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Review Article

Management of Hypertension in Adults with Diabetes

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Introduction

Hypertension and diabetes mellitus are common diseases in the Kingdom of Saudi Arabia (KSA), related in part to improved living conditions and increasing rates of obesity. [1-5] One in five adults in the KSA has hypertension [6] and more than three million adults have diabetes. [7,8] It is projected that the incidence of diabetes will continue to grow and that the majority of the cases will be type II diabetes. Diabetes Mellitus (DM) is a strong predictor of cardiovascular events. [9,10] The increased risk of cardiovascular morbidity and mortality is about 2-fold in men and 4-fold in women, and cardiovascular disease is the leading cause of death among diabetic patients. DM is also the most important cause of end-stage renal disease in KSA, accounting for almost 40% of the cases. [11] Diabetic retinopathy is one of the major causes of blindness in the general population. [12] Taken together, the health burden of DM is enormous. Hypertension and DM frequently coexist. [13,14] Among type II diabetics, 40 to 50% have hypertension compared to 20% of matched non-diabetic patients. Also, hypertensive patients have a 2-fold increased risk of developing type II diabetes in their lifetime. The presence of hypertension in diabetic patients dramatically increases the rate of complications. In the United Kingdom Prospective Diabetes Study (UKPDS), for example, the incidence of any aggregate end-point related to diabetes was strongly and linearly associated with systolic blood pressure (BP) and over the range of systolic BP from less than 120 mm Hg to greater than 160 mm Hg the likelyhood of a cardiovascular event increased 2-fold. [15] Additionally, the absolute event rate in diabetic patients is substantially higher than that in non-diabetic patients at the same level of BP.

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Clinical trials in hypertensive diabetic patients

Benefits of treatment to control blood pressure

The health benefits of lowering BP in hypertensive diabetic patients are well documented in a large number of clinical trials. Additionally, there is trial evidence of improved outcomes with aggressive treatment to a lower goal pressure than that recommended for uncomplicated hypertension. These findings have led to recommendations that all hypertensive diabetic patients should be treated with antihypertensive medication and the goal of therapy should be to decrease BP to less than 130/80 mm Hg. [16-20]

Choice of pharmacological therapy

All the major classes of antihypertensive agents (diuretics, beta-blockers, angiotensin converting enzyme (ACE) inhibitors and calcium channel antagonists) are highly effective in reducing cardiovascular events in diabetic patients. [15,21-23] Although the beneficial effects in hypertensive trials have been attributed to the fall in BP with active therapy, data from HOPE and LIFE trials suggest that agents disrupting the function of the renin-angiotensin system improve outcomes by means beyond their effects on BP. [24,25] In the HOPE trial, the addition of the ACE inhibitor, ramipril, to standard therapy significantly reduced the rates of death and major cardiovascular events in a broad range of high-risk patients including those with diabetes and hypertension, despite modest differences in office BP readings compared to placebo.[24] The LIFE trial demonstrated that, despite comparable reductions in BP, angiotensin II receptor blocker (ARB)-based treatment with losartan significantly reduced the incidence of the composite endpoint of cardiovascular morbidity and mortality to a greater extent than atenolol-based therapy in older (55-80 years) patients with essential hypertension and electrocardiographic left ventricular hypertrophy. [25] On the other hand, the UKPDS trial showed that BP lowering with the ACE inhibitor, captopril, or atenolol-based treatment was equally effective in reducing the incidence of diabetic complications in type-2 diabetic hypertensive patients. [15]

There is considerable evidence supporting the use of specific classes of agents in treating and preventing diabetic nephropathy. Experimental studies provide compelling support for a major role of angiotensin II in the pathogenesis of diabetic renal disease, and these findings have been confirmed in human studies. Starting with the hallmark study in type I diabetic patients with overt nephropathy, [26] there are now many large-scaled trials in patients with diabetic renal disease demonstrating the importance of including an ACEi or ARB as initial therapy compared with conventional agents (diuretics/betablocker) or a dihydropyridine antagonist. [27-30] These agents, possibly because of their anti-proteinuric action, have a greater relative benefit in patients with significant proteinuria as this abnormality is a strong predictor of decline of glomerular filtration rate.[31] Some studies have demonstrated that the non-dihydropyridine calcium channel antagonists can also reduce urinary protein excretion [32] but their effectiveness in providing renal protection has not been convincingly shown, particularly in comparison with an ACEi or ARB. There are no head-to-head studies comparing the relative effectiveness of an ACEi and ARB in renal outcomes, and studies of their use in combination are only beginning to appear. [33,34] Thus, until more information becomes available, it would appear that the choice between an ACEi and an ARB as initial

therapy will be based largely on cost and side effect profile.

