

Psychiatric management of substance abuse

Dr. Lee Wing-King
Specialist in Psychiatry

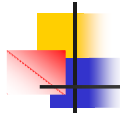
Clinical Associate Professor (honorary),
Department of Psychiatry, CUHK

Clinical Associate Professor (honorary),
Department of Community and Family
Medicine, CUHK

Honorary Clinical Supervisor, Hong Kong
College of Family Physicians

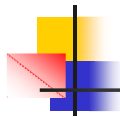
Outline

- Management principles
- Cannabis
- Cocaine
- Amphetamine
- Ecstasy
- Ketamine
- Benzodiazepines
- Z-drugs (non-BDZ hypnotics)



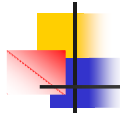
Management principles

- As with treatment models for chronic diseases, treatment for individuals with substance use disorders occurs in temporal phases that include
 - 1) initial assessment,
 - 2) acute intervention,
 - 3) long-term intervention and/or maintenance, with frequent reassessment during episodic flares in substance use



Management principles

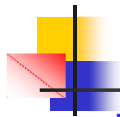
- Immediate intervention to provide safety to the patient in a medically monitored environment
- is recommended for individuals who present with high-risk intoxication or withdrawal states or altered mental states (e.g., psychosis, suicidality, agitation) that are associated with a risk of danger to self or others.



Management principles

- It is recommended that individuals in the patient's family or social network be included in the treatment process so they may learn about the disorder, help monitor the patient's progress, and assist in the patient's maintaining existing relationships or repairing troubled ones

Weiss RD: Adherence to pharmacotherapy in patients with alcohol and opioid dependence. *Addiction* 2004; 99:1382-1392



Street names of illicit drugs

- Heroin : no. 3 三仔, no. 4 四仔
- Cannabis : 草、Hashish 大麻精、Hash oil 大麻油
- Lysergic acid diethylamide (LSD) : 迷幻藥、方糖、郵票、黑芝麻
- Phencyclidine (PCP) : angel dust, 天使塵
- Amphetamines : 大力丸、methamphetamine 冰
- Methylene-dioxy-methylamphetamine (MDMA) : Fing 頭、E仔、忘我、狂喜、designer's drug
- Cocaine : C, coke, 可卡因、crack、可樂、霹靂
- Chlordiazepoxide (librium) : 綠豆仔
- Diazepam (valium) : 五仔



Street names of illicit drugs

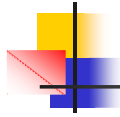
- Flunitrazepam (rohypnol) : 十字架
- Midazolam (dormicum) : 羅氏藍精靈
- Triazolam (halcion) : 藍精靈、藍瓜子
- Nitrazepam (Morgadon) : 魔鬼黨、睡覺幫
- Zolpiclone (imovane) : 白瓜子
- Zolpidem (stilnox) : 思諾施
- Mandrex : 忽得、MX、糖仔
- Ketamine : K仔
- Gamma hydroxybutyrate (GHB) : G水、迷姦水、X水
- Dextromethorphan (Romila) : O仔



Treatment goals

- The evidence to date suggests that substance-dependent individuals who achieve sustained abstinence from the abused substance have the best long-term outcomes (1,2).
- Clinicians will, however, frequently encounter individuals who wish to reduce their substance use to a “controlled” level (i.e., use without apparent functional consequences).

