Comparison of the insulin pump and multiple daily insulin injections in intensive therapy for type 1 diabetes

SUMMARY

AGENCE D'ÉVALUATION DES TECHNOLOGIES
ET DES MODES D'INTERVENTION EN SANTÉ

Québec

Comparison of the insulin pump and multiple daily insulin injections in intensive therapy for type 1 diabetes

Report prepared for AETMIS
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MISSION

The mission of the *Agence d'évaluation des technologies et des modes d'intervention en santé* (AETMIS) is to contribute to improving the Québec's health-care system and to participate in the implementation of the Québec government's scientific policy. To accomplish this, the Agency advises and supports the Minister of Health and Social Services as well as the decision-makers in the health care system, in matters concerning the assessment of health services and technologies. The Agency makes recommendations based on scientific reports assessing the introduction, diffusion and use of health technologies, including technical aids for disabled persons, as well as the modes of providing and organizing services. The assessments take into account many factors, such as efficacy, safety and efficiency, as well as ethical, social, organizational and economic implications.

FOREWORD

Diabetes is a chronic, incurable disease, and its prevalence in the Québec population is on the rise. Approximately 30,000 Quebecers have type 1 diabetes, and the only treatment currently available is insulin therapy. Treatment with insulin injections can be conventional (two injections per day) or intensive (four to seven injections per day), but in both cases, the goal is normoglycemia. Glycemic control is essential, both for preventing short-term problems, such as hypoglycemic and ketoacidotic episodes, and for preventing long-term complications, such as diabetic retinopathy, nephropathy and neuropathy.

For several years now, continuous subcutaneous insulin infusion, or the insulin pump, has been an alternative to multiple daily insulin injections in intensive therapy for type I diabetes. Pump therapy, which is not covered by the public plan in Québec, avoids repeated injections and offers greater flexibility in adjusting the insulin dose on the basis of the level of physical activity and food intake.

In this context, the *Ministère de la Santé et des Services sociaux* asked the *Agence d'évaluation des technologies et des modes d'intervention en santé* (AETMIS) to assess insulin pump therapy. This report examines the safety and efficacy of this technology and the economic aspects of introducing it into Québec's health-care system, and presents the patient and health professional perspectives in the Québec context.

An evaluation of the evidence indicates that this technology is safe for motivated patients who are adequately trained and supported by a specialized team and that the improvement in glycemic control offered by the pump, though very modest for the general population of diabetic patients, could be significant for a specific subgroup of patients. Although the cost-effectiveness data for the insulin pump are limited, they do seem to indicate that its use is efficient when it is prescribed to selected patients.

In light of this analysis, AETMIS recommends, among others: 1) that a clear, consistent policy be developed for the use of the insulin pump as a treatment modality for a limited, selected group of patients with type 1 diabetes, with specific prescription and coverage modalities; and 2) that a multidisciplinary task force be formed and specifically charged with defining insulin pump use (patient selection, prescription and follow-up criteria and tools) and procedures for implementing an insulin pump access program (designated centres, care teams, evaluation) in the current Québec context.

In submitting this report, AETMIS wishes to contribute to the optimal use of the insulin pump in intensive type 1 diabetes therapy for the greater benefit of all patients with this disease.

Luc Deschênes
President and Chief Executive Officer

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Any risk or error is the authors' responsibility.

CONFLICT OF INTEREST

None declared.

SUMMARY

INTRODUCTION

This report examines the safety, efficacy and cost-effectiveness of the insulin pump compared to multiple daily insulin injections for the treatment of type 1 diabetes, a chronic, incurable disease whose onset generally occurs at an early age. Insulin therapy and its modalities have evolved in the past few years, and the intensive therapy recommended in all the practice guidelines can be administered by continuous subcutaneous insulin infusion (pump) or by multiple daily insulin injections. Clinical studies identify two types of basal insulin used in multiple daily injections: NPH[1] and glargine[2].

DESCRIPTION OF THE TECHNOLOGY

Insulin pump therapy is technically referred to as continuous subcutaneous insulin infusion. It is a method of administering fast-acting insulin subcutaneously by means of a portable, battery-operated, programmable pump with a tube and a Teflon or metal cannula specially designed for this purpose.

