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BENZODIAZEPINES, DEPENDENCE AND WITHDRAWAL SYMPTOMS

There has been concern for many years regarding benzodiazepine dependence (Br. Med. J. 1980: 280, 910-912). Such dependence is becoming increasingly worrying.

Withdrawal symptoms include anxiety, tremor, confusion, insomnia, perceptual disorders, fits, depression, gastrointestinal and other somatic symptoms. These may sometimes be difficult to distinguish from the symptoms of the original illness.

It is important to note that withdrawal symptoms can occur with benzodiazepines following therapeutic doses given for short periods of time.

Withdrawal effects usually appear shortly after stopping a benzodiazepine with a short half life, or up to several days after stopping one with a long half life. Symptoms may continue for weeks or months. No epidemiological evidence is available to suggest that one benzodiazepine is more responsible for the development of dependency or withdrawal symptoms than another.

The Committee on Safety of Medicines recommends that the use of benzodiazepines should be limited in the following ways:

USES
As Anxiolytics
1. Benzodiazepines are indicated for the short-term relief (two to four weeks only) of anxiety that is severe, disabling or subjecting the
individual to unacceptable dis-
 distress, occurring alone or in
 association with insomnia or
 short-term psychosomatic,
 organic or psychotic illness.

2. The use of benzodiazepines to
treat short-term ‘mild’ anxiety is
inappropriate and unsuitable.

As Hypnotics

3. Benzodiazepines should be used
to treat insomnia only when it is
severe, disabling, or subjecting the
individual to extreme distress.

DOSE

1. The lowest dose which can control
the symptoms should be used. It
should not be continued beyond
four weeks.

2. Long-term chronic use is not
recommended.

3. Treatment should always be
tapered off gradually.

4. Patients who have taken benzo-
diazepines for a long time may
require a longer period during
which doses are reduced.

5. When a benzodiazepine is used as
a hypnotic, treatment should, if
possible, be intermittent.

PRECAUTIONS

1. Benzodiazepines should not be
used alone to treat depression or
anxiety associated with depres-
sion. Suicide may be precipitated
in such patients.

2. They should not be used for phobic
or obsessive states.

3. They should not be used for the
treatment of chronic psychosis.

4. In cases of loss or bereavement,
psychological adjustment may be
inhibited by benzodiazepines.

5. Disinhibiting effects may be
manifested in various ways. Suicide
may be precipitated in
patients who are depressed, and
aggressive behaviour towards self
and others may be precipitated.
Extreme caution should therefore
be used in prescribing benzo-
diazepines in patients with
personality disorders.

THE “RED ALERT” SCHEME

The Committee on Safety of Medicines
and the Drug Safety Research Unit have
begun a trial of a new drug monitoring
scheme called “Red Alert”. Its aim is to
encourage doctors to report serious
adverse reactions to new drugs.

The scheme will cover every new drug
(new active substance) marketed over
the trial period. Inclusion of a drug does
not imply any special concern about its
safety at the present time.

During the trial, GPs in England who
prescribe drugs included in the scheme
will be sent specially modified yellow
cards marked with red triangles. These
“red alert” cards are printed with the
patient’s name and the name of the
drug, and should be used only to report
SERIOUS OR LIFE THREATENING
adverse reactions or the death of the
patient. Other reactions should be
reported direct to the Committee on
Safety of Medicines on an ordinary
yellow card. Detailed guidance is given
with each “red alert” card, and doctors
are asked to follow it carefully.

SPIRONOLACTONE

It has become known to the Committee
on Safety of Medicines that potential
human metabolic products of
spironolactone are carcinogenic in
rodents.
As a result, the licences for all products containing spironolactone have been amended so that the drug is no longer indicated for essential hypertension and idiopathic oedema.

Products containing spironolactone remain licensed for use in cirrhosis with ascites and oedema, malignant ascites, nephrotic syndrome, and in the diagnosis and treatment of primary hyperaldosteronism and in congestive heart failure.

The forthcoming publication by McPherson and colleagues suggests that there may be a two and a half fold increase in the risk of breast cancer in women up to 45 years of age who have had four or more years of oral contraceptive use before their first full term pregnancy. The authors point out that their data do not directly reflect upon the use of the modern low dose oral contraceptive pills. In addition, this study has found no association between oral contraceptive use after first full term pregnancy and breast cancer either in women under 45 years of age or in older women. The paper extends the previously reported results of these authors (published in December 1983), which were fully considered by the Committee on Safety of Medicines at the time of their appearance.

The Committee on Safety of Medicines has considered the additional results now being made available in the light of all the current evidence. It will continue to monitor the several studies which are still in progress on this subject but agrees with the view of McPherson and others that the newly reported findings do not indicate the need to change at this time the current advice regarding the use of the presently available oral contraceptive agents. Thus the Committee remains of the view that women receiving oral contraceptives should be prescribed a product with the lowest suitable content of both oestrogen and progestogen.

A W ASSCHER*
COMMITTEE ON SAFETY OF MEDICINES

ADR REPORTING: WHAT, HOW AND WHERE

What to Report

NEW Drugs ▼ Report ALL suspected reactions, that is any adverse or unexpected event, however minor, which could conceivably be attributed to the drug.

Please report even if the reaction is well recognised or if you are unsure of the causal relationship.

New drugs have an inverted black triangle ▼" ▼ in the British National Formulary, MIMS and the Data Sheet Compendium.

ESTABLISHED Drugs

Report SERIOUS suspected reactions, including those which are fatal, life-threatening, disabling, incapacitating, or which result in or prolong hospitalisation.

Please report a serious reaction even if it is already well-recognised.

Please do not report minor reactions for established drugs.

How to Report

Two yellow cards are enclosed. Others can be found in:

— the British National Formulary
— FP10 prescription pads
— the ABPI Data Sheet Compendium
— by dialling 100 and asking for CSM Freephone

When reporting, please give details of BRAND NAME and BATCH NUMBER, especially for

— over the counter drugs
— slow or delayed release formulations
— biotechnology products, eg human growth hormone
— vaccines

Please print your name and address clearly, or use a legible stamp. A copy of the report will be returned to you in a window envelope.

Where to Report

CSM, FREEPOST, London SW8 5BR

or if you are in one of the following NHS regions:

CSM West Midlands, FREEPOST, Birmingham B15 1BR

CSM Northern, FREEPOST 1085, Newcastle-upon-Tyne NE1 1BR

CSM Wales, FREEPOST, Cardiff C44 1ZZ

(Yellow cards with red triangles only should be sent FREEPOST to the Drug Safety Research Unit at the address shown on them.)