Editors' view

Over-the-counter medicines

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The history of over-the-counter medicines has been a roller-coaster. The Rose case, which culminated in a decision from the House of Lords in 1704, established that apothecaries could prescribe and dispense medicines, breaking the monopoly of the College of Physicians [1]. After that, over-the-counter medicines continued to be generally available in Britain until 1860, when drugs of abuse were designated as prescription-only medicines. However, most other medicines remained generally available until the 1960s, when, in the hope of improving safety, most of them became prescription-only medicines, following a report of the Interdepartmental Committee on Drug Addiction, chaired by Sir Russell Brain [2]. The attempt may not have been successful. We don't know what the risks of adverse effects were in those days, but they are currently quite high and the hoped-for improvement may not have transpired. Now the roller-coaster is tumbling down the slope again, and more and more medicines are becoming available over the counter.

Take simvastatin. On 12 May 2004 the Secretary of State for Health for England and Wales, John Reid, announced that simvastatin, which is off patent, would become available from July 2004 for over-the counter sale in the UK in a 10 mg formulation.

The announcement was welcomed by the Royal Pharmaceutical Society [3]. According to Gill Hawsworth, its President, 'The Society believes that there is a clear public health benefit to be gained from making this important medicine available through pharmacies. The switch will give pharmacists more opportunities to use their skills'. However, the Consumers' Association was not so impressed [3]: 'The switch is tantamount to using the UK public as guinea pigs and smacks of a cost-cutting exercise'. A spokesman for the Royal College of

General Practitioners said [4], 'We understand that while a range of health tests will be offered before simvastatin is dispensed by a pharmacist the tests are not obligatory and we are concerned by this news. . . . Pharmacists currently do not have access to a patient's medical record which would help them judge whether simvastatin is necessary and help patients get appropriate and optimum treatment while protecting them against interactions and adverse effects'. And The Lancet gave the announcement the full benefit of a typical anonymous broadside entitled 'OTC statins: a bad decision for public health' [5].

Should simvastatin be available over the counter? Well, there are criteria. They have recently been reviewed in a US context [6], although surprisingly the author failed to distinguish between necessary criteria, such as efficacy and safety, and desirable criteria, such as making medicines more readily available.

I shall mostly refer to medicines that are only available in pharmacies, rather than those on the General Sales List, which are available through supermarkets and other outlets without the supervision of a pharmacist. I shall also assume that pharmacists are alive to the problems of self-medication by patients and will take steps to advise them about seeking medical advice when appropriate. This is not true in all countries, and I shall therefore mostly restrict my comments to the UK, where it is.

Necessary criteria for making medicines available over the counter

The diagnosis

The patient should be able to make the diagnosis, or should at least know what the diagnosis is, based on an authoritative opinion. For example, hay fever is easily

diagnosed by the sufferer, and effective medicines, such as antihistamines and cromoglicate, are available for purchase without question over the counter.

In some cases the patient may need counselling by the pharmacist. For example, various histamine H_2 receptor antagonists are available over the counter in the UK for the short-term symptomatic relief of heartburn, dyspepsia, and hyperacidity, in packs containing no more than 2 weeks' supply. The diagnosis is not difficult, but a pharmacist would advise any patient who was repeatedly buying these drugs to consult their doctor.

In some cases, even if the patient cannot make the initial diagnosis, over-the-counter purchase can be permissible, in the case of a chronic condition, once the diagnosis has been made by a medical practitioner. This applies, for example, to the use of hyoscine butylbromide in the treatment of irritable bowel syndrome, available to patients over the counter provided the diagnosis has been made by a doctor. Some do not believe that hyoscine butylbromide is effective in this condition, but the decision to make it available over the counter was made on the basis of safety not efficacy.

Efficacy

Currently in the UK it is possible for a medicine to be granted over-the-counter status because it is considered to be sufficiently safe, without consideration of its efficacy. To those who are concerned about balancing the benefits and harms of therapies [7] this seems odd: no matter how safe a drug is, lack of efficacy should militate against its use. It has also been argued that if ineffective medications become readily available, patients might choose them, rather than more effective but less readily available treatments [6], although it is not clear how justified that fear is.

