Diabetes

Blood pressure and risk of cardiovascular events in type 2 diabetes

A large cohort study has found that lower systolic blood pressure (BP) is associated with reduced cardiovascular risk in type 2 diabetes patients with no previous cardiovascular disease (CVD). However, there was evidence of a J-shaped relationship between systolic BP and heart failure, and also all cause mortality.

The retrospective population-based cohort study used data on patients who entered the Swedish national diabetes register between 2006 and 2012. Criteria for inclusion were patients aged up to 75 years with type 2 diabetes for at least a year but no previous CVD or other major comorbidity. A total of 187,106 patients were eligible for inclusion, and the mean duration of follow-up was five years.

Outcome measures were obtained from hospital discharge and death registers. Hazard ratios (HR) were estimated for different levels of baseline BP and adjusted for potential covariates. Systolic BP was divided into six categories: 110-119 mmHg; 120-129 mmHg; 130-139 mmHg; 140-149 mmHg; 150-159 mmHg and ≥160 mmHg.

Compared with the reference group (130-139 mmHg) the group with the lowest systolic BP (110-119 mm Hg) had significantly lower risks of:

- Non-fatal acute MI; HR 0.76 (95% CI: 0.64-0.91)
- Total acute MI; HR 0.85 (95% CI: 0.72-0.99)
- Non-fatal CVD; HR 0.82 (95% CI: 0.72-0.93)
- Total CVD; HR 0.88 (95% CI: 0.79-0.99)
- Non-fatal CHD; HR 0.88 (95% CI: 0.78-0.99)

There was no evidence of a J-shaped relationship between systolic BP and these endpoints. However, there was evidence of a J-shaped relationship between systolic BP and heart failure, and also all cause mortality.

The authors conclude that by adjusting for comorbidities, mainly by excluding patients with previous CVD, the J curve relation between systolic BP and MI and CHD disappears.

They postulate that the association between low BP and increased mortality might be caused by concomitant disease, rather than by antihypertensive treatment.

However, the authors caution: 'One limitation of our study is that it did not include individuals with complications or those over 75. We believe that caution should be exercised when using observational studies to draw conclusions about recommended treatment goals for blood pressure among high risk patients.'

The debate is ongoing on optimum systolic BP targets. It may be that the way forward for systolic BP targets will turn out to be the same as for HbA_{1c} levels i.e. individual targets, depending on the age, duration of diabetes, and comorbidities.

DR MATTHEW LOCKYER

Adamsson Eryd S, Gudbjörnsdottir S, Manhem K et al. Blood pressure and complications in individuals with type 2 diabetes and no previous cardiovascular disease: national population based cohort study. *BMJ* 2016;354:i4070

Is frequent self-monitoring and on-line reporting of blood glucose worthwhile?

Frequent self-monitoring of blood glucose had a significant effect on HbA_{1c} only when combined with frequent on-line reporting, in a study from Canada.

A total of 229 patients with type 2 diabetes, treated with oral hypoglycaemic agents only and registered with the Internet-based Blood Glucose Monitoring System, were evaluated. The patients had similar baseline characteristics.

They were asked to test their blood glucose before meals, and to submit a standardised report to the endocrinologist every two weeks, which showed the mean glucose and standard deviation of values. The endocrinologist was asked to reply to each report with a brief feedback of two to four sentences. As well as the on-line advice, the patients received all the normal face-to-face care expected.

Data on 191 patients who produced results eligible for the study were analysed. The researchers then retrospectively reviewed their records for: HbA_{1c}, frequency of self-monitoring of blood glucose and on-line communication with an endocrinologist during the preceding six months.

The analysis divided patients into two groups according to frequency of blood glucose testing. There were 73 patients in the infrequent testers group and 118 in the frequent testers. Infrequent testing was defined as once or less per day, and frequent testing as twice or more a day. There was no significant difference in other baseline characteristics between the frequent and infrequent testing groups. Reporting frequency was defined as the average number of reports per three months over the most recent six-month period.

There was a statistically significant difference in HbA_{1c} between the group who tested frequently and also reported frequently when compared with those who only tested frequently but did not report frequently: 7.4±0.2% (57±2 mmol/mol vs 7.9±0.4% (63± 5 mmol/mol).

