Fatal attraction

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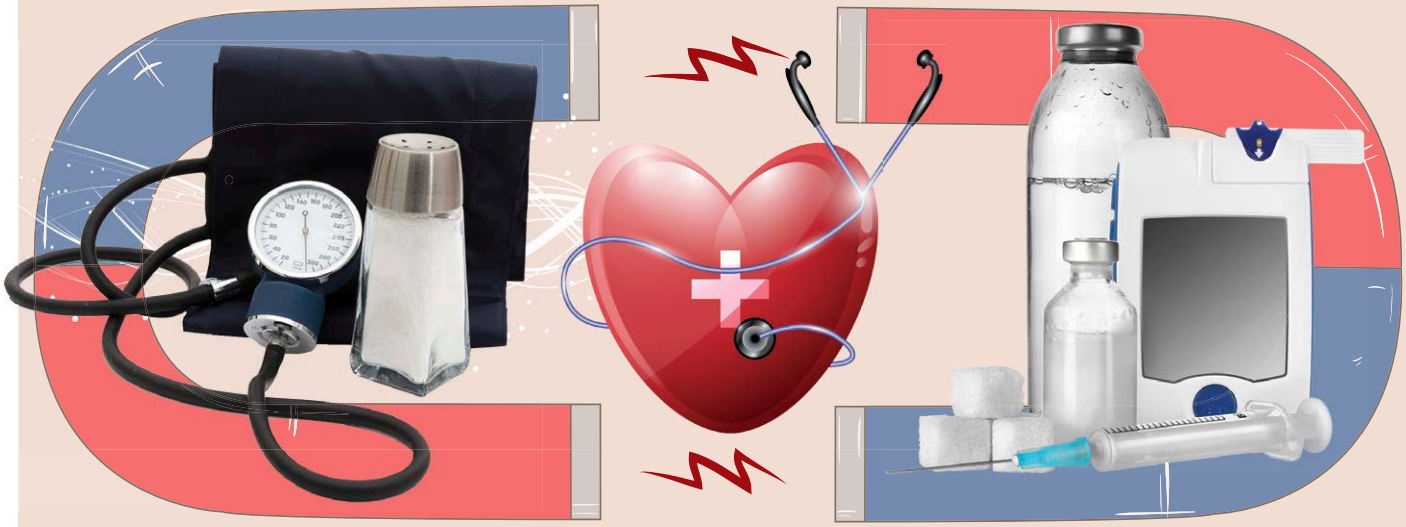
Hypertension and diabetes are linked and could be considered a fatal attraction.[1] Elevated blood pressure is twice as common in people with diabetes as compared to people without diabetes.



When hypertension occurs in diabetes, the risk to develop micro-vascular and macro-vascular complications are greatly increased. This greatly increased susceptibility to blood pressure-mediated vascular injury in the two bad companions has a number of possible mechanisms. There are disturbed BP circadian rhythms such as increased nocturnal BP levels, a higher 24-hour BP load for any given clinic-measured blood pressure. There are also impaired blood flow autoregulation, increasing micro-vascular perfusion pressures and stiffening of large arteries with increased pulse pressure and greater blood pressure variability. All of these changes in hypertensive people with diabetes have led to an approach to assume that the blood pressure level where to start treatment and the goal of treated blood pressure should be different in diabetic people with hypertension.[2] This concept was adopted by many guidelines on the treatment of hypertension and a goal BP for treatment was stated as lower than 130/80mmHg as compared to the general BP goal of lower than 140/90mmHg.

In 2010 the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial reduced blood pressure to lower than 120mmHg vs. the more conservative below 140/90mmHg.[3] They reported that a lower blood pressure target did not lead to a significant reduction in cardiovascular events and that there were more adverse effects with a blood pressure target lower than 120mmHg in hypertensive patients with diabetes mellitus.

