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Position Statement

When to treat a diabetic patient using an external insulin pump. Expert consensus. Société francophone du diabète (ex ALFEDIAM) 2009


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Received 15 July 2009; received in revised form 22 September 2009; accepted 26 September 2009
Available online 13 January 2010

Abstract

For years, external insulin pumps have enjoyed proven efficacy as an intensive diabetes treatment to improve glycaemic control and reduce hypoglycaemia. Since the last ALFEDIAM guidelines in 1995, however, basal-bolus treatment using a combination of long- and short-acting insulin analogues have emerged and could challenge, at a lower cost, the efficacy of pumps using rapid-acting insulin analogues, considered the ‘gold standard’ of insulin treatment. Nevertheless, given its theoretical and practical advantages, some patients will derive more benefit from pump treatment. These cases have been carefully evaluated in the literature by a panel of experts appointed by ALFEDIAM to determine the indications for pump treatment. In patients with type 1 diabetes, persistent elevated HbA1c despite multiple daily injections (MDI), and repeated hypoglycaemia and high glycaemic variability, represent the most validated indications. In patients with type 2 diabetes, pump treatment may be indicated in cases of MDI failure to achieve HbA1c targets. Absolute contraindications are rare, and comprise severe psychiatric disorders, rapidly progressing ischaemic or proliferative retinopathy before laser treatment and exposure to high magnetic fields. Relative contraindications are mostly related to the patient’s lack of compliance or inability to cope with the treatment, and need to be evaluated individually to clearly assess the benefit/risk ratio for the given patient. However, as these conditions are progressive, there should also be annual reassessment of the appropriateness of pump treatment. Specific education on pump treatment initially and throughout the follow-up, delivered by experienced medical and paramedical teams, are the best guarantees of treatment efficacy and safety.

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Keywords: Insulin pump; Intensified treatment of diabetes; Basal-bolus insulin; SFD recommendations

Résumé

Quand traiter un patient diabétique par pompe à insuline externe ? Référentiel de la société francophone du diabète (ex Alfediam) 2009.

Pendant des années, le traitement par pompe à insuline externe a fait la preuve de son efficacité chez les patients diabétiques de type 1 et avec les analogues rapides de l’insuline a été considéré comme l’élan-orce des traitements par insuline. L’apparition des analogues lents de l’insuline qui, combinés aux analogues rapides réalisent un traitement basal-bolus par injections a remis en cause, à moindre coût, la supériorité de la pompe. Toutefois, en raison des avantages théoriques et pratiques de la pompe, certains patients vont tirer un bénéfice plus important de ce traitement. Ces situations qui permettent de définir les indications du traitement par pompe externe ont été évaluées par un groupe d’experts mandatés par la Société francophone du diabète (ex Alfediam), à la lumière de la littérature et de leur expérience. Chez les diabétiques de type 1, une...

Mots clés : Pompe à insuline ; Traitement intensifié du diabète ; Insuline basal-bolus ; Recommandations SFD

1. Introduction

Since the last recommendations for insulin pump treatment by Association de langue française pour l’étude du diabète et des maladies métaboliques (ALFEDIAM; French-speaking Association for the Study of Diabetes and Metabolic Diseases) in 1995 [1], rapid-acting insulin analogues have been developed and, when used in pumps, they appeared to be more efficient than human insulin, according to a review of the literature [2]. In addition, when long-lasting analogues were associated with short-acting ones, the so-called ‘basal-bolus regimen’, using multiple injections, became possible. With the exception of pump treatment, this regimen is currently regarded as the reference treatment. In comparison, external pumps theoretically have three advantages: the infusion is continuous; the basal dose rate is adjustable; and boluses can be given as frequently as necessary with no additional injections. This suggests that these two therapeutic methods need to be compared to determine which patients might benefit the most from which treatment.

The decrees published by Le Journal Officiel (Official Gazette of the French Republic) on 10 November 2000, 25 August 2006 and 17 December 2008 [3–5] specify guidelines for the management and refunding of pump treatment. The short-term costs of the treatment are greater than those based on multiple injections, but the improvements in metabolic control and quality of life easily counterbalance the extra costs. Thus, an expected short-term benefit of pump treatment might be a favourable benefit/risk ratio (concerning hypoglycaemic events) while, in the long run, patients may also benefit from the avoidance or slower development of complications linked to diabetes.