Multidrug therapy in hypertensive diabetic patients

To achieve the desired reduction in BP (<130/80), over 80% of hypertensive diabetic patients will require two or more antihyper-tensive drugs. [35] Data from several major recent trials demonstrate that attainment of such low levels of BP is virtually impossible to achieve with monotherapy. [15,22-24,30] An appropriate combination of therapy generally includes ACEi or ARB, diuretic and calcium channel blocker, supplemented often with a beta-blocker or possibly an alpha-adrenergic blocker.

Achieving good blood pressure control

A major challenge in managing hyper-tensive patients is not whether to initiate treatment or use a specific therapeutic agent, but rather the failure to treat patients aggressively enough to achieve the desired BP goal. Community-based epidemiological studies have repeatedly found poor BP control in treated hypertensive patients. Reasons for this discouraging observation include patient-related factors such as non-compliance, difficulties in accessing care, financial barriers, failure to understand the consequences of the disease, and adverse events during therapy. Equally important, however, are physician-related factors. Physicians are often not aggressive enough in managing hypertensive patients. They fail to follow recommended guidelines in initiating antihypertensive therapy in patients who would benefit from treatment and increasing the dose and types of BP lowering agents until good BP has been achieved. Several studies have shown that physicians fail to intensify therapy in as much as two-thirds of the visits when the patients present with BP values above the desired goal.

Several physician-related barriers may contribute to their reluctance to follow guidelines including the lack of awareness or knowledge of the guidelines, disagreement with consensus statements, lack of self-efficacy and outcome expectancy and inertia of previous practice. [36] In a recent study, the most frequently cited reason for non-initiation or change in therapy was related to the physician being satisfied with the current BP even though it was above the guideline recommended level. [37,38]

Home blood pressure monitoring

The BP can be monitored at the office and at home using conventional or ambulatory BP monitors (ABPM). Measurement of BP outside the office setting may allay physicians' concerns about a possible "white-coat syn-drome". There is a sizeable body of literature showing the superiority of ABPM over casual office measurement for predicting prognosis, [39-42] but this type of monitoring has not been used to make ongoing treatment decisions largely because of cost, inconve-nience and poor patient acceptance of repeated measurements. Having patients measure their own BP regularly at home has proven to be an acceptable alternative. Home BP monitoring is relatively cheap and convenient. Multiple readings can be obtained over a prolonged period of time, thereby better defining true pressure and eliminating the 'white-coat' effect. Home BP monitoring may also be used to increase patient compliance with medications, improve BP control, reduce the number of office visits related to hypertension and decrease the cost of care.[43]

Health care professionals are often concerned about using patient-measured readings to make treatment decisions. Home BP readings are often inaccurate because of the use of faulty devices or inadequate training of the patients. Moreover, patients may select the readings that they report to the physician. In addition there is limited prospective data relating home BP readings to health outcomes; consequently, there is a lack of consensus on reference values to guide decision-making. Despite these limitations, most organizations providing recommendations on hypertension management advocate the use of home BP monitoring, undoubtedly encouraged by the finding that home readings correlate more closely with cardiovascular mortality than do those recorded in the clinic.[44]

Disease management

Disease management may be defined as "a systematic, population-based approach to identify persons at risk, intervene with specific programs of care, and measure clinical and other outcomes". [45,46] It can be divided into strategies that are designed to facilitate usual care with their primary care physician and those that are planned as alternative means of managing patients such as multidisciplinary teams or specialized clinics.[47] Several trials have examined various strategies to facilitate usual care to improve BP control including appointment reminders, home BP monitoring, written treatment protocols and computer assisted feedback on hypertension management. Although these strategies often improve elements of the process of care such as better clinic attendance, in general they have failed to improve BP control. Similarly, in meta-analysis of heart failure studies, McAlister et al showed that there was no effect on morbidity or mortality of programs designed to increase patient attendance with their primary care physicians. [48]

There are many examples of alternative ways of managing hypertension, ranging from limited interventions to programs involving multiple health-care workers. Most multidisciplinary programs have shown benefit, but generally they are very expensive to establish and maintain. The key, therefore, to their acceptance is to develop a model that is clinically effective, safe and cost-effective.

