

## ABCs: B is for blood pressure

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Case studies in this series focus on the ABCs of diabetes care ( $A_{1c}$ , blood pressure, cholesterol, smoking, salicylates), how to get them closer to target and how to keep them there.

### Case scenario

Bob is 64 years old and has had type 2 diabetes for 11 years. His weight is 82 kg and his height is 1.82 m, which means he is overweight (BMI, 25.9 kg/m<sup>2</sup>); his weight has been steady over the last few years. He walks for 20 to 30 minutes several times a week with his wife and an ageing Labrador and enjoys 'a few beers' on weekends. His father died suddenly of a heart attack at the age of 66 years, and Bob is well aware of his own coronary risk.

Four of Bob's ABCs are pretty good. He is close to target with his glycosylated haemoglobin level ( $A_{1c}$ ) of 7.6% (target, <7%) and his cholesterol is 3.1 mmol/L (target, <4.0 mmol/L). He quit smoking at the age of 60 years and started taking prophylactic aspirin when he was diagnosed with diabetes.

It is Bob's blood pressure that is the problem. Despite taking an ACE inhibitor and a selective beta blocker each day and

a diuretic (frusemide) three days a week (on Monday, Wednesday and Friday), his systolic blood pressure consistently exceeds 150 mmHg. His other medications include:

- metformin (850 mg three times daily)
- glipizide (10 mg twice daily)
- pantoprazole (20 mg once daily, at night)
- diclofenac (50 mg twice daily)
- vitamin E (10 mg once daily)
- a multivitamin supplement (once daily, with breakfast).

### Questions

- Considering that Bob's other ABCs are pretty good, how important is his elevated blood pressure?
- Are there potentially correctable

contributors to his hypertension?

- What further management options are available?

### Hypertension in patients with diabetes

It is easy for patients with diabetes to focus solely on glycaemic goals – for many, diabetes is 'sugar'. Doctors also may overrate the importance of controlling blood glucose and underrate the importance of controlling other complication risk factors. In a survey of American doctors, glucose lowering was found to be the most commonly assigned top priority in diabetes management, whereas in fact both blood pressure lowering and cholesterol lowering are associated with greater reductions in risk for cardiovascular outcomes in the medium term (Figure).<sup>1</sup> The HOT and UKPDS studies have shown the importance of blood pressure control, with reduced rates of both cardiovascular and microvascular events being associated with lower blood pressure.<sup>2,3</sup>

Having diabetes puts any patient into a high risk category for cardiovascular events,<sup>4</sup> but Bob has several additional risk factors (Table 1). We don't know if he

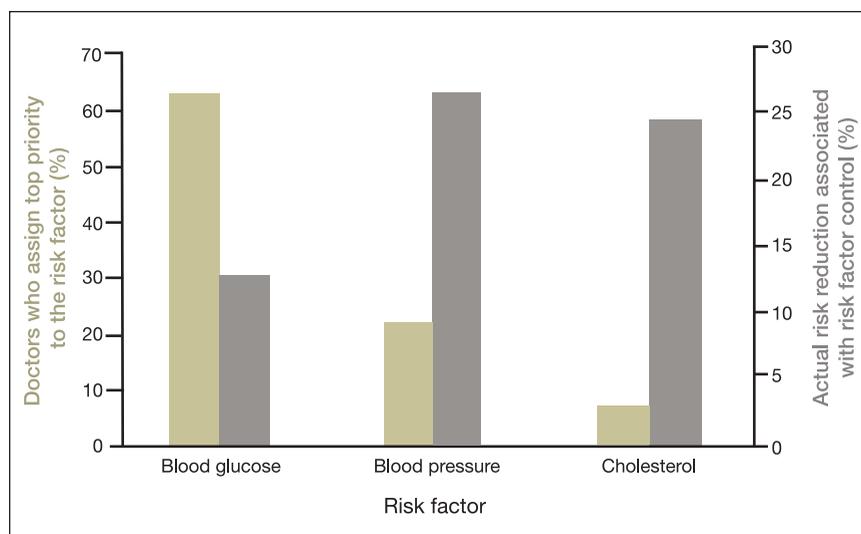


Figure. Ranking risks in diabetes management – doctors' perception and reality. Doctors' ranking of the top priorities in diabetes management are shown (left-hand axis ■) along with actual risk reductions for cardiovascular outcomes in the medium term (right-hand axis ■).<sup>1</sup>

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**Table 1. Risk factors for cardiovascular complications****Nonmodifiable**

Past history of cardiovascular events  
 Family history of cardiovascular events prior to age 60 years  
 Age (every extra decade past 50 years is equivalent to an additional risk factor)  
 Menopausal status

**Modifiable****Lifestyle**

Smoking  
 Low level of physical activity  
 High intake of fat and/or energy

**Medical**

Microalbuminuria  
 Hypertension  
 Dyslipidaemia  
 Dysglycaemia

has microalbuminuria or left ventricular hypertrophy but it would be important to find out – the presence of either would make controlling his blood pressure even more important. Microalbuminuria is an indicator of endothelial damage throughout the cardiovascular system, not just in the kidney, and, if present, would be a treatment target itself. Left ventricular hypertrophy would indicate damage of other end organs (particularly the eyes and kidneys) as well as the heart, and it would be useful to arrange an ECG to identify this. A baseline ECG would also be useful in case Bob later presents with symptoms that might be an atypical presentation of a myocardial infarct. Remember that autonomic neuropathy may mean an infarct does not present with crushing chest pain but with much more nonspecific symptoms (e.g. weakness, vague discomfort, nausea and shortness of breath).

