Studies on the Evidence Base in Support of Digoxin Therapeutic Drug Monitoring

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Submitted in fulfilment of the requirements for the degree of
Doctorate of Philosophy in December 2005

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Abstract

Despite being available for over 3 decades, there is a dearth of high level evidence for the benefit of digoxin therapeutic drug monitoring (TDM) on clinical endpoints. A pilot randomised controlled trial of digoxin TDM was conducted in hospital inpatients. Clinical endpoints were difficult to collect without considerable additional resources. The main barrier to performing a full-scale randomised trial of digoxin TDM would be the required sample size, which would be over 1,500 patients for a hard endpoint such as incidence of toxicity.

The benefit of the knowledge of the serum digoxin concentration (SDC) in determining the likelihood of digoxin toxicity was assessed by presenting blinded clinicians clinical and SDC data using a computerised interface. The main benefit of the knowledge of the SDC was to reduce the percentage of patients classified as "possibly toxic", and to increase the agreement between clinicians. Those who were assessed as being more likely to be toxic after the knowledge of the SDC were also more likely to have symptoms of digoxin toxicity.

The impact of determining the SDC on all patients prescribed digoxin admitted to medical units of a tertiary referral hospital was assessed. Approximately one fifth of all patients had their management altered as a result of the knowledge of the SDC. In patients, in whom there was no indication for a digoxin assay, and the intended management was to "continue the same", approximately one tenth had a change in their management as a result of the knowledge of the SDC. It is possible to predict, on clinical grounds, patients who are more likely to have such an alteration, and in whom the test has greater clinical utility.

A systematic survey of symptoms and electrocardiographic changes associated with digoxin toxicity was conducted in hospital inpatients. The only symptoms found to be significantly associated with higher SDCs were anorexia, nausea, vomiting, fatigue, and subjective changes in colour vision. Although some colour vision tests can also identify patients with high SDCs, the only symptoms which are clinically useful for the assessment of toxicity, in current clinical practice, are assessment of digoxin's emetic effects. The predominant effect of increasing SDCs on the electrocardiogram was increasing prevalence and severity of bradycardic rhythms, without an increase in automaticity.

An increase in the prevalence of cardiac and non-cardiac manifestations of digoxin toxicity became clear at approximately 1.0 ng/ml which is at the lower end of the currently quoted therapeutic range. In light of these findings the current therapeutic range for digoxin should be revised.