

# US experience of intensive insulin therapy in older people

Ali Rizvi, Elizabeth Todd-Heckel

## Article points

1. Older people with diabetes often have other chronic conditions that may contraindicate, or increase the side effects of, oral antidiabetic agents.
2. Early, aggressive use of insulin is being advocated by some US clinicians.
3. Appropriate and 'physiological' use of insulin via injections or pump therapy has been shown to improve control, reduce hypoglycaemia, and improve treatment satisfaction.
4. Insulin should not be withheld on the basis of age alone; the educated and well-informed older patient is suitable for such therapy.

## Key words

- Older people with diabetes
- Intensive insulin therapy
- 'Basal-bolus' regimen
- Subcutaneous injection
- Insulin pump

Ali Rizvi is Associate Professor of Medicine, Department of Medicine, University of South Carolina School of Medicine, Columbia, USA, and Elizabeth Todd-Heckel is Site Director at The Diabetes Initiative of South Carolina, Columbia, USA.

**In response to an increasingly ageing population and growing prevalence of diabetes, some clinicians in the USA are advocating early aggressive use of insulin for the management of diabetes in older people. This article presents recommendations for optimising insulin use in this age group through multi-dose injections or pump therapy. While not reflecting common practice in the UK, this article is intended to serve as a platform for debate on the use of intensive insulin therapy.**

**D**iabetes is a chronic condition that is increasing in prevalence and is poised to become a global health epidemic. At the same time, the geriatric population is growing, secondary to medical breakthroughs and advances in life expectancy and living standards. Nearly one-fifth of people over 60 years of age suffer from diabetes (Gregg et al, 2000). Although older patients may have long-standing type 1 diabetes, the majority have type 2 diabetes. This may remain undiagnosed for many years, and its incidence increases with age, physical inactivity and weight gain (Franse et al, 2001). Older patients often have suboptimal glycaemic control, leading to microvascular complications (neuropathy, retinopathy and nephropathy) and macrovascular disease.

The emphasis on 'tight' glycaemic control has given a big impetus to early, aggressive use of insulin (Leahy, 2003). However, both provider- and patient-related barriers exist to thwart our efforts at utilising insulin effectively in clinical practice. It is often difficult to mimic physiological insulin delivery and attain a satisfactory insulin-to-glucose match with traditional insulin therapy. The results are frequent hypoglycaemia, unpredictable glycaemic excursions, lifestyle restrictions and decreased treatment satisfaction.

Older people perhaps suffer most in

this respect. Preconceived notions and misconceptions are probably the major limitations and hurdles. If used appropriately, however, insulin can be highly effective in this age group. Recent work in this field is reviewed in this article and recommendations for optimising insulin use in older people through multi-dose injections or pump therapy are presented.

## Initiating insulin treatment in older patients with diabetes

Insulin therapy in type 2 diabetes is commonly relegated to a treatment of 'last resort' after all other avenues have been exhausted (Holmwood and Philips, 1999). Providers are reluctant to initiate insulin, while most patients have an aversion to injections. Studies have revealed a lack of awareness of the potential benefits of insulin (Riddle, 2004). Clinicians worry about hypoglycaemia, weight gain and increased cardiovascular risk, but these concerns are, for the most part, unfounded misconceptions (McCarren, 2003). Early insulin therapy is now being advocated for improving glycaemic control and reducing the risk of diabetic complications in type 2 diabetes (Marre, 2002). However, the potential drawbacks of complex regimens, the need for frequent glucose monitoring, increased cost, hypoglycaemia and weight gain should be kept in mind (*Table 1*).

The benefits and risks of insulin therapy should therefore be weighed carefully in the individual patient. The decision to implement a particular insulin regimen should be individualised. In this respect, it is worth spending some time exploring the patient's attitudes towards insulin treatment, answering his/her questions, involving family members, and seeking the assistance of a nurse educator and nutritionist. Ultimately, an informed decision by patients regarding insulin initiation, type of regimen, and continuation stands the best chance of being congruent with their long-term goals.

### **Instituting a multi-dose insulin regimen using the basal–bolus concept**

The use of multi-dose insulin injections in type 1 or insulin-requiring type 2 diabetes has undergone a transformation in recent years. In order to mimic normal physiological pancreatic function, therapeutic regimens designed to treat both fasting and post-meal hyperglycaemia are being utilised.

