AREA STROKE NETWORK

TIA & Stroke Clinic
Royal North Shore Hospital

Health
Northern Sydney
Local Health Network

20.02.2012

Submission regarding anticoagulation for Atrial Fibrillation

Dear ladies and gentlemen,

I am the Stroke and Neuroscience Director of the Northern Sydney Local Health District and overlook all stroke services in Northern Sydney and personally treat a large number of patients with Atrial Fibrillation (AF) and stroke.

As you are well aware AF is increasingly common with age and further more increases in significance with regard to causing sever strokes.

The Framingham study investigated the impact of nonrheumatic atrial fibrillation, hypertension, coronary heart disease, and cardiac failure on stroke incidence (Wolf et al. Stroke 1991;22:983-988). Compared with subjects free of these conditions, the age-adjusted incidence of stroke near fivefold excess when atrial fibrillation was present (/»<0.001), which was the most significant independent risk factor! Advancing age, however, did not reduce the significant impact of atrial fibrillation, which is contrary to the other examined risk factors. For persons aged 80-89 years, atrial fibrillation was the sole cardiovascular condition to exert an independent effect on stroke incidence ($p<0.001$). The attributable risk of stroke for all cardiovascular contributors decreased with age except for atrial fibrillation, for which the attributable risk increased significantly ($p<0.01$), rising from 1.5% for those aged 50-59 years to 23.5% for those aged 80-89 years. While these findings highlight the impact of each cardiovascular condition on the risk of stroke, the data suggest that the elderly are particularly vulnerable to stroke when atrial fibrillation is present.

AF induces strokes are in all cases embolic event (in contrast to lacunar strokes) with a high probability of death, sever disability and dependency!

Anticoagulation reduces this risk by 62% (Hart RG et al. Ann Intern Med. 1999;131:49), whereas platelet inhibitors reduce this risk to a much lesser degree (approximately 22%).

In current National Stroke Audit Acute Services Clinical Audit Report 2011 (www.strokefoundation.com.au) on page 16 only 30% of patients with known and preexisting AF are treated with anticoagulation when presenting with a stroke to the participating audited hospitals. The NSF Audit is attached to this email for your convenience.

There are many barriers for anticoagulation in patients with stroke. Certainly one of the greatest is the therapy with warfarin.

As you are well aware warfarin interacts with food containing vitamin K, with a multitude of medication, and genetic polymorphism can make it impossible to reach stable INR's in patient on this medication. It takes 3 to 7 days to titrate to a steady stage and many patients are not diligent enough to monitor their INR which then makes this a very dangerous therapy. For this reason the majority of patients with AF do not receive this urgently necessary therapy. Self measuring of INR, which would possibly increase compliance with e.g. CoaguChek® is hugely expensive for patients and many are not able to afford such a system which is subsidized in some European countries like Germany.

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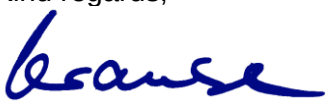
Many patients with AF are hospitalized after e.g. TIA for sole purpose of warfarinisation which would not be necessary if an alternative medication is subsidized in Australia which would provide a faster anticoagulation.
Fortunately there are now anticoagulants available which do not have these interactions with food or other drugs, which do not require monitoring and provide fast and reliable anticoagulation.
Most of the direct thrombin inhibitors like dabigatran or direct Xa inhibitors like rivaroxaban have shown at least non inferiority with regard to efficacy and safety to warfarin. In fact dabigatran has demonstrated superiority compared to warfarin (Connolly, SJ; Ezekowitz, MD; Yusuf, S et al N Engl J Med 361 (12): 1139–51).
Studies are certainly always an artificially optimal situation as they select patients very carefully and impose rigid testing, which might not happen in the “real” world. Since dabigatran or rivaroxaban do not require INR monitoring the artificial study environment works in favor of warfarin, which still remained inferior. In the “real” world many patients are treated poorly with warfarin and do not maintaining a reasonable INR control, which is reflected in the low numbers of treated patients in the NSF audit.
Warfarin has been licensed for more than half a century. Plenty of programs have evaluated ways to improve compliance. However none of these have led to larger penetration of this treatment.
I find it rather difficult to understand how the event of a new medication – an alternative to warfarin - would suddenly make these programs more effective and reduce the need for an alternative after more than 50 years of futile attempts!

Some of my patients are on dabigatran. One particular patient, a 75 year old lady with a cerebellar stroke due to AF, had an allergy to warfarin with an anaphylactic shock and had been on twice daily clexane injections for years. She is now taking dabigatran tablets, which makes a huge difference to her quality of life. She could not afford to buy the medication and not many can.
It is abundantly obvious prevention is the most cost effective therapy. I firmly believe an oral anticoagulation which does not require constant monitoring and does not interact with food or other medication, will lead to more patients being inclined to take this medication and remain on it.
The delay in approval or subsidization in my opinion is the wrong decision and will lead to preventable strokes and poor outcomes. On the contrary I believe the approval process for all new drugs for anticoagulation needs to be expedited for the sake of patients who are struggling with warfarin. I fully agree that warfarin will remain the man treatment of AF for socioeconomic reasons. But if INR control is poor or side effects occur we urgently need a subsidized and approved alternative!
Please do not hesitate to contact me if anything requires clarification.

Kind regards,



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