Atrial fibrillation: rate as important as rhythm

Scott Gottlieb *New York*

Drugs that regulate heart rate are just as effective as drugs and procedures that control rhythm in the treatment of atrial fibrillation, as well as being cheaper and safer, according to two new studies. The new approach may also lead to fewer hospital admissions, presumably because of fewer side effects from the drugs that control heart rate.

To treat atrial fibrillation most doctors have preferred a strategy of restoring normal heart rhythm, which can involve electrically shocking the heart, partly on the assumption that this strategy results in fewer complications such as strokes than a strategy to control heart rate. The prevailing approach was largely uncontested and was based mostly on intuition.

Among the drugs that doc-

tors most commonly use to restore a normal rhythm in cases of atrial fibrillation are amiodarone, sotalol, propafenone, procainamide, quinidine, flecainide, disopyramide, moracizine, and dofetilide.

A smaller group of doctors, many in Europe, already favoured the less aggressive strategy, choosing to control the rate and allowing the atrial fibrillation to continue. These doctors prescribed digitalis, β blockers, and calcium channel blockers.

One of the new studies, both of which were published in the *New England Journal of Medicine*, was conducted in the United States and Canada (2002;347:1825-33), the other in the Netherlands (2002;347:1834-40).

The North American study was led by Dr D Wyse of the

Atrial Fibrillation Follow-up Investigation of Rhythm Management Investigators. The study involved 4060 patients at 213 hospitals, and the patients were followed for an average of 3.5 years (maximum six years). Each patient had atrial fibrillation and at least one other risk factor for stroke or death, including an age of at least 65, high blood pressure, diabetes, and heart failure.

One group, of 2027 patients, received drugs to control heart rate. Drugs that were acceptable in the protocol for this purpose were β blockers, calcium channel blockers (verapamil and diltiazem), digoxin, and combinations of these drugs.

The other group, of 2033 patients, received drugs to control rhythm.

At the end of the study, the number of patients in the rhythm control group who had died, of any cause, was 356, compared with 310 in the rate control group. The mortality at five years was 23.8% in the rhythm control group and 21.3% in the rate control group, corresponding to a hazard ratio of 1.15 (95% confidence interval 0.99 to 1.34, $P=0.08$).

The Dutch study, led by Dr Isabelle Van Gelder of the University Hospital in Groningen, involved 522 patients at 31 hospitals in the Netherlands. After an average of 2.3 years, 60 of the 266 participants (23%) in the rhythm control group had died of a cardiac cause, compared with 44 of the 256 patients (17%) in the rate control group. □

FDA limits research of former AHA president for submitting false information

Janice Hopkins Tanne *New York*

Just days before he completed his year as president of the American Heart Association on 30 June, Dr David Faxon signed a consent agreement with the Food and Drug Administration limiting his clinical research.

On 19 June 2002 Dr Faxon agreed that for three years he would not be the principal investigator for more than two FDA regulated clinical investigations at any one time, and that he would not be the principal clinical investigator for a study that enrolled more than 25 subjects.

The agreement follows an investigation into Dr Faxon's work, which was held from October to November in 1999 when he was chief of cardiology at the

University of Southern California in Los Angeles. The FDA inspected his clinical study, comparing a new drug with aspirin to see which gave better protection from ischaemic heart events after acute coronary syndromes.

After its investigation, the FDA complained that Dr Faxon failed to personally conduct or supervise the clinical investigation, that he submitted false information to the trial sponsor, and that he failed to conduct the study in accordance with the approved protocol. He was also found not to have kept adequate and accurate case histories and not to have provided a Spanish version of the informed consent document to

people whose first language was Spanish, not English.

The complaint cited examples of records being falsified to alter the duration of chest pain; changes in the records that led to the inclusion of patients who were not eligible for inclusion; patients being included despite being enrolled after the time limits; patients being included when they were receiving drugs that should have excluded them.

Dr Faxon answered the FDA in December 1999, saying his study's coordinator was responsible for misrepresentation of data and he had no knowledge of the practice. The FDA rejected his response: "We remind you that you are responsible for personally conducting and supervising the clinical investigations since you are the investigator of record. Therefore, we consider your explanation unacceptable."

In April 2000, the FDA sent Dr Faxon a "Notice of Initiation of Disqualification Proceedings

Dr David Faxon, who said his coordinator was responsible for misrepresenting data

and Opportunity to Explain (NIDPOE)." Few clinical investigators receive such a notice. In 2000, Dr Faxon was one of only six to receive one. In 2001 there were four, and so far this year there have been two.

In July 2000, Dr Faxon became section chief of cardiology and professor of medicine at the University of Chicago. □