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A breath of pragmatism

Invited commentary on … Cardiovascular monitoring with acetylcholinesterase inhibitors[†]

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Abstract What cardiovascular screening is needed before prescribing cholinesterase inhibitors in the memory clinic has led to much debate and contradictory advice – especially concerning the need for electrocardiograms (ECGs). Having looked at the current evidence base Rowland *et al* have produced simple and pragmatic advice that should be adopted immediately across the many memory clinics currently in operation. It is rare to have simple protocols these days – it is a relief to have such a breath of pragmatism.

Rowland *et al*'s (2007, this issue) comprehensive and properly evidence-based review on cardiovascular screening when using the three licensed acetylcholinesterase inhibitors (donepezil, rivastigmine and galantamine) is very timely, as what to do routinely in terms of cardiovascular work up with patients receiving these drugs has been a commonly asked question at various memory clinic and old age psychiatry conferences. Many cardiologists have been asked to give their opinion, both in practice and at the same conferences. Responses have ranged from do nothing to do everything, so an unbiased review based on the available literature is a valuable contribution to practice – especially since most memory clinics in the UK are staffed by psychiatric staff, whose knowledge of cardiology is often fairly basic, supported by cardiologists who, as a rule, have no experience with acetylcholinesterase inhibitors.

As a result of this pairing of specialties, each of which has half the information, clinical judgements are often based on a misconstrued relationship between two facts – that increasing vagal tone can have physiological effects on the heart and that acetylcholinesterase inhibitors can increase peripheral acetylcholine at the synapse. The real association between them has in fact not been demonstrated – the only clear reports of acetylcholinesterase inhibitors actually directly causing a bradycardia are in significant overdose. However, because the assumption of a connection is made, some clinics dogmatically perform an ECG on everybody. Others attempt to define 'at-risk' groups, and others do no cardiac assessment at all. This is not a healthy situation, as such variation in practice exposes an organisation to risk – both in terms of clinical governance and over-utilisation of resources.

Clinical evidence

The relevant question then is not what might happen in theory, but what does happen in the clinical setting. The best approximation to this can be gained from the results of clinical trials, which, when pooled, involve quite large numbers of patients. The proviso is that patients selected for clinical trials are relatively healthy and specifically do not usually have significant unstable diseases, including coronary disease and certain conduction disorders on ECG. Given this, the data analysed from the published studies and meta-analyses in Alzheimer's disease do not give rise to concern that using acetylcholinesterase inhibitors has any clinical effect on standard cardiac variables in either those with no existing heart disorder or, in fact, in those who were on stable treatment for known heart disease. Safety is further supported by the relative lack of drug–drug interaction with the acetylcholinesterase inhibitors, especially perhaps rivastigmine.

Open-label and case studies sometimes report that acetylcholinesterase inhibitors have unmasked cases of potential silent parasympathetic weakness. However, this is very rare and does not justify wholesale screening, especially as the most likely

[†]See pp. 178–184, this issue.

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tool is the ECG, which clinical trials have shown to be a poor predictor of cardiac events. It is therefore reasonable to conclude, as do Rowland *et al*, that routine ECG screening for all patients is not going to reduce the risk of an adverse event when treating patients with Alzheimer's disease with acetylcholinesterase inhibitors. It is therefore an unnecessary expense for the memory clinic.

Heart block

That is not to say some patients should not have ECGs before anticholinesterase inhibitors are prescribed. The most important cardiac risk with these drugs is heart block. This will be manifested clinically in a slow pulse, frequently, but not always, associated with syncope. It is definite therefore that everybody should have their pulse documented prior to treatment, and this is wisely where Rowland *et al* start their protocol.

First-degree heart block is relatively benign and most cardiologists would be happy for acetylcholinesterase inhibitors to be used in that circumstance. Third-degree heart block demands a pacemaker, and treatment should be withheld until one has been fitted. Once the pacemaker is in situ, then acetylcholinesterase inhibitors are fine. The biggest area of controversy is second-degree or Mobitz heart block (Ariyarajah *et al*, 2005) – especially if it is asymptomatic. Some cardiologists feel that Mobitz type I heart block (Wenckebach phenomenon) is as benign as first-degree block as far as acetylcholinesterase inhibitors are concerned. Others disagree. Mobitz type II heart block is considered more unstable and, although not always paced for clinical reasons, merits the use of caution with acetylcholinesterase inhibitors – even though to date, there are no data to suggest they do increase the chance of moving from one degree of heart block to another. Obviously, separating these different heart blocks requires a knowledge of the ECG, which is why the protocol suggests GP or specialist help. It is probably the confidence and experience of the memory clinic clinicians and ease of availability of an ECG that will determine whether the slow pulse is examined within the memory clinic or not.

A pragmatic approach

Rowland *et al*'s protocol is straightforward and very simple to use. It can be followed by any member of the memory clinic team, as it relies on simple clinical findings that can be taught in minutes and have high interrater and test–retest reliability.

The protocol means that every person exposed to a acetylcholinesterase inhibitor can have a basic assurance that the treatment they are being offered will not do them any cardiac harm. This is of paramount importance in terms of clinical governance, as variability in practice and differences in opinion are difficult to resolve when sudden adverse events occur. Many memory clinics are provided by mental health trusts that are carrying out more and more physical care. Simple rules such as these help the staff and the trust to feel they are doing their best, without forcing them to resort to unnecessary use of their own resources or those of the primary care or acute trust.

In their article Rowland *et al* have balanced risk, governance and cost-effectiveness in a pragmatic and sensible way. Their protocol should be the adopted standard for both procedure and audit for all memory clinics from the moment it is published.

Declaration of interest

None.

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