Intuitively the greatest benefit of a polypill is the simplicity of the regimen, resulting in improved adherence and better clinical outcomes, but surprisingly, few clinical trial data are available.[4] Nevertheless, fixed-dose combinations of four or more medications are being developed for tuberculosis and HIV. For people with cardiovascular disease, in whom the separate ingredients are recommended, only a small minority receive the full combination.[5] This may result from confusion due to complicated regimens, the sheer inconvenience of managing large numbers of pills, a reluctance to take (or prescribe) multiple medicines, and cost.

A polypill could be very inexpensive because its ideal components are now off-patent. World Health Organization (WHO) analyses show that combination therapy given to people at high absolute risk of cardiovascular disease is more cost-effective than current treatment patterns based on single risk factors (for example treating 'hypertension'). Population approaches like salt reduction in foods are the most cost-effective of all, according to the WHO report.[6]

So why don't we have a polypill already? Innovator companies are reluctant to invest, because profit margins are likely to be thin. Generic manufacturers do not have large research and development budgets. This leaves a gap that government agencies are not ready to fill. What is more, the regulatory hurdles for combinations of three or more ingredients are poorly defined. Despite all this, there are now 'mini' versions of the polypill. For example, last year the United States Food and Drug Administration approved a combination of amlodipine and atorvastatin. The authors of the BMJ paper have a patent on their version of the polypill, though it is difficult to know how defensible this would be, given the components are all generics and the concept is based on published evidence.

At present there seems more heat than light in the polypill debate. It is time to move on and seek direct evidence from trials. Relatively small studies could investigate whether adherence is improved in patients with established indications for the component medications. An even bigger question is what works best for primary prevention; long-term trials with several thousand participants will be needed to show a reduced event rate. Before casting the polypill as 'friend' or 'foe', we need better information on acceptability, safety and effectiveness.

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References

1. Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. Br Med J 2003;326:1419-24.
2. Rodgers A. A cure for cardiovascular disease? Combination treatment has enormous potential, especially in developing countries. Br Med J 2003;326:1407-8.
3. The assessment and management of cardiovascular risk. Best practice evidence-based guideline. Wellington, NZ: New Zealand Guidelines Group; 2003.
4. Connor J, Rafter N, Rodgers A. Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systematic review. Bull World Health Organ 2004;82:935-9.
5. Lawlor DA, Bedford C, Taylor M, Ebrahim S. Geographical variation in cardiovascular disease, risk factors, and their control in older women: British Women's Heart and Health Study. J Epidemiol Community Health 2003;57:134-40.
6. Murray CJ, Lauer JA, Hutubessy RC, Niessen L, Tomijima N, Rodgers A, et al. Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular-disease risk. Lancet 2003;361:717-25.

Dr Rafter is applying for funding for a randomised controlled trial of combination cardiovascular medication.

Transparency – in the eye of the beholder?

Editorial Executive Committee, Australian Prescriber

Key words: drug regulation, drug industry.

(Aust Prescr 2005;28:83–4)

The Editorial Executive Committee of *Australian Prescriber* is concerned about the increasing difficulty of obtaining good information about new drugs. It is not unusual for a drug to be marketed in Australia despite a lack of published peer-reviewed information to support its manufacturer's claims. This is particularly the case for adverse effects and for 'head-to-head' comparisons with older drugs used to treat the same conditions as the new drug. The data (both published and unpublished) may have been evaluated by drug regulatory authorities so there is a strong argument that their evaluations should be available to health professionals and consumers.

A lot of prominence has recently been given to the need for 'transparency' in the drug regulatory system. For example, there have been calls for an international register of clinical trials so that unfavourable results are not hidden.[1,2] Greater transparency in the process for subsidising drugs was also an important part of the free trade agreement between Australia and the USA. However, transparency means different things to different people.

The Australian pharmaceutical industry sees increased transparency as the right to scrutinise the deliberations of the Pharmaceutical Benefits Advisory Committee (PBAC). Currently, companies are informed why their drugs are not recommended for subsidy on the Pharmaceutical Benefits Scheme. Increased transparency will give them an opportunity to interact with and scrutinise the basis of the decision.

Disclosing information about the PBAC may improve understanding of its decisions, but the corollary the industry makes is that increased transparency is meaningless unless there is a process for challenging a decision. The call for increased transparency can then be confused with calls for an appeals mechanism.

There are two sides to transparency. Drug companies have been reluctant to make public the information they have submitted to the PBAC, despite the argument that the data for drugs submitted for public subsidy should be open to public scrutiny. The free trade agreement has however enabled the PBAC to release a public summary containing information about how it reaches its decisions. Time will tell how useful this will be to clinicians.

The industry may be concerned about transparency because its dealings with the PBAC include commercially sensitive information about cost-effectiveness. There therefore should be less concern about data which do not include cost information. The data submitted to the Therapeutic Goods Administration (TGA) to support the registration of a drug in Australia deal only with quality, safety and efficacy. This is important information for health professionals and patients, but it is often deemed to be commercial-in-confidence. The TGA does not release any details of its evaluations, unlike the Food and Drug Administration in the USA and the European Medicines Evaluation Agency. We would expect that similar standards of transparency would apply in Australia to help good prescribing. Instead, Australian health professionals and patients often have to rely solely on published information. As the formulations or use of drugs overseas may be different, we cannot always depend on international information.

The withdrawal of rofecoxib in 2004 is a salutary reminder of the difficulty of identifying the adverse effects of a new drug. It is also salutary that the decision to remove rofecoxib from the market was made by the manufacturer, not by the regulatory authorities. The manufacturer was in possession of important safety information that even the regulatory authorities, let alone the prescriber or the public, were not. There have even been suggestions that some companies have tried to limit the dissemination of data for commercial reasons.[3]

The Editorial Executive Committee supports the call of the International Committee of Medical Journal Editors for a register of clinical trials.[1] The need for a register would be less urgent if the drug regulation process was as transparent as possible. Transparency should not be limited to industry's desire to scrutinise the PBAC. There is a far greater need for the clinical information supporting a new drug to be made public. To explore issues around access to information, National Prescribing Service is holding a seminar in September 2005.*

In future, when *Australian Prescriber* publishes its summary of a new product in the New Drugs section, it will inform readers whether or not the company involved was prepared to provide the journal with the clinical information which was evaluated by the TGA, but has not been made public (see page 103). Companies are gradually accepting the need for transparency and those that are willing to share their information should be recognised.

* Informing Judgements about Medicines. 7–8 September 2005, Sydney. http://www.nps.org.au/events

References

1. Clinical trial registration [editorial]. A statement from the International Committee of Medical Journal Editors. Med J Aust 2004;181:293-4.
2. Is this clinical trial fully registered? [editorial]. A statement from the International Committee of Medical Journal Editors. Med J Aust 2005;182:609-10.
3. Dyer O. GlaxoSmithKline faces US lawsuit over concealment of trial results. Br Med J 2004;328:1395.

Letters

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Intravenous potassium chloride

Editor, – Recommendations from the Safety and Quality Council regarding the 'High-risk medication alert: intravenous potassium chloride' (Aust Prescr 2005;28:14–16) warrant further comment.

Many elderly and frail patients requiring parenteral potassium supplementation are readily at risk of volume overload if administered potassium salts in dilute infusions, as illustrated in the article. High dependency and intensive monitoring areas are now being approached to admit and supervise patients merely for the intravenous administration of concentrated potassium salt, or at worst to manage the