SEARCH METHOD

The literature search identified two health technology assessment (HTA) agency reports, one published in August 2002 by an HTA agency in Great Britain, the other in 2000 by the Catalonian HTA agency. To complement this information, we examined the literature published since 2002. The perspective of patients who use the pump and of health professionals who have experience with it was also explored by means of a self-administered questionnaire (patients) and face-to-face interviews (health professionals).

RESULTS

Indicators

Safety is evaluated in terms of mortality and severe hypoglycemic episodes and ketoacidotic episodes due to pump malfunction. The standard indicator of quality of glycemic control is glycosylated hemoglobin (HBA_{1c}). The HBA_{1c} level is an indicator of glycemic control over the past two to three months. The higher this level, the higher the frequency of complications. The HBA_{1c} concentration and the mean blood glucose level are widely used in clinical and research settings as surrogate outcome for predicting long-term complications. These two indicators are the ones used in this report to assess therapeutic efficacy. The Diabetes Quality of Life (DQOL) questionnaire, which measures the impact of diabetes on four areas of daily life, and the version adapted for youth, the DQOLY (Diabetes Quality of Life for Youth), were used as quality-of-life indicators.

Safety

Randomized, controlled trials have not found any difference, in children or adults, in the incidence of severe hypoglycemic episodes with the pump compared to multiple injections. Nonrandomized studies reported fewer severe hypoglycemic episodes in pump-treated patients, but this can be explained by the choice of subjects in nonrandomized studies, where pump therapy is offered to those patients who are most likely to benefit from it. Two nonrandomized studies, one involving adults selected at the beginning of the study, the other involving children, found that pump therapy and mul-

1. Neutral Protamine Hagedorn (NPH) is a lente insulin.

2. A novel lente insulin that has been approved but which is not yet available in Canada.

tiple injections with basal insulin glargine are more effective than multiple injections with basal NPH insulin in reducing the incidence of severe hypoglycemic episodes. As for the incidence of ketoacidotic episodes, studies have not found any significant difference between pump therapy and multiple injections, although the absolute number of ketoacidotic episodes is higher with the pump.

Efficacy

Comparison of pump therapy and multiple injections with basal NPH insulin

As regards efficacy, data from randomized, controlled trials indicate that for the general population of adult diabetic patients, the pump can lead to a modest improvement in glycemic control (mean decrease of 0.51 to 0.6% in the HBA_{1c} level) compared to multiple injections with NPH, with no additional risks. For the general population of diabetic children, randomized, controlled trials have not found the pump to have any advantage over multiple injections with NPH. In patients selected because of inadequate glycemic control (HBA_{1c} level $\geq$ 8.5%), one randomized, controlled trial noted a greater improvement with the pump in the adults (0.84% decrease in the HBA_{1c} level). Non-randomized studies involving children selected according to various criteria report a greater improvement with the pump as well, although it cannot be quantified.

Comparison of pump therapy and multiple injections with basal insulin glargine

In terms of glycemic control, the pump is as effective as multiple injections with glargine in adults. However, for some patients who fail to achieve glycemic control with multiple injections with glargine, the pump could be an option. The effect of insulin glargine on glycemic control is difficult to evaluate in children, but this new treatment modality does not seem to confer the same benefits as it does for adults, except that it reduces the incidence of severe hypoglycemic episodes.

Quality of life

The data on the impact of the pump on quality of life from randomized or cohort studies involving the general population of type 1 diabetics do not indicate any improvement. In adult patients selected because of inadequate glycemic control, two studies report that the pump led to a significant improvement in various aspects of quality of life. Randomized, controlled trials do not report any significant effect on the quality of life of children who use the pump. Only one such trial found a tendency in favour of pump therapy with regard to certain domains covered by the DQOLY questionnaire, particularly satisfaction with the treatment.

PERSPECTIVE OF PATIENTS WHO USE THE PUMP

In all, 34 people, including 30 pump users, voluntarily responded to a survey conducted in Québec. Since the sample was small, the respondents' comments cannot be generalized to all type 1 diabetics who use or used the pump. It emerges from all the responses that diabetics who presently use the pump derive from it benefits they consider important with regard to several aspects of their daily life. A number of characteristics differentiated the pump users who participated in our survey from most other type 1 diabetics. They were more motivated than average, and some of them were highly organized. They were using the pump successfully and were generally enthusiastic about the technology. These patients had come to use the pump after experiencing considerable difficulty controlling their diabetes (severity bias). They were therefore more likely to benefit from the pump than the typical diabetic patient.

