Antihypertensive concordance in elderly patients

In spite of overwhelming clinical evidence to support the cardiovascular benefits of antihypertensive treatments, less than half of treated hypertensive individuals achieve good blood pressure control. Poor concordance remains one of the major obstacles in preventing adequate control. It is estimated that between 50% and 80% of hypertensive patients do not take all of their prescribed medication, resulting in potentially major adverse consequences. Involvement of patients in decisions about their treatment, adapting consultation style to meet patients' needs, simplification of treatment regimens using combination therapy with flexible dosing components are just some of the ways that may enhance concordance.

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Almost 50% of elderly patients have high blood pressure and adequate treatment has been shown to significantly reduce cardiovascular disease morbidity in those older than 65 years.[1] A reduction in systolic blood pressure by 10 mmHg or diastolic blood pressure by 5 mmHg reduces the risk of stroke by almost 35% and the risk of ischaemic heart disease events by about 25% at the age of 65 at all levels of blood pressure in Western populations.[2–5]

Current data strongly support early, aggressive management of hypertension, irrespective of age, as a fundamental component of the management of the global risk of cardiovascular disease.[6] Proportional reduction in risk across various age ranges translates into substantially higher benefit in older patients.[7,8] The number-needed-to treat for five years in order to prevent one major cardiovascular event in patients with isolated systolic hypertension at 70 years or older is as low as 19.[7]

Despite overwhelming clinical evidence supporting the cardiovascular benefits of antihypertensive treatment, less than 50% of treated hypertensive individuals have good blood pressure control.[9] Poor concordance with antihypertensive treatment is a well recognised cause of inadequate blood pressure control.[10] Unfortunately, poor concordance is difficult to measure and remains largely undiagnosed or misinterpreted as a poor response to treatment or as resistant hypertension.

Rates of concordance are usually represented as a percentage of prescribed medication actually taken by the patient over a specified time.[11] Part of the difficulty in measuring concordance with therapy is the lack of consensus in what constitutes adequate adherence to treatment. Some trials regard rates of 80% as acceptable whereas others may set more stringent criteria.[11] Clinical trials report concordance rates of 43–78% in patients receiving treatment for chronic conditions.[12,13] This figure is probably higher than the concordance rate in the real-world population. Treatments for chronic conditions, such as hypertension and dyslipidaemia, are particularly vulnerable to poor concordance by virtue of their asymptomatic nature.

Poor antihypertensive concordance is widely prevalent. It is estimated that between 50 and 80% of patients with hypertension do not take all of their prescribed medication.[14,15] Generally, one third of patients always take their antihypertensive treatment, one third take it sometimes, and one third never take it. The adverse consequences are huge, with unnecessary investigations, drug and dose adjustments, and (most importantly) progression and complications of cardiovascular disease.[9] Moreover, abrupt withdrawal of certain treatment regimens may lead to harmful effects (eg, rebound hypertension or tachycardia) and this may result in target organ damage such as acute pulmonary oedema or worsening congestive heart failure.[16]

Reasons for poor concordance

Commonly perceived barriers to concordance include both patient and physician factors. Side-effects, polypharmacy (particularly with co-existent conditions), cost, formulary restrictions, complexity of treatment schedules, need for life-long treatment, lack of understanding of treatment

targets, and limited patient involvement in treatment decisions are some of the issues that contribute to poor concordance. Physicians treating elderly patients with hypertension often face difficult patient challenges, some of which are psychosocial and others medical.[17]

Psychosocial challenges

Although elderly individuals are generally more likely to adhere to antihypertensive treatment than younger people,[18] a number of psychosocial factors may hamper concordance:

- Older men, especially widowers, take limited interest in their health and tend to skip outpatient visits[17]
- Elderly people living alone may find it difficult to travel to attend clinic visits
- Engrained beliefs that high blood pressure is an expected consequence of growing older.

Medical challenges

- Elderly individuals are more likely to have concomitant medical conditions requiring multiple medications, increasing the risk of drug interactions and side-effects[19]
- Cognitive impairment and depression are more common in the elderly population, posing a challenge to patients understanding the need for concordance with long-term medical therapy[17]
- Visual and hearing impairment make following treatment instructions difficult
- Use of non-steroidal-anti-inflammatory drugs, alcohol, and over-the-counter medications can all adversely affect hypertension management
- Lifestyle measures, such as diet and exercise, are often more difficult to institute in older age groups.

All these factors need to be given particular attention when ensuring adequate concordance with an antihypertensive regimen in an elderly patient.

When to suspect non-concordance

An empathetic, non-judgmental approach to concordance assessment during clinic review is essential when dealing with individuals with chronic disease, who will probably be on multiple medications. Asking a patient, "How often are you likely to miss a dose?" is far better than asking whether they are really taking all of their tablets. Enquiring sympathetically about side-effects is good practice and finding the opportunity to ask patients whether they realise the merits of treatment and to reiterate the potential risk of sudden unauthorised withdrawal of medication should pay dividends.