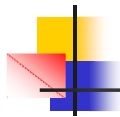
1. Vaillant GE: A long-term follow-up of male alcohol abuse. Arch Gen Psychiatry 1996; 53:243–249
2. Vaillant GE: A 60-year follow-up of alcoholic men. Addiction 2003; 98:1043–1051



Assessing readiness for change

- Motivational interview
- Client-centered directive method for facilitating change by helping people to explore and work through ambivalence
- Motivation as defined by Motivational Theory can be classified into
 - 1. reliable stage
 - 2. predictable stage
 - 3. well-defined stage

Miller WR, Rollnick S. Motivational interviewing : Preparing people for change. Guilford Press, 2002



Motivating patients for change

- The therapist to identify the stage the patient is in and to apply the stage-appropriate counseling approaches to get the best results
- Family doctors can do that with training as an effective time-limited counseling approach.
- If not responsive, refer to specialist for more specialized treatment

Miller WR, Rollnick S. Motivational interviewing : Preparing people for change. Guilford Press, 2002



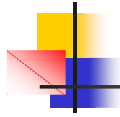
Urine toxicology

- Confirm suspected patients
- Detect the nature and number of illicit substances involved
- Beware of the detectability of drugs



Urine toxicology-longest detection time after last use by days

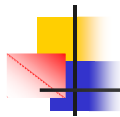
- Amphetamines : 3
- Benzodiazepines : 3
- Cannabis : 14
- Cocaine : 3
- Dextromethorphan : 2
- GHB : 0.5
- Ketamine : 2
- LSD : 2
- MDMA : 3
- Methadone : 7
- Opiates : 3
- PCP : 14
- Zolpiclone : 3



Treatment goals

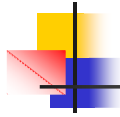
- Although some of these individuals, particularly those with less severe problems, may be helped to reach a stable level of use (e.g., “controlled” drinking) that does not cause morbidity, a goal of “controlled” substance use is unrealistic for most individuals presenting with a substance use disorder.
- Furthermore, setting “controlled” use as a primary goal of treatment may initially dissuade individuals from working toward abstinence.

Marlatt GA, Larimer ME, Baer JS, Quigley LA: Harm reduction for alcohol problems: moving beyond the controlled drinking controversy. *Behav Res Ther* 1993; 24:461–504



Treatment goals

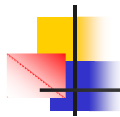
- However, treatment may be initially facilitated by the clinician’s accepting the patient’s goal for moderation while sharing with the patient any reservations the clinician may have about the likelihood of success.
- If the clinician believes that any level of substance use for the individual carries a risk of acute or chronic negative consequences, he or she should share with the patient this concern and the belief that long-term abstinence would be the best course of action.



Treatment goals

- In certain circumstances it may be reasonable, however, for an individual to begin treatment by setting a short-term goal of reducing or containing dangerous substance use as a first step toward achieving the longer-term goal of sustained abstinence

Marlatt GA, Witkiewitz K: Harm reduction approaches to alcohol use: health promotion, prevention, and treatment. *Addict Behav* 2002; 27:867–886



Treatment goals

- 1) Treatment retention and substance use reduction or abstinence as initial goals of treatment
- 2) Reduction in the frequency and severity of substance use episodes
- 3) Improvement in psychological, social, and adaptive functioning

American Psychiatric Association, Practice Guideline for the treatment of patients with substance use disorders, second edition, 2006, p.17



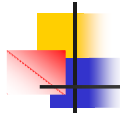
Treatment principles

- motivating the patient to change,
- establishing and maintaining a therapeutic alliance with the patient,
- assessing the patient's safety and clinical status, managing the patient's intoxication and withdrawal states,
- developing and facilitating the patient's adherence to a treatment plan, preventing the patient's relapse,
- educating the patient about substance use disorders, and reducing the morbidity and sequelae of substance use disorders.



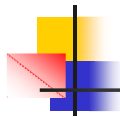
Treatment principles

- generally combined with specific treatments carried out in a collaborative manner with professionals of various disciplines
- at a variety of sites, including community-based agencies, clinics, hospitals, detoxification programs, and residential treatment facilities.
- many patients benefit from involvement in self-help group meetings, and such involvement can be encouraged as part of psychiatric management.



