HEALTHY SCEPTICISM

A second opinion on Drug Promotion for NZ GPs

November 1998, Vol. 1 No. 1

This edition

Introducing Healthy Scepticism

Delaying the Complications of Hypertension. Part 1

Contents

Introducing Healthy Scepticism

Four good reasons for reading Healthy Scepticism

1. Promotion is a growing influence. Increasingly our patients are being influenced by promotion (Direct to Consumer advertising, Public Relations activities etc.).[1]
2. Promotion is often misleading.[2]
3. Misleading promotion may be difficult to detect.[3]
4. *Healthy Scepticism* aims to help you to assess promotional claims and make the best recommendations for your patients.

Healthy Scepticism is written by the MaLAM Secretariat and funded by PHARMAC. MaLAM aims to defend appropriate, compassionate, scientific medical care, health professionals and the public from marketing practices which may be detrimental to health. Please address feedback to Dr Peter Mansfield, c/o PO Box 10-545, Wellington or E-Mail: peter.mansfield@flinders.edu.au.

MaLAM
Medical Lobby for Appropriate Marketing Inc

Who will benefit from Healthy Scepticism?

If *Healthy Scepticism* is successful then:

- It will be easier for Doctors and Pharmacists to provide better care for Patients.
- Taxpayers will get better value for money.
- The Companies with the best products backed up by the best information will be able to gain increased market share.

About MaLAM

The Medical Lobby for Appropriate Marketing (MaLAM) is an international organisation for health professionals.[4] MaLAM aims to defend appropriate, compassionate, scientific medical care, health professionals and the public from marketing practices which may be detrimental to health. MaLAM encourages pharmaceutical companies to provide more reliable information to assist appropriate therapy. Commencing in 1983, MaLAM focused on misleading promotion in developing countries. MaLAM has continued that work and expanded to include inappropriate marketing in any country.

The principal author of *Healthy Scepticism* is Dr Peter Mansfield, a part time GP in Adelaide, Australia and part time Director of MaLAM. During Peter's medical student elective in Bangladesh in 1982 he saw dramatic examples of inappropriate marketing such as the promotion of anabolic steroids for malnourished children. He conceived an international organisation using the methods of Amnesty International for dialogue about pharmaceutical marketing. MaLAM International News now has subscribers in over 30 countries.

Healthy Scepticism is based on an approach to critical appraisal of pharmaceutical promotion developed by MaLAM with funding from the World Health Organisation's Drug Action Program. Further information about MaLAM is available at www.camtech.net.au/malam. If you have a specific question not answered by the MaLAM Web site or do not have Internet access then feel welcome to contact MaLAM via one of the addresses given.

Funding

Healthy Scepticism is funded by PHARMAC under an arrangement that provides MaLAM with full editorial responsibility.

A request for feedback

If you have any comments, questions, suggestions (including suggestions for future topics) or complaints about *Healthy Scepticism* and/or about pharmaceutical promotion then please contact:

Dr Peter Mansfield, c/o PO Box 10-545, Wellington or E-Mail: peter.mansfield@flinders.edu.au.

We believe that feedback is a gift from you, that will help us improve the *Healthy Scepticism* editions. Consequently we will consider all feedback carefully.

How we analyse advertisements

Most people only take in the headlines and images in advertisements.[5] Advertisements are written accordingly. Consequently we focus on headlines and images.

The first step is to identify the appeals being used. Advertising usually uses appeals to "logic" and "emotions". Appeals may work at conscious or subconscious levels. Emotional appeals may seek to motivate us by associating the drug with getting something we desire or by presenting the drug as a way to avoid something we fear.[6] Advertisers usually use what they believe are the strongest appeals available for justifying increased use of their product. We call attention to the appeals, which we believe are being used, to enable you to decide for yourself whether or not you should be influenced by them.

Advertising appeals are often open to different interpretations. Advertisements usually suggest or imply that the promoted product has an advantage. Consequently for each advertisement we have tried to clarify the appeals in terms of "possible" advantages over other drugs. We have tried to do that by writing "possible interpretations". We do not claim that our "possible interpretations" are necessarily what was intended by the advertiser. However, in our opinion, they would be reasonable interpretations for readers to make if they were relying on the advertisement.

"Possible interpretations" which, in our opinion, are:

- unjustified are indicated with: ✗
- justified are indicated with: ✔
- borderline are indicated with: ?

Finally, we provide a second opinion on whether or not the evidence cited in the advertisement justifies the appeals used by the advertiser.

Delaying the Complications of Hypertension. Part 1

What are the best therapies?

