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of the Swiss Society of Hypertension

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Comments to the 2007 recommendations for the treatment of essential hypertension by the Swiss Society of Hypertension¹

Focus on beta-blockers in the treatment of uncomplicated essential hypertension

Introduction

The new 2007 guidelines of the Swiss Society of Hypertension have just been released and are available at the website www.swisshypertension.ch/guidelines.htm. They are essentially an update of the guidelines 2003, but with some important changes in the recommendations on the medical treatment of hypertension. The rationale of these and the few other changes are outlined in this brief report. It represents a consensus that may not necessarily reflect the opinion of each individual member of the committee.

Beta-blockers in the treatment of essential hypertension

Twenty years ago the Committee of the Swiss Society of Hypertension dropped the recommendation to treat elevated blood pressure in younger hypertensive patients dominantly with beta-blockers and hypertension in the elderly preferentially with calcium antagonists.

Beta-blockers have been widely and successfully used for the treatment of uncomplicated essential hypertension for years. However, this strategy has been challenged, first by Messerli et al. [1], who demonstrated in a meta-analysis of randomised trials that, compared to diuretics, beta-blockers did not reduce stroke or myocardial infarction. A subsequent analysis of the effects of different blood-pressure-lowering regimens on major cardiovascular events concluded that treatment with any commonly used regimen reduces the risk of total major cardiovascular events, and larger reductions in blood pressure produce larger reductions in risk [2]. Most of the beta-blocker studies included in this meta-analysis were carried out with atenolol, and Carlberg et al. addressed the question whether atenolol is a wise choice for the treatment of hypertension [3]. Indeed, the Carlberg meta-analysis demonstrated the inferiority of atenolol in pre-

venting cardiovascular events when compared to other active anti-hypertensive treatments, and essentially the lack of effect when compared to placebo [3]. A subsequent meta-analysis by the same authors investigating the role of all beta-blockers concluded that this class of anti-hypertensive drugs, but especially atenolol, should not remain first choice in the treatment of primary hypertension [4]. The conclusions relied on their findings showing a much less effective reduction of stroke and other cardiovascular events in hypertensive patients treated with beta-blockers compared to patients treated with other antihypertensive drugs. More recently, this topic was extensively reviewed by others on behalf of the Cochrane Collaboration [5].

In view of these challenging analyses most of the Hypertension Societies have revisited their recommendations for the treatment of hypertension and among those, the British Hypertension Society does no more see a primary role for beta-blockers in hypertension (<http://guidance.nice.org.uk/CG34/guidance/pdf/English>).

A committee of the Swiss Society of Hypertension tried unsuccessfully to collect the original data of all of the major beta-blockers studies for further analysis (P. Jüni, Bern, P. Erne, Lucerne; personal communication). Some of these studies were carried out more than twenty years ago and the individual results could not be retrieved in many of them. Furthermore, it was sometimes even not possible to define the exact proportion of the study population which was treated with beta-blockers alone or in combination with diuretics.

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Based on the aforementioned available evidence, the committee of the Swiss Society of Hypertension took into consideration the following facts for the writing of its new 2007 guidelines:

- (1.) Most of the beta-blocker trials were carried out 20–25 years ago and we recognise that during this period of time the morbidity and mortality of coronary artery disease and stroke has been substantially reduced and it might therefore be very difficult to compare these older with more recent trials.
- (2.) In many of these older beta-blocker trials target blood pressure is far away from what is targeted in more recent trials. Moreover, in some trials blood pressure goal was weakly defined and in some others, the percentage of patients at goal was not even reported.
- (3.) We do realise that in about three quarters of the studies which were used for the aforementioned meta-analyses [3, 4], atenolol was the used beta-blocker, whereas oxprenolol or metoprolol were mainly used in the remaining studies. On the other hand, newer beta-blockers with a high selectivity or dual blood-pressure-lowering mechanism such a bisoprolol, carvedilol or nebivolol were never extensively studied in hypertension, especially with regard to hard endpoints such as myocardial infarction, stroke or mortality, or a combination of them. Therefore, strong evidence for effectiveness of newer beta-blockers is lacking.
- (4.) While older studies on the efficacy of beta-blockers or diuretics addressed a population with mostly uncomplicated primary hypertension, newer studies with angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (sartans) investigated hypertensive populations with high cardiovascular risk and often even end organ damage. Therefore, in uncomplicated hypertension, there is no head to head comparison of efficacies between beta-blockers and other antihypertensives.
- (5.) The mean age of the patient populations included in the studies considered in the aforementioned meta-analyses [3–5] was around 63 years. It has been argued, that age could be the confounder responsible for the lack of efficacy of beta-blockers since the daily clinical experience was that beta-blockers were highly effective in young hypertensive patients. Therefore, the Cana-

