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Progress in Diabetes Care: Introduction

OPTIMIZED GLYCEMIC CONTROL has for many years been a cornerstone in the treatment of patients with type I and type II diabetes. This concept was further supported by the publication of the Diabetes Control and Complications Trial (DCCT). Several studies in type II diabetes also strongly support the role of optimal glycemic control in preventing microvascular complications. This was further reinforced by the UK prospective study on diabetes (UKPDS), which is the equivalent of the DCCT study in type II diabetes.

Despite the fact that optimal diabetes control is important, many patients, for several reasons, are still not optimally controlled. Researchers and clinicians have therefore looked for alternatives to prevent microvascular complications and also diabetic heart disease and macrovascular involvement. Over the past few decades, we have seen several attempts to answer the question: Can we prevent diabetic complications even in patients with rather poor diabetic control? An important concept was the introduction of the polyol pathway activated by increased activity of, eg, aldose reductase enzymes in patients in poor glycemic control. Several aldose reductase inhibitors have been proposed, but this concept has not yet reached the clinical arena, although work is still in progress. Modification of advanced-glycation end products (AGEs) is another major concept in diabetes research, and aminoguanidine has been proposed. However, this is again a concept whose clinical realization is still some way off.

However, we have seen a major breakthrough in the management of diabetes with the introduction of antihypertensive treatment to prevent microvascular and also macrovascular complications. This approach has been even further improved by the use of angiotensin-converting enzyme (ACE) inhibitors, the major topic of these proceedings. Indeed, over the past few years, we have seen attention increasingly focused on microvascular disease, especially diabetic nephropathy (DN), where there also seems to be an effect on structural damage according to new studies. It is now commonplace to screen patients for microalbuminuria for the purpose of early intervention. ACE inhibition is even being proposed in normoalbuminuric type II patients to prevent progression to microalbuminuria; however, this is not yet standard practice. It is, however, the practice in most centers to use ACE inhibitors in the management of microalbuminuric patients and patients with clinical proteinuria. ACE inhibition is central to the antihypertensive strategy and is often supplemented by other drugs such as diuretics and/or other antihypertensive agents. Interestingly, the mechanism of action may not simply involve the antihypertensive effect and a specific effect on renal function, reducing filtration pressure. New studies suggest that the modification of endothelial dysfunction and cytokines, as well as growth factors, may be equally important in explaining the beneficial results. A new extension of the indication is the potential to treat patients with diabetic retinopathy. New studies suggest that the progression of diabetic retinopathy can be inhibited by the use of ACE inhibitors, and, here again, a multiple mechanism of action—both hemodynamic and metabolic—may be involved. The vasculature elsewhere may also benefit, as discussed in this volume.

The use of ACE inhibitors is in most cases fairly uncomplicated if patients do not have advanced renal disease. There has been some discussion about the dose of ACE inhibitors. It is usually not enough to administer a small dose; a medium or sometimes even high dose is often indicated to achieve efficacy. However, generally, it is proposed to start with a small dose and increase gradually, with albuminuria, including microalbuminuria, and blood pressure as effect parameters. Obviously, physicians should be alert for the well-described side effects also with respect to renal function, mainly elevated serum potassium. Some reduction in the glomerular filtration rate (GFR) is observed initially. However, a slight reduction in GFR is an actual part of the mechanism of action, and a 10% to 20% increase in serum creatinine acutely should not be of concern, but of course such patients should be monitored carefully for stabilization, the purpose of long-term treatment.

Other avenues of treatment are still on the horizon such as inhibition of protein kinase C and growth factors, but again clinical implementation of this is a long way off, although we have evidence that part of the effect of ACE inhibitors may be mediated through these pathways. Clearly, diabetologists must be concerned with more than blood glucose values alone. Management of blood pressure related to complications is equally important, as outlined in the proceedings from this meeting. There must be an intensified multifactorial intervention.

In conclusion, I would say that the major progress in diabetes care over the past several decades has been the introduction of self-monitoring, followed by implementation of HbA_{1c} monitoring. Achieving optimized glycemic control is a cornerstone, but clearly the introduction of antihypertensive treatment, mainly ACE inhibitors, has been the major breakthrough in the clinical care of diabetic patients. Again, this was confirmed by the UKPDS, published in September 1998.

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