Genetic testing for warfarin therapy initiation

Hynicka L M, Cahoon W D, Bukaveckas B L

**CRD summary**
This review concluded that the routine use of pharmacogenomic testing for the initiation of warfarin therapy was not supported by the evidence. Given the lack of reporting of the review process and quality assessment, the small number of participants and the likelihood that the review did not include the entire evidence base, the reliability of the conclusions are uncertain.

**Authors' objectives**
To evaluate the efficacy of genetic testing for determining the appropriate initial dose of warfarin and the effect of testing on the safety and efficacy of therapy.

**Searching**
MEDLINE (1966 to May 2008) and The Cochrane Library (1993 to May 2008) were searched for English-language publications; search terms were reported. Bibliographies of included studies were also scanned.

**Study selection**
Studies of pharmacogenomic testing to improve outcomes with initiation of warfarin therapy were eligible for inclusion. All patients were adults, however, the included studies varied in their population and treatment regimens. The genotypes included CYP2C9 and VKORC1 wild-types and variants. The authors stated neither how studies were selected for the review nor how many reviewers performed the study selection.

**Assessment of study quality**
The authors did not state that they assessed study quality.

**Data extraction**
Data were extracted on the therapeutic and supra-therapeutic international normalised ratio and the number of adverse events. The authors stated neither how data were extracted for the review nor how many reviewers performed the data extraction.

**Methods of synthesis**
The studies were described individually, with a brief summary of results. Study details were tabulated.

**Results of the review**
Four studies met the inclusion criteria: two randomised controlled trials (n=238) and two prospective cohort studies (n=345). None of the studies reported a significant difference in efficacy between dosing strategies, although the prospective cohort studies reported a tendency towards fewer adverse events in patients with pharmacogenomic-guided dosing.

**Authors' conclusions**
The use of pharmacogenomic testing in the initiation of warfarin therapy does not show improved outcomes in either safety or efficacy with warfarin therapy.

**CRD commentary**
The authors addressed a clear review question, but had poorly defined inclusion criteria. The search for studies was limited and restricted to studies published in English. The review process was poorly reported, and it was unclear whether methods were used to reduce error and bias. The authors did not assess the quality of the included studies. The number of participants included in the review was extremely small. The decision to combine studies in a narrative seemed appropriate. Given these limitations, the reliability of the results of the included studies and the proportion of available evidence that was identified and included in the review are uncertain, therefore, the reliability of the conclusions are uncertain.
Implications of the review for practice and research

**Practice:** The routine use of pharmacogenomic testing for warfarin initiation was not supported by the evidence.

**Research:** The authors did not state implications for practice.

**Funding**
Not stated.

**Bibliographic details**

**PubMedID**
18682545

**DOI**
10.1345/aph.1L127

**Original Paper URL**
http://www.theannals.com/cgi/content/full/42/9/1298

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Anticoagulants /adverse effects; Genetic Predisposition to Disease; Hemorrhage /chemically induced /genetics; Humans; Warfarin /adverse effects

**AccessionNumber**
12009100698

**Date bibliographic record published**
31/03/2009

**Date abstract record published**
29/07/2009

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.