First: Lifestyle action

No smoking. More exercise eg walking. More fruit, vegetables, fish and potassium. Less animal fat and salt. No more than 2 standard drinks of alcohol a day.[7-12]

The Guidelines for management of mildly raised blood pressure in New Zealand recommend:

"In the first instance, non-pharmacological management of raised blood pressure and modification of other cardiovascular risk factors should be attempted. The most important modifiable risk factors are smoking cessation, diet modification (fat and salt restriction), excess weight reduction, exercise and alcohol moderation."[13]

Second: If Lifestyle action is not enough, then use

Thiazides, Beta-Blockers, ACE Inhibitors (in that order)

The Guidelines for management of mildly raised blood pressure in New Zealand recommend:

"When pharmacological treatment is required for mild hypertension, diuretics and beta-blockers should be considered first because there is randomised controlled trial evidence of reduction in cardiovascular morbidity and mortality with these agents."[13]

For more specific advice the MaLAM Secretariat suggests:

1. Consider using a Thiazide as first line drug therapy for all hypertensives except if it causes recurrent gout or if the patient has one of the following indications.
2. Consider using a beta-blocker for hypertensives who also have angina, recurrent migraine, anxiety, non-insulin dependent diabetes mellitus, tachycardia or palpitations, except if they have asthma or obstructive lung disease.
3. Consider using an ACE inhibitor for hypertensives who also have insulin dependent or non-insulin dependent diabetes mellitus, congestive heart failure, or left ventricular dysfunction after a myocardial infarction.

Be aware of surrogate endpoints!

The aim of therapy for people who have hypertension is to delay premature morbidity and mortality from complications. The complications include cerebral or coronary artery disease, heart failure and aortic aneurysm and microvascular disease of the brain, kidney and retina.[14]

Consequently, when evaluating antihypertensive therapies we need to focus on evidence for morbidity and mortality benefits.

Drug companies are allowed to promote drugs for hypertension if they lower blood pressure. Lowering blood pressure may, or may not, affect the clinically important endpoints: morbidity and mortality from complications. Lower blood pressure is used as a surrogate for the endpoints that matter. Surrogate endpoints are quicker to measure than clinically important endpoints. Changes to an ideal surrogate endpoint would reliably predict changes to clinically important endpoints.[15] Unfortunately, many surrogate endpoints may turn out to be misleading "red herrings". For example, flecainide was believed to be beneficial because it reduced arrhythmias (a surrogate endpoint). However the CAST trial found that flecainide increased the death rate (a clinically important endpoint).[16]

Thiazides have been shown to reduce mortality.[17] There is a range of views about Beta-Blockers.[14,18] The other drugs remain unproven for reducing mortality due to uncomplicated hypertension.[18] Consequently, promoters of ACE Inhibitors and Calcium Channel Blockers often use surrogate endpoints in their advertising.

The following examples show how surrogate endpoints may be misleading:

- Mibefradil (Posicor) did lower blood pressure but caused so many adverse drug interactions that it was withdrawn worldwide.[19]
- The UK Medical Research Council trial found that atenolol and hydrochlorothiazide / amiloride both lowered blood pressure a similar amount but only hydrochlorothiazide / amiloride lowered the risk of stroke and coronary events.[17]
- Thiazides may have adverse effects on potassium levels, and minor effects on cholesterol, triglyceride and uric acid levels but thiazides reduce stroke rates, myocardial infarct rates and total death rates.[13]

Advertisements for ACE Inhibitors for hypertension

Below are opinions on advertisements for ACE inhibitors promoted for hypertension published in "*New Zealand GP*" during 1998 in alphabetical order. We plan to provide opinions on advertisements for other drugs later.

ACE Inhibitors

Advertisement 1: Capoten (captopril, Bristol-Myers Squibb BMS)

Headlines: "Diabetic? Hypertensive? Or Capoten. You can't argue with the evidence."

Images: Picture 1 - Feet of a corpse with a tag giving cause of death as Diabetic Renal Failure. Picture 2 - Diver's flippers

Second Opinion

Appeals: Fear of death of patients, Fear of failure as a doctor, Appeal to evidence based medicine.

Possible interpretations:

1. **?** There is evidence to show that Capoten reduces mortality from diabetic renal failure.

How good is the evidence?

1. We can argue about the evidence! BMS cite a good quality trial of captopril for insulin dependent diabetics with abnormal urinary protein and serum creatine levels.[20] In the captopril group, 8 of the 207 patients died. In the placebo group, 14 of 202 patients died. In both groups, 2 patients were lost to follow up. The investigators did not say whether or not the difference was statistically significant, presumably because it was not. However, there was a significant difference in the combined endpoints of death or dialysis or transplantation. We can conclude that captopril is better than placebo for clinically important endpoints combined. However, we do not know if this can be generalised to non-insulin dependent diabetics or not. Also, the trial does not tell us the size of the impact of captopril on mortality. Furthermore, this trial does not tell us whether captopril is better or worse than other drugs. The only other citation used by BMS is "data on file". A recent UK Prospective Diabetes Study found that captopril did not have more impact than atenolol on clinically important endpoints.[21]

Advertisement 2: Gopten (trandolapril, Knoll)

Headlines: "Hyperliving: Busy lives, not enough exercise, too much of the wrong food. Gopten for hyperliving hypertensives."