Predictors of poor concordance include poor clinic attendance records, erratic repeat prescription ordering, cognitive impairment, depression, side-effects of treatment prescribed, complexity of treatment schedules, multiple pharmacological therapies for asymptomatic conditions, lack of patient insight into the illness, and lack of belief in the merits of preventive treatment.[11]

The NICE guidance for the management of hypertension[20] stresses the importance of concordance with prescribed antihypertensive medication. A meta-analysis of eight studies found the average concordance rates to be significantly higher for patients with once daily dosing regimes versus those on multiple daily doses of antihypertensive medications (91% versus 83%; $p<0{\cdot}001$). Additionally, the concordance rates for those taking once daily dosage regimens compared with twice daily doses were also higher (93% versus 87%).[20] While citing this meta-analysis, NICE cautions that simplification of dosing regimens is often insufficient on its own to result in adequate concordance and, therefore, stresses the importance of combining a wide range of interventions.

NICE has now published guidance[21] for medication adherence. The principles of the guidance are centred on better communication and engaging patients in treatment decisions. The document encourages health-care professionals to adapt their style to meet the individual needs of patients and to make information about chronic conditions and their treatment as accessible as possible. The recommendations remind us that even after receiving all the relevant information, patients still have the right to refuse treatment. They also reminds us that although medication adherence can be improved, there is no specific measure to suit all patients and interventions must be tailored to address the specific difficulties that a patient is facing with adherence.

The cost burden of poor concordance is impossible to quantify in the management of chronic diseases. Randomised controlled trials have proven unequivocally that treating high blood pressure substantially reduces the risk of stroke and myocardial infarction. Despite the availability of effective treatment, suboptimum management of hypertension is a worldwide problem

and lack of antihypertensive concordance is a major factor in poor blood pressure control. The financial effect of cardiovascular disease events (eg, myocardial infarction) is huge, but the human cost to patients and their families is immeasurable. In the USA, 33-69% of medication-related hospital admissions are due to poor medication concordance, with a resulting cost of $100 billion per year.[22]

Management of the non-concordant patient

There is little doubt that measures designed to improve concordance with antihypertensive treatment will help to achieve blood pressure goals and contribute to a substantial reduction in cardiovascular disease complications.

Interventions to improve concordance may be classified into three main groups: patient-centred, physician centred, and drug-specific factors.[23]

Patient-centred interventions

Empowering patients and educating them about treatment goals and reducing risk helps to create an incentive for concordance when dealing with a chronic, asymptomatic condition such as hypertension. In a selected group of patients, blood pressure self-monitoring may be useful in encouraging concordance. Counselling patients on the importance of concordance and how to organise their medication and enlisting the help of family members and relatives is also useful, and so is telephone and computer-assisted monitoring. Objective monitoring of concordance using electronic dispensing devices may be beneficial in some patients, but can be subject to inaccuracies and misinterpretation. Increasing convenience of care provision and taking time to understand patients' fears and reservations about treatment is paramount. This can be ascertained by the physician during clinic visits and also by dedicated specialist nurses. In fact, nurse-led initiatives through coronary disease risk factor clinics have proven to be effective in modifying lifestyle behaviours, reducing blood pressure, promoting medical education, and—eventually—reducing mortality.[20,24,25]

Community pharmacists can play an important role in reassuring patients and helping concordance. The Federal Study of Adherence to Medications in the Elderly (FAME)

was the first prospective randomised trial to specifically address medication concordance in this population. The study tested the effect of a comprehensive pharmacy care programme on medication concordance and control of blood pressure and low-density-lipoprotein (LDL) cholesterol. 200 patients aged 65 years or older were studied. All patients were taking four or more chronic daily medications and were living independently. Following a run-in-phase, all scheduled medications were custom packaged in blister packs sorted by time of day (morning, noon, evening, and bedtime) and used throughout the adherence phase by all study patients. All participants were also given the pharmacy education programme, which included the blister packs, during the adherence phase of the study. In the persistence phase of the study, patients were randomised to either receive a continued pharmacy programme care or usual care (defined as the original method of medication administration at baseline). There were marked improvements in the rate of medication concordance. Mean baseline concordance was 61·2% (+/-13·5%), which increased to 96·9% (+/-5·2%; p<0·001) during the 6 months of pharmacy programme intervention. There was a 16-fold increase in the number of participants who achieved 80% or more concordance with all medications. At the conclusion of the trial (14 months), concordance associated with usual care had fallen to near baseline levels, but continued pharmacy care was associated with a continued high concordance rate (p<0·001). Improved concordance was associated with clinically significant improvements in systolic blood pressure (p=0·02 versus baseline) and LDL cholesterol (p=0·001).[26]

Further evidence supporting health education interventions comes from the five-year blood pressure control and mortality following health education for hypertensive patients study.[27] Three interventions for urban poor hypertensive patients were introduced sequentially in a randomised factorial design: an exit interview to increase understanding and adherence to medication, a home visit to encourage a family member to support the patient, and an invitation to a group educational session designed to boost patient confidence in management of the condition. The cohort consisted of 400 hypertensive patients and the five-year analysis of the study confirmed a positive impact of the interventions on appointment keeping, weight, and blood pressure control. The all-cause mortality rate for the experimental group was 57·3% less than for the control group, and the hypertension-related mortality rate was 53·2% less.

