Effect of setting, monitoring intensity and patient experience on anticoagulation control: a systematic review and meta-analysis of the literature

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CRD summary
This review assessed whether oral anticoagulation control differed for monitoring under different settings. The authors concluded that significant differences in International Normalised Ratio (INR) control were associated with different settings. Given a number of shortcomings in the review process, the authors' conclusions should be interpreted with caution.

Authors' objectives
To assess whether oral anticoagulation (OAC) control differed with respect to monitoring intensity and patient setting in treatment-experienced and treatment-naïve atrial fibrillation (AF) patients.

Searching
PubMed, EMBASE and Cochrane Central Register of Controlled Trials were searched from 1995 to 2005 without language restrictions. Search terms were reported. Reference lists of retrieved articles and review articles were reviewed to identify additional studies.

Study selection
Studies of patients receiving adjusted-dose OAC for AF, which reported the proportion of time spent within a maximum International Normalised Ratio (INR) range of 2.0 to 3.5 and had a mean duration of six months follow-up were eligible for inclusion. Excluded studies were those with more than 25 per cent of subjects with heart valve replacement and where the INR calculation had not used the patient-time approach. Most of the included studies were restricted to patients with AF; some studies included patients with a range of other cardiovascular conditions. The range of INR was 2.0 to 4.5. The most frequently used anticoagulant was warfarin; others used included acenocoumarol and phenprocoumon. Monitoring regimens varied between studies. Patient years of follow-up ranged from 8.5 to 12,958.

The authors stated neither how the papers were selected for review nor how many reviewers performed the selection.

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

Data extraction
The data were extracted using a standard proforma. The proportion of time spent in the therapeutic range was extracted for each study and expressed as an incidence density with 95% confidence intervals (CIs).

The authors stated neither how the data were extracted for the review nor how many reviewers performed the data extraction.

Methods of synthesis
Summary estimates of the proportion of time spent in the therapeutic range and 95% CI were calculated. These were combined using a random-effects model weighted by the inverse of the variance of the proportion of time spent in therapeutic range. Statistical heterogeneity between the studies was assessed using the Q statistic. Sensitivity analysis was undertaken according to: frequent versus infrequent monitoring; organised versus usual care; and existing OAC users versus naïve users.

Results of the review
A total of 36 studies met the inclusion criteria (number of patients not reported): 22 were restricted to patients with AF and used for primary analyses; and 14 included mixed populations and were used for secondary analyses. Statistical
heterogeneity was present for all pooled estimates.

The pooled overall mean time for AF patients in the INR range of 2.0 to 3.0 was 61.3 per cent (95% CI: 58.8, 63.8). Pooled mean time in INR was 59.1 per cent (95% CI: 55.5, 62.8) for infrequent monitoring and 64.3 per cent (95% CI: 60.5, 68.0) for frequent monitoring; the difference between the groups was not significant. Significantly more time was spent in range in specialist care settings than usual care 11.3 per cent (95% CI: 0.1, 21.7). Naïve OAC users spent less time in range 56.5 per cent (95% CI: 45.5, 67.5) than existing users 61.2 per cent (95% CI: 57.2, 65.2); the difference between the groups was not significant.

**Authors’ conclusions**
INR control is dependent on monitoring intensity and the duration of anticoagulant treatment.

**CRD commentary**
The review question was stated clearly. Relevant sources were searched with no restrictions placed on language (no foreign language papers met the inclusion criteria). There was no specific search for unpublished studies, so some studies might have been missed. The methods used for study selection and data extraction were not reported, making it unclear whether methods were used to reduce error and bias. There was no formal assessment of the validity of the included studies. Highly significant statistical heterogeneity was observed for all analyses and the study details indicate substantial clinical heterogeneity, thus the reliability of the pooled estimates was uncertain. Given such limitations, the author's conclusions should be interpreted with caution.

**Implications of the review for practice and research**
Practice: It may be inappropriate to extrapolate data on efficacy and safety of anticoagulants from the studies to clinical practice.

Research: Further studies reporting INR control in standard clinical settings should be published to reflect efficacy and safety of anticoagulation with vitamin K antagonists.

**Funding**
Boehringer Ingelheim International GmbH.

**Bibliographic details**

**PubMedID**
18402715

**DOI**
10.1185/030079908X297349

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Administration, Oral; Aged; Aged, 80 and over; Anticoagulants /administration & dosage /adverse effects; Atrial Fibrillation /complications /diagnosis /drug therapy /mortality; Dose-Response Relationship, Drug; Drug Administration Schedule; Female; Humans; Male; Maximum Tolerated Dose; Meta-Analysis as Topic; Monitoring, Physiologic /methods; Patient Compliance /statistics & numerical data; Prognosis; Randomized Controlled Trials as Topic; Risk Assessment; Severity of Illness Index; Stroke /prevention & control; Survival Analysis; Time Factors; Treatment Outcome
AccessionNumber
12008105587

Date bibliographic record published
02/03/2009

Date abstract record published
06/05/2009

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.