**Table 1. Benefits and risks of insulin therapy in older people.**

#### **Benefits**

- Improved glycaemic control
- Improved treatment of the dawn phenomenon
- Better postprandial glucose management
- Increased lifestyle and meal flexibility
- Avoidance of oral agent side effects

#### **Risks/cautions**

- Need for multiple injections and regimen complexity
- Frequent daily blood glucose monitoring
- Increased risk of hypoglycaemia and possible weight gain
- Need for education/training of patients and healthcare providers
- Possible increased patient anxiety

Daily glucose self-monitoring is necessary in order to identify trends and patterns, and implement the 'basal–bolus' concept (McDonald, 2003).

Components of multi-dose insulin therapy

comprise different types of insulin with specific pharmacokinetic profiles. A combination of long-acting (such as NPH or glargine) and short-acting (such as regular, lispro or aspart) insulin is usually used. Adjustments are based on the daily self-monitored blood glucose readings, with the aim of dovetailing insulin to glucose levels.

The optimal type and regimen of insulin is another hurdle that is often overlooked or not properly addressed. Insulin therapy is commonly used in improper dosage, frequency or timing, and is associated with glycaemic variations and increased risk of hypoglycaemia (DeWitt and Dugdale, 2003). The goal with insulin treatment is to mimic normal physiology by using it in a basal-bolus fashion, with the emphasis on duplicating the natural release of insulin when normal pancreatic function is present. This approach consists of the administration of a long-acting 'basal' insulin required to maintain euglycaemia in the fasting state, and 'bolus' insulin during times of hyperglycaemia (e.g. in the postprandial state). Ideally, doses of bolus insulin should be calculated at each meal by taking into account the blood glucose level and the amount of food (grams of carbohydrates) to be consumed. This approach is widely recognised and accepted in the management of type 1 diabetes, and requires precise insulin timing and calculations.

However, with the emphasis on aggressive therapy and early insulin use, the basal-bolus approach is increasingly advocated in type 2 diabetes as well (Raskin et al, 2003). In addition to inherent pharmacokinetic insulin properties, other variables that determine the dose and pattern of insulin requirements in a particular patient are ambient glucose levels, carbohydrate intake and physical activity.

We have successfully used the basal-bolus multi-dose insulin approach in older patients with diabetes in our practice. We utilise the advantages of the newer insulin analogues, which have certain superior pharmacological characteristics that make them better suited for use in a basal-bolus fashion. Insulin aspart and lispro are rapid-acting preparations for control of postprandial glycaemic excursions, while glargine is a once-daily, peakless, long-acting insulin.

Our preliminary experience (Baldwin and Rizvi, 2004), although limited by short follow-up, has

shown a statistically significant decrease in HbA<sub>1c</sub>, and a patient-reported subjective improvement in hypoglycaemia and treatment satisfaction.

More importantly, it has encouraged us to continue the multi-dose combination of basal and bolus insulin regimen through multidisciplinary diabetes education. A complex multi-dose insulin regimen might appear daunting and formidable, yet with patience and persistence it is amenable to implementation in the practices of most primary care providers. Rapid-acting insulin calculations based on insulin sensitivity factor and carbohydrate counting can be taught in the office setting and are preferable to the 'sliding scale' regimen. The latter does not take into account individual sensitivity to insulin or variations in carbohydrate content of food. Similarly, therapy with premixed insulin has unpredictable peaks and limited flexibility for making modifications (DeWitt and Dugdale, 2003).

### Continuous subcutaneous insulin infusion

#### Advantages of the insulin pump

Basal-bolus insulin therapy is easier to implement when continuous short-acting insulin is given using an insulin pump. The pump delivers continuous insulin at a pre-programmed basal rate, while insulin boluses can be calculated and delivered at mealtimes to treat postprandial glycaemic elevations.

Insulin pumps are a valuable tool that help in improving glycaemic control, decreasing the risk of hypoglycaemia and reducing cost by minimising the need for acute medical care and hospitalisations (Hirsch et al, 2005). Proper candidate selection and close follow-up are critical. Type 1 diabetes and pregnancy are good indications for pump therapy, which has also been used to great advantage in type 2 diabetes (Raskin et al, 2003).