Safety

If a medicine can cause a serious adverse effect it should not be made available over the counter. Of course, many drugs can cause serious adverse effects from time to time, but a rare serious effect need not obviate over-the-counter status if the potential benefit is considered to outweigh the potential harm. The antihistamines terfenadine and astemizole were withdrawn from over-the-counter sales when it was realized that they could cause ventricular arrhythmias, such as torsade de pointes, especially when taken with grapefruit juice [8, 9] and kava was withdrawn in many countries because of concerns over liver damage [10]. In both cases the balance of benefit to harm was considered to be unfavourable. And teratogens, such as thalidomide and oral retinoids, should not be given over-the-counter status.

The risks of unwanted effects can be reduced by limiting the dosage strengths of over-the-counter formulations. For example, over-the-counter ranitidine comes in tablets of 75 mg as opposed to the usual strengths of 150 or 300 mg available on prescription. Furthermore, the number of tablets that can be sold at any time is often also limited. This gives pharmacists a chance to offer advice to patients who may need a medical opinion.

Desirable criteria for making medicines available over the counter

Improved accessibility

Over-the-counter availability makes a medicine more readily accessible to patients; it is hard to think of a case against any medicine on these grounds, except those that have an abuse potential.

Rapid accessibility

When my hay fever strikes I know that I am likely to awaken that night with an acute attack of asthma. I should be able to go to the pharmacist to obtain, say, a salbutamol inhaler. To argue that I should have anticipated the problem by a visit to the doctor ignores the realities of my busy life and forgetfulness, and an antihistamine doesn't always do the job. On the other hand, cromoglicate eye-drops and nose-drops, which rapidly relieve my other symptoms, are readily available over the counter.

Shifting costs

Making medicines available over-the-counter shifts the cost from the health-care system to the patient. There is no drug for which this is not an argument in favour of over-the-counter availability. Although patients who cannot afford to buy their medicines over the counter will be disadvantaged, in the UK they can still get a prescription for such medicines from their doctor if they are really necessary. Those who can afford to buy over the counter should not be penalized by a high-minded desire for apparent equality.

Should simvastatin be available over the counter?

How does simvastatin meet these criteria?

Diagnosis is not an issue, since the main intention of over-the-counter simvastatin is in primary and secondary prevention of heart attacks and strokes, not the management of primary hyperlipidaemias.

Efficacy is undoubted [11]. Of course, the dose of 10 mg day^{-1} is at the lower end of the effective range and has been estimated to lower serum cholesterol by only about 0.5 mmol l^{-1} [12]; but this is a start, and when evidence of the benefit to harm balance becomes avail-

able the dosage can be increased. The major outcomes will be small reductions in the risks of heart attacks and strokes, although disappointingly not type 2 diabetes mellitus, according to Jick *et al.* in this issue of the *Journal* (pp. 303–9).

Safety is excellent. In clinical trials only 0.1% of patients taking higher dosage equivalents of statins than simvastatin 10 mg day⁻¹ developed unwanted symptoms, and withdrawal was warranted in fewer than that [11]. And in a meta-analysis of 48 trials there was no difference in the incidence of adverse events between statins and placebo, even at a dosage of 80 mg day⁻¹ [12]. In this issue of the *Journal* de Graaf *et al.* (pp. 326–8) describe eight patients who complained of reversible loss of libido while taking a statin; given the large numbers of patients who take statins, this possible adverse effect is probably uncommon.

Rapid accessibility is not an issue, but increased accessibility is. As Mantel-Teeuwisse *et al.* show in this issue of the *Journal* (pp. 310–16), in the Netherlands even those with hypercholesterolaemia are being undertreated. And a paper that featured in a previous Editors' View [13] showed that patients who were taking lipid-lowering drugs prescribed by UK GPs were more likely to be elderly smokers with more concomitant severe cardiovascular comorbidity than patients who were not. In short, we are not currently targeting those who would benefit from lipid-lowering drug therapy in primary prevention (everyone over the age of 55 years) or even in established disease.

