  3. Continue to monitor mood

Worsening depression in a middle age male

- A 56 year old male is brought to Psych ED by his wife
- 1 week worsening depressive Sx, 3 yr. total treatment for "resistant depression", little benefit.
- Clothes are rumpled, he is unshaven, agitated, wringing hands, despairing, says, "I just can't go on like this, I don't know what to do"
- He says the past few days he is having SI with vague plan to jump from a parking deck, When asked to talk about what's wrong, mumbles, "I don't know, everything"

Worsening depression in a middle age male

- No prior suicide attempts, no family history of suicide, or psychiatric problems, no pre-morbid psychiatric history
- Second marriage, now 20 years, lives with wife who is supportive but feels helpless
- middle class, both are high school teachers
- PMH: hypertension on lisinopril, migraines
- Meds: venlafaxine XR 300mg/d (3 mo.), bupropion SR 150mg bid (2 wk.), Ambien® 10mg at hs (8 mo.)

Worsening depression in a middle age male

- Labs: TSH, LFT's, renal function, electrolytes, CBC all WNL
- VS on admission: P. 88 b/p 150/84

****

1) what is your differential dx ?
2) you've just spoken with patient, looked at the outpatient notes, what is your intuitive diagnosis ?
3) what would you do next?
4) any additional information or diagnostics?

Worsening depression in a middle age male

- MAPS report
- Comprehensive Urine Toxicology screen (ELISA + GC/MS)
- Interview wife alone - collateral (with patients permission)

Worsening depression in a middle age male

MAPS: 2 Rx's for small quantities Tylenol #3® w/codeine
3 Rx' for Ambien® 10mg, #30, at monthly intervals

- UDS + for barbiturates (GC/MS identified butalbital)
- Wife concerned, non-drinker but he occasionally slurs words in the evenings, says "I'm just tired"
- Arguing more about $$$, she thinks he is hiding it from her, they can't seem to reduce credit card balances, thinks he might be having an affair

What do you think is going on with this patient ?

Urine drug testing

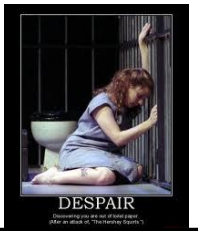
- ELISA (urine dip test) first done, most common
- Be aware of cross reactants (false +) , panel contents specific to your test strip (read circular)
- Approach to patient – empathic, clear, ally not enemy
- GC/MS to confirm (takes time, $$$, no false +)

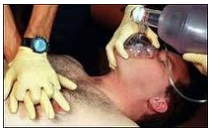
Worsening depression in a middle age male

- 24 hrs. after admission, increasing agitation, sweaty, P. 110, b/p, 170/110, B UE tremor on exam. Asked for repeat zolpidem night before, no effect with 1 dose noted by RN.
- When asked to help us understand his barbiturate + urine he had “no idea”
- An hour later called the resident to his room, tearfully admitted has been buying APAP/butalbital (Fioricet®, Esgic®, etc.) over the Internet for 3 1/2 years, 8-16 tabs/day. Stopped it 2 days PTA, “I was trying to quit, tired of lying to everyone”
- Met DSM IV for sedative-hypnotic dep.

Great Idea !!!!

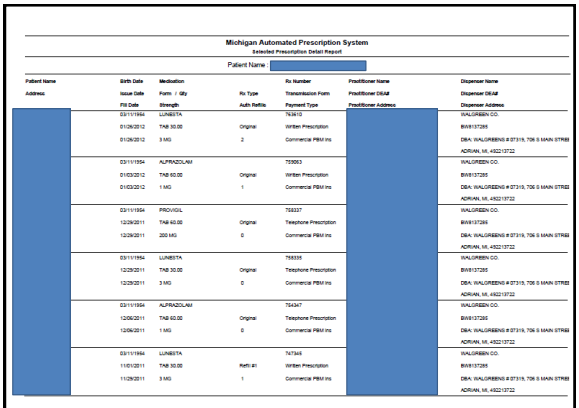
Reality……





Worsening depression in a middle age male, *points to consider*

- Always ask about substances & get UDS (only reason for patient refusal is it’s going to be positive)
- Some drugs aren’t on the Controlled Substance list and won’t show on MAPS, i.e., Fioricet (but Fiorinal® , ASA + butalbital is CIII), tramadol, Soma ®, etc.
- Many drugs are available w/o Rx on the Internet
- ALWAYS THINK CRITICALLY, are there other possible explanations for what you’re seeing ?



