Fluoxetine - The Big Seller - Its side effects & Interactions

Fluoxetine (Prozac) has fast become a big seller in the relatively short period it has been on the market. Although not inexpensive, one of its main claims to fame is the advantage that in overdose it is safer than the tricyclic antidepressants (TCA's) which are potentially severely cardiotoxic. It is claimed to be equivalent in efficacy to imipramine. All existing treatments for depression, in particular the tricyclics have drawbacks. The tricyclic antidepressants (viz; imipramine (Tofranil), amitriptyline (Tryptanol etc) are associated with some unpleasant side-effects which reduce compliance and compromise treatment.

The clinical implications of a deficiency in the serotonin (5-hydroxytryptamine) system has been a long-standing area of research into drugs for depression, and discussion has focused on whether drugs that work on either the serotonin or the noradrenergic systems have a pre-eminent role in treatment. Fluoxetine is a specific 5-HT uptake inhibitor and may be compared to the efficacy of a specific noradrenaline uptake inhibitor such as imipramine. It has become apparent that antidepressants may initiate a clinical response by direct effects on either amine system and that relationships between the systems are rather more complex than previously thought. The side-effect profile of the TCA's include: dry mouth, prostatism in the elderly male, postural hypotension and being potentially epileptogenic. Their drug interactions such as cardiotoxicity with ephedrine-like compounds, inhibition of blood pressure control with reserpine and guanethidine as well as their potentially serious interactions with monoamine oxidase inhibitors (MOAI's) are well documented.

As fluoxetine is a relatively new agent more information about it is likely to become available with time. Fluoxetine has the advantage of a once-a-day dosage not being sedative as opposed to the TCA's, but there have been reports of side-effects in the international literature. Reports reaching our Centre have included sleep disturbance, weight loss, hypertension, anxiety, nausea, tremor, dizziness, sexual dysfunction, flu-like symptoms, seizures, mania and extra-pyramidal symptoms. It must at once be admitted that depressed patients do show a higher incidence of side-effects (and placebo effect up to 30%!) and that the TCA's have a similar side-effect profile.

Fluoxetine has been shown to have enzyme inhibiting properties as it raises the level of TCA's when given concomitantly. The obvious answer to this would be to reduce the dose of the TCA, but toxicity may be a potentially serious problem before it is recognised.

It is in the area of weight reduction that we wish to sound a note of warning. Its use as an anorexiant is not a registered indication and anyone using it for this purpose would be well advised to study the literature carefully because if anything should go wrong, there could be serious consequences medicolegally. (This applies of course to any drug when used for unregistered indications.)

As is the case with the TCAs, the use of monoamine oxidase inhibitors with fluoxetine is a potentially dangerous combination as hyperthermia and hypertensive crisis can be provoked. Fluoxetine may antagonise the anxiolytic action of buspirone, while combination of fluoxetine with lithium may have a use in refractory depression, while other reports suggest that the combination may precipitate mania and lithium toxicity.

It is in the area of suicide and overdose that fluoxetine outshines the TCA's. The tricyclics are potentially dangerous in overdose. Overdose of fluoxetine, while apparently not life-threatening, is likely to produce nausea, vomiting, agitation, hypomania, insomnia and tremor. Fluoxetine does not cause impairment of psychomotor function nor does it potentiate the effects of alcohol.

Cardiac toxicity with fluoxetine has not been reported.

Safety in human pregnancy or lactation has not yet been proven although animal studies have shown no harm to the foetus.

References from various sources available on request.

Articles compiled by: Joe Talmud & Laubi Walters

MEDICINES SAFETY CENTRE

A link between Valproate and Spina Bifida?

Spina bifida has occurred in 9 children born to Australian women with epilepsy who took valproate (Epilim, Convulex) during pregnancy. The Australian Drug Evaluation Committee (ADRAC) has published warnings about this association and suggests that pregnant women undergo ultrasound and amniocentesis to allow prenatal diagnosis. Spina bifida is estimated to occur in 1-2% of offspring exposed to valproic acid in the first trimester. Women with epilepsy are 3-fold more likely to have offspring with abnormalities than the normal population (which is about 2,5%). However, the dangers to the mother and child of uncontrolled seizures far outweigh the risk of fetal abnormalities.

Refs: ADRAC Bulletin May 1990.

Are your patients losing their hair?

Alopecia is often considered to be a minor adverse effect (unless you are the one suffering from it!) Drugs most likely to be offenders in this regard include the antineoplastics, valproic acid 11, (Epilim, Convulex); clofibrate 7 (Atromid S), propranolol 7 (Inderal etc); allopurinol (Zyloprim, Puricos etc)), clonidine (Dixarit, Catapres), terfenadine (Tildane) 6 reports each; as well as atenolol (Tenormin), naproxen (Naprosyn, Nafasol), captopril (Capoten) and piroxicam (Feldene) .. 3-6 each. [The numbers indicate reports received by the Australian adverse reaction monitoring committee since 1972.] Other offenders include bezafibrate (Bezalip), carbamazepine (Tegretol, Degranol etc), colchicine, ketoconazole (Nizoral), oral contraceptives and sulphasalazine (Salazopyrin).

(ADRAC Bulletin May 1990).

UNIVERSITY OF CAPE TOWN: MEDICINES SAFETY CENTRE

(an incorporated association not for gain)

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DRUG EXPERIENCE REPORT

(Names of reporter and patient will remain confidential and you will be kept informed of our findings)

PATIENT (name or identification)

Age:
Sex:
Race:

ADVERSE REACTION DESCRIPTION:

Date of onset of reaction
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Drug therapy: Asterisk suspected drug(s) *Trade names please*	Daily dosage and route	Date begun	Date stopped	Reasons for use
.....	.....	.....	.....	.....
.....	.....	.....	.....	.....
.....	.....	.....	.....	.....
.....	.....	.....	.....	.....

TREATMENT:

OUTCOME: Recovered ☐ Not recovered ☐ Unknown ☐ Fatal ☐

SEQUELAE: No ☐ Yes ☐ (describe)

COMMENTS: (e.g. relevant history, previous exposure to this drug, allergies)

REPORTING DOCTOR, PHARMACIST etc. (please specify)

Name:

Address:

Signature: .....

Date / / 199