SEDATIVE-HYPNOTICS: Barbiturates (p.1)

History

these drugs were the major tx option for anxiety & insomnia from 1912 to 1960

they were very likely to be abused

often used in suicide and attempted suicide

caused accidental deaths in *Ss* who took them w/ ETOH or in combination with other S-Hs

1.Pharmacokinetics:

are often *classified by the length of their ½ lives*, which can vary over large time spans (from minutes to several days)

ultra-shorts and short-acting barbs may be used for a brief medical procedure or for a "pre-anesthetic"

e.g. Pentothal/thiopental, 3 minute distribution ½ life
action terminated by re-distribution
Brevital/methohexital, 1-2 hour ½ life

moderate acting barbs may be used for surgeries taking hours, with ½ lives from 24-48 hours

e.g. Amytal/amobarbital, 10-40 hour ½ life

e.g. Nembutal/pentobarbital

e.g. Seconal/secobarbital

long acting barbs, may have 80-100 hour ½ lives

what clinical problem would require such a long duration?...

e.g. Luminal/phenobarbital, 24-140 hour ½ life

these moderate to long acting barbs have their action terminated by liver enzyme metabolism & excretion (not re-distribution)

barbs are usually taken PO, completely absorbed and well distributed to most body tissues

degree of lipid solubility has major impact on ½ lives

the short-acting barbs lipid solubility > mod.-long acting barbs

next day "hang over" effects are common for the mod.-long acting barbs

SEDATIVE-HYPNOTICS: Barbiturates (p.2)

1. Pharmacokinetics (cont.):

"hang over" effects due to slow elimination (often reabsorbed from urine)
urine can show barbs still being eliminated for long time after drug D/Cd

protein binding of barbs.

2. Pharmacodynamics:

barbs do not block incoming pain signals, so why are they used as anesthetics?

in small doses barbs can decrease response to pain…why?

sometimes barbs will lead to an increase is aggression, esp. with pain or with paranoid ideation…why?

barbs used a sleeping pills will increase TST, decrease SOL & WASO
do change sleep "architecture", esp. decreasing REM
implications…?

implications of the next day "hang over" effects

barbs can depress respiration at high dose levels (no effect on heart)
implications…?

barbs induce liver enzymes (non-specific)
implications?

barbs have a similar behavioral effects to ETOH: disoriented, disinhibition, decreased anxiety, impulsiveness, poor judgment, increased depression, slurred speech, aggression/violence, ataxia, loss of motor coordination (including lack of awareness of loss)

SEDATIVE-HYPNOTICS: Barbiturates (p.3)

2. Pharmacokinetics (cont.)

tolerance develops via metabolic tolerance & cellular tolerance

esp. sedative effects (gradually decreasing TST)…implication?

depression of reaction time

reinforcing effects ("intoxication")…implication?

tolerance does *not* develop quickly to respiratory depression effects implications….

tolerance does *not* develop quickly to the antiseizure effects either implications….

physical dependence on barbs – a serious problem when attempt to D/C

REM rebound, "dream anxiety attacks", severe insomnia (that lessens over time), convulsions/seizures, hallucinations, restlessness, disorientation, delusions, delirium

plus, S will show *craving behavior* (potential for abuse in fairly high)

Barb use and *pregnancy*

barbs do affect fetus, occasional congenital defects

post-natal respiration depression

avoid if possible; use barbs only as an antiseizure med. w/ pg woman

3. Neurophysiological Effects

barbs are more potent drugs vs. BZDs because:

at high doses barbs can independently open Cl- ion channels, even in absence of GABA (BZDs cannot)

all GABA receptors have a barb binding site; many lack a BZD site

barbs probably inhibit non-GABA neurons too; BZDs probably do not