better compliance. Is it worth saving one life through the prescription of non-toxic drugs if the overall increase in costs averages at several hundreds of thousands of pounds? More lives might be saved for the same outlay on, for example, kidney transplantation or health education. Costs are therefore central to the debate about new versus old.

On closer scrutiny the cost advantages of the cheap tricyclic antidepressants may be more apparent than real. Firstly, the cost differentials, although wide, are starting to narrow. Secondly, the costs of treatment abandoned because of unwanted side effects of tricyclic antidepressants, failures of recovery, and the increased risks of suicide must be taken into account. Thirdly, the side effects of tricyclic antidepressants could result in extra expenditure on treatment for dental decay, hip fractures, and trauma from road traffic accidents. A simulated costing analysis based on data available from clinical trials estimated that when the cost of drop outs and poor compliance are taken into account, the selective serotonin reuptake inhibitors are no more expensive than tricyclics, despite the higher initial prescription costs.⁹

Of course, an old friend such as amitriptyline is not

yet ready to be pensioned off completely. Not all patients respond to their first antidepressant treatment and certain depressed patients may require a broader spectrum of synaptic blockade than that offered by the selective serotonin reuptake inhibitors. Tricyclics will continue to form an important part of doctors' armoury. But for the first line treatment of patients seen everyday in surgeries and psychiatric clinics, new is better.

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Benefits of new drugs are exaggerated

David Owens

Lately there has been a good deal of clamour from those who think that the recent additions to the antidepressant drug list known as selective serotonin reuptake inhibitors (fluoxetine, fluvoxamine, paroxetine and sertraline) should replace older, largely tricyclic, antidepressant drugs as the treatment of choice for depressive illness. How strong is their case?

Effectiveness

Randomised trials have shown the new drugs to be more effective than placebo, but the debate is about trials comparing serotonin reuptake inhibitors with tricyclic antidepressants. Selected studies have found greater recovery with serotonin reuptake inhibitors and are widely quoted by enthusiasts. However, several influential reviews have concluded that efficacy is about equal.¹⁻³ A recent systematic review of 64 randomised controlled trials comparing serotonin reuptake inhibitors with established antidepressant drugs found similar benefit from new and old treatments; where data could be pooled in a meta-analysis no clear difference was found.⁴

Because the treatment trials have mainly examined depression in primary care, specialists may be premature to count on equal effectiveness when treating patients referred to clinics and hospitals. Interest is shifting towards other clinical situations and we will soon be (or already are being) treated to claims that serotonin reuptake inhibitors are ideal for severe depression, resistant depression, continuing treatment, prophylaxis, and so on. In view of the lack of extra benefit so far shown, canny clinicians will look for independent systematic reviews in each of these areas before changing practice.

Unwanted effects

No more effective, but do the serotonin reuptake inhibitors prevail when it comes to unwanted actions: either troublesome side effects or toxicity in overdose?

The side effects of new and old drugs have little in common. For example, serotonin reuptake inhibitors are less likely than tricyclic antidepressants to cause sedation, anticholinergic actions, and cardiac arrhythmias. On the other hand, serotonin reuptake inhibitors commonly affect the gut (especially causing nausea and diarrhoea) and may affect the central nervous system producing insomnia, agitation, extrapyramidal symptoms, and withdrawal effects.

It is a common assertion that serotonin reuptake inhibitors are less troublesome to patients, thereby improving compliance and wellbeing. This claim does not, however, bear close scrutiny. As with tricyclic antidepressants, many patients find serotonin reuptake inhibitors unpleasant to take. When drop out rates from 58 trials were reviewed systematically there was no clinically important difference between the new drugs and tricyclic and related antidepressants; when the data were pooled one third of patients dropped out of each drug group.⁴

Antidepressant poisoning accounts for about 5% of suicides. Serotonin reuptake inhibitors are probably safer in overdose than older tricyclic antidepressants. Some clinicians have already argued that this should affect routine choice of antidepressant⁵ and that tricyclic antidepressants should be consigned to second or lower choice.⁶

There were around 3600 deaths due to overdose of single antidepressants in the United Kingdom between 1975 and 1989—an average of 240 deaths each year.⁷ But substitution of serotonin reuptake inhibitors for tricyclics is unlikely to eradicate all these deaths. Firstly, a few people have already committed suicide using serotonin reuptake inhibitors; precise figures for fatal toxicity in overdose will emerge only after several more years of use. Secondly, serotonin reuptake inhibitors, like older drugs, are often not tolerated or are ineffective; some patients at risk of suicide will necessarily be switched to other drugs. Thirdly, where self poisoning with a prescribed drug has not been fatal an unknown proportion of suicidal patients will substitute another method.

