

mindovermatter

by Professor Gordon Parker

Which antidepressant?

Working out the right antidepressant for the right patient.

AVIS, a single clerk in her early 40s, had experienced unipolar 'clinical' depressive episodes since her teens.

She sought referral, having been prescribed six different antidepressant drugs in the past: two with no side-effects but no benefit; two with some temporary benefit before "pooping out"; and two being clearly beneficial but with troubling side-effects.

Patients' non-response to multiple antidepressant drugs is not uncommon, and can be handled in several ways. It may be that medication is the inappropriate treatment option, and there is need for a management paradigm shift.

If medication does appear appropriate, practitioners vary in their approaches. Assuming the patient has not received the practitioner's preferred drug, the option of trialling it is common. Otherwise, practitioners may refer the patient for a second opinion, or choose from the list of untried drugs. If the last, what factors should shape that decision?

COMMON PRACTICES

As there is a well-propagated myth that all antidepressant drugs are of equal efficacy, many practitioners are inclined to choose an antidepressant that – in their hands – has a low rate of side-effects.

Others will prescribe the drugs favoured by consultants they respect. Some choose the most recently released antidepressant drug. In essence, we variably observe practicality and eclecticism in drug choice. Can a logic be advanced?

BENEFITS VERSUS SIDE-EFFECTS

While all antidepressant drugs (within and across differing drug classes) appear of equal efficacy in their licensing studies, they do vary in their real world effectiveness.

When we have asked experienced clinical psychiatrists to rank antidepressants in terms of their effectiveness (and ignoring the side-effect profile), a distinct gradient is generated: the tricyclics (TCAs) rate as more effective than the dual-action drugs, which in turn rate as more effective than the SSRIs, which in turn rate as more effective than drugs such as moclobemide.

For side-effect profiles, the gradient is almost reversed. Thus, there is an immediate problem if drug prescription logic is based on any side-effect/benefit ratio, especially as side-effects commonly emerge before any benefits.

ANOTHER LOGIC

An alternative logic assumes there are different types of depression, with each having a differential response to differing antidepressant strategies and drug classes.

A further step is to question

the purpose of the antidepressant – which may be to take the edge off the depression, or actually intended to address underlying neurotransmitter perturbations, or perhaps have some other role.

The Black Dog Institute's hierarchical 'structural' model of depressive disorders assumes a set of non-melancholic conditions and two (melancholic and psychotic) categorical depressive disorders, with the latter two distinguished by class-specific features (psychomotor disturbance and psychotic features respectively) from the non-melancholic class.

Its related 'functional' model assumes that any neurotransmitter perturbation contributing to a non-melancholic depression is principally a serotonergic one.

Thus, broad-action drugs (such as tricyclics) generally have no advantage over SSRIs for those with a non-melancholic depression (demonstrated in our two independent studies), even when augmented (e.g. with lithium, atypical antipsychotic drugs or other options).

In case of non-response, the clinician might better trial a second SSRI or possibly a dual-action drug, and if they failed, consider non-drug options rather than proceeding to broad-action strategies.

For melancholic depression, we assume a greater contribution of noradrenergic (and possibly dopaminergic)



dysfunction, which logically argues for broader action antidepressants. Thus, a dual-action drug is more likely to be beneficial than an SSRI, and a TCA even more effective. We have shown the superiority of TCAs over SSRIs in both prospective and retrospective melancholia studies, though that superiority is somewhat age-dependent, with the chance of an SSRI being beneficial for melancholic depression decreasing with age.

If a broader action antidepressant alone is ineffective, augmenting strategies have a logic here.

For psychotic depression, we assume a dopaminergic contribution to be distinctive, arguing for an antipsychotic drug in addition to an antidepressant, although there are no data informing us whether there is greater benefit from broad-action antidepressants over narrow-action ones in effecting such combination therapy.

Meta-analyses have quantified an antidepressant alone as

having about a 25% chance of benefit, an antipsychotic drug alone about 33%, and their combination about 80% – a quite striking differential.

CONCLUSIONS

Just as all roads do not lead to Rome, not all antidepressant drugs are equal in their effectiveness or salience for differing expressions of depression – and improved road maps of depressive disorders would assist practitioners to their destination.

And Avis? She linked up with Axel at a group therapy course enhancing social skills for depressed people. Both are on the road to recovery. ☺

A Rational Model for Antidepressant Drug Prescription can be found at <http://www.blackdoginstitute.org.au/clinicians/clinicianaids/>

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References available from author.

clinicaltrials

COPD study

RESEARCHERS from Sydney's Woolcock Institute of Medical Research are looking for current and past smokers with chronic lung disease to take part in a study evaluating a treatment regimen for the condition.

The study aims to determine the safety and efficacy of taking one inhalation of Symbicort Turbuhaler (320/9 µg) twice a day on top of one inhalation of Spiriva (18 µg) daily compared to taking one inhalation of Spiriva daily alone.

Participants in the study will be asked

to attend six visits over the 12-week duration of the trial. Each visit will take approximately 1-2 hours and will involve a series of questionnaires, as well as spirometry testing.

In addition, subjects will be given questionnaires to complete at home and will also be expected to undertake peak

flow monitoring 2-3 times a day.

To be eligible for the study, volunteers need to be current or past smokers, older than 40 years and have a diagnosis of COPD, emphysema or chronic bronchitis.

For further information about the study, please contact Camilla Hoyos on (02) 9515 8583.