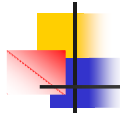
Treatment scenarios

- Intoxication state
- Withdrawal state
- Dependence state



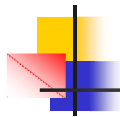
Treatment modalities

- Pharmacological treatments :
 - 1) medications to treat intoxication and withdrawal states,
 - 2) medications to decrease the reinforcing effects of abused substances,
 - 3) agonist maintenance therapies,
 - 4) antagonist therapies,
 - 5) abstinence-promoting and relapse prevention therapies,
 - 6) medications to treat co-morbid psychiatric conditions



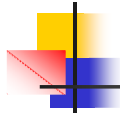
Treatment modalities

- Evidence-based psychosocial treatments :
- cognitive-behavioral therapies (CBTs, e.g., relapse prevention, social skills training),
- motivational enhancement therapy (MET),
- behavioral therapies (e.g., community reinforcement, contingency management), 12-step facilitation (TSF),



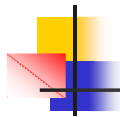
Treatment modalities

- psychodynamic therapy/interpersonal therapy (IPT),
- self-help manuals,
- behavioral self-control,
- brief interventions,
- case management,
- group, marital, and family therapies.



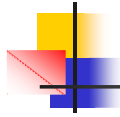
Treatment plan

- 1) psychiatric management;
- 2) a strategy for achieving abstinence or reducing the effects or use of substances of abuse;
- 3) efforts to enhance ongoing adherence with the treatment program, prevent relapse, and improve functioning;
- 4) additional treatments necessary for patients with a co-occurring mental illness or general medical condition.



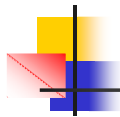
Treatment plan

- The duration of treatment should be tailored to the individual patient's needs and may vary from a few months to several years.
- It is important to intensify the monitoring for substance use during periods when the patient is at a high risk of relapsing, including during the early stages of treatment, times of transition to less intensive levels of care, and the first year after active treatment has ceased



Out-patient treatment setting

- a comprehensive approach is optimal, using, where indicated, a variety of psychotherapeutic and pharmacological interventions along with behavioral monitoring
- clinical and research experience suggests the effectiveness of intensive outpatient treatment in which a variety of treatment modalities are simultaneously used and in which the focus is the maintenance of abstinence



In-patient treatment setting

- 1) have a substance overdose
- 2) are at risk for severe or medically complicated withdrawal syndromes
- 3) have co-occurring general medical conditions that make ambulatory detoxification unsafe;
- 4) have a documented history of not engaging in or benefiting from treatment in a less intensive setting



In-patient treatment setting

- 5) have a level of psychiatric co-morbidity that would markedly impair their ability to participate in, adhere to, or benefit from treatment or have a co-occurring disorder that by itself would require hospital level care (e.g., depression with suicidal thoughts, acute psychosis);
- 6) manifest substance use or other behaviors that constitute an acute danger to themselves or others; or
- 7) have not responded to or were unable to adhere to less intensive treatment efforts and have a substance use disorder(s) that endangers others or poses an ongoing threat to their physical and mental health



Cannabis

- often considered benign,
- common in individuals with other psychiatric disorders, including major mood, anxiety, and personality disorders (1)
- can precipitate initial episodes of psychosis in vulnerable individuals (2) and is associated with an earlier age at first psychotic episode in male patients with schizophrenia, 6.9 years younger than in non-cannabis users (3)

1. Brook JS, Cohen P, Brook DW: Longitudinal study of co-occurring psychiatric disorders and substance use. *J Am Acad Child Adolesc Psychiatry* 1998; 37:322-330
2. Arseneault L, Cannon M, Witton J, Murray RM: Causal association between cannabis and psychosis: examination of the evidence. *Br J Psychiatry* 2004; 184:110-117
3. Veen ND, Selten JP, van der Tweel I, Feller WG, Hoek HW, Kahn RS: Cannabis use and age at onset of schizophrenia. *Am J Psychiatry* 2004; 161:501-506



Cannabis

- Drug treatments for marijuana dependence have been studied infrequently, perhaps because of the belief held by many that marijuana is a benign substance whose use is easy to stop when desired.
- evidence from animal and clinical studies
- has suggested that a withdrawal syndrome occurs if chronic heavy use of cannabis is discontinued (1).
- Common symptoms are primarily emotional and behavioral, although appetite change, weight loss, and physical discomfort are frequently reported.