Blood pressure is an important risk factor in any patient with diabetes, but

it becomes even more important as coronary risk increases and when there is evidence of end organ damage. In fact, Bob did have confirmed microalbuminuria (albumin:creatinine ratios, 8.1 and 6.4 mg/mmol; normal range for men <2.5 mg/mmol). He is, therefore, at very high risk for coronary events.

**Potentially correctable contributors to hypertension****Adherence, adherence, adherence**

Generally in clinical trials, participants are required to take at least 80% of the prescribed medication, otherwise they are excluded. In the real world, the rule of thirds often applies:

- one-third of patients don't take the medication at all
- one-third don't take it as prescribed
- one-third do take it as prescribed.

Checking medication adherence is part of a diabetes review. This may be done informally, using an approach such as, 'Most people find it hard to take all their medication, how often do you miss yours?' This type of questioning makes it easier for a nonadherent patient to tell you the truth. A more formal approach may involve reviewing the frequency of prescription or involving a pharmacist in a Home Medications Review.

Bob's medication schedule should be simplified by reducing the number of medications he is taking and/or the medication-taking occasions. He is supposedly taking 10 medications – 13 tablets on four days a week and 14 tablets on the other three days. The chances are that he is missing some of his pills.

Measures that could be considered for Bob include:

- using a combination ACE inhibitor and diuretic preparation
- switching to extended release metformin with a twice daily dosing schedule (1 g twice daily)
- switching to a once daily sulfonylurea (e.g. modified release gliclazide [Diamicon MR] or glimepiride

[Amaryl, Aylide, Diapride, Dimirel])

- improving his sleep position to prevent reflux so he can stop taking the proton pump inhibitor.

Bob is also taking medications that have been shown not to help (vitamin E and the multivitamin supplement). Perhaps he could stop taking the tablets that don't work and try harder to take those that do.

**Misleading hypertension**

Don't forget that the blood pressure readings you obtain may be misleading or nonrepresentative. Not many of us measure blood pressure as carefully as we could – that is, using a correctly sized cuff and a calibrated sphygmomanometer in an unhurried environment after giving the patient adequate time to relax. Given that Bob is (correctly) concerned about his blood pressure, he would be a prime candidate for white coat hypertension. Either a 24-hour ambulatory blood pressure recording or home monitoring would show if the surgery readings are misleading.

Diabetes can also be associated with calcified arteries, which are not compressible. A heavily calcified aortic arch on chest x-ray might prompt you to check that the brachial artery is compressible.

**Correctable hypertension**

Together, the NSAID, ACE inhibitor and diuretic make a 'triple whammy' that is putting Bob at high risk of acute renal failure.<sup>5</sup> Stopping the NSAID will reduce his renal risk and it may also help control his blood pressure. Even though he is not very overweight, sleep apnoea should be considered. It would be useful to check his neck size (>42 cm would identify him as being at high risk) and to ask about night time snoring and daytime naps to determine if a sleep study is warranted. Treating sleep apnoea can have dramatic effects on blood pressure, and it could have other benefits for Bob (as well as sleep benefits for his wife).

**Table 2. The pros and cons of 'add on' hypotensive agents\***

	Pros	Cons
<b>Alpha blockers</b>	No metabolic effects	Increased risk of cardiac failure and coronary events Postural hypertension
<b>Angiotensin receptor antagonists<sup>†</sup></b>	Indicated if micro- or macroalbuminuria is present Same advantages as ACE inhibitors if ACE inhibitor not used	First dose hypotension Decreased glomerular filtration Hyperkalaemia Cough and angioedema (rarely)
<b>Calcium channel blockers<sup>‡</sup></b>		
– centrally acting (diltiazem, verapamil)	–	Risk of heart block Constipation Oesophageal reflux
– vasodilating (dihydropyridines)	–	Peripheral oedema Flushing Headache
<b>Sympatholytics</b>	–	Postural hypotension Depression

\* Modified from reference 9.

<sup>†</sup> ACE inhibitors and angiotensin receptor antagonists are contraindicated in pregnancy and may not be wise choices in women of childbearing potential who are not using reliable contraception. Advice from an obstetrics specialist may be helpful.

