

HISTORY OF BENZODIAZEPINES

WHAT THE TEXTBOOKS MAY NOT TELL YOU

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ANXIOLYTIC DRUGS THROUGH THE AGES

Alcohol 8000 years

Opium 1000s of years

Bromides 1870s

Also chloral hydrate, paraldehyde

Barbiturates 1903-1912

Also carbromal, glutethimide, methaqualone etc

Benzodiazepines 1960 Librium; 1963 Valium

Z drugs zopiclone 1998; eszopiclone 2005

Morbidity in 50 long-term benzodiazepine users

After starting benzodiazepines:

20% - took drug overdose requiring hospital admission

20% - developed incapacitating agoraphobia

18% - had GI investigations (irritable bowel)

10% - had neurological investigations

(3 wrongly diagnosed as MS)

62% - received other psychotropic drugs (antidepressants)

28% - were taking 2 prescribed benzodiazepines

Some Common Acute Benzodiazepine Withdrawal Symptoms

Symptoms common to all anxiety states

Anxiety, panic attacks, agoraphobia
Insomnia, nightmares
Depression, dysphoria
Excitability, jumpiness, restlessness
Poor memory, concentration
Dizziness, lightheadedness
Weakness, “jelly legs”
Tremor
 Muscle pain, stiffness
 (limbs, back, neck, jaw, head)
Sweating, night sweats
Palpitations

Symptoms less common in anxiety states; relatively specific to benzodiazepine withdrawal

Perceptual disturbances, sense movement
Depersonalisation, derealisation
Hallucinations (visual, auditory),
 misperceptions
Distortion of body image
Tingling, numbness, altered sensation
Formication
Sensory hypersensitivity (light, sound,
 taste, smell)
Muscle twitches, jerks, fasciculation
Tinnitus
Psychotic symptoms
Confusion, delirium
Fits

SOME PROTRACTED BENZODIAZEPINE “WITHDRAWAL” SYMPTOMS

Anxiety

Depression

Gastrointestinal

Neurological

tinnitus

?peripheral neuropathy

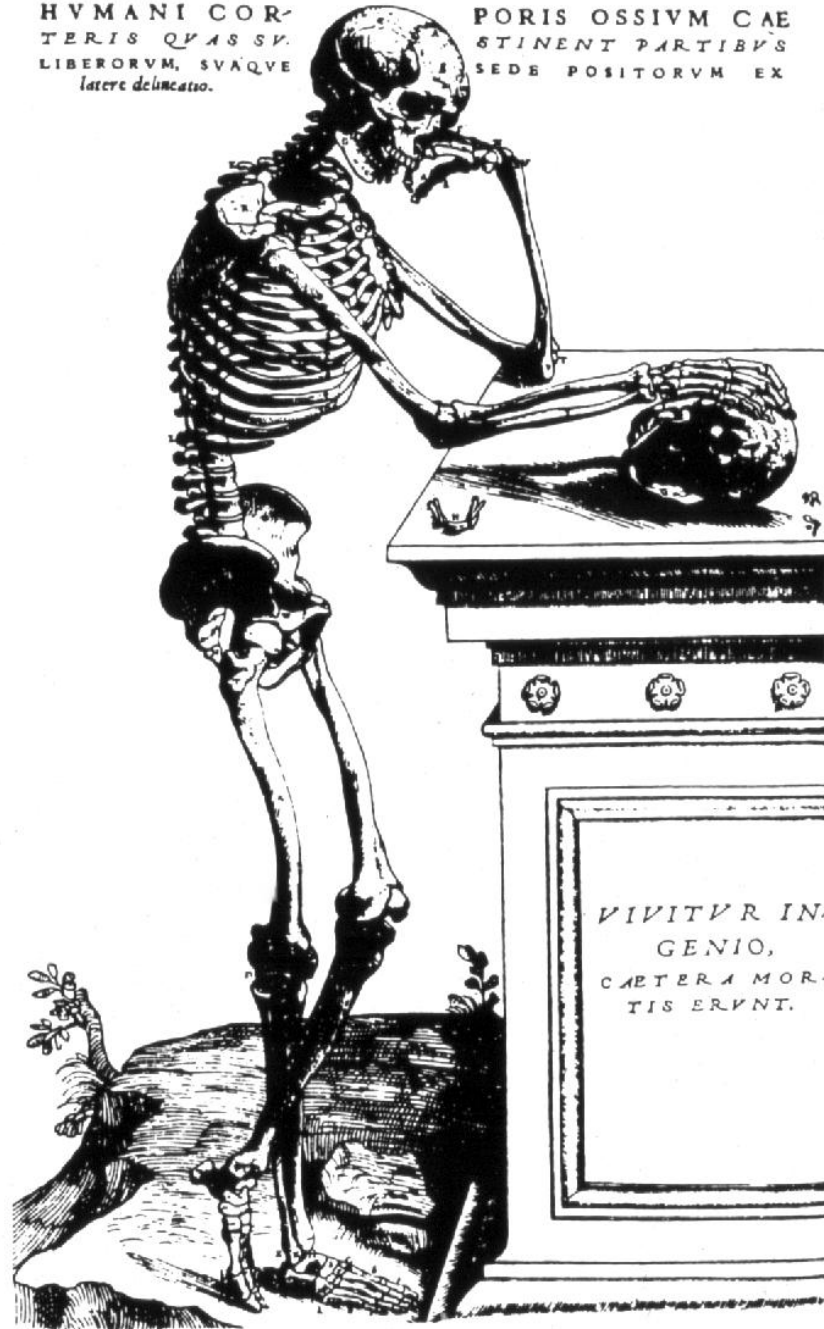
motor - muscle spasms, ticks, jerks

“restless legs syndrome”

