

Cochrane corner

Is digitalis effective in congestive heart failure in patients in sinus rhythm?

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Although the utility of digitalis glycosides for controlling the heart rate in patients with rapid atrial fibrillation is well recognised, the current review is restricted to the use of digitalis in patients who are in normal sinus rhythm. In this situation any benefits resulting from treatment would not be due to rate control, but to other properties of digitalis such as effects on inotropy or neurohumoral balance.

Digitalis no longer first line therapy in heart failure

The use of ACEI and beta-blocking agents is based upon randomised clinical trials which decisively show that both agents decrease mortality and improve clinical status. Because the clinical benefits of treating congestive failure with digitalis appear to be less striking than for ACEI and beta-blocking agents, and because there is no reduction in mortality, use of digitalis can probably no longer be considered first-line therapy.

Based upon these findings, treatment with digitalis in patients who

remain symptomatic after already receiving appropriate therapy with diuretics and ACEI is quite reasonable. The same may also be true for patients who are being treated with beta-blocking agents or spironolactone, though data on this point are lacking.

Mortality

A meta-analysis of mortality figures for the eight studies that provided this data clearly showed that treatment with digoxin had no effect on death rates. This observation is based almost entirely upon findings in the trial conducted by the Digitalis Investigation Group (Dig 1997).

Hospitalisations

Regarding hospitalisation, the data provided by the large study conducted by the Digitalis Investigation Group (Dig 1997), as well as data from three smaller studies, indicated that hospitalisation during the course of the study was significantly less common in patients taking digoxin. This resulted in a Relative Risk Reduction of 32% (95% CI 25%–39%). This gives a Numbers Needed To Treat from 27 to 114.

Clinical deterioration

There is evidence to support the conclusion that digitalis therapy results in a better clinical status than placebo.

Point estimates show a Relative Risk Reduction of 71% (95% CI 58%–80%). The numbers needed to treat to prevent a clinical deterioration at three months ranged from four to 75.

Ejection fraction

Ejection fraction was measured in five studies (Dig captopril 1988, Dig milrinone 1989, Lee 1982, PROVED 1993, RADIANCE 1993), and the measurement was significantly better with digoxin than placebo therapy in four of them. One may conclude that digitalis does have favourable effects, but that they are not very pronounced, and may not be observed in all patients.

Benefits of high doses of digoxin

It may be noted that the effects of digitalis therapy were unequivocally positive in all four studies reported somewhat higher than normal doses of digoxin, ranging from 0.375 to 0.425 mg/day, were administered (Guyatt 1988, Lee 1982, PROVED 1993, RADIANCE 1993). The mean or median serum levels ranged from 0.7 to 2.5 mg/mL.

Diastolic dysfunction

There was also no obvious benefit of digitalis treatment in these patients, and it remains uncertain whether there is a therapeutic role for this agent in patients with 'diastolic dysfunction'.

Continuing Medical Education

Age, gender and duration of congestive heart failure

There is no clear-cut evidence that age, gender, or duration of congestive failure have a bearing on the question of which groups are most eligible for treatment with digitalis.

Reviewers' conclusions Implications for practice

The findings of this review demonstrate that digitalis has a useful role in treating symptomatic congestive

heart failure, and has both clinical benefits, and the ability to reduce hospitalisations. Although some authors have stated that the agent is of limited value, adequate control of symptoms in patients with NYHA Class II–IV congestive heart failure may be difficult to achieve through use of diuretics and ACEI alone, and additional clinical gains can often be made by adding digitalis to the regimen. Patients with impaired cardiac function who have few or no symptoms

(NYHA Class I) are not appropriate candidates for treatment with digitalis, since the agent does not reduce mortality, and is not known to prevent progression of the disease. These recommendations are consistent with the draft version of the new National Heart Foundation of New Zealand guidelines for heart failure, The Scottish Intercollegiate Guideline Network (www.sign.ac.uk) and the Institute for Clinical Systems Improvement in Minnesota (www.ICSI.org).

References

References are available from B Arroll or from the web <http://www.cochrane.org/>