<sup>‡</sup> All calcium channel blockers have the full range of side effects but gastrointestinal effects and heart block are more common with the centrally acting agents and vasodilating effects with the dihydropyridines. The risk of heart block is increased if a beta blocker is being taken.

Bob may be prepared to consider life-style changes. By eating less and walking more, cutting back on his beer consumption and losing a few kilograms, he could reduce his systolic blood pressure by 5 to 10 mmHg.<sup>6</sup> Either a 24-hour urinary sodium measurement would tell you whether he (or more likely his wife) should be advised to 'sack the salt' – both from the kitchen and the table – and to check food labels for low salt products.<sup>6</sup> The recommended salt intake is less than 100 mmol/day (equivalent to 2300 mg/day of sodium), but the average Australian intake is over 200 mmol/day.<sup>7</sup>

### Secondary causes

Secondary causes of hypertension include coarctation of the aorta and renal artery stenosis as well as adrenal diseases (Cushing's syndrome, hyperaldosteronism, pheochromocytoma) and renal disease. Recreational drugs should also be remembered.

Secondary causes should be considered when hypertension starts in a younger or elderly patient or when it is resistant to therapy, accelerating or severe (e.g. over 180/115 mmHg). In Bob's case, it would be useful to check that his blood pressure is the same in both arms, and to look for an abdominal bruit or hypokalaemic alkalosis. If a secondary cause is suspected, discussion with a specialist would help determine if further investigation is appropriate.

### Further management options

In the RACGP guidelines *Diabetes Management in General Practice*, the suggested medication steps for reducing blood pressure to target (that is, <130/80 mmHg; <125/75 mmHg if proteinuria is greater than 1 g/day) are to start with an ACE inhibitor (or an angiotensin receptor antagonist if an ACE inhibitor is not tolerated), then to add a diuretic, and then a beta blocker.<sup>8</sup> Bob is already taking all

three of these, which is not unusual. In both the HOT and UKPDS studies quoted earlier, one-third or more of participants required three or more medications to manage their blood pressure.<sup>2,3</sup>

Assuming that maximum doses are already being prescribed, that Bob is taking his medications as instructed, that the blood pressure readings you are getting are correct and that Bob has modified his medication schedule and lifestyle as recommended, adding a fourth hypertensive agent could be considered. However, there are various pros and cons to consider (Table 2).<sup>9</sup>

Choosing a fourth medication is difficult because all additional hypotensive agents have significant disadvantages. The alpha blockers do not have metabolic effects but have been associated with excess risk of cardiac failure and coronary events.<sup>10</sup> Combining an angiotensin receptor antagonist with an ACE inhibitor is theoretically attractive because both

angiotensin production and its receptor are blocked; however, the combination does make hyperkalaemia a real risk.

Adding a centrally acting calcium channel blockers to a beta blocker makes heart block more likely – particularly if there is already some block (e.g. lengthening of PR interval >0.12 second). This is less likely with long acting peripheral calcium channel blockers, but there is the disadvantage of peripheral oedema, especially if autonomic neuropathy is present. (This is because autonomic neuropathy causes arteriovenous shunting, raising capillary and filtration pressure. Vasodilating calcium channel blockers also increase capillary and glomerular filtration pressure.) The sympatholytics often cause troublesome hypotension and may be associated with depression (especially if beta blockers are also being taken). Slow acting oral nitrate therapy and hydralazine are other options but are rarely used.

Once again, discussion with a specialist may help guide the treatment decision. Many would consider adding a long acting peripheral calcium channel blocker to be the next step, with precautions to prevent peripheral oedema (e.g. use of support stockings, especially in hot weather). Alternatives would include an angiotensin receptor antagonist (with monitoring for hyperkalaemia) or an alpha blocker (with monitoring for postural hypotension and worsening of heart failure).

### Key points

- Blood pressure is an important risk factor for both micro- and macro-vascular complications of type 2 diabetes.
- Microalbuminuria and left ventricular hypertrophy are markers of endothelial and end organ damage throughout the body.
- When blood pressure is difficult to control:
  - check adherence and consider reducing the number of medications and the number of occasions on

which they are taken

- consider home or ambulatory monitoring to define the 24-hour blood pressure profile
  - check for correctable causes of hypertension, particularly NSAIDs, sleep apnoea and lifestyle factors
  - consider secondary causes involving two arteries (aortic coarctation and renal artery stenosis), two organs (adrenal gland and kidney) and recreational drugs (e.g. cocaine).
- The medication steps suggested by the RACGP to achieve target blood pressure (<130/80 mmHg; <125/75 mmHg if proteinuria >1 g/day) are to start with an ACE inhibitor (or angiotensin receptor antagonist if an ACE inhibitor is not tolerated), then to add a diuretic and then a beta blocker. Selecting a fourth medication (if necessary) can be difficult – possible choices include a long acting peripheral calcium channel blocker, angiotensin receptor antagonist, alpha blocker and centrally acting sympatholytic. Discussion with a specialist colleague may be helpful. **MT**

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