Haney M, Ward AS, Comer SD, Foltin RW, Fischman MW: Abstinence symptoms following oral THC administration to humans. *Psychopharmacology (Berl)* 1999; 141:385–394



Cannabis

- Human trials of medications to ameliorate symptoms of marijuana withdrawal have included bupropion (1), divalproex (2,3), naltrexone, and nefazodone (4); all these trials have had negative results.
- No pharmacotherapy trials to prevent marijuana reinstatement after abstinence have been reported. Thus, no specific pharmacotherapy can be recommended at this time.

1. Haney M, Ward AS, Comer SD, Hart CL, Foltin RW, Fischman MW: Bupropion SR worsens mood during marijuana withdrawal in humans. *Psychopharmacology (Berl)* 2001; 155:171–179
2. Levin FR, McDowell D, Evans SM, Nunes E, Akerele E, Donovan S, Vosburg SK: Pharmacotherapy for marijuana dependence: a double-blind, placebo-controlled pilot study of divalproex sodium. *Am J Addict* 2004; 13:21–32
3. Haney M, Hart CL, Vosburg SK, Nasser J, Bennett A, Zubarán C, Foltin RW: Marijuana withdrawal in humans: effects of oral THC or divalproex. *Neuropsychopharmacology* 2004; 29:158–170
4. Haney M, Hart CL, Ward AS, Foltin RW: Nefazodone decreases anxiety during marijuana withdrawal in humans. *Psychopharmacology (Berl)* 2003; 165:157–165



Cannabis

- Given the lack of pharmacotherapy for marijuana dependence, psychosocial treatments such as motivational therapy and relapse prevention are recommended
- brief motivational approach and a more intensive relapse prevention approach that combines motivational approaches with coping skills development
- A recent study of a manual-guided, group-based treatment for adolescents with mild to moderate substance abuse found that marijuana use (but not alcohol use) was significantly reduced at 6 months, with the reduction sustained at 12 months (1)

Battjes RJ, Gordon MS, O'Grady KE, Kinlock TW, Katz EC, Sears EA: Evaluation of a group-based substance abuse treatment program for adolescents. *J Subst Abuse Treat* 2004; 27:123-134



Cocaine

- Treat intoxication :
- usually self-limiting
- there is no specific antidote to cocaine
- treatment is typically supportive and aimed at treating symptoms such as delusions or autonomic hyperactivity, like hypertension, tachycardia, cardiac arrhythmias, coronary artery vasospasm, myocardial infarction, stroke, and seizures
- Although the beta-blocker labetalol has been cited as being helpful in reducing this cocaine toxicity, animal studies and some clinical experience suggest that the use of adrenergic blockers and dopaminergic antagonists should be carefully monitored when treating acute cocaine intoxication (1,2,3).

1. Perrone J, Hoffman RS: Cocaine, amphetamines, caffeine, and nicotine, in *Emergency Medicine: A Comprehensive Study Guide*, 6th ed. Edited by Tintinalli JE, Kelen GD, Stapczynski JS. New York, McGraw-Hill, 2004, pp 1075-1079
2. Jin C, McCance-Katz EF: Substance abuse: cocaine use disorders, in *Psychiatry*, 2nd ed. Edited by Tasman A, Kay J, Lieberman JA. Chichester, UK, John Wiley & Sons, 2003, pp 1010-1036



Cocaine

- Benzodiazepines are used for acute cocaine intoxication in patients who become extremely agitated and/or potentially dangerous (1).
- Although antipsychotic medications have been reported to be effective in treating delusions associated with cocaine/ amphetamine intoxication, most individuals recover spontaneously within hours (2) and thus require no treatment (3).
- There is no evidence that anticonvulsants prevent stimulant-induced seizures, and they are not recommended for this purpose.