?cognitive impairment

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SOCIOECONOMIC COSTS OF INAPPROPRIATE BENZODIAZEPINE PRESCRIBING

- 1. Increased mortality from overdose, suicide**
- 2. Increased risk of accidents
traffic. Home, work, falls and fractures in elderly**
- 3. Increased risk of aggressive behaviour, assault, antisocial acts**
- 4. Contribution to marital/domestic disharmony**
- 5. Increased risk to foetus, infants, children**
- 6. Contribution to job loss, unemployment, loss of work through illness**
- 7. Cost of medical consultations, hospital admissions/ investigations**
- 8. Dependence and withdrawal reactions**
- 9. Recreational abuse - AIDS, hepatitis, unwanted pregnancy**
- 10. Costs of drug NHS prescriptions**
- 11. Costs to DHSS due to disability**
- 12. Costs of litigation**

THERAPEUTIC ACTIONS OF **BENZODIAZEPINES**

Actions

Hypnotic

Anxiolytic (tranquillising)

Anticonvulsant

Amnesic

Muscle relaxant

Clinical uses

Short-term treatment of insomnia

Short-term treatment of severe anxiety

Short-term aid to alcohol withdrawal

Acute treatment of violent psychotic states

Epileptic and drug-induced convulsions

Premedication before surgery

Muscle spasms, dystonias

ADVERSE EFFECTS OF BENZODIAZEPINES

1. Over-sedation

Depressed psychomotor performance, poor memory, ataxia contribute to car accidents, shoplifting

Most marked in the elderly, may produce mental confusion contribute to falls and fractures

2. Additive effects with other CNS depressants

e.g. alcohol, drug overdose

3. Disinhibition

Aggressiveness ? Contribute to baby battering, wife beating

4. Depression, emotional blunting

5. Cognitive impairment

6. Adverse effects in pregnancy

Neonatal depression

7. Abuse

8. Tolerance, dependence, withdrawal effects

HALF-LIVES AND EQUIVALENT POTENCIES OF BENZODIAZEPINE ANXIOLYTICS

Benzodiazepine	Half-life (hrs) [active metabolite]	Approximate equivalent oral dosages (mg)
<u>Alprazolam</u> (Xanax)	6-12	0.5
<u>Clonazepam</u> (Klonopin)	18-50	0.5
<u>Lorazepam</u> (Ativan)	10-20	1
<u>Diazepam</u> (Valium)	20-100 [26-200]	10
<u>Chlordiazepoxide</u> (Librium)	5-30	25
<u>Clorazepate</u> (Tranxene)	[36-200]	15
<u>Oxazepam</u> (Serax)	4-15	20

HALF-LIVES AND EQUIVALENT POTENCIES OF BENZODIAZEPINE HYPNOTICS

Benzodiazepine	Half-life (hrs) [active metabolite]	Approximate equivalent oral dosages (mg)
<u>Triazolam</u> (Halcion)	2	0.5
<u>Flunitrazepam</u> (Rohypnol)	18-26 [36-200]	1
<u>Nitrazepam</u> (Mogadon)	15-38	10
<u>Temazepam</u> (Restoril)	8-22	20
<u>Flunitrazepam</u> (Dalmane)	[40-250]	15-30
<u>Diazepam</u> (Valium)	20-100 [36-200]	10

PATIENTS VULNERABLE TO INCREASED RISKS OF BENZODIAZEPINES

Condition

Risks

Older age (>65yrs)

Mental confusion, amnesia, falls
and fractures

Chronic respiratory disease

Respiratory depression

Liver disease

Oversedation

Depression

Exacerbation, suicide risk

Other sedative drugs

Additive effects

Pregnancy

Neonatal depression, withdrawal

Alcohol/drug abuse

Increased risk of dependence

Genetic factors

Slow metabolisers

SOME STEPS NEEDED TO REDUCE BENZODIAZEPINE PRESCRIBING (1)

New Patients

- Short-term prescriptions (2-4 weeks only) in minimal dosage
- Avoid potent benzodiazepines (alprazolam, lorazepam, clonazepam)
- Consider rescheduling benzodiazepines
- Develop non-drug treatments for anxiety and insomnia with suitable training and provision of staff
- Educate doctors and health care workers about potential dangers of new drugs (e.g. Z drugs and others)

SOME STEPS NEEDED TO REDUCE BENZODIAZEPINE PRESCRIBING (2)

Long-term patients (already dependent)

- Educate doctors and health care workers in withdrawal methods
- Financial aid for patient support groups and dedicated withdrawal clinics

General measures

- Research into long-term effects of benzodiazepines
- Greater openness about results of drug-company sponsored clinical trials
- Keep up pressure on government health authorities and the public