However, clinicians may hesitate to prescribe insulin pump therapy in older people, for a variety of reasons (Farkas-Hirsch and Hirsch, 1994). Older people may be seen as unable to retain new information, to have slow reaction times, and as unable to learn pump features and carbohydrate counting. Safety considerations, perceived lack of patient motivation, and cost concerns may make care-givers reluctant to entrust older people with insulin pumps. The presence of diabetic

1. The newer insulin analogues have certain pharmacological characteristics which make them better suited for use in the basal-bolus multi-dose insulin regimen.
2. Insulin aspart and lispro are rapid-acting preparations for control of postprandial glycaemic excursions, while glargine is a once-daily, peakless, long-acting insulin.
3. Basal-bolus insulin therapy is easier to implement when continuous short-acting insulin is given using an insulin pump.
4. The pump delivers continuous insulin at a pre-programmed basal rate, while boluses of insulin can be calculated and delivered at meals.
5. Clinicians may be reluctant to prescribe pump therapy for older people, for a variety of reasons.

complications and change from a previously familiar routine can cause apprehension in some older individuals, contributing to the perception of older patients as poor candidates for pump therapy.

A growing body of experience now suggests that carefully selected older patients can benefit enormously from the advantages offered by the insulin pump. Case studies and anecdotal reports have been published demonstrating the feasibility of pump use in patients in their seventh and eighth decades of life (Mecklenburg et al, 1982; Farkas-Hirsch and Hirsch, 1994). Kamoj (2002) described good long-term quality of life and freedom from complications in a 72-year-old woman with type 1 diabetes treated for 20 years with continuous subcutaneous insulin therapy.

Our group has previously reported success in older people switched from injections to pump therapy (Rizvi et al, 2001). These individuals had long-standing type 1 diabetes with suboptimal glycaemic control and complications. HbA<sub>1c</sub> was significantly better on the pump after more than a year of follow-up. Concurrent with improved metabolic control, there was a reduction in insulin requirements and decreased propensity to hypoglycaemia. In other words, pump therapy offered a more physiological and effective use of available insulin.

Of note, Siegel-Czarkowski et al (2004) recently reported the efficacy of insulin pump therapy in 34 patients with type 1 diabetes switched from injections to pumps and followed up for 1 year. An improvement in glycaemic control (decrease in HbA<sub>1c</sub> from 7.6% to 7.0%) and a reduction in the frequency of severe hypoglycaemic events were seen.

We have also accumulated favourable experience with pump use in older patients with type 2 diabetes, especially those requiring large amounts of injected insulin (signifying underlying insulin resistance). Obese patients with type 2 diabetes have been shown to achieve better HbA<sub>1c</sub> levels with pumps compared with multiple daily injections without significant change in weight or insulin dosage (Wainstein et al, 2005). Other reports of pump therapy in patients with type 2 diabetes have included older individuals (Lenhard and Maser, 2001; Raskin et al, 2003).

The pharmacokinetics of continuous basal-bolus insulin can make more efficient use of available insulin and prove very valuable in treating the dawn

phenomenon (Koivisto et al, 1986), which is often extremely difficult to manage with injections. The overnight basal insulin rate can be precisely programmed and tailored to attenuate the early morning and pre-breakfast glucose elevations. The reproducible insulin delivery afforded by pump use also decreases variability in blood glucose levels (Lauritzen et al, 1983).

Iatrogenic hypoglycaemia, blunted hormone counter-regulation, and hypoglycaemic awareness are significant causes of psychosocial and physical morbidity and mortality in older, insulin-treated people. They perpetuate a vicious cycle of fear, anxiety and psychological distress (Irvine et al, 1992). Pump therapy can reduce or eliminate frequent, debilitating hypoglycaemic episodes and provide freedom from bothersome and frustrating symptoms (Hirsch et al, 1991). Thus the possible psychosocial advantages, lifestyle benefits, and improved treatment satisfaction make pump therapy an attractive option in many older patients with diabetes.

#### Initiating and maintaining pump therapy

Important prerequisites for successfully initiating pump therapy in older people (*Table 2*) include careful selection of candidates with intact cognitive skills, an understanding of the basics of pump therapy, its risks and benefits, and the effort required for the transition.

The availability of an experienced and professional multidisciplinary diabetes care team is desirable (American Association of Diabetes Educators, 1997; *Table 3*). The team educates the patient in the preparation phase (during several outpatient visits) and provides round-the-clock contact to troubleshoot problems in pump initiation (self-monitoring of blood glucose results are faxed or called in to the prescribing team on a daily basis, and out-of-hours assistance is provided by an on-call physician). Costs are not significantly increased because patients are not admitted to hospital. Patients receive instruction in diabetes self-management and pump mechanics, and sessions in carbohydrate counting or food exchanges. Frequent self-monitoring of plasma glucose and management of high and low glucose readings is reinforced. Practical aspects, including insulin replenishment, timely replacement of tubing, care of needle insertion sites, and procedures to follow in case of

**Table 2. Requirements and components of a successful insulin pump programme.**

- Motivated patient
- Selection of suitable candidates
- Detailed pre-assessment and training
- Services of a pump trainer/nurse educator
- Availability of a qualified nutritionist
- Cohesive pump therapy team
- Ability to maintain close contact with patient during pump initiation
- 24-hour availability of staff and manufacturer support

1. However, a growing body of experience now suggests that carefully selected older patients can benefit enormously from the advantages of the insulin pump.
2. The authors have accumulated favourable experience with pump use in older patients with type 2 diabetes, especially those requiring large amounts of injected insulin (signifying underlying insulin resistance).