Images: Three middle-aged men smiling or laughing.

Second Opinion

Appeals: The easy solution, no effort by the patient, easy for the doctor.

Possible interpretations:

1. ✗ Trandolapril is a more appropriate therapy for hypertensives with high-risk lifestyles.
2. ✗ Use of trandolapril reduces the need to modify high-risk life styles.

How good is the evidence?

Knoll have not provided any evidence to support either of those possible interpretations. To our knowledge, no such evidence is available.

Advertisement 3: Odrik (trandolapril, Hoechst)

Headlines: "The pressure in the morning is too much for some hearts to bear. Odrik Consistent and extended blood pressure control."

Images: A dead middle aged man and a crying child.

Second Opinion

Appeals: Fear of providing the wrong treatment, Fear of causing children to suffer bereavement.

Possible interpretations:

1. ✗ Odrik is better at preventing mortality because it provides better control of blood pressure in the early morning.
2. ✗ Doctors who do not prescribe Odrik will cause children to suffer unnecessary bereavement.

How good is the evidence?

1. This advertisement uses morning blood pressure as a surrogate endpoint. Trandolapril is not the only drug that lowers blood pressure for more than 8 hours. Hoechst have not provided any evidence to show that longer duration of action leads to mortality benefits. If you want to feel confident about reducing mortality then see the recommendations in the "What is the best therapy?" section.
2. Emotive images that arouse fears are used to increase sales. Images that arouse fear may work in the subconscious mind in ways that bypass rational decision making.[6]

Advertisement 4: Prinivil (lisinopril, Douglas Medical)

Headlines: "ACE Improvement. Hypertension. Prinivil Smart thinking."

Images: Jigsaw pieces

Second Opinion

Appeals: The desire to be and to be seen to be smart.

Possible interpretations:

1. ✗ Use of lisinopril improves morbidity or mortality for hypertensives.
2. ✗ Doctors who prescribe lisinopril are smarter than other doctors.

How good is the evidence?

1. The only reference cited for "Hypertension" is the data sheet. Douglas has not provided any evidence of morbidity or mortality benefits. To our knowledge, no such evidence is available.
2. Douglas has not provided evidence that doctors who prescribe lisinopril are smarter than other doctors. Appeals to desires, (such as doctors' desires to be and to be seen to be intelligent), are used to increase sales. Appeals to desires may work in the subconscious mind in ways that bypass rational decision making.[6]

1 Mintzes B. Blurring the Boundaries. HAI Amsterdam 1998

2 Wilkes MS, Doblin BH, Shapiro MF. Pharmaceutical advertisements in leading medical journals: experts' assessments. Ann Intern Med 1992; 116: 912-9

3 Ziegler MG, Lew P, Singer BC. The accuracy of drug information from sales representatives. JAMA 1995;273:16:1296-8

4 Mansfield P. MaLAM, a medical lobby for appropriate marketing of pharmaceuticals. Med J Aust 1997;167:11/12;590-592

5 Ogilvy D. Ogilvy on advertising. Prion. London 1995

6 Scott DK, Ferner RE. "The strategy of desire" and rational prescribing. Br J Clin Pharmac 1994;37:217-9

7 Elmer PJ, et al. Lifestyle intervention: results of the Treatment of Mild Hypertension Study (TOMHS). Preventive Medicine. 24(4):378-88, 1995

8 Galgali G, et al. Potential for prevention of premature death and disease in New Zealand. N Z Med J. 1998;23;111:7-10.

9 Oliver MF, Conway S. Cholesterol lowering diets and coronary heart disease. BMJ 1998;317:1253

10 Appel LJ, et al. A clinical trial of the effects of dietary patterns on blood pressure. N Engl J Med 1997;336:1117-24

11 Whelton PK, et al. Effects of oral potassium on blood pressure. JAMA 1997;227:1624-32

12 Whelton PK, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons. JAMA 1998;279:839-46

13 Guidelines for the management of mildly raised blood pressure in New Zealand. Wellington 1995

14 Missan G, Rossi S, Gabb G, Vitry A, et al. Australian Medicines Handbook. Adelaide 1998;6-19 www.amh.net.au

15 Greenhalgh T. How to read a paper. BMJ Publishing. London 1997

16 Echt DS et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The Cardiac Arrhythmia Suppression Trial. N Engl J Med 1991;324:781-8

17 Drugs of Choice in the Treatment of Hypertension (Part 1) www.ti.ubc.ca/pages/letter7.html

18 Drugs of Choice in the Treatment of Hypertension (Part 2) www.ti.ubc.ca/pages/letter8.html

19 Li Wan Po A, Zhang WY. What lessons can be learnt from withdrawal of mibefradil from the market? Lancet 1998:351:9119:1829-30

20 Lewis EJ et al. Captopril and renal function in diabetic nephropathy. New Engl J Med 1993;329:1456-62

21 UK Prospective Diabetes Study Group. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. BMJ