For this reason, a group of experts met at the request of ALFEDIAM to rigorously evaluate, based on the literature (see Table 1 for grading of the recommendations) and experience, the conditions under which a patient would most benefit from pump treatment, and to define the most relevant indications for this therapeutic method. This would also mean that the success of this treatment and the safety of the patient would be best guaranteed by such guidelines of good care as stated in such recommendations [3–5]. Being rigorous in terms of indications and contraindications as well as adherence to the rules of good care is the best way to deliver pump treatment with the optimal benefit/risk ratio for the patient and as the most cost-effective healthcare.

2. Treatment objectives

Recommendations for healthcare professionals define treatment objectives for diabetic patients as a composite of the following, while maintaining an optimal quality of life:

- HbA1c concentrations;
- capillary blood glucose levels;
- frequency of hypoglycaemic episodes.

2.1. HbA1c

The HbA1c goal recommended for adults and children with type 1 diabetes is < 7.5% [6]. However, this target does not reflect any international consensus: the American Diabetes Association (ADA) recommends < 7% [7], whereas National Institute for Health and Clinical Excellence (NICE) [8] and International Society for Pediatric and Adolescent Diabetes (ISPAD) [9] have selected < 7.5%.

Table 1
Grading of recommendations.

<table>
<thead>
<tr>
<th>Level of scientific evidence from the literature</th>
<th>Grade of recommendation</th>
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<tbody>
<tr>
<td><strong>Level 1</strong></td>
<td></td>
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<tr>
<td>Randomized controlled trials of high power</td>
<td>A</td>
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<tr>
<td>Meta-analysis of randomized controlled trials</td>
<td></td>
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<tr>
<td>Decision analysis based on well-conducted studies</td>
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<tr>
<td><strong>Level 2</strong></td>
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<tr>
<td>Randomized controlled trials of low power</td>
<td>B</td>
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<tr>
<td>Non-randomized comparative studies, but well conducted</td>
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<tr>
<td>Cohort studies</td>
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<tr>
<td><strong>Level 3</strong></td>
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<td>Case-control studies</td>
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<td><strong>Level 4</strong></td>
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<tr>
<td>Comparative studies with major bias(es)</td>
<td>Low level of scientific evidence</td>
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<tr>
<td>Retrospective studies</td>
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<tr>
<td>Case reports</td>
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<tr>
<td>Descriptive epidemiological studies (cross-sectional, longitudinal)</td>
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</table>
For type 2 diabetes, the HbA1c goal recommended in France is < 6.5% or 7%, depending on the type of treatment [10].

2.2. Capillary blood glucose

- In both types of diabetes, postprandial capillary blood glucose goals are < 180 mg/dL after 1–2 h [11] or, more recently, < 140 mg/dL [12].
- In children, capillary blood glucose goals vary according to age, and are less strict in young children [13].
- During pregnancy, glycaemic goals are lower: < 95 mg/dL in the fasting state; and < 120 mg/dL postprandial after 2 h [7] in gestational diabetes.
- The ADA has no recommendations for glycaemic targets in pregestational diabetes.

2.3. Hypoglycaemia

As hypoglycaemia should be avoided as much as possible, glycaemic targets in the fasting state and before meals can be set at 70–120 mg/dL [14].

However, it is often difficult to reconcile these objectives, whatever the insulin regimen. Continuous subcutaneous insulin infusion (CSII) via an external pump, thanks to its flexibility, makes it easier to achieve these different objectives at the same time. However, the cost/benefit balance of the treatment should also be taken into account.