**Table 3. The multidisciplinary diabetes care team.**

**Core members**

- Patient with diabetes
- Physician with expertise in diabetes management
- Diabetes nurse educator
- Registered dietitian

**Other members**

- Ophthalmologist
- Podiatrist
- Nephrologist
- Psychologist
- Exercise physiologist
- Pharmacist
- Social worker

pump malfunction are emphasised. Long-term support and guidance are necessary to address questions and provide prompt solutions to unique daily challenges. As in other age groups, mishaps in older patients are probably no more common with pump use than with other intensive forms of treatment (combination oral medications or multi-dose insulin injections; Radermecker and Scheen, 2004).

In general, patients should be considered for pump therapy when insulin injections are inadequate in achieving treatment goals (suboptimal metabolic control, unacceptable hypoglycaemia, lack of lifestyle flexibility, etc). Factors influencing the decision include general health status, life expectancy, comorbid conditions, cognitive abilities and the presence of advanced diabetes complications. The goals of pump use should therefore be tailored to the individual patient.

We prefer to initiate pump therapy in older people with a 23-hour observation status. The daily insulin dose is calculated as 80 % of the pre-pump amount, of which half is given in a constant basal rate while the rest is divided into three meal boluses. Outpatient monitoring during the first few weeks is achieved by telephone or fax, and patients are seen in the office every week. Close communication is vital in achieving treatment goals.

**Conclusion**

A substantial amount of accumulated evidence reveals the benefits of ‘physiologically’ delivered insulin in older patients with diabetes. For optimal results it is important that patients are selected carefully, educated thoroughly and followed closely by clinicians who understand the dynamics of glycaemic variations and insulin pharmacokinetics.

The population of older people with diabetes will continue to increase into the 21st Century, contributing to health challenges worldwide. With better types of insulin and easier methods of insulin delivery (pens, pumps and expected availability of inhaled insulin), it is imperative that primary care physicians become familiar with the basal-bolus concept and utilise it on a larger scale in their practices.

The recommendations for an intensive insulin injection regimen as outlined above can form the basis of introducing this therapy to the older

patient. The nuances of treatment can be tailored to the individual patient. If pump therapy is felt to be outside the scope of the GP, the patient should be referred to a specialist. In our view, age alone should not be considered a barrier to providing older patients with the benefits of appropriate insulin use. ■

American Association of Diabetes Educators (AADE; 1997) AADE position statement: education for continuous subcutaneous infusion pump users. *American Association of Diabetes Educators. Diabetes Education* 23(4): 397–8

Baldwin A, Rizvi AA (2004) Efficacy of a basal-bolus insulin regimen in patients with type 2 diabetes. *Tenth Annual Diabetes Fall Symposium*, Abstract Presentation, Scientific Poster Session, 23.09.2004, Charleston, South Carolina, USA

DeWitt DE, Dugdale DC (2003) Using new insulin strategies in the outpatient treatment of diabetes: clinical applications. *Journal of the American Medical Association* 289(17): 2265–9

Farkas-Hirsch RE, Hirsch IB (1994) Continuous subcutaneous insulin infusion: a review of the past and its implementation for the future. *Diabetes Spectrum* 7(2): 80–4, 136–8

Franse LV, Di Bari M, Shorr RI et al (2001) Type 2 diabetes in older well-functioning people: who is undiagnosed? Data from the Health, Aging, and Body Composition study. *Diabetes Care* 24(12): 2065–70

Gregg EW, Beckles GL, Williamson DF et al (2000) Diabetes and physical disability among older US adults. *Diabetes Care* 23(9): 1272–7

Hirsch IB, Farkas-Hirsch R, Cryer PE (1991) The use of continuous subcutaneous insulin infusion for the treatment of hypoglycemia unawareness. *Diabetes, Nutrition & Metabolism* 4: 41–3

