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Review of Anticoagulation Therapies in Atrial Fibrillation

This submission is on behalf of the Victorian Cardiac Clinical Network. The short time frame has not permitted consultation so this submission is a personal one by the author on behalf of the network.

1. The terms of reference refer to the RE-LY trial basing its comparison of warfarin against dabigatran as comparing dabigatran against poorly managed warfarin.

In 1999 working as a general physician and cardiologist I was increasingly frustrated by the poor management of warfarin by doctors in the my area. I wrote and developed a computer program to assist in my management of these patients. I offered and maintained a service for patients at particularly high risk and for patients who were being poorly managed. I have enrolled 490 pts since then and have made 15,627 dosage decisions since. To my knowledge I have not had a major haemorrhagic event nor a stroke in pts on this management program. I have compared the percentage of target INRs against the local pathology company which manages a large number of pts and the efficacy rate is much higher with my program.

My conclusions from this experience is that carefully managed warfarin using a purpose built software program involving 1 or 2 clinicians with a superior knowledge and understanding of warfarin pharmacology and risk assessment and who is intimately familiar with the medical problems of the pts can be extremely safe, quite probably eliminating the apparent benefit of dabigatran.

However what is also very clear is that it is hopeless to expect busy GPs in multi doctor practices to be able to achieve anything like this level of quality. If anything medical education recently produces graduates with poor understanding of pharmacology and their treatment decisions are often inconsistent with good management.

GPs have been encouraged to operate in large practices and it is no longer possible to maintain close contact with all their pts, so a pt with atrial fibrillation who has had bleeding issues in the past will be managed mostly by other than the pts usual doctor to suit the efficiency of the clinic rather than the needs of the pt.

Admitting their inadequate ability to manage these pts many GPs defer management to pathology companies. This is totally unacceptable. The pathology company does not know the patient, cannot make a refined assessment of risk and ideal INR ranges in a pt they don't know and cannot manage the many individual issues that occur when the pt may have a blood nose or has to go on antibiotics or if they are heavy drinkers, or need to go on medications that interact with warfarin.

Very few specialists who might have the necessary understanding of pharmacotherapy are interested in maintaining management of these pts they are mostly sent back to the GP.

If we were forced to continue using warfarin then I would be advocating certification for GPs using warfarin. It is the only way to ensure a minimum level of expertise in doctors managing this drug. I would be quite certain that a high percentage of doctors would fail a basic test on how to safely and optimally manage warfarin.

The answer to the suggestion in the terms of reference that there may be an opportunity to improve the quality of management is simply NO. It's not possible to significantly improve the quality of management without massive education programs which may or may not help.

2. A major part of the irritation and frustration of clinical practice for me as a hospital based clinician is the time taken to manage patients needing warfarin management. Currently a pt who presents to casualty with atrial fibrillation who is at high, medium or unknown risk of thromboembolism will need to be stabilized on warfarin. In an ideal world this patient will be covered with sc clexane once daily and will need daily INR tests to stabilize the warfarin. It is often impossible to get a GP who can see the patient immediately to perform these tests in a reliable manner so the hospital generally has to make the pt a 'hospital in the home' patient. A nurse then has to see the patient every day. Take blood tests and try to find a doctor who will decide on dosage of warfarin. This will take from 4 to 7 days of daily visits, involving major costs to the hospital and inconvenience to the doctor and the patient. At some stage the patient is transferred to a GP who may or may not be competent at managing the INRs. In the weekend or after hours the pt will either be kept in hospital unnecessarily or if the bed pressure is great (and it always is) the patient is sent home without warfarin in the hope that he doesn't have a stroke. This is bad medicine but we are constantly under pressure to perform bad medicine because of the pressure on beds in hospital.

The alternative with dabigatran is simple. 1 shot of clexane and start dabigatran. No nursing visits no interrupting busy doctors to try to get dosage decisions, no unnecessary clexane injections for the patient, and no longer subjected to the constant risk of bad management. He or she can be sent home within hours and see his GP in a weeks time.