Criticisms

The change to over-the-counter status for simvastatin has been criticized on various grounds:

- *It is an experiment – there have been no randomized trials of over-the-counter simvastatin.* This is disingenuous. Trials are not possible until it is available. Once it is, there should certainly be postmarketing surveillance of some sort to determine the benefit to harm balance. But a priori, increased availability of simvastatin is likely to improve public health at minimal cost in adverse effects.
- *It is a cost-cutting exercise.* It is not. It is a cost-diverting exercise – from the body of taxpayers to individuals. In any case, what is wrong with Governmental efforts to reduce public spending?
- *Pharmacists will not have the time or even be able to decide whether a patient needs the treatment.* The serum cholesterol concentration is not a good screening test for the use of a statin, since only 10% of those with an increased risk of a heart attack or stroke have a raised cholesterol. Age and a history of cardiovascular disease are the best screening tests and are easily ascertained over the counter. Then, no matter what your cholesterol is, it can always be beneficially lower.
- *The potential for adverse effects will be increased.* This is true, but benefit will also accrue and it is likely that the latter will outweigh the former. The contraindications are simple.
- *The potential for interactions will be increased; pharmacists will not have access to patients' medical records.* This is a real concern and one that will have to be tackled by good labelling of the products and careful advice from pharmacists. It is not generally appreciated, however, that the problem of multiple prescribing is one that we are going to face more and more as the numbers of prescribers (doctors, nurses, pharmacists, and others) increases. I have already learnt of one patient who was given paracetamol by more than one prescriber, each unaware of the others; the concern that he might have accidentally developed paracetamol poisoning was unfounded, as it turned out, but worrisome nevertheless. We should consider giving patients of the future smart cards detailing their medical history or perhaps encourage them to develop their own medical website to which their carers can have access.
- *There is no evidence about patient adherence to over-the-counter simvastatin.* That is true, but not an argument against over-the-counter availability. It is in any case likely that those who are prepared to spend money on the drug will take it. And if they don't, they are no more likely to take it if their doctor prescribes it. Indeed, it may be that encouragement from the pharmacist will be more effective than encouragement from the doctor.
- *Those who buy the drug will use it as a substitute for lifestyle modifications.* Even if there were any evidence that the UK public is currently enthusiastic about espousing the relevant lifestyle changes, this would be a specious argument, lacking evidence.
- *Extra sales will benefit pharmaceutical companies.* This argument, aired in The Lancet [5], is an interesting one. The anonymous editorialist was prepared to believe that the move to over-the-counter sales would benefit the pharmaceutical industry by creating a new market of 'perhaps 8 million more people in the UK', while at the same time implying that adherence to therapy would be poor. But in any case, why shouldn't the pharmaceutical industry benefit from selling its products for legitimate purposes?
- *Privatization increases inequalities in access to health care.* I have dealt with the politics of envy above.

Conclusions

There is nothing new about over-the-counter availability of powerful drugs. Those who are interested in the history of drug availability in ancient times should read Griffin's article in this issue of the *Journal* (pp. 317–25). Today 'over-the-counter' medicines are much more widely available than ever before, whether or not Governments sanction them. Just type 'buy simvastatin' into Google and goggle at the gaggle of online pharmacies willing to sell you tablets (5–80 mg) at about 80 pence a time. And while you're at it, try looking for all the other statins too – even cerivastatin seems to be available.

Over-the-counter statins will improve public health at a small cost in adverse drug reactions. Products will have to be carefully labelled, and pharmacists will have to advise patients appropriately. But you don't have to overhear many conversations in pharmacists' shops to know that they are expert at informing patients about appropriate remedies and their risks.

So, if you are of a certain age, or have a history of cardiovascular disease, on the way home stop at your local pharmacy and buy your simvastatin.

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