Hirsch IB, Bode BW, Garg S et al (2005) Continuous subcutaneous insulin infusion (CSII) of insulin aspart versus multiple daily injection of insulin aspart/insulin glargine in type 1 diabetic patients previously treated with CSII. *Diabetes Care* 28(3): 533–8

Holmwood C, Philips C (1999) Insulin and type 2 diabetes. Last resort or rational management? *Australian Family Physician* 28(5): 429–35

Irvine AA, Cox D, Gonder-Frederick L (1992) Fear of hypoglycemia: relationship to physical and psychological symptoms in patients with insulin-dependent diabetes mellitus. *Health Psychology* 11(2): 135–8

Kamoi K (2002) Good long-term quality of life without diabetic complications with 20 years of continuous subcutaneous insulin infusion therapy in a brittle diabetic elderly patient (Letter). *Diabetes Care* 25(2): 402–4

Koivisto VA, Yki-Jarvinen H, Helve E et al (1986) Pathogenesis and prevention of the dawn phenomenon in diabetic patients treated with CSII. *Diabetes* 35(1): 78–82

Lauritzen T, Pramming S, Deckert T, Binder C (1983) Pharmacokinetics of continuous subcutaneous insulin infusion. *Diabetologia* 24(5): 326–9

Leahy JL (2003) What is the role for insulin therapy in type 2 diabetes? *Current Opinion in Endocrinology and Diabetes* 10(2): 99–103

Lenhard MJ, Maser RE (2001) Continuous subcutaneous insulin infusion (CSII) in patients with type 2 diabetes. *Diabetes* 50(Suppl 2): 1837

Marre M (2002) Before oral agents fail: the case for starting insulin early. *International Journal of Obesity and Related Metabolic Disorders* 26(Suppl 3): S25–30

McCarren M (2003) *Insulin and Type 2 Diabetes: Fears, Myths, Truths*. American Diabetes Association, Alexandria, Virginia, USA



- McDonald K (2003) Insulin therapy today: focusing on the basal-bolus balance. *Advance for Nurse Practitioners* **11**(7): 40–4
- Mecklenburg RS, Benson JW, Becker NM et al (1982) Clinical use of the insulin infusion pump in 100 patients with type 1 diabetes. *New England Journal of Medicine* **307**(9): 513–18
- Radermecker RP, Scheen AJ (2004) Continuous subcutaneous insulin infusion with short-acting insulin analogues or human regular insulin: efficacy, safety, quality of life, and cost-effectiveness. *Diabetes Metabolism Research and Reviews* **20**(3): 178–88
- Raskin P, Bode BW, Marks JB et al (2003) Continuous subcutaneous insulin infusion and multiple daily injection therapy are equally effective in type 2 diabetes: a randomized, parallel group, 24-week study. *Diabetes Care* **26**(9): 2598–603
- Riddle MC (2004) Timely initiation of basal insulin. *American Journal of Medicine* **116**(Suppl 3A): 3S–9
- Rizvi AA, Petry R, Arnold MB, Chakraborty M (2001) Beneficial effects of continuous subcutaneous insulin infusion in older patients with long-standing type 1 diabetes. *Endocrine Practice* **7**(5): 364–9
- Siegel-Czarkowski L, Herold KC, Golando RS (2004) Continuous subcutaneous insulin infusion in older patients with type 1 diabetes. *Diabetes Care* **27**(12): 3022
- Wainstein J, Metzger M, Boaz M et al (2005) Insulin pump therapy vs. multiple daily injections in obese Type 2 diabetic patients. *Diabetic Medicine* **22**(8): 1037–46

## The UK perspective:



The need for earlier initiation of insulin is accepted in type 2 diabetes, after other avenues, including lifestyle measures, have been explored. In 2003 the National Institute for Health and Clinical Excellence

advised that pump therapy should not be considered for people with type 2 diabetes regardless of age; also, in 2002 it stated that insulin glargine should be confined to those requiring once-daily injections, and not used as part of a basal–bolus regimen ([www.nice.org.uk](http://www.nice.org.uk); accessed 23.09.2005). Since then, newer insulin regimens have proved effective and are in general use. However, perhaps we can learn here from the American experience. Those of us in primary care would need a high degree of education and new ways of working to emulate the practice outlined – in particular the out-of-hours support. Although insulin is increasingly initiated in primary care, the intensive regimens advocated in this article are generally managed in specialist care. Should well-motivated, older people not be given the choice of insulin regimens to suit them? As the authors point out, people would need to be carefully selected and we need to bear in mind that older people will get even older. That will have implications for their care in the future.

*Gwen Hall, Practice Nurse / Trainer, Haslemere*