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EDITORIAL

"ALL ANTIDEPRESSANTS ARE CREATED EQUAL" (SOME ARE MORE EQUAL THAN OTHERS)

"All antidepressants have a 60-70% response rate". "Nobody has ever proved that one antidepressant is better than another".

How far are these statements true? Does this mean that antidepressants are interchangeable?

All marketable drugs are categorized as belonging to a particular class depending upon specific biochemical or pharmacological properties. Grouping together drugs in this fashion has certain advantages and disadvantages.

To assume that drugs belonging to a particular class can be used interchangeably may not be true. Interchangeability does not take into account the benefit, risk or cost of the drug. Drug selection within a class may depend on marketing strategies (Furberg et al.,1999).

Drug regulating agencies assume that all drugs within a class are related by structure, activity or adverse effects. This assumption is qualitative i.e., whether the drug is effective when compared to standard drug or plecebo. The agency is not concerned with quantitative differences in terms of efficacy or safety. It is the marketing department, which often decides this issue. Certain drugs may have long term side effects, which become obvious only by post marketing surveillance or anecedotal reports by practitioners (pharmacovigilance).

Why should an antidepressant be changed?

The three main reasons are lack of efficacy, troublesome side effects, or the high cost of the drug.

Traditionally, antidepressants are classified into three group viz., tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and monoamine oxidse inhibitors (MAOIs).

Drugs belonging to a particular group are supposedly interchangeable. But there are limitations.

Dothiepin, doxepin and amitriptyline are all sedative tricyclic antidepressants. If a switchover is made from dothiepin to doxepin or amitriptyline for some reason, there is a risk of developing acute urinary retention, or frequent falls and fractures because of marked anticholinergic and adrenargic side effects with amitriptyline and doxepin which can be disastrous (Kaplan & Sadock,1991).

When changing over from a TCA to a SSRI, the SSRI may not prove as effective as the TCA (Preskorn,1994). TCAs are more effective than SSRIs, especially in severely depressed inpatients (DUAG,1988; DUAG,1990; Roose et al.,1994; Anderson & Tomenson,1994). Simultaneous administration of a TCA and a SSRI can increase the TCA levels and cause severe side effects like seizures or cardiotoxicity or a serotonergic syndrome during the change over period (Montgomery,1998).

In comparative drug trials between two drugs, the statistical conclusion "no significant difference between two groups" does not mean the two drugs are equally effective. At periodic follow-up assessments during the trial, a patient on drug 'A' may say "Doctor I feel great, can I stop the pills?" In contrast, the patient on drug 'B' may say "Doctor, like that, I am alright, but ------". This could mean that drug 'B' is probably not as effective as drug 'A'. The two drugs may be quantitatively different though statistically not different. Statistical significance is not the same thing as clinical efficacy. Inadequate recovery

or residual symptoms of depression after antidepressant treatment, is one of the chief reasons for treatment resistant depression and relapses

Approximately 20% of patients on antidepressant treatment will develop side effects of which about 90% will become treatment resistant if the same antidepressant is continued. TCAs are more liable to produce side effects than SSRIs because of action on multiple receptor systems. SSRIs act predominately on a single receptor system. A single dose of a TCA can produe pharmacological effects similar to a "cocktail" of various drugs. For instance, a 25 mg dose of amitriptyline can produce effects as if a combination of chlorpheniramine, benzodiazepine, desipramine sertraline, cimetidine, prazosin and quinidine had been administered (Preskorn,1994) However it is naive to assume that a SSRI will have effect on the serotonin system alone It is not possible to modulate the serotonin system without modulating the norepinephrine system also, because of their anatomical and physiological proximity (Richelson 1994) So SSRIs also have their own side effects But they are a different set of side effects.

In the present state of knowledge, antidepressants can be continued indefinitely (Herschfield,1994) If there is a long-term side effect e.g., tardive dyskinesia which can occur with amoxapine, a change over may be required (Hsin-Tung et al.,2000) An SSRI would then be the antidepressant of choice because of minimal long-term side effects SSRIs especially fluoxetine can interfere with cytochrome enzyme P450 which is involved in the metabolism of several drugs. (De Vane 1994) The long term consequences of prolonged interference with cytochrome enzyme P450 are not known (Preskorn,1994)

Medically compromised patients with depression are preferably treated with a SSRI because of the mild degree of depression, and the minimal risk of side effects. Most of these patients are on polypharmacy Concurrent SSRI administration can create problems because of drug interactions, which would not be the case with TCAs (Preskorn,1994).

With some SSRIs, prolonged administration may worsen the depressive symptoms through sensitization (Fava,1999) or induce tolerance requiring higher doses of the drug to produce the same effect (Lieb,1984) (a form of tachyphylaxis). Conversely, some TCAs may show therapeutic effects only after prolonged administration. This becomes relevant at time of switching over from one class of drugs to another.

It may be necessary to change over from an expensive antidepressant to less expensive one for economic reasons. In the long term the new drug may not be cost effective because of hidden expenses which were not apparent initially The drug may have a delayed onset of action, may require several daily doses, may need constant monitoring or expensive investigations, may be difficult to obtain, or have high overdosage toxicity etc. The purchase price of the drug is by no means the only criterion for overall cost effectiveness

Therefore, antidepressants should not be interchanged indiscriminately unless there are solid reasons like health benefit and long term safety Most people are reluctant to change their barbers, their dentists or their spouses The same caution should be exercised when changing antidepressants.

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