1. Goldfrank LR, Hoffman RS: The cardiovascular effects of cocaine. *Ann Emerg Med* 1991; 20:165–175
2. Gawin FH, Kleber HD: Abstinence symptomatology and psychiatric diagnosis in cocaine abusers: clinical observations. *Arch Gen Psychiatry* 1986; 43:107–113
3. Chen CK, Lin SK, Sham PC, Ball D, Loh EW, Hsiao CC, Chiang YL, Ree SC, Lee CH, Murray RM: Pre-morbid characteristics and co-morbidity of methamphetamine users with and without psychosis. *Psychol Med* 2003; 33:1407–1414



Cocaine

- Treat withdrawal :
- The clinical features and duration of the cocaine abstinence syndrome are still somewhat controversial.
- many people do experience a characteristic withdrawal syndrome within a few hours to several days after the acute cessation of, or reduction in, heavy and prolonged cocaine use.
- studies characterized withdrawal as progressing from a “crash” associated with intense depression, anxiety, anhedonia, fatigue, and suicidal ideation, sleep difficulties (insomnia or hypersomnia), lasting 1–10 weeks, increased appetite, and psychomotor retardation, which decrease steadily over several weeks. (1,2,3)

1. Gawin FH, Kleber HD: Abstinence symptomatology and psychiatric diagnosis in cocaine abusers: clinical observations. *Arch Gen Psychiatry* 1986; 43:107–113
2. Weddington WW, Brown BS, Haertzen CA, Cone EJ, Dax EM, Herning RI, Michaelson BS: Changes in mood, craving, and sleep during short-term abstinence reported by male cocaine addicts: a controlled, residential study. *Arch Gen Psychiatry* 1990; 47: 861–868
3. Coffey SF, Dansky BS, Carrigan MH, Brady KT: Acute and protracted cocaine abstinence in an outpatient population: a prospective study of mood, sleep and withdrawal symptoms. *Drug Alcohol Depend* 2000; 59:277–286



Cocaine

- Dopamine agonists, such as amantadine (200–400 mg/day)(1), and bromocriptine yielded controversial results in the treatment of cocaine withdrawal (2).
- Finally, a large study of pergolide (3) found no difference from placebo in either symptom reduction or continued cocaine use.
- Propranolol use limited to those with relatively severe withdrawal symptoms (4).

1. Handelsman L, Chordia PL, Escovar IL, Marion IJ, Lowinson JH: Amantadine for treatment of cocaine dependence in methadone-maintained patients. *Am J Psychiatry* 1988; 145:533
2 Dackis CA, Gold MS: Bromocriptine as treatment of cocaine abuse. *Lancet* 1985; 1:1151–1152
3. Malcolm R, Kajdasz DK, Herron J, Anton RF, Brady KT: A double-blind, placebo-controlled outpatient trial of pergolide for cocaine dependence. *Drug Alcohol Depend* 2000; 60:161–168
4. Kampman KM, Volpicelli JR, Mulvaney F, Alterman AI, Cornish J, Gariti P, Cnaan A, Poole S, Muller E, Acosta T, Luce D, O'Brien C: Effectiveness of propranolol for cocaine dependence treatment may depend on cocaine withdrawal symptom severity. *Drug Alcohol Depend* 2001; 63:69–78



Cocaine

- Treat dependence :
- For many patients, pharmacological treatment is not ordinarily indicated as an initial treatment because no medication has been found to have clear-cut efficacy
- No FDA-approved pharmacotherapy
- However, a number of studies have shown promising results with pharmacotherapeutic agents, and patients with more severe forms of cocaine dependence (e.g., those with more severe cocaine withdrawal symptoms) (1,2) or patients who do not respond to psychosocial treatment may be candidates for a pharmacotherapy trial.