3. Results according to type of diabetes

3.1. Type 1 diabetes

- A 0.4–0.6% reduction in HbA1c levels has been reported in three meta-analyses of trials comparing CSII with multiple daily injections (MDI) [15–17]. However, in four further studies [18–21] — three of which were randomized [18,20,21] — comparing CSII with MDI in adults using insulin glargine and short-acting insulin analogues, the benefit from pump therapy to the whole population was small. On the other hand, the higher the baseline HbA1c, the greater the superiority of CSII over MDI, reaching an absolute difference of 1% in lowering HbA1c in patients with baseline HbA1c > 12% [22].
- In children, four trials — including one randomized study [23] — comparing CSII with MDI, and using glargine and short-acting insulin analogues, showed greater efficacy with CSII [23–26].
- A recent meta-analysis of trials, including patients at high risk of severe hypoglycaemia (> 10% patient-years), showed a significant reduction in severe hypoglycaemic events with CSII compared with MDI, the number of events being divided by 2.9 in randomized trials and by 4.3 in observational studies [27]. The higher the frequency of severe hypoglycaemic events at baseline, the greater the benefit of pump therapy.

In studies that included patients not particularly prone to severe hypoglycaemia, and comparing an MDI regimen using glargine and short-acting insulin analogues with CSII, no difference was seen in the frequency of hypoglycaemic events. However, the small number of hypoglycaemic episodes reported in these studies, and their short duration, does not allow any firm conclusions to be drawn.
- In the paediatric population, numerous observational studies [28–31] have shown a reduction in the frequency of both severe and mild hypoglycaemic events with pump therapy compared with MDI, whereas randomized studies [32–34] could find no such differences. However, once again, it is difficult to draw any clear conclusions, as the frequency of hypoglycaemic events was low, and the duration of the studies was short.

Nevertheless, two consensus reviews of the indications for pump therapy in children were based on these results [35,36].
- Glycaemic variability is reduced in CSII compared with MDI using various types of insulin [37], including glargine as the basal insulin [20], and the more marked the glycaemic variability, the greater the benefit with CSII [38].
- In recent studies, the following parameters of glycaemic control were concomitantly improved by pump therapy: HbA1c, and frequency of hypoglycaemic events and ketoacidosis [26]; and HbA1c, frequency of hypoglycaemic events and glycaemic variability [37].
- In those rare cases of insulin allergy, pump therapy has proved its efficacy in type 1 diabetes, according to one review [39].
- No controlled randomized trial used quality of life as a primary endpoint. However, a recent case-controlled, large-scale study [40] showed the benefit of CSII on quality of life, thanks to its greater flexibility in day-to-day life, less fear of hypoglycaemia and greater treatment satisfaction. In recent randomized trials including quality of life as a secondary endpoint, the results were better [21,37] or the same [23,32,33] with pump therapy vs MDI. These results, however, need to be confirmed. Also, as they are strongly related to device performance, the results may continue to improve as the technology is developed.

3.2. Type 2 diabetes

The experience of external pumps in patients with type 2 diabetes is much more recent and limited. The results of four randomized studies comparing the insulin pump with MDI using rapid-acting analogues and NPH [41–43] or glargine [44] revealed that treatment with the pump had greater efficacy if the previous treatment had been intensified (to at least two injections per day), while quality of life was maintained or improved. A fifth study [45] showed sustained improvement of blood glucose with the pump used simply (without frequent adjustments) in association with antidiabetic oral agents.

The pump allows more predictable insulin uptake in patients with high insulin requirements and/or major insulin resistance [46,47], and probably offers desensitization in the rare cases of insulin allergy [39].

4. Indications for pump therapy

The indications for insulin pump therapy described in the 1995 ALFEDIAM recommendations [1] can now be updated in
the light of increased experience since then. Also, the text of the French *Journal Officiel* of 10 November 2000 [3], which covers the reimbursement of such treatment, states that “care is provided for type 1 or 2 diabetes that cannot be properly controlled through multiple insulin injections”.

The purpose of the present update is to clarify the debate based on rigorous analysis of the literature and experience by an expert panel to allow grading of the new recommendations according to the level of scientific evidence and professional experience. This should help to better define the benefit/risk ratio for patients and the cost-effectiveness of the treatment. Of these indications, only a few are absolute, whereas the motivation of the patient (or parents in paediatric cases) is an essential consideration. It is crucial that physicians and patients take the time to carefully weigh the various factors, as this will limit the chances of failure.

