Effect Of Endogenous Noradenaline Release On Peak Exercise Heart Rate In Subjects With Chronic Heart Failure Receiving Carvedilol Versus Metoprolol

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Background

Dose equivalency of metoprolol and carvedilol for beta-1 blockade remains subject of ongoing debate. The degree of beta-1 blockade is best assessed in vivo by blunting of the exercise induced heart rate. Accordingly, we examined baseline and peak exercise heart rate in subjects with chronic heart failure (CHF) treated with carvedilol or metoprolol. To correct for possible differences in norepinephrine (NE) release due to beta-2 blockade, we also measured NE levels at baseline and peak exercise.

Methods

Thirty-three subjects treated chronically with carvedilol (34.5 +3.4 mg; n=23) or metoprolol XL (77.5+17.3 mg; n=10) referred for cardiopulmonary exercise testing were studied prospectively. All subjects were in normal sinus rhythm, achieved RER > 0.95, and received the long acting form of metoprolol, metoprolol XL, which has 75% bioavailability of the short acting metoprolol IR. Carvedilol versus metoprolol XL subjects did not differ

($p < 0.05$) with respect to age (52 vs 56 yrs), LVEF (25 vs 29 %), LVEDD (6.2 vs 6.3 mm), MAP (83.5 vs. 88.3 mmHg), baseline HR (73.6+2.4 vs 71.5+4.7 bpm), peak Vo2 (16.7 vs 15.7 ml/kg/min), exercise time (9.3 vs 9.1 min), or baseline (3.49 vs 4.01 nmol/l) plasma norepinephrine (NE) levels. However, despite similar peak NE levels (17.1+1.8 vs 18.6+4.9 nmol/l), heart rate at peak exercise was higher in subjects receiving carvedilol (131.7 + 4.6 bpm) compared to those receiving metoprolol (112.6 + 6.0 bpm), $p=0.029$.

Conclusion

Similar NE release and more complete beta-1 blockade as assessed by peak heart rate is observed in otherwise well matched subjects with CHF treated with a mean daily dose of 77.5 mg metoprolol XL as compared to 35.5 mg carvedilol. Assuming a 75% bioavailability of metoprolol XL, 58 mg metoprolol IR should provide a higher degree of beta-1 blockade than 35 mg carvedilol.

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