1. Kampman KM, Volpicelli JR, Mulvaney F, Alterman AI, Cornish J, Gariti P, Cnaan A, Poole S, Muller E, Acosta T, Luce D, O'Brien C: Effectiveness of propranolol for cocaine dependence treatment may depend on cocaine withdrawal symptom severity. *Drug Alcohol Depend* 2001; 63:69–78
2. Kampman KM, Volpicelli JR, Alterman AI, Cornish J, O'Brien CP: Amantadine in the treatment of cocaine-dependent patients with severe withdrawal symptoms. *Am J Psychiatry* 2000; 157:2052–2054



Cocaine

- Studies of desipramine (1), fluoxetine (2) and bupropion (3) have yielded inconsistent findings
- The evidence for using dopamine agonists, like dexamphetamine in treating cocaine dependence is also mixed. (4)

1. Gawin FH, Kleber HD, Byck R, Rounsaville BJ, Kosten TR, Jatlow PI, Morgan C: Desipramine facilitation of initial cocaine abstinence. *Arch Gen Psychiatry* 1989; 46:117–121

2. Batki SL, Manfredi LB, Jacob P III, Jones RT: Fluoxetine for cocaine dependence in methadone maintenance: quantitative plasma and urine cocaine/benzoyllecgonine concentrations. *J Clin Psychopharmacol* 1993; 13:243–250

3. Margolin A, Kosten T, Petrakis I, Avants SK, Kosten T: An open pilot study of bupropion and psychotherapy for the treatment of cocaine abuse in methadone-maintained patients. *NIDA Res Monogr* 1991; 105:367–368

4. Shearer J, Wodak A, van Beek I, Mattick RP, Lewis J: Pilot randomized double blind placebo-controlled study of dexamphetamine for cocaine dependence. *Addiction* 2003; 98:1137–1141



Cocaine

- carbamazepine showed controversial evidence (1)
 - more recent research (2), suggested some promise for another anticonvulsant, topiramate
 - GABAB agonist baclofen has shown some success in treating cocaine dependence (3)
 - a recent double-blind clinical trial of tigabine, a GABA reuptake blocker, was superior to placebo for reducing cocaine use (4)
 - Modafinil (400 mg/day) has recently shown some efficacy for reducing cocaine abuse (5)

1. Montoya ID, Levin FR, Fudala PJ, Gorelick DA: Double-blind comparison of carbamazepine and placebo for treatment of cocaine dependence. *Drug Alcohol Depend* 1995; 38:213–219

2. Kampman KM, Pettinati H, Lynch KG, Dackis C, Sparkman T, Weigley C, O'Brien CP: A pilot trial of topiramate for the treatment of cocaine dependence. *Drug Alcohol Depend* 2004; 75:233–240

3. Ling W, Shoptaw S, Majewska D: Baclofen as a cocaine anti-craving medication: a preliminary clinical study. *Neuropsychopharmacology* 1998; 18:403–404

4. Gonzalez G, Sevarino K, Sofuoglu M, Poling J, Oliveto A, Gonsai K, George TP, Kosten TR: Tigabine increases cocaine-free urines in cocaine-dependent methadone-treated patients: results of a randomized pilot study. *Addiction* 2003; 98:1625–1632

5. Dackis CA, Kampman KM, Lynch KG, Pettinati HM, O'Brien CP: A double-blind, placebo-controlled trial of modafinil for cocaine dependence. *Neuropsychopharmacology* 2005; 30:205–211



Cocaine

- For many patients with a cocaine use disorder, psychosocial treatments focusing on abstinence are effective.
- In particular, CBTs, behavioral therapies, interpersonal therapies, and 12-step-oriented individual drug counseling can be useful, although efficacy of these therapies varies across subgroups of patients.
- Recommending regular participation in a self-help group may improve the outcome for selected patients with a cocaine use disorder