Worsening depression in a middle age male

Treatment plan changes:

- stop bupropion (why?)
- start phenobarbital taper, problem solve to access substance use treatment on discharge
- Support patient with engaging family, secrets lead to relapse!!

Worsening depression in a middle age male, references

CE Romero, et al, Barbiturate Withdrawal Following Internet Purchase of Fioricet. Archives of Neurology, 2004

NS Miller, M Gold. Management of Withdrawal Syndromes and Relapse Prevention in Drug and Alcohol Dependence. American family physician(1970) 58:11, 119-146, American Academy of Family Physicians, 1998

Graham A et al. Principles of Addiction Medicine. American Society of Addiction Medicine. 3rd Edition, Chevy Chase , MD , 2003

RF Forman, DB Marlowe, AT McLellan. The Internet as a source of drugs of abuse. Current Psychiatry Reports, 2006 - Springer

Therapy session #20, 30 y.o. woman, panic, anxiety and depression

- "stuck" in therapy, little progress, still having panic attacks, depressed
- Confesses, "I think I'm hooked on the Xanax my doctor gave me, not doing good, feel guilty, tired of all the lying"

What do you do next?

a. **Tell her to stop it if she can't take it the way she is supposed to.**
b. **Increase therapy to deal with her resistance to treatment, anxiety**
c. **Send her to a doctor or substance use program**
d. **Feel guilty, you should have "caught it" sooner**

Questions

- Comments ?
- Cases ?

A case of cross dependence

A case of cross dependence

- 52 y.o. Veterinarian, stable in recovery for 18 months after a 3 year dependence on Ultram® (tramadol).
- 4 mo. ago sought help for anxiety, having cravings for alcohol (had alcohol abuse history in her early 20's)
- Citalopram (SRI) started along with baclofen® titrated to 120mg/d (rec. max is 80mg/d)
- 6 weeks ago began asking for early refills, had started writing Rx's for self

A case of cross dependence

- Says baclofen® “really works”, anxiety “goes away” but “it doesn't last that long”
- Disclosed that she had felt a sedative effect, “calm, relaxed, good” with the first dose, didn’t tell anyone, “thought I found a legal high”, increased dose on own to 150-180mg/d.
- Now can’t reduce her dose without anxiety, tremor, sleeplessness, GI upset.
- “I didn’t plan this to happen, I should have known better”

A case of cross dependence

- Baclofen® being used “off label” for suppression of ETOH craving, treatment of anxiety in recovering alcoholics (1)
- Some evidence for efficacy in small open-label trials, case reports, larger double blind study in progress (1,2)
- Side effects include: drowsiness, dizziness (common) and euphoria (rare) – no studies of abuse liability in persons known to be ETOH or other drug dependent (5)

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- Side effects include: drowsiness, dizziness (common) and euphoria (rare) (5)
- No studies of abuse liability in persons known to be ETOH or other drug dependent (5)

A case of cross dependence

Abrupt d/c of high dose baclofen® after several months or more can produce withdrawal syndrome similar to severe ETOH or sedative-hypnotics. Can include: seizures, delirium, autonomic instability (3,5)

Management:

Involved family to handle meds

Tapered off by 10-20mg q 4-7 days

Patient self reported to MHPRC as “relapsed”, rec: IOP, no clinical practice until re-evaluation

A case of cross dependence, Caveats:

- Use caution when prescribing drugs that involve (directly or indirectly) the patients know receptor pattern vulnerability *(even though their brain has never seen the new drug)
- Other gaba-ergic drugs such as gabapentin and pregabalin have also been abused by recovering patients (4,5)
- Limited information on managing withdrawal of these agents, most shows poor cross coverage with high dose BZD’s, phenobarbital.
- Most effective way is to re-start drug and slowly taper (3)

A case of cross dependence, gaba-like drugs/some references

(1) Alcohol and Alcoholism, 2002. Baclofen efficacy in reducing alcohol cravings and intake: a preliminary double-blind study. G Addolorato, F Caputo, E Capristo

(2)Alcohol and Alcoholism, 2007. Suppression of symptoms of alcohol dependence and craving using high dose baclofen. W Bucknam

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