Division of Psychiatry and
Behavioural Sciences,
Leeds University, Leeds
LS2 9LT
David Owens, senior lecturer

Commentary: new drugs increase doctors' choice

The appeal of drugs that are selective in their action is that they are more likely to do what you want and not do what you don't want. However, they will not necessarily do what you want any better than the drug which is less selective. For example, in a person with stable angina propranolol should alleviate cardiac symptoms as well as a β blocker which acts only on the heart. Unfortunately, because propranolol also has actions outside the heart patients may experience a wide range of side effects, and if they do the more selective β blocker would obviously be more appropriate. The problem with new and old antidepressants is that this β blocker analogy is not really transferable. In angina we know that we want to block β_1 receptors in the heart. But we do not yet know the biochemical mechanisms involved in depression, and it is likely that several different mechanisms operate in the broad spectrum of depressive diseases. Where inhibition of serotonin reuptake will suffice to lift the depression the newer drugs in this class clearly have an important role. However, the meta-analysis showing equal effectiveness of old and new treatments gives a useful guide to clinical practice. The main advantage of the advent of new antidepressants seems to be that it has substantially increased the therapeutic options for depression.—PETER C RUBIN, *professor of therapeutics, University of Nottingham*

Costs

Because there are high rates of drop out from treatment and of long term therapy, it is difficult to estimate cost per treatment episode. Nevertheless, it is clear that the new drugs are much more expensive. For example, six months' treatment with 150 mg of imipramine costs about £6 whereas six months of a recommended dose of a serotonin reuptake inhibitor costs from £150 to £500.⁸ By late 1992, although only around 15% of antidepressant prescriptions in England were for serotonin reuptake inhibitors, they already accounted for half the cost.⁹ It has been estimated that substitution of older tricyclics will require over £100m extra for the health service drug budget in England each year.⁹

Conclusion

Serotonin reuptake inhibitors should not replace tricyclic drugs as first line treatment for depression in the expectation of either increased effectiveness or fewer side effects. In some patients, for example, when sedation or cardiotoxicity must be avoided, the new drugs are the first choice. Prescribing for potentially suicidal patients, however, is not straightforward. Seeing the patient regularly, building a relationship, and providing access to support are all part of reducing risk of suicide; safe prescribing is not just a question of always prescribing a safe drug. If concern about safety in overdose persuades doctors to abandon tricyclic antidepressants we will be responsible for doubtful benefit to the public health but enormous cost.

Doctors have repeatedly been too readily persuaded that patients need the latest available treatment. Past experience with new drugs, especially those that have been excessively promoted and used, should by now have taught us to moderate prescribing in the early years of a drug's availability.¹⁰ We should stick with treatments whose effectiveness and long term ill effects are known from years of experience until change seems certain to be of benefit. In this case the degree of certainty has been exaggerated.

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Medicine in Europe

The greying of Europe

John L C Dall

About a quarter of the population of Europe is now of pensionable age. Facilities for caring for very old or disabled people differ throughout Europe in scope and means of funding, and the countries of the European Union are far from equity in the status of pensioners. Health expectations have increased in older people—most of the calculated gain in life expectancy is likely to be without disability. Most countries now have specialist geriatric medicine facilities, and international research programmes are under way.

The most striking feature of the last century may well be the change in the shape of populations. In the early years of the twentieth century, when the old age pension was initiated and made available to those reaching a retirement age of 65 years in several countries of Europe, around 5% of the populations of these countries was eligible. Now roughly a quarter of the population of Europe is of pensionable age.

One factor in this change is the reduction in the number of children and consequently the relative

increase in the number of older people—this helps to explain why Mediterranean countries have taken longer to reach this stage than has northern Europe. Figure 1 shows that there will be a substantial percentage increase in each age decade. Some of this is due to an improvement in life expectancy as well as a reduction in the number of children. A child born now can expect to live 10 years longer than one born in 1950 and 25 years longer than one born at the beginning of this century.¹

The European Year of Older People and Solidarity Between the Generations (1993) was intended to highlight the challenge an aging population presents to society and to encourage an exchange of ideas which collectively might enhance the quality of life of older people. It was launched in the knowledge that people are living longer, in better conditions, and with higher expectations, and it intended that the European Community particularly would make efforts to meet those expectations and ensure that, as years are added to life, improved quality of life is added to years.

The European Commission has published two

This is the 10th in an intermittent series of articles looking at medical issues in Europe

Victoria Infirmary National Health Trust,
Glasgow G42 9TT
John L C Dall, *chairman*

BMJ 1994;309:1282-5