Amphetamines

- pharmacotherapy of amphetamine dependence is expected to be similar to that of cocaine. Neither disorder has an FDA-approved pharmacotherapy (1)
- very few clinical trials have been completed with amphetamine-dependent patients, with none of these studies showing different results than those described later for cocaine dependence (2,3)
- A possibly significant difference between cocaine and amphetamine is cocaine's interaction with alcohol to form cocaethylene. This metabolite has cocaine-like effects and toxicity (4)

1. American Psychiatric Association, Practice Guideline for the treatment of patients with substance use disorders, second edition, 2006, p.105

2. Rawson RA, Huber A, Brethen P, Obert J, Gulati V, Shoptaw S, Ling W: Status of methamphetamine users 2–5 years after outpatient treatment. *J Addict Dis* 2002; 21:107–119

3. Srisurapanont M, Jarusuraisin N, Kittirattanapaiboon P: Treatment for amphetamine dependence and abuse. *Cochrane Database Syst Rev* 2001; 4:CD003022

4. McCance EF, Price LH, Kosten TR, Jatlow PI: Cocaethylene: pharmacology, physiology and behavioral effects in humans. *J Pharmacol Exp Ther* 1995; 274:215–223



Ecstasy

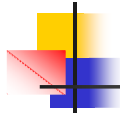
- MDMA (3, 4-Methylenedioxyamphetamine)
- a psychoactive synthetic drug possessing stimulant and hallucinogenic properties.
- analogous to amphetamine and LSD in terms of its hallucinogenic properties.
- pharmacotherapy of MDMA dependence is expected to be similar to that of cocaine (1)
- Most treatment programs offer counseling, behaviors modification, and with the use of sedatives (2)

1. American Psychiatric Association, Practice Guideline for the treatment of patients with substance use disorders, second edition, 2006, p.105
2. Tanner-Smith EE. Pharmacological content of tablets sold as "ecstasy". Drug and Alcohol Dependence 2006. 83:247-254



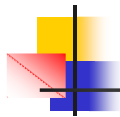
Ketamine

- an NMDA receptor antagonist
- at high, fully anesthetic level doses, ketamine has also been found to bind to opioid mu and sigma receptors
- like other drugs of this class such as phencyclidine (PCP), it induces a state referred to as "dissociative anesthesia"
- No evidence-based treatment guideline available
- Symptomatic and supportive treatment



Benzodiazepines (BDZ)

- Change to long-acting benzodiazepines
- Use medication for withdrawal symptoms
- Tail off all medication in the long-run
- Pronounced respiratory depression may occur in combination with alcohol, antidote is flumazenil



Benzodiazepines (BDZ)

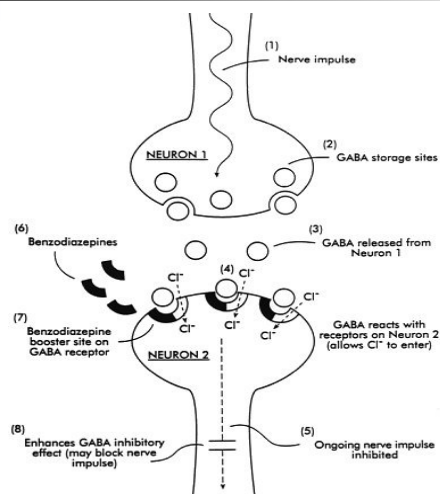
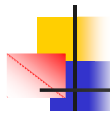


Diagram of mechanism of action of the natural neurotransmitter GABA and benzodiazepines on nerve cells (neurons) in the brain



Benzodiazepines (BDZ)

