Should beta-blockade continue to be withheld from patients with chronic heart failure and asthma?1

We would like to congratulate the Task Force (for the diagnosis and treatment of acute and chronic heart failure 2008) in producing an excellent revision of the heart failure guidelines.1 We are very confident that this document will assist physicians tremendously in the management of this complex cardiovascular condition. One of the central aims of such a document is to help ensure that patients who typically carry poor prognoses, benefit from the administration of potentially life prolonging treatments. With this in mind, we wonder why the Task Force continues to view bronchial asthma as a contra-indication to patients with chronic heart failure (CHF), as opposed to a caution under specialist supervision. This subject remains an area of frequent debate, given the high incidence of asthma in the general population.

We understand that this group of patients have been excluded from previous randomized, controlled trials assessing the benefit of beta-blockers in CHF. Therefore, direct conclusions from specific CHF trials are difficult to draw upon. Nevertheless, the original contra-indication to beta-blockade in asthmatics came mainly from observational reports of propranolol use many years ago.2,3 Since that time, several cardioselective agents have been developed, some of which are now proved to substantially improve outcome in CHF.4,5 An extensive Cochrane meta analysis reported on the relative safety of cardioselective beta-blockers in patients with asthma, for treatment exposures of up to 1 month in duration.6 Although there is a paucity of data for time periods outside of this, the evidence suggests that the first dose of beta-blockade is the most likely to cause bronchospasm, in comparison to continuing treatment. In response to this, careful observation over the initial dosing could be employed for many patients. Conversely, over the longer term (3 days to 1 month), beta-blockade may even improve airways resistance and reduce the tachyphylaxis phenomenon of salbutamol.7 It thereby might even offer benefit to asthmatics in the long term, which is a theory currently under much discussion.7–9

Therefore, in contrary to common practice, particularly when we take into account the magnitude of potential benefit derived from beta-blockade in CHF, we continue to feel uncomfortable withholding these agents from (non-brittle) asthmatics. We believe that there is little evidence of serious harm from using cardioselective agents, when given carefully under specialist supervision and at low starting doses. On the other hand, there is very strong evidence that patients with CHF who are not given beta-blockers fare poorly.

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Should beta-blockade continue to be withheld from patients with chronic heart failure and asthma?: reply

We are pleased that Drs Shaw and Williams are confident that the new heart failure guidelines will assist physicians in the management of patients with complex cardiovascular conditions.1 We appreciate their concern that patients with asthma and heart failure might be excluded from the potential benefits of beta-blockade. The ESC 2008 heart failure guidelines state that asthma is considered a contraindication, but we emphasize that chronic obstructive pulmonary disease (COPD) is not a contraindication.2

In the meta-analysis referred to, the chronic dosing studies indentified a total of less than 200 patients randomized to a relatively selectively beta-1 receptor antagonist, with about half the studies using an agent with beta-1 agonist activity. The duration of treatment ranged from only 3 days to 4 weeks. This does not represent sufficiently large-scale or
long-term experience from which safety can be inferred. While it is theoretically possible to identify patients who might be given a relatively selective beta-1 receptor antagonist, e.g. non-smokers with mild–moderate airways disease, no previous hospitalization, only Stage 1 or 2 treatment, a stable peak expiratory flow rate, no nocturnal symptoms, little wheeze, and the sense to know when to seek help, such advice is based upon clinical assumptions and not on evidence. What might happen to patients who develop an exacerbation of asthma while taking a beta-blocker? Additionally, the patients’ response to rescue beta-agonist therapy during that attack remains a concern. While in time recommendations may change, we believe that, at present, it is unwise to recommend in a general guideline such as ours that relatively beta-1 selective beta-blockers be given to patients with asthma in the absence of convincing evidence of safety.

Although guidelines are evidence based, anecdotal experience frequently generates strong hypotheses. We would encourage Drs Shaw and Williams to address their hypothesis in a prospective, randomized trial with appropriate endpoints. We agree that the role of selective beta-blockade in patients with asthma and heart failure deserves more rigorous attention.

Albert Einstein put it well: ‘In theory, theory and practice are the same. In practice they are not’.

References

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doi:10.1093/eurheartj/ehp166

Prediction of fatal or near fatal arrhythmias in patients with a depressed left ventricular function after an acute myocardial infarction

The ambitious study by Huikuri et al.1 for the CHARISMA study group deserves our attention, careful reading, and contemplation about our current practices in predicting malignant arrhythmias in patients with an acute myocardial infarction and depressed left ventricular function, and what we should go from here. Methodologies employed in the study of 312 patients included standard electrocardiogram, heart rate variability/turbulence, ambient arrhythmias, signal-averaged electrocardiogram, T-wave alternans (TWAs), and programmed electrical stimulation (EPS). Ventricular fibrillation or symptomatic sustained ventricular tachycardia, the primary endpoint, was documented by implantable ECG loop-recorder. During a follow-up of 2 years, measurement of heart rate variability was shown to be an independent non-invasive predictor of outcomes with the best performance. T-wave alternans was assessed by exercise stress testing, and for patients with incomplete or indeterminate tests, during the EPS by atrial and atrial/ventricular pacing. While many investigators have recommended the employment of quantitative results of TWAs,2,3 the authors of this report have not reported actual values of TWA, but resorted to the currently prevailing trichotomy of positive/negative/intermediate and dichotomy of negative/non-negative study results. In the context of previously expressed opinions,2,3 it would be useful to have information about the contribution of quantitation of TWA results. Accordingly, was the magnitude of TWA a better predictor of the arrhythmic outcomes than mere characterization of negative/non-negative results? What were the correlates (i.e. other test results) of patients with relatively high values of TWA? Another notion recently expressed4 is whether the magnitude of the TWA is T-wave amplitude dependent. In this vein, was there any relationship between the magnitude of the TWA values and the corresponding T-wave lead(s) used for the TWA calculations? The authors have employed all the 12 standard ECG leads, and X, Y, Z orthogonal leads for the TWA assessment, and thus an opportunity exists to evaluate whether such a relationship underlies TWA. Although the spectral assessment of TWA does not reflect only the amplitude of the corresponding T-wave, some insight on the above issue could be forthcoming from a correlation of the values of TWA magnitude in μV in the 15 leads used and the values of the amplitude of the corresponding T-waves in μV or mV. A response to this inquiry may provide an insight whether a different TWA magnitude in a repeat assessment in a particular patient is a reflection of changing of the degree of vulnerability to malignant arrhythmias, or merely the often unexplained change in the morphology, amplitude, or polarity of T-waves.

References
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