Effect of antihypertensive treatment at different blood pressure levels

Mattias Brunström

Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt försvar i Hörsal D, Unod T9, 9 tr Norrlands Universitetssjukhus fredagen den 26 januari, kl. 13:00.
Avhandlingen kommer att försvaras på svenska.

Fakultetsopponent: Professor Sverre Kjeldsen
Institutt for klinisk medisin, Oslo Universitet, Oslo, Norge.

Department of Public Health and Clinical Medicine
Effect of antihypertensive treatment at different blood pressure levels

Cardiovascular disease is the most common cause of death worldwide. Elevated systolic blood pressure is the most important risk factor for cardiovascular disease, causing approximately 10 million deaths annually. Treatment of high blood pressure effectively reduces the risk of cardiovascular disease and death, but the optimal cut-off for treatment is debated.

This thesis includes two systematic reviews and meta-analyses of randomized controlled trials, assessing the effect of antihypertensive treatment at different systolic blood pressure levels. The first paper was restricted to people with diabetes, whereas the second paper included trials regardless of participants’ comorbidities. The potential interaction between blood pressure level and treatment effect was analyzed through metaregression, and treatment effects at each blood pressure level was estimated through random-effects meta-analyses. The third paper assessed the effect of standardization of study results, according to blood pressure lowering within trials, in meta-analyses of antihypertensive treatment.

In people with diabetes, antihypertensive treatment reduced the risk of all-cause mortality and several cardiovascular disease outcomes if baseline systolic blood pressure was 140 mm Hg or higher. Below this level, treatment was not associated with any benefit but an increased risk of cardiovascular death. In primary prevention, regardless of diabetes, we found a similar pattern. Treatment reduced the risk of all-cause mortality and composite major cardiovascular events if baseline systolic blood pressure was 140 mm Hg or higher. At lower levels, treatment was neither harmful nor beneficial. In people with previous coronary heart disease, antihypertensive treatment reduced the risk for major cardiovascular events, without any mortality benefit. The average systolic blood pressure in this group was 138 mm Hg. Standardization of study results in meta-analyses was associated with increased heterogeneity, making analyses sensitive to choice of statistical method. Further, study weights shifted from trials with many participants and events to trials with large blood pressure differences, leading to biased overall effect estimates in meta-analyses.

In conclusion, antihypertensive treatment reduces the risk of death and cardiovascular disease in people with systolic blood pressure 140 mm Hg or higher. Treatment effect below this level depends on comorbidity status, with potential benefit in coronary heart disease secondary prevention, no effect in primary prevention, and potential harm in people with diabetes. Standardization of study results in meta-analyses introduces bias and should thus be avoided.

Keywords
Blood pressure, hypertension, antihypertensive treatment, cardiovascular disease, randomized controlled trial, systematic review, meta-analysis, standardization

Language: English
ISSN: 0346-6612
Number of pages: 77 + 3 papers (incl. appendices)