Guideline writers responded by relaxing the target of blood pressure in diabetics to lower than 140/90mmHg.[4] An important issue that emerged was whether applying these new targets of blood pressure in diabetics, would not lead to undertreatment of some patients with a consequent increase in the risk of both micro-vascular and macro-vascular events, which could have been avoided.[2]

REBOLDI META-ANALYSIS

This meta-analysis was done evaluating 31 randomised clinical trials and 73 913 people.[5] Overall there were statistically significant reductions of stroke (9%) and myocardial infarctions (11%). In the more tight blood pressure reduction group as compared to less tight reduction, the Relative Risk Reduction of stroke was 31% (95%CI: 21-52%) but the reduction of myocardial infarction was not significantly reduced by more tight blood pressure reduction. A meta-regression of the data showed that for every 5mm reduction of systolic blood pressure the risk of stroke was reduced by 13% (95%CI: 5-20%). The relative risk reduction in the risk of myocardial infarction was not significantly reduced by the extent of blood pressure reduction.

BANGALORE META-ANALYSIS

This meta-analysis examined 13 randomised clinical trials on 37 736 patients with type 2 diabetes mellitus and patients with impaired fasting glucose and in patients with impaired glucose tolerance.[6] They compared a systolic blood pressure of <135mmHg versus a systolic blood pressure of <140mmHg. All-cause mortality was significantly reduced by 9.4% (95%CI: 2-10%) with a number-to-treat (NNT) of 161 (95%CI: 95-809). Stroke was also significantly reduced by 17% (95%CI: 2-26%) with NNT 210 (95%CI: 132-715) to prevent one stroke. Nephropathy was also significantly reduced by 25% (95%CI: 15-34%) with NNT 49 (95%CI: 37-84). There were, however, no significant reductions of CV mortality, MI or heart failure.

MCBRIEN META-ANALYSIS

This was a meta-analysis of five randomised clinical trials and 7513 patients aged 53 - 62.[7] Patients with different target blood pressures were evaluated. Systolic blood pressure (SBP) <120mmHg/ Diastolic blood pressure 75-80 mmHg and SBP <140mmHg/DBP 85-90mmHg. Only stroke was significantly reduced by more intense blood pressure reduction: Relative Risk Reduction 39% (95%CI: 17-55%) NNT 82 (95%CI: 58-188).

EMDIN META-ANALYSIS

This is a new meta-analysis published in 2015 that evaluated 40 randomised clinical trials on 100 354 patients spanning the time period 1966 to October 2014.[8] These trials were considered to be of low bias. For every 10mmHg reduction in SBP there was a significant reduction of all-cause mortality of 13% (95%CI: 4-22%), NNT 32 995%CI: 19-111) over 10 years of treatment a reduction of CVD events of 11% (95%CI: 5-17%),NNT 26 (95%CI: 17-64), a reduction of coronary events of 12% (95%CI: 2-20%), NNT 55 (95%CI: 32-284) and a reduction of stroke of 27% (95%CI: 17-36%), NNT 25 (95%CI: 19-40).

Heart failure and renal failure events were not significantly reduced with a lower than recommended SBP. There were also significant reductions of micro-vascular events with a 10mmHg reduction of SBP. For 10mmHg reduction in SBP there were significant reductions in retinopathy of 13% (95%CI: 1-24%) and of albuminuria of 17% (95%CI: 13-21%).

Analyses of these results that were not standardised to a 10mmHg reduction of BP showed similar results. For all the significant outcomes, reductions in events were demonstrated for BP targets of less than 140mmHg but reduction of SBP to levels lower than 130mmHg only reduced stroke and albuminuria outcomes.

CONCLUSIONS

1 The general guideline recommendation that blood pressure should be lowered to <140/90 mmHg is still valid as demonstrated in this very large meta-analysis.

2 There are, however, indications that in certain subgroups among hypertensive diabetic patients, lower SBP levels may be beneficial and that the recommended blood pressure targets may be too conservative.

3 Those patients with a history suggestive of a cerebrovascular incident and those patients with albuminuria should probably have their SBP lowered to below 130mmHg.

4 Most clinical trials have recruited older patients with complex multisystem diseases and a high risk of complications. Clinicians should question how to use the evidence from trials of these older patients and translate the data and findings to use in younger patients who have not yet developed the complications of diabetes. The younger patients may be better at tolerating lower blood pressure levels (below 130/80mmHg) than the typical older more complex diabetic patients in the clinical trials.[2]

5 For these reasons it would be appropriate to consider a bolder approach to blood pressure treatment in younger patients with hypertension and diabetes mellitus, especially in those with albuminuria and other early micro-or macro-vascular complications of diabetes. However, it should be pointed out that these findings translated into clinical practice on the treatment of younger patients are extrapolated from the findings on older diabetic patients with hypertension.

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