Physician factors

Physician-related barriers for concordance have lessened in the UK following the introduction of clearer guidelines and the target-driven General Medical Services contract. However, physicians in both primary and secondary care settings may not be sufficiently aggressive with hypertension management, particularly in the elderly population for fear of side-effects, or there simply may be an acceptance of systolic hypertension as part of the ageing process. These attitudes cause concern when dealing with an ageing population in which the relative risk of cardiovascular disease is greater at any level of blood pressure. The latest Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC) analysis[6] shows that the relative risk reduction of cardiovascular disease events with tighter blood pressure control occurs irrespective of age. In a meta-analysis of 31 trials involving more than 190,000 patients, the reduction in blood pressure with various antihypertensive drugs was independent of the patients' ages. The BPLTTC analysis provides strong supportive evidence for the use of blood pressure lowering therapy in all elderly patients with hypertension. The Hypertension in the Very Elderly Trial (HYVET) showed that in patients older than the age of 80 years, lowering blood pressure systolic (>160 mmHg) or diastolic (>90-109 mmHg) to below 150/80 reduced the risk of fatal and non-fatal stroke by 30%.[8]

Drug specific factors

The British Hypertension Society's rule (ACD) in the management of hypertension adopts a physiological rationale when basing treatment decisions predominantly on age.[28] Plasma renin activity falls with increasing age and there is an increase in alpha adrenoceptor mediated calcium influx vasoconstriction in the ageing individual.[6,28] These physiological processes would favour the use of a diuretic or calcium-channel blocker as first choice in an elderly hypertensive patient. Diuretic therapy stimulates renin release,[29] thus elderly patients are more responsive to therapy with an angiotensin-converting-enzyme (ACE) inhibitor or angiotensin-receptor blocker (ARB) when combined with a diuretic. An example of how this strategy has been successfully tested is evident through the aforementioned HYVET trial, in which nearly 80% of

individuals in the treatment arm were taking indapamide (thiazide-like diuretic) and perindopril (an ACE inhibitor). A significant reduction in total mortality, death from stroke, and development of heart failure was shown in those receiving active treatment.[30]

Simplification of the treatment schedule and reducing the number of daily doses is effective in increasing concordance. Patients should be encouraged to take medication in the morning whenever possible to make sure this becomes part of their daily routine. Choosing long-acting antihypertensive agents that provide genuine control over 24 hours and beyond may be beneficial and more forgiving in the event of a missed dose. Regimens that are effective and well-tolerated are fundamental to concordance.[11,31] ARBs, followed by ACE inhibitors and calcium-channel blockers have the lowest discontinuation rates among all antihypertensive drug classes.[32] Olmesartan medoxomil is a long-acting ARB with an excellent 24-hour blood pressure lowering capability, and a very favourable safety and tolerability profile.[33] Both of these attributes facilitate concordance. It is not metabolised and does not interfere with cytochrome P-450, which reduces the risk of interactions.[34] In elderly patients with isolated systolic hypertension, olmesartan is similar in efficacy to dihydropyridine calcium antagonists, such as nitrendipine. It also has similar efficacy to amlodipine in patients with mild-to-moderate hypertension.[35,36] A recent meta-analysis involving 7,040 patients treated with ARB monotherapy showed significant benefits in favour of olmesartan compared with other commonly used ARBs.[37]

Fixed-dose combinations (FDCs) reduce the risk of poor concordance as they simplify dosing regimes.[38] The availability of more modern combinations with flexible dosing components is likely to encourage their use in patients on polypharmacy, where concordance may be a major issue.

The ACCOMPLISH study showed the cardiovascular benefits of a FDC that included an ACE inhibitor and a calcium-channel blocker.[39] Compared with conventional treatment, the combination reduced the risk of mortality and morbidity by 20%. A recently approved FDC that combines olmesartan and amlodipine is due to be launched in the UK. This particular FDC successfully treated patients with uncontrolled hypertension to the universally accepted blood pressure goal of less than 140/90 mmHg, a threshold considered significant in reduction of cardiovascular risk.[40]

Conclusion

In summary, poor concordance is an important contributor to the failure of optimum blood pressure control in elderly populations. A high index of suspicion is important, particularly in patients who fail to respond to conventional regimens. An empathetic approach to patients suffering with multiple comorbidities and polypharmacy is essential. It is important to pause and consider poor concordance before deciding to add yet another new drug. Medications will not work if left in the medicine cabinet.

Conflict of interest: I have attended and contributed to advisory boards and speaker meetings for Daiichi Sankyo, Novartis and Merck, Sharp & Dohme

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