Atrial fibrillation is an epidemic as the hypertensive population ages it takes up more and more of our time and the current issues of managing warfarin is very burdensome to the doctor, the nurses and the hospital. 1 of the driving forces behind a rhythm management approach is the wish to avoid the use of warfarin.

3. As mentioned in the background to the Submissions statement item d: A number of pts who might not otherwise take warfarin may take dabigatran. This is most certainly true. There are a large number of patients who currently will not take warfarin or simply cannot cope with the complexity of tests and reviews that would happily take dabigatran with a huge benefit to the health of the community. It is the elderly who are most at risk of stroke in atrial fibrillation and it is this group that are least likely to cope with warfarin. It is the poorly educated lower socioeconomic pt that can't manage warfarin that is at greatest risk.

4. Unecessary medicalization.
It isn't possible to quantify the emotional and inconvenience costs of having to have blood tests at least once a month and to see a doctor as often, usually for the rest of the patients life. Consider that 8% of the population over the age of 80 have atrial fibrillation and that these pts nearly all need warfarin. We are consigning all these individuals to monthly blood tests and visits to their doctors for the rest of their lives.

5. Low risk pts unnecessarily transferred to dabigatran. This indeed could be an issue and should be monitored as with any drug. This could easily be achieved if the PBS took a more active role in providing expensive drugs for general use.

In 2001 I performed a study of use of PBS guidelines by doctors prescribing lipid lowering drugs (LLDs)[1]. The study showed that a high percentage of doctors prescribed LLDs to pts that did not meet the PBS requirements. It also showed that the PBS requirements were poor indicators of risk. The study showed that possibly hundreds of millions of dollars of drugs were being prescribed to pts who were at low risk and didn't need them. I still remain astonished at the lack of interest this study generated and the inability of the PBAC to consider innovative ways to avoid this massive waste of the health dollar.

I have argued before that the PBAC should set up a web based approval service whereby the details of the case could be entered before approval is obtained. This would reduce inappropriate prescribing and provide a database from which the patterns of prescribing could be studied and also enable research to assess efficacy, compliance and complications.

Such a program would not be expensive (compared with the cost of the drug), it would <u>almost certainly save a great deal more money than it would cost</u> by reducing overuse of the drug. It would undoubtedly save lives and save money.

IN SUMMARY

The current management of pts with warfarin is badly done with significant morbidity and cost.

The continued use of warfarin places a significant stress on hospital casualties and wards.

The management of atrial fibrillation would be simplified with availablility of dabigatran with reduced doctor dependence and quality of life for the patient. The quality of life issues involve a life long obsession with careful regulation of diet and alcohol intake in many patients for the rest of their lives. It required at least monthly visits to their GPs to review blood tests.

The inconvenience and dangers of initiating therapy, and of interrupting therapy for surgery and other issues such as overseas trips would be abolished with availability of dabigatran.

There is no easy way to improve the quality of warfarin management which is currently in my opinion and based on my research poor. The RE-LY trial if anything includes warfarin pts who I suspect are BETTER managed than those in Australia, being involved as they are in a major trial.

The PBAC should change their paradigm and set up a web based application service to improve the quality of decision making in doctors prescribing drugs. This should also be utilised in research so that the PBAC or other academic bodies can then determine if their decisions are wise or not.

Warfarin is an extraordinary impost on the lives of patients and doctors. It is inconceivable that we are forced to continue using it when a superior alternative is available.

Brett Forge MBBS FRACP
Consultant physician and cardiologist
West Gippsland Hospital

On behalf of the Victorian Govt Cardiac Clinical Network.

1. Forge BH, Briganti EM. Lipid lowering and coronary heart disease risk: how appropriate are the national guidelines? *Med J Aust* 2001; 175: 471-475.

Conflict of interest.
I have received an honorarium for a talk I gave on dabigatran.