The authors recommend that on-line management of self-monitoring of blood glucose should be incorporated into practice on the basis of their results. However, the average duration of diabetes in both groups was well over ten years, making the value of tight control of HbA_{1c} of relatively less value than tight control of blood pressure and lipids. The difference in HbA_{1c} demonstrated was relatively modest for significant input from both patients and healthcare professionals.

Previous studies of self-monitoring of blood glucose, such as ESMON and DIGEM which used intensive but conventional follow-up of larger populations and for longer duration not only failed to demonstrate improved HbA_{1c} levels, but also suggested worse outcomes in terms

of psychosocial wellbeing.[1,2]

This study seems to me to confirm that even with internet review, self-monitoring of blood glucose has a limited role in improving glycaemic control in type 2 diabetes patients on oral hypoglycaemic agents. I feel that the main role of self-monitoring of blood glucose in this group is the detection of hypoglycaemia.

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Chow N, Shearer D, Aydin Plaa J et al. Blood glucose self-monitoring and internet diabetes management on A1C outcomes in patients with type 2 diabetes. *BMJ Open Diabetes Research and Care* 2016;4:e000134

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2 Farmer A, Wade A, Goyder E et al on behalf of the Diabetes Glycaemic Education and Monitoring Trial Group. Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomized trial. *BMJ* 2007;Jul 21;335(7611):132

Mental health

Women on hormonal contraception at raised risk of depression

Women who use hormonal contraception are more likely to become depressed, a large Danish prospective cohort study has found.

The cohort comprised all adolescents and women aged between 15 and 34 who were resident in Denmark and without a previous history of depression, antidepressant use, other major psychiatric diagnosis, cancer, venous thrombosis or infertility treatment. Data were obtained from national registers of dispensed prescriptions and secondary care psychiatric diagnoses.

A total of 1,061,997 women were followed up for a mean period of 6.4 years. Compared with nonusers, women who took combined hormonal contraception (CHC) were 23% more likely to be prescribed antidepressants; adjusted incidence rate ratio (RR):

- RR 1.23 (95% CI: 1.22-1.25).

Women who took progestogen-only pills (POPs) were 34% more likely to be given antidepressants:

- RR 1.34 (95% CI: 1.27-1.40).

The rate ratios for use of a patch (norelgestromin), ring (etonogestrel) and intrauterine system (levonorgestrel) were respectively:

- RR 2.0 (95% CI: 1.76-2.18)
- RR 1.6 (95% CI: 1.55-1.69)
- RR 1.4 (95% CI: 1.31-1.42)

The rate ratios for a first diagnosis of depression were similar or slightly lower. The association between use of hormonal contraception and subsequent use of antidepressants was greater in adolescents (age 15-19), with rate ratios for those using CHC and POP of 1.8 (95% CI: 1.75-1.84) and 2.2 (95% CI: 1.99-2.52) respectively. The highest level of antidepressant use occurred six months after starting hormonal contraception.

The Faculty of Sexual and Reproductive Healthcare (FSRH) advises that use of CHC or POP may be associated with mood changes but that there is no evidence of a causal relation between their use and depression.[1,2] The present study is an observational study and cannot demonstrate causality. However, a causative link is very plausible given the high concentration of oestrogen and progesterone receptors in many regions of the brain and the complex effects of sex hormones on several neurotransmitters including GABA and serotonin.[3]

When discussing the potential risk of depression, it is important to present information on absolute, not relative risk. Given an annual incidence of depression in women of approximately 4%,[4] a 23% relative risk equates to an absolute risk of only around 1%. Similarly, although there is a greater relative risk in adolescents, this will be offset by the fact that the incidence of depression is more than 50% less in those aged 16-24 compared with those aged 25-44.[4]

The study excluded those with a previous history of depression, so we should be cautious about extrapolating the results to this group of patients.

For those with bipolar disorder the possible increased risk of depression needs to be balanced with the importance of adequate contraception in view of the high risk of postpartum relapse.[5]

In conclusion, I suggest that before prescribing hormonal contraception we should:

- Ask if there is any personal or family history of depression
- Advise that depression is a potential adverse effect
- Advise that the absolute risk is small
- Weigh this against other benefits and risks including that of pregnancy.

If women become depressed when taking hormonal contraception, we should discuss switching to non-hormonal contraception, particularly when depression occurs within the first 12 months of use.

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Skovlund CW, Mørch LS, Kessing LV, Lidegaard Ø. Association of hormonal contraception with depression. *JAMA Psychiatry* 2016;73:1154-62

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