

## Beta-blockers: A Second Rate Treatment for Hypertension?

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Hypertension is a major risk factor for stroke and myocardial infarction. Lowering blood pressure by 5-6 mmHg reduces the stroke risk by 38%.<sup>1</sup> It is astonishing that the treatment of hypertension is so beneficial when the efficacy of currently available antihypertensive drugs is so modest. Thus, any drug, which lowers blood pressure and is safe, is approved for clinical use. In the last decade, large clinical trials have been conducted to compare antihypertensive drugs in terms of cardiovascular outcome.<sup>2,3</sup> One of the latest trials was the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), the results of the blood pressure lowering arm of which have recently been reported at the American College of Cardiology Annual Scientific Session.<sup>4</sup> The database is not complete yet, but the preliminary results already show that the amlodipine-perindopril arm (new drugs) had better outcomes than the diuretic-beta-blocker arm (old drugs). Furthermore, there were more new cases of diabetes in the latter arm.

The results of ASCOT were unexpected, because previous trials of old versus new drugs had been a tie.<sup>5-7</sup> In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT),<sup>8</sup> diuretics performed as well as amlodipine and lisinopril, but because thiazide diuretics have been in use for a long time and are economical, they are promoted as first line

treatment in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7).<sup>9</sup> However, beta-blockers are not advocated as first line treatment in JNC7. In the British guidelines, there are explicit reservations regarding beta-blockers.<sup>10</sup> In older trials on hypertension, beta-blockers were used together with thiazide diuretics and so took a share of the credit for the benefits shown.<sup>1</sup> On their own, they are less than impressive.<sup>11</sup> In the Medical Research Council trial of treatment of hypertension in older adults, beta-blockers were no better than placebo and significantly inferior to diuretics.<sup>12</sup> In the Losartan Intervention For Endpoint reduction in hypertension study (LIFE), atenolol was inferior to losartan with regard to stroke, although it was non-significantly better than losartan in terms of myocardial infarction.<sup>13</sup> A recent meta-analysis showed that atenolol performs consistently less well than other antihypertensive drugs in clinical trials.<sup>14</sup>

ASCOT was an unequal race between old war-horses and young thoroughbreds. Diuretics and beta-blockers need to be used at low doses, limiting their blood pressure lowering effect. These drugs also worsen the metabolic profile whereas angiotensin-converting enzyme inhibition prevents diabetes.<sup>15</sup> Amlodipine is a very efficacious antihypertensive agent.<sup>16,17</sup> Small differences in blood pressure control can be translated to significant differences in clinical outcome, as in the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial.<sup>18,19</sup> Amlodipine also has an anti-atherosclerotic effect in carotid and coronary arteries.<sup>20,21</sup>

Beta-blockers remain valuable in the treatment of angina pectoris and myocardial infarction, and their use in heart failure clearly reduces mortality.<sup>22</sup> They are contraindicated in asthma and peripheral vascular

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disease. In the light of the latest evidence, the use of a beta-blocker should not be a reflex but a carefully considered action. The American and World Health Organization guidelines may require revision,<sup>9,23</sup> whereas the European guidelines characteristically give equal weight to each antihypertensive drug class.<sup>24</sup> The British guidelines hold up rather well.<sup>10</sup> The British Hypertension Society, adopting the Cambridge ABCD rule, proposes that beta-blockers are less suitable as first-line treatment in the elderly.<sup>25</sup> I would not discard them for the moment, not least because they are surprisingly the best tolerated antihypertensive drug class apart from angiotensin receptor blockers.<sup>26</sup> The majority of patients require a number of drugs to reach current blood pressure targets (140/90 mmHg and lower targets for patients with diabetes or nephropathy).<sup>9,10,23,24</sup> Beta-blockers may therefore be one of the drugs used to attain good blood pressure control.<sup>27</sup> Drug companies are keen to emphasise and exploit small differences between drugs, but these pale into insignificance when compared to the paramount importance of good blood pressure control. Beta-blockers are out of favour for hypertension for the moment, but the full results of ASCOT are still awaited. The pendulum may swing this way and that way from time to time, but it will finally come to rest in the middle.

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