Inhaled insulin in diabetes mellitus

The clinical effectiveness and cost-effectiveness of inhaled insulin in diabetes mellitus: a systematic review and economic evaluation

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Executive summary

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Executive summary

Background

The two main types of diabetes are type 1 (formerly called insulin-dependent diabetes) and type 2 (formerly called non-insulin-dependent diabetes). In type 1, insulin is always required because the insulin-producing islet cells in the pancreas have been destroyed. In type 2, the pancreas can still produce insulin, and treatment is initially with diet and exercise, but the disease often progresses, with deteriorating control and rising blood glucose levels, and a need next for oral hypoglycaemic agents (OHAs), and later for insulin in about 30%. The aim of insulin therapy is to reduce blood glucose to normal levels, without going too low and causing hypoglycaemia.

Insulin currently has to be given by injection. There are various types according to duration of action – short, intermediate and long. Short- and long-acting insulin both come in two forms: traditional and the newer analogues. The traditional form of short-acting insulin is known as soluble. It is given by injection using an insulin pen, or a syringe and needle. Insulin can also be given by continuous subcutaneous infusion by an insulin pump, usually only in selected patients with type 1 diabetes.

Objective

The aim was to review the clinical effectiveness and cost-effectiveness of a new technology, the inhaled insulin, Exubera® (Pfizer and Sanofi-Aventis in collaboration with Nektar Technologies), a short-acting insulin.

Methods

A systematic literature review was conducted and economic modelling carried out. Literature searches were done up to November 2005. The industry model, EAGLE, was used for modelling.

Results

Clinical effectiveness

Nine trials of inhaled insulins were found, but only seven used the Exubera form of inhaled insulin. The other two used inhaled insulins that have not yet been licensed. There were five trials in type 1 and two in type 2 diabetes.

Inhaled insulin is clinically effective, and is as good as short-acting soluble insulin in controlling blood glucose. The frequency of hypoglycaemia is similar. It works slightly more quickly than soluble insulin. None of the published trials compared it with short-acting analogues, which would have provided a better comparison since they also work slightly more rapidly than soluble. There is also a problem in most of the trials in that patients were on combinations of short-acting, and either long- or intermediate-acting insulin, and both were changed, making it more difficult to assess the effects of only the change from soluble to inhaled insulin.

The only significant difference between inhaled and soluble insulin in the trials was in patient preference. Most patients preferred inhaled to injected short-acting insulin, and this has some effect on quality of life measures. However, there could be some bias operating in the trials. The control groups mostly used syringes and needles, rather than pens. As pens are more convenient, their use might have narrowed the patient satisfaction difference.

The manufacturer, Pfizer, argues that this patient preference could lead to improved control in some type 1 patients, through improved compliance with treatment, and in some type 2 patients poorly controlled on oral agents, because a switch to insulin therapy would be more acceptable if people could use inhaled rather than injected insulin. These assertions are unproven.

There were no trials of inhaled insulin against continuous subcutaneous insulin infusion (CSII).

Safety

Concern has been raised about the long-term effects of inhaled insulin in the lung. So far, no serious adverse effects have been seen, but until many thousands of people have used inhaled insulin for many years, one cannot rule out some uncommon or rare, but serious, adverse effects.

Cost-effectiveness

The manufacturer's model (EAGLE) appears to be a high-quality one. However, the results depend more on the assumptions fed into the model than on the model itself. The key assumptions are the size of the gain in quality of life utility from inhaling rather than injecting insulin, the effect of having an inhaled option on the willingness to start insulin among people with poor diabetic control on oral drugs, and the effect on glycaemic control. We consider that the assumptions used in the industry submission make the cost-effectiveness appear better than it really would be. The manufacturer's submission assumed utility gains of 0.036–0.075 in patients with type 1 diabetes, and 0.027–0.067 in those with type 2, based on an unpublished utility elicitation study sponsored by the manufacturer. We thought that these gains were optimistic and that gains of 0.02 or less were more likely, on average. However, patients with particular problems with injection sites might have more to gain, although they might also be a group with much to gain from CSII.

A key factor is the cost of inhaled insulin. Much more insulin has to be given by inhaler than by injection, and so the cost of inhaled insulin is much higher than injected. The extra cost depends on dosage, but ranges from around £600 to over £1000 per patient per year.

Conclusion

The inhaled insulin, Exubera, appears to be effective and safe, but the cost is so much more that it is unlikely to be cost-effective.

Recommendations for the further research

Additional research is recommended into the safety, efficacy and cost-effectiveness of inhaled insulin.

Publication

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NIHR Health Technology Assessment Programme

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