Possibilities and Problems in Clinical Research on Benzodiazepine Use

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Potential conflicts of interest
Consultant/Advisory Board
Lundbeck, Trancept
Various firms of solicitors
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Research into Benzodiazepine Addiction - 1

1. Poor control of the independent variable, namely the drug taken – identity, preparation (bases vs. salts), purity, doses, co-administered drugs
2. Inability to allocate subjects randomly to treatments
3. Heterogeneity of different forms of addiction (e.g., middle-aged housewife steadily overusing tranquillizers vs. polydrug abuser)
4. Personality structures (e.g., impulsive, risk-taking)

Solutions tried include epidemiological surveys using birth cohorts, surrogate models - both animal and human.
Research into Benzodiazepine Addiction - 2

- Biological aspects intensively researched
- Pharmacology now much clearer
- Many receptors and ligands (neurotransmitters) now defined and some genes known
- Common factors such as dopamine and reward mechanisms

Outstanding questions – Research - 1

- Is there some way of predicting who will become dependent on normal doses?
- Is there some way of predicting who will abuse BZDs?
- Can safer drugs substitute or does cross tolerant drug substitution merely postpone withdrawal

Outstanding issues – Clinical

- Poor knowledge of extent and severity of problem
- Extent and severity of prolonged withdrawal
- Setting up clinics to treat non-abuser dependent patients separately from Addiction Units
- Development of methods of treatment
- Does tapering work?
- Tailor treatment to expectations
- Medico-legal implications
Use of flumazenil:

- LADER, Malcolm H. and MORTON, Sally V.
- Some other studies from Brazil and Sweden

Agonist and antagonist treatment

- ?maintenance slow onset on-acting BZD agonists
- May need new formulations such as programmed release or depots
- Similarly for flumazenil formulations

Summary

- Neglected area
- Perception of BZD dependence as minor condition
- Epidemiology unclear
- Few resources devoted to BZD dependence compared with diamorphine or cocaine