Telemonitoring systems

Technologies are available that may be used to collect, transmit and store data on patients with chronic health problems. They provide opportunities for outreach models and can be used for patient self-monitoring at home and to disseminate this information to health care providers and medical laboratories. Studies using first generation systems in patients with essential hypertension achieved a greater reduction in BP than usual care. [49,50] However, the magnitude of the change in BP was modest and the proportion of patients achieving a pre-specified treatment goal was not assessed. The principal focus of these systems was home BP monitoring, and physicians and patients were provided with a printed version of the results. Other capabilities of computerized systems such as trend analysis, application of treatment algorithms and internet communications were not exploited. Past studies of home BP monitoring have shown that monitoring alone is not an effective method to improve hypertension control. [51]

The Internet has generated unprecedented opportunities to enhance patient-provider communication and improve the provision

of health related services. A recent systematic review on comparative studies evaluating internet-mediated communication, [51,52] reported better health outcomes in a variety of conditions [53] and other reviews have described better quality of care and increased patient satisfaction. [54] Its use can also improve access to services and co-ordination of activities by clinicians. Studies have demonstrated that informed patients gain control of their conditions, reduce their anxiety levels, improve medication and treatment compliance, create realistic expectations, promote self-care and participation, and generate feelings of safety and security. [55] Moreover, satisfaction with information has been shown to correlate with quality of life. [56] Patients who feel satisfied with the adequacy of information given are more likely to feel happy with their level of participation in the overall process of decision-making. [57] To date, there are no studies assessing the role of the internet for type II diabetic patients with uncontrolled hypertension.

Goal-oriented, protocol-driven treatment of hypertension

Beginning in the 1970s, several clinical trials (Hypertension Detection and Follow-up Program [HDFP], Systolic Hypertension in the Elderly Program [SHEP], Controlled Onset Verapamil Investigation of Cardio-vascular Events [CONVINCE], Hypertension Optimal Treatment [HOT] study and the Antihypertensive Lipid Lowering Trial to Prevent Heart Attack [ALLHAT]) used a BP treatment algorithm to treat hypertensive patients and achieved better BP control than those reported in national surveys. [21,58-61] In the CONVINCE trial, for example, the proportion achieving goal pressures stabilized around 70% during 2.5 years of follow-up, whereas only 20% of the participants taking drug therapy for hypertension at the time of enrolment had their BP under good control. [59] The findings in these trials, while impressive, cannot readily be generalized, since only highly compliant patients are recruited in these trials and cost was not a constraint to the delivery of care.

Logan and colleagues used a similar paradigm to treat patients with uncomplicated hypertension at the worksite. [62] They found that hypertensive workers, randomly allocated to receive protocol-driven treatment delivered by a specially trained nurse working under physician supervision, were significantly more likely to be put on antihypertensive medications (94.7% vs. 62.7%), reach goal BP in the first six months of therapy (48.5% vs. 27.5%) and take medicine as prescribed (67.6% vs. 49.1%), compared to those receiving standard care provided by general practitioners. The improved BP control was attributed to convenience of the site for the delivery of care, more vigorous application of therapy and better compliance with therapy. Others have reported similar results. [63,64] While the cost of delivering care was higher in the nurse-managed group in the study of Logan et al, it was also more cost-effective. [65]

Recently, Singer et al observed that physicians trained in hypertension management achieved better control of BP among patients referred to a specialty referral clinic by primary care physicians, because of difficult-to-manage hypertension. [66] Overall, 63% achieved systolic BP goal, 86%, the diastolic BP goal and 59% both systolic and diastolic goals. The results of the subgroup with diabetes, however, were much less impressive with only 15% reaching the <130/80 mm Hg goal set by and Canadian Hypertension Society (CHS) and American Diabetes Association/National Kidney Foun-

dation (ADA/NKF).[19,20,67] Treating physicians in this study, while encouraged to treat to a specific BP goal, were not required to follow a formal drug treatment algorithm. Moreover, the study lacked a control group with which to make direct comparisons.

Conclusion

Chronic illness accounts for significant proportion of national health care expenditures. The majority of patients with such chronic health problems as hypertension, diabetes mellitus or hyperlipidemia are inadequately treated. Increasingly, illness and death are due to chronic disorders in which an abnormal blood value or clinical measurement may be the only manifestation of disease. Good management of these conditions requires physicians to respond in a timely fashion to indicators of inadequate or ineffective treatment, particularly in the absence of symptoms. Most importantly, patients need to take a more active role in managing their personal health care.

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