- Short acting BZD (T_{1/2} varies from 5-12 hours)
 - Temazepam (abuse potential), Lorazepam, Lormetazepam
- Longer acting BZD (T_{1/2} varies from 1-2 days)
 - Nitrazepam, flurazepam, flunitrazepam (addictive potential)



Benzodiazepines (BDZ)

- Prolongs the total duration of sleep; but it disturbs normal sleep architecture; reduces sleep latency;
- Hangover: it impairs daytime performance, memory disturbances and psychomotor activity e.g. driving
- Dependence
- Tolerances / Withdrawal symptoms (risk of Rebound insomnia)
- Pronounced respiratory depression may occur in combination with alcohol, antidote is flumazenil
- Commonest prescribed hypnotics but far from an ideal hypnotic
- Possibility of drug induced somnambulism / automatism at sleep



Benzodiazepines (BDZ)

- Short-term use; intermittent if possible
- Avoid high dose; avoid short acting high potency BDZ
- Avoid abrupt withdrawal
- Avoid in addiction-prone people and respiratory failure
- Reduce dose in elderly



Non-BDZ hypnotics (z-drug)

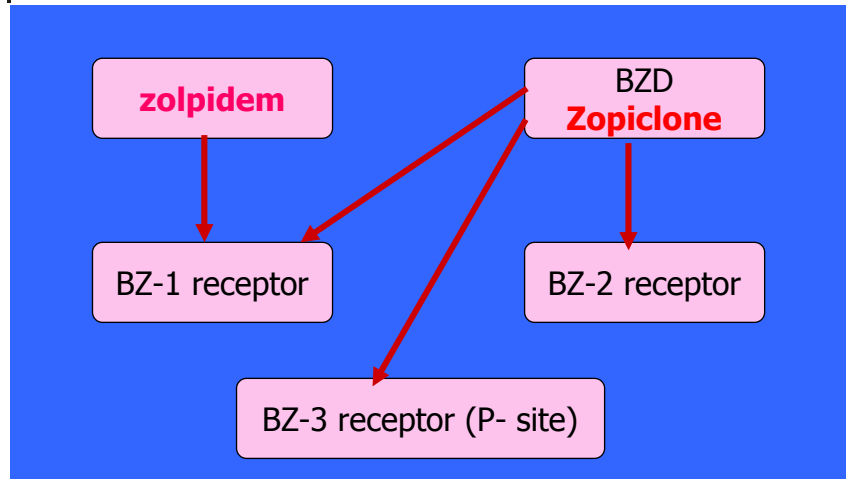
Zolpidem, imidazopyridine

- GABA-A receptor α -1 selective
- Onset 30 to 60 minutes, lasts for 3 to 4 hours
- Short term use

Zopiclone, cyclopyrrolone

- Pharmacologic binding spectrum that resembles classic BDZ but structurally different
- Onset in 1 hour, lasts for 6 to 8 hours
- Bitter taste, 40 % of patients experience it, genetically determined

Differences of zolpidem vs. zopiclone & BDZ



Non-BDZ hypnotics (z-drug)

- Zolpidem (Stilnox) has a preferential hypnotic effect due to its selectivity for BZ-1 receptors, while zopiclone (Imovane) has a BDZ-like pharmacological profile
- Zolpidem (Stilnox) has a shorter half-life (2.4 vs 5 hours), suggesting a smaller incidence of hangover/residual effects
- Sleep architecture was better preserved with Zolpidem (Stilnox)
- zopiclone (Imovane) is associated with a bitter after-taste



Conclusion

- Assess and decide treatment plan
- Decide the treatment setting
- Treat the substance abuse disorder at different phases
- Treat co-morbid medical and psychiatric conditions
- Supportive and symptomatic drug treatment
- Only relatively more specific treatment recommended for opioid, alcohol and nicotine substance abuse disorders by APA guideline, not for others
- Combine pharmacological and psychosocial intervention for abstinence or controlled use
- Refer to specialist care when necessary