

Drug therapy in older people with heart failure

Editor – We read with interest the review article by Mukhtar and Jackson entitled *Drug therapy in older adults (part 2)*.¹ In the article the authors provide an overview on the drug treatment of heart failure in older patients. However, we were surprised that digoxin, one of the oldest drugs in the management of heart failure was not mentioned as a treatment option. Clinical evidence is in favour of digoxin in diastolic heart failure as well as systolic heart failure through improvement of early diastolic function and possible reduction in sympathetic humoral activity.

The benefits are not restricted to patients with heart failure in atrial fibrillation but also in sinus rhythm. In a systematic review of 13 trials which included over 7,000 patients with heart failure in sinus rhythm, digitalis had a positive effect on improving symptoms and reducing hospitalisation.²

The earlier Digitalis Investigation Group trial had also showed, in addition to 6% less hospitalisation in the treatment, a trend toward a beneficial effect of digoxin in pump failure death, but this was offset by mortality from non-cardiovascular causes³.

Therefore in older patients with moderately severe heart failure who remain symptomatic despite optimum treatment with diuretics, angiotensin-converting-enzyme inhibitors and beta blockers, it is worthwhile considering the addition of digoxin. It is important to point out that the benefits of digoxin occur with low maintenance dosage which is usually between 62.5–125 µg daily.

The benefits of digoxin mentioned above cannot be over-emphasised in the vast majority of the older frailer population with heart failure. This is important as the NHS is aiming towards keeping the frail elderly in their own environment for as long as possible rather than hospitalisation. Clinicians working in acute frailty units are likely to come across more of these patients and can best serve this cohort of patients well by asking why they cannot be on digoxin. Every little helps especially on a frailty ward!

References

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- 3 The Digitalis Investigation Group. The effect of digoxin on mortality and morbidity in patients with heart failure. *N Engl J Med* 1997;336:525–33.

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Response

Editor – We thank the correspondents for their letter in response to our recent article 'Drug therapies in older adults (part 2)'.¹ While digoxin is well established in the management of older patients with atrial fibrillation with or without heart

failure, the evidence base for digoxin in frail older patients is not established.

The Digitalis Investigation Group study referred to in your letter enrolled 6,800 patients with documented left ventricular ejection fractions of 45% or less.² We are concerned that in this study, as the serum digoxin concentration increased, the absolute risk in mortality rose versus patients receiving placebo. In such patients the absolute mortality rate was 11.8% (95% confidence interval 5.7–18.0%; $p < 0.001$) higher than those receiving placebo. The effect of frailty on this association is unknown.

We included the section on neprilysin inhibitors to establish that there is a pipeline of newer agents, but we made the point that their role is not established. We agree, however, that we should have included digoxin here discussing its newer roles rather than the indication established described by Sir William Withering. Clinicians managing frailty units should restrict their therapeutic choices to those that have an evidence base in frail patients, or where clinical circumstances are in favour of extrapolating from fitter populations.

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A cough that doesn't fit the mould

Editor – We read with interest the lesson of month entitled *A cough that doesn't fit the mould* (*Clin Med* 2015;15:492–4). This is an interesting case report, which we believe highlights the difficulty in making a diagnosis and classifying *Aspergillus*-related pulmonary disease. Baggott *et al* have made a diagnosis of *Aspergillus* tracheobronchitis and mention that it is part of the spectrum of invasive *Aspergillus* disease. We believe it would be worth adding that both saprophytic (non-invasive) and invasive forms of *Aspergillus* tracheobronchitis exist.^{1,2} The latter requires the demonstration of fungal hyphae invading the bronchial mucosa, which was not demonstrated in this case. Where fungal hyphae are found in the bronchial tree without invasion this could be due to obstructing bronchial aspergillosis, which requires the absence of allergic disease,¹ or mucoid impaction that is a non-specific sign of *Aspergillus* bronchial disease and is also a feature of allergic bronchopulmonary aspergillosis (ABPA). The case presented by Baggott *et al* had mucoid impaction resulting in obstruction and collapse of the right middle lobe. However, the patient developed features of an allergic reaction to *Aspergillus* evidenced by the positive grade-III specific *Aspergillus* IgE, high total IgE level (1,519 kU/L) and

pulmonary eosinophilia ($1.94 \times 10^9/L$). Therefore, we wonder if this patient developed seropositive ABPA following sensitisation and repeated exposure to *Aspergillus* species. What is interesting in the presented case is the absence of pre-existing respiratory disease, as ABPA does not usually present as an acute primary condition. ABPA is more often found in patients with asthma and cystic fibrosis, and certainly the presence of asthma is considered essential for the diagnosis of classical ABPA; however it is not infrequent that it is reported in individuals without a past history of asthma.^{3–5}

References

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Response

Editor – We would like to thank the correspondents for their interest in our case report. We are in complete agreement that this case illustrates the difficulty in diagnosing the various respiratory conditions that can be caused by *Aspergillus* and the considerable overlap between them. We also agree that the distinction between non-invasive and invasive forms of *Aspergillus* tracheobronchitis is important and in our case, the disease was non-invasive.

We read with interest their comments that allergic bronchopulmonary aspergillosis (ABPA) has been reported

in individuals without a history of asthma,¹ and whether this patient had developed ABPA rather than *Aspergillus* tracheobronchitis as we proposed. ABPA was one of the differential diagnoses considered while the patient was under our care; however several factors influenced our final diagnosis, based on the diagnostic criteria of Rosenberg and Patterson.^{2,3}

Radiologically, no fleeting opacities or bronchiectasis were present on chest radiograph or computed tomography of the chest. In this case, the radiological manifestation of disease was limited to right middle lobe collapse, which subsequently resolved. While he did develop features of allergic sensitisation to *Aspergillus* – demonstrated by raised total serum IgE, *Aspergillus* specific IgE and serum eosinophilia – we felt this was a consequence of his exposure to a significant burden of *Aspergillus* spores, as demonstrated by the fungal hyphae from his mucous plug. Finally, his response to treatment was more rapid than is usually seen in ABPA.

We would like to thank the correspondents for highlighting that ABPA can rarely be seen in patients without a diagnosis of asthma or cystic fibrosis, further illustrating the complexity of *Aspergillus*-related pulmonary disease.

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