dian Hypertension Society asked for a more detailed analysis with respect to age groups and it was concluded that in studies performed in older (mean age >60 years) populations, beta-blockers were inferior to calcium antagonists, angiotensin-converting enzyme inhibitors or sartans while this was not the case in populations younger than 60 years [6]. As a consequence, the Canadian Hypertension Society adopted a policy that includes beta-blockers as potential first line drug therapy in a younger population while beta-blockers are not recommended for patients above 60 years of age.

- (6.) In the majority of trials, target blood pressure could only be achieved with the use of combinations of various antihypertensive classes. We emphasise again, that achieving blood pressure target, whatever the treatment used, remains the primary goal of antihypertensive therapy.

Rationale for the 2007 guidelines of the Swiss Society of Hypertension

Based on these facts, the Committee of the Swiss Society of Hypertension has outlined the 2007 recommendations for the antihypertensive drug therapy as follows:

- (1.) Due to their effective reduction of coronary and cerebrovascular events and their non-negative effect on lipid and glucose metabolism, we recommend angiotensin-converting enzyme inhibitors, angiotensin II antagonists (sartans) and calcium antagonists as first choice antihypertensive drug classes.
- (2.) We do still recommend beta-blockers and diuretics as alternative antihypertensive drugs for the initial therapy of uncomplicated primary hypertension in particular cases. Beta-blockers can be used in younger patients with uncomplicated hypertension not at risk for the metabolic syndrome and in whom there is no co-morbidity which prevents their use. We do favour highly selective beta-blockers or beta-blockers with dual antihypertensive action. Highly selective beta-blockers can even be used in stable patients with asthma or chronic obstructive lung disease if monitored appropriately and if there is a good indication for the choice of a beta-blocker therapy, *eg* hyperkinetic syndrome, elevated heart rate, or others. Di-

- uretics are very effective and recommendable in the treatment of hypertension in the elderly.
- (3.) In the 2007 recommendations we do differentiate between mild, uncomplicated hypertension and more severe hypertension with blood pressure values above 160/100 mm Hg. If blood pressure is only mildly elevated and in the absence of end organ damage or important co-morbidities, we do consider a low-dose mono-therapy sequentially tested as appropriate. If blood pressure is above 160/100 mm Hg, we recommend to initiate drug therapy with low-dose combination.
- (4.) If the patient has end organ damage or cardiovascular co-morbidities, then the adapted compelling drug(s) should be chosen to initiate therapy, either alone or in low-dose combination. In these patients, if initial blood pressure values are above 160/100 mmHg, full-dose bi-therapy is recommended and, if not at goal at follow-up, triple combination therapy must be initiated.
- (5.) The rationale of low-dose combination is to achieve more easily target blood pressure, to minimise side effects and to improve compliance. For this purpose, first-choice antihypertensive drugs can be combined with alternative drugs.
- (6.) To combine three or more different antihypertensives, alpha-blocking agents, centrally acting sympatholytics or minoxidil can also be considered.

References

- 1 Messerli FH, Grossman E, Goldbourt U. Are beta-blockers efficacious as first-line therapy for hypertension in the elderly? A systematic review. *JAMA*. 1998;279(23):1903–7.
- 2 Turnbull F. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. *Lancet*. 2003; 362(9395):1527–35.
- 3 Carlberg B, Samuelsson O, Lindholm LH. Atenolol in hypertension: is it a wise choice? *Lancet*. 2004;364(9446):1684–9.
- 4 Lindholm LH, Carlberg B, Samuelsson O. Should beta blockers remain first choice in the treatment of primary hypertension? A meta-analysis. *Lancet*. 2005;366(9496):1545–53.
- 5 Wiysonge CS, Bradley H, Mayosi BM, et al. Beta-blockers for hypertension. *Cochrane Database Syst Rev*. 2007;24(1): CD002003.
- 6 Khan N, McAlister FA. Re-examining the efficacy of beta-blockers for the treatment of hypertension: a meta-analysis. *CMAJ*. 2006;174(12):1737–42.