PERSPECTIVE OF HEALTH PROFESSIONALS

All the health professionals consulted agree that the current pumps are safe if the patient is conscientious, serious, motivated and disciplined, and has received complete training. In Québec, a number of them prescribe the insulin pump and train their patients, both adults and children. For adults, opinions are divided as to the comparative efficacy of the pump in terms of glycemic control. All of the professionals in question say that the pump is effective in a minority of carefully selected patients. For children, clinical opinions are more categorically in favour of the pump. All the clinicians interviewed conclude that the pump is not for everyone, but only for selected candidates.

ECONOMIC ASPECTS

The only thorough study published to date indicates that pump therapy is an efficient investment if prescribed to those patients who are most likely to benefit from it, namely, those who experience more than two severe hypoglycemic episodes per year and who have to be hospitalized at least once a year for hypoglycemia. Two other economic studies were published recently, but only as abstracts, with the result that the methodological quality and assumptions underlying the modeling cannot be assessed. A paper presented at a recent conference maintains that pump therapy is more effective in the long term than multiple injections, but at a much higher cost. The present Québec-based cost analysis includes the cost of the pump, accessories, patient training and supplies. Compared to multiple insulin injection therapy, the equivalent annual cost differential of pump therapy is estimated at CAN$4,756 per user. This estimate takes into account the fact that a pump is replaced every five years and that, at that point, training is required, which is a major disbursement. It should be noted that the total anticipated cost for each diabetic who uses an insulin pump will be proportional to the mean life expectancy of the diabetics thus treated.

CONCLUSION

According to the scientific literature, the insulin pump is effective and does not involve greater risks than the comparator therapy, multiple injections with NPH, if precautions are taken. However, the efficacy gain is clearly more pronounced for patients—both adults and children—who meet specific clinical and psychosocial criteria. Study data indicate that the pump's efficacy is comparable to that of multiple injections with glargine for all adult diabetic patients. Since the pump is very expensive, and since insulin glargine should soon be available in Québec, there is less interest in pump therapy for adult diabetics. Nonetheless, for some adult patients who may not be able to achieve adequate glycemic control via multiple injections with glargine, the pump could prove to be an efficient option. For children, insulin glargine seems to be less promising than for adults.

RECOMMENDATIONS

AETMIS recommends that:

1) as set out in the Canadian practice guidelines, the preferred therapeutic approach to type 1 diabetes, in both adults and children, be based on intensive therapy with multiple daily insulin injections;

2) therapy by continuous subcutaneous insulin infusion (insulin pump) be recognized in Québec as a treatment modality that might be indicated for a limited, selected group of type 1 diabetics (various selection criteria based on expert opinions are cited in this report);

3) the *Ministère* considers setting up a multidisciplinary task force (including *Diabète Québec*, and the clinical and research communities) charged with:

- identifying consensus criteria for patient selection and for prescribing and monitoring insulin pump therapy;
- designating clinics that would participate in the implementation of pump therapy

and determining the composition and role of the professional team required;
- developing common candidate selection, patient education and follow-up tools;
- monitoring the implementation of pump therapy; and
- reevaluating the use of pump therapy in Québec some time after it is introduced;

4) the consensual criteria for the use of the pump be reviewed periodically in light of the new evidence that becomes available after this report, in particular, from studies comparing the insulin pump and multiple injection therapy with basal insulin glargine, since the latter may soon be available in Canada (technology watch);

5) a clear, consistent policy governing the use of the insulin pump be developed and made part of a broader initiative for managing diabetes in Québec that would take into account the need to increase the ability of Québec's health-care system to offer intensive therapy to all type 1 diabetics;

6) two options for standardizing the prescription and coverage modalities be examined:

- consider the pump an exceptional treatment modality for exceptional patients, with access granted by the *Régie de l'assurance maladie du Québec* (RAMQ) on a case-by-case basis according to the criteria established by the above-mentioned task force and/or on request by a physician;
- institute systematic pump prescription and utilization auditing and monitoring procedures based on set criteria in collaboration with the clinical settings concerned, possibly by creating a registry of pump-treated patients or developing tools for selecting priority cases within a predetermined budget allowance;

7) a full range of technical services be provided in French in Québec by the manufacturers and distributors of insulin pumps; and

8) research on patient selection criteria and the cost-effectiveness of insulin pumps in the Québec context be considered an important avenue of investigation by the *Fonds de la recherche en santé du Québec* (FRSQ).

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