4.1. Type 1 diabetes

4.1.1. HbA1c persistently elevated despite intensified MDI

After intensification of healthcare by a multidisciplinary team and optimization of the patient’s education, an HbA1c persistently >7.5% is an indication to initiate therapy by insulin pump. This treatment will be even more effective in patients with an elevated HbA1c at baseline.

**Grade A recommendation**

4.1.2. Recurrent hypoglycaemia (severe or moderate, but frequent)

a. Incidence of severe hypoglycaemia (requiring the assistance of a third party): more than one episode per year;
b. Incidence of moderate hypoglycaemia: more than four episodes per week;
c. Inability to maintain HbA1c target without increasing episodes as described in a or b.

**Grade A recommendation**

4.1.3. Marked glycaemic variability

Glycaemic variability from day to day or within the same day needs to be documented by a panel of parameters, including clinical (frequent hypoglycaemia) and biological (high HbA1c) data, self-monitoring of blood glucose, index of variability (SD, MAGE, MODD) and/or continuous interstitial glucose monitoring using sensors.

**Grade B recommendation**

4.1.4. Variability of insulin requirements

The main advantage provided by the pump compared with MDI is the possibility of programming several basal rates to adapt insulin delivery according to varying needs throughout the day and to manage the dawn phenomenon.

**Expert consensus**

4.1.5. Treatment with MDI results in good metabolic control, but undermines the patient’s social/professional life

This includes people who are shift workers, business travelers — especially those who must deal with ‘jetlag’ — participants in competitive sports activities, and have variable times for sleeping and eating.

**Expert consensus**

4.1.6. Planned or current pregnancy

Before and during pregnancy, excellent glycaemic control is of vital importance. If not achieved by MDI, then pump therapy may be considered in accordance with the previously mentioned indications.

Given the increased risk of ketoacidoses during pregnancy and the subsequent risk to the fetus, an individualized risk/benefit analysis upon initiation of pump therapy is required.

**Expert consensus**

4.1.7. Specific indications in children and adolescents

All indications for adult patients are equally valid for children and adolescents, although incremental indications may result on consideration of:

- glycaemic instability in very young children;
- pain and/or needle phobia;
- practical reasons limiting the feasibility of MDI;
- nocturnal hypoglycaemia;
- very low insulin requirements (especially at night) in very young children;
- neonatal diabetes or very early onset of diabetes.

In such cases, consider the pump as the first-line therapy.

**Expert consensus**

4.1.8. Insulin allergy

**Grade C recommendation**

4.2. Type 2 diabetes

As the use of pump therapy in type 2 diabetes is much more recent, the following recommendations are based on limited experience only.

4.2.1 Failure of intensified MDI regimen (at least 2 injections/day)

4.2.2 Patients with insulin resistance or very high insulin requirements

**Expert consensus**

4.2.3 Pregnancy (mother has type 2 diabetes)

While this situation appears more frequently in clinical practice, the therapeutic value of the insulin pump has yet to be established. Indications may be similar to those outlined in 3.2.1 and 3.2.2.

**Expert consensus**

4.2.4 Insulin allergy
Grade C recommendation

4.3. Other indications

4.3.1. Major perturbations of glycaemic control in extreme and/or long-term pathophysiological situations
- Diabetes and parenteral nutrition
- Secondary diabetes (for example, following interferon treatment)
- Lipodystrophic diabetes
- Association with insulinopenic state and major insulin resistance

4.3.2. Outlook

Forthcoming indications might include pump therapy as a first-line treatment upon diagnosis of diabetes or as a way to improve patients’ quality of life. Likewise, in line with technical innovations, guidelines differentiating the use of intraperitoneal implantable insulin pumps vs external insulin pumps need to be established.

5. Contraindications for pump therapy

Both absolute and relative contraindications depend on the patients, their environment and/or the pump itself, and refer to situations in which pump therapy is not effective and/or dangerous to the patient.

All contraindications are based on expert consensus.

5.1. Absolute contraindications

5.1.1. Severe psychiatric illness

This includes the parents in cases of children with diabetes.

