Review and evaluation of PiP strategy for PAF compared to episodic IHT or continuous AADs

Systematic review and cost-effectiveness evaluation of 'pill-in-the-pocket' strategy for paroxysmal atrial fibrillation compared to episodic in-hospital treatment or continuous antiarrhythmic drug therapy

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Executive summary

Health Technology Assessment 2010; Vol. 14: No. 31
DOI: 10.3310/hta14310

Health Technology Assessment
NIHR HTA programme
www.hta.ac.uk

Executive summary

Objectives

1. To summarise the results of the rapid reviews of the clinical effectiveness and cost-effectiveness literature describing the pill-in-the-pocket (PiP) approach for the treatment of patients with paroxysmal atrial fibrillation (PAF).
2. To develop an economic model to assess the cost-effectiveness of PiP compared with in-hospital treatment (IHT) or continuous antiarrhythmic drugs (AADs) for the treatment of patients with PAF.

Background

Atrial fibrillation (AF) is a tachyarrhythmia characterised by unco-ordinated atrial activation with consequent deterioration of impairment of atrial function and a rapid, irregular heartbeat. The patient may experience palpitations, chest pain, dizziness or, in severe cases, loss of consciousness. In some cases, patients with AF may present without any symptoms. An incidence of AF may be self-terminating or require clinical intervention (for example, pharmacological or medical cardioversion). The annual incidence rate of PAF has been estimated at 1.0 per 1000 person-years (95% confidence interval 0.9 to 1.1), and reported prevalence rates show wide variations depending on age and country.

The classification of AF is called the 3 'P' classification: paroxysmal, persistent and permanent. When a patient experiences two or more AF episodes that terminate within 7 days (usually within 48 hours), AF is classified as paroxysmal. If a patient suffers more than one attack and the AF attack lasts longer than 7 days, the AF is classified as persistent. If the AF episode does not resolve for over a year and/or is not successfully terminated by cardioversion, the pattern is classified as permanent.

Conventional treatment strategies for PAF focus on the suppression of paroxysms of AF and return to normal sinus rhythm (NSR). AAD treatment can consist of (i) continuous prophylactic treatment or (ii) episodic IHT. Prophylactic treatment (daily dose) can include the use of beta-blockers, class Ic agents (e.g. flecainide, propafenone) or class III agents (sotalol, amiodarone). Episodic treatment of PAF consists of pharmacological cardioversion usually involving an intravenous infusion of AADs in a hospital setting or, if this fails, electrical direct current cardioversion.

Methods

Electronic searches were conducted to identify clinical effectiveness and cost-effectiveness evidence describing the use of a PiP strategy for the treatment of PAF, published since the release of the Royal College of Physicians' national guidelines on AF in June 2006. An additional search was also undertaken, excluding the term 'pill-in-the-pocket' in order to identify economic evaluations and costing studies describing the comparator treatments to support the development of the economic model.

A Markov model was constructed to examine differences between three PAF strategies (PiP, AAD and IHT) in terms of cost per quality-adjusted life-year (QALY). A Markov model structure was chosen because it is assumed that PAF is a condition that causes patients to move between a limited number of relevant health states during their lives. This type of model allows a large number of cycles to be simulated without having to create a new decision tree in each cycle. The three PAF strategies have the same five health states:

- NSR
- persistent/chronic atrial fibrillation (CAF)
- post-stroke without CAF
- post-stroke with CAF
- death state.

The economic evaluation has been undertaken from an NHS and Personal Social Services perspective. The model has been developed with a cycle length of 1 year and is simulated for the remaining lifetime of all patients.

Results

The search strategies for clinical studies identified 201 randomised controlled trials (RCTs). None of the identified RCTs compared PiP with any other treatment for PAF and therefore did not meet the inclusion criteria for the review. No relevant studies were identified by the search for ongoing trials.

Of the 201 RCTs identified, 12 were deemed to be relevant to the decision problem as they included drugs used to treat PAF; summary data were abstracted from these studies in order to inform the development of the economic model only. The 12 RCTs were all conducted in a hospital setting and prior to the publication of the current national guidelines. One additional study was identified that had informed the evidence considered in *Atrial fibrillation: national clinical guideline for management in primary and secondary care* developed by the National Collaborating Centre for Chronic Conditions in 2006.

The model results indicate that the PiP strategy is slightly less effective than the other two strategies, but also less costly (incremental cost-effectiveness ratio of £45,916 per QALY when compared to AAD, and £12,424 per QALY when compared to IHT). The one-way sensitivity analyses performed do not show substantial changes in relative cost-effectiveness except in relation to the age of patients, where PiP dominates AAD in men over 65 years and in women over 70 years.

The probabilistic sensitivity analysis demonstrates how close the three strategies are to each other, and the uncertainties in the data. All conclusions need to be considered in relation to these uncertainties.

Conclusions

The systematic review of clinical evidence did not identify any new studies that had not been included in the previously available guidelines.

Overall, a PiP strategy seems to be slightly less effective (i.e. fewer QALYs gained) than AAD and IHT, but is associated with cost savings.

A PiP strategy seems to be more efficacious and cost-effective than an AAD strategy in men over 65 years and women over 70 years, but this is principally due to a very slight difference in QALY gained by the PiP strategy.

A change in clinical practice that includes the introduction of PiP may save costs, but also involves a reduction in clinical effectiveness compared to existing approaches used to treat patients with PAF.

Uncertainty in the available clinical data means there was insufficient evidence to support a recommendation for the use of PiP strategy in patients with PAF. Further research should identify outcomes of interest such as adverse events and recurrent AF episodes in an RCT setting because the only clinical study addressing these issues, even partially, is not an RCT but a descriptive analysis.

Patient preferences also need to be considered in any future research designs.

Publication

Martin Saborido C, Hockenhull J, Bagust A, Boland A, Dickson R, Todd D. Systematic review and cost-effectiveness evaluation of 'pill-in-the-pocket' strategy for paroxysmal atrial fibrillation compared to episodic in-hospital treatment or continuous antiarrhythmic drug therapy. *Health Technol Assess* 2010;**14**(31).

NIHR Health Technology Assessment programme

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Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this issue of the journal was commissioned by the HTA programme as project number 08/46/01. The contractual start date was in May 2009. The draft report began editorial review in September 2009 and was accepted for publication in March 2010. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

ISSN 1366-5278

Published by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk), on behalf of NETSCC, HTA.

Printed on acid-free paper in the UK by the Charlesworth Group.