5.1.2. Severe, rapidly progressive or proliferative retinopathy

Any treatment aiming to rapidly normalize glycaemia is contraindicated in these patients prior to laser treatment.

5.1.3. Regular exposure to strong magnetic fields

Strong magnetic fields such as those emitted by magnetic resonance imaging (MRI) machines can cause pumps to overdeliver insulin.

5.2. Relative contraindications

These situations require careful evaluation of the benefits/risks related to pump therapy. Expert teams in charge of the decision-making process should be experienced with pump therapy, and include physicians, nurses, dietitians and psychologists.

5.2.1. Suboptimal adherence to diabetes treatment

This includes patients who fail to visit their doctor regularly, neglect blood glucose self-monitoring and do not test for ketone bodies. For children, this includes families who are unable to get to an appropriate medical institution within 3 h due to logistical/geographical reasons, or those who have difficulties reaching their parents.

5.2.2. Suboptimal acceptance of treatment by the patient

Indeed, the patient’s motivation and cooperation are essential for the success of pump therapy.

5.2.3. Poor hygiene and participation in violent sports

Such patients have the risk of causing localized infection or bleeding at the site of infusion.

5.2.4. Sensory (particularly visual) or gestural impairment (physically handicapped)

5.2.5. End-stage renal failure and the risk of acidosis

This situation indicates the need for capillary surveillance for ketonaemia.

5.2.6. Living in extremely cold or heated environments for professional or personal reasons

These situations (experienced by patients who are, for example, cooks and refrigeration workers) can lead to insulin inactivation.

5.2.7. Underwater diving (as a sport or profession)

Pumps are water-resistant, but not waterproof, so their submersion in water is not recommended.

5.2.8. Participation in extreme sports

This requires great caution and precise insulin dose adjustments on a case-by-case basis.

For most relative contraindications, it is extremely important to increase the frequency of checking for blood glucose and capillary ketonaemia or ketonuria to avoid diabetic ketoacidosis.

6. Need for ongoing evaluation of appropriate pump treatment

The patient, physician and technology may all change. Certain transient indications may be acceptable, but what was once the correct indication may become adverse or a contraindication. This emphasizes the need for continuous reevaluation of the patient, his theoretical knowledge and everyday ability to manage the pump treatment, and requires careful verification of the patient’s metabolic control, quality of life and satisfaction. Making such an assessment at each medical consultation with the diabetologist, and at each annual check-up with the multidisciplinary medical and paramedical team of the initiating centre, allows every patient to appreciate the benefits and risks of pump treatment. Regular patient evaluation, motivation and observation are the three main points for achieving success with this mode of treatment.

6.1. Criteria for interruption of pump treatment

6.1.1. Carelessness (or parents’ carelessness towards their diabetic child) or non-compliance with the following conditions

- Insufficient frequency of blood glucose determinations and testing for ketone bodies
- Insufficient and irregular follow-up
- No annual check-up

6.1.2. Misuse of treatment
Making wrong dose adjustments that are ineffective or even dangerous.

6.1.3 Occurrence of acute situations
Two or more episodes of diabetic ketoacidosis with no medical explanation, or more frequent severe hypoglycaemic episodes than with MDI.

6.1.4 Significant increase of HbA1c levels over therapeutic goals

6.1.5 Patient’s reluctance to use the insulin pump and desire to stop treatment is so strong that it leads to complaints

6.1.6 Occurrence of contraindications

6.2. Relative failures

The following conditions require reinforcement of education about the therapy:

- Recurrent skin infections at the infusion site
- Localized lipohypertrophic reactions at the same site
- Infrequent replacement of catheter
- Inappropriate adjustment of insulin doses
- Misuse of pump equipment

6.3. Transient interruptions

Transient interruption of pump treatment is usually necessary in hospitalized patients without a diabetologist present, with diseases that cause the patient to be unable to care for himself and by patient’s request (during the summer holidays, for instance).

7. Conclusion

The indications and contraindications for insulin pump treatment have been summarized in this review. Ultimately, however, the motivation of the patient, and specific education at the time of treatment initiation and follow-up, delivered by experienced medical and paramedical teams, are the best guarantees of its efficacy and safety.

Conflicts of interest

None.

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