Treatment of diabetes mellitus using an external insulin pump in clinical practice

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Abstract

Before the initiation of insulin pump therapy, patients must be aware of the different aspects of this form of intensive insulin therapy. Most healthcare professionals recommend a sequential approach to inform patients about CSII. Factors that need to be considered in choosing an insulin pump include its safety features, durability of the device, tolerability and comfort of the catheter, user-friendliness, technical features and appearance. The initial insulin requirements need to be individualized for the given patient, using different methods to determine the appropriate dosages for the basal rate and prandial boluses. Glycaemic targets and algorithms for insulin dose adaptation need to be learned by the patients to enable them to avoid and/or correct hypo- and hyperglycaemia/ketosis episodes. Patients are also advised on how to carry out frequent self-monitoring of blood glucose—and of ketone bodies, if necessary. Insulin pumps are now able to deliver a range of basal rates and boluses that increase the flexibility of CSII. One specific issue is the approach to meal-planning, based on carbohydrate-counting or the equivalent: this method of so-called ‘flexible insulin therapy’ can improve metabolic control (for instance, by diminishing postprandial excursions) as well as the quality of life of patients. Evaluation of the knowledge and practices of the patient can be made through a continuous educational programme carried out by experienced nurses and physicians at the start of therapy and during follow-up. In addition, it may be necessary to identify the reasons for lack of improvement in metabolic control after several months of therapy, which include pump malfunction, cannula problems, miscalculated insulin dosages and insufficient metabolic control in specific clinical situations with a high risk of metabolic deterioration (illness, exercise, concomitant drugs). Annual assessment of the patient using an itemized checklist is required to verify the continued efficacy and safety of insulin pump therapy, two main factors of success with CSII treatment.

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Résumé

Traitement du diabète par pompe à insuline externe en pratique clinique

Avant l’initiation du traitement par pompe à insuline, les patients doivent être informés des différents aspects de cette insulinothérapie intensive. La majorité des professionnels de santé recommandent une approche séquentielle pour l’éducation des patients au traitement par pompe. Certains facteurs doivent être pris en compte dans le choix de la pompe à insuline, en particulier la sécurité du matériel, sa durabilité, la tolérance et le confort des cathéters, la facilité d’utilisation, les spécificités techniques, et l’attractivité. Les besoins initiaux en doses d’insuline doivent être individualisés selon différentes méthodes, afin de déterminer respectivement la répartition des doses de base et des bolus prandiaux. Les objectifs glycémiques et les algorithmes d’adaptation des doses d’insuline sont enseignés aux patients, en particulier pour prévenir et corriger les épisodes d’hypo- et d’hyperglycémies avec ou sans cétose. Afin de favoriser un autocontrôle glycémique régulier, et la recherche de corps cétoniques si nécessaire, des conseils sont donnés aux patients. Les pompes à insuline d’aujourd’hui permettent différentes modalités de débits de base et de bolus, afin d’augmenter la flexibilité du traitement par pompe. Une des spécificités repose sur

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un plan alimentaire basé sur le comptage des glucides ou des équivalents glucidiques: cette méthode appelée insulinothérapie flexible peut améliorer le contrôle métabolique (en particulier les excursions postprandiales), mais aussi la qualité de vie des patients. Une évaluation des connaissances et des pratiques du patient est réalisée à l’aide d’un programme continu d’éducation sous contrôle d’infirmières et de médecins expérimentés, au début du traitement et durant tout le suivi des patients. Par ailleurs, il est nécessaire d’identifier au cours du suivi médical les causes de non amélioration de l’équilibre métabolique après plusieurs mois de traitement par pompe: dysfonction de la pompe, problèmes de cathéters, erreurs d’adaptation des doses d’insuline, insuffisance de surveillance métabolique dans certaines situations cliniques à risque (maladie, exercice, traitements intercurrents...). Une réévaluation annuelle à l’aide d’une « check-list » est également requise pour vérifier l’efficacité et la sécurité du traitement par pompe à insuline, deux points essentiels de succès du traitement par pompe à insuline.

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Keywords: External insulin pump; Self-monitoring of blood glucose; Hypoglycaemia; Hyperglycaemia; Ketosis; flexible insulin therapy; Quality of life; Devices; Review.

Mots clés : Pompe à insuline externe ; Autocontrôle glycémique ; Hypoglycémie ; Hyperglycémie ; Cétose ; Insulinothérapie fonctionnelle ; Qualité de vie ; Matériel ; Revue générale.

1. Initiation of CSII

As patients should be aware of the various aspects of intensive diabetes management, they need to receive ongoing education and psychological support. In most cases, pump therapy is initiated when the patient is in hospital for 3 to 5 days [1]. During the initial selection consultation with the patient, the diabetologist must be clear on several points:

- confirmation of the indication;
- an explanation of what continuous subcutaneous insulin infusion (CSII) is;
- the fact that the device must be worn 24 hours a day (except for 1.5 h);
- the need for the patient to be responsible in terms of self-management of blood glucose, which should be measured at least three times a day.

The patient may then choose a pump and catheter based on the technical features offered by the devices (possible infusion rates, dose increments, number of possible different basal rates per day) and on personal preferences (see General pump function and comparaison of available insulin pumps in 2008). The initial treatment is programmed into the device only when the patient has achieved a complete understanding of the principles behind the workings of the device, and his technical skills have been evaluated. Rapid-acting insulin analogues such as lispro, aspart or glulisin may be prescribed with the pump [2], except in a few specific medical situations such as gastroparesis.

1.1. Initial insulin dose determination

It is difficult to specify what comes under bolus action as opposed to basal rate action, except when the boluses or basal rates are very low, or at around 6 hours after the insulin bolus was delivered, suggesting that its action has come to an end.

1.1.1. Basal rate

Numerous methods can be used to determine the initial basal rate for a patient currently using multiple daily insulin injections (MDI). If the patient had been on a ‘basal-bolus’ MDI regimen, then gradually reducing the total daily basal insulin dose by 10-20% may be considered, while keeping the same prandial bolus doses using a rapid-acting analogue. As for other MDI regimens, the total daily insulin dose (including long- and rapid-acting insulin) can be divided into two parts, with 50-60% becoming the total basal dose, and 40-50% becoming the total bolus dose. In both these situations, the basal rate has to be divided by 24 to arrive at units per hour (U/h). It is often necessary to progressively increase the basal rate, notably in the late afternoon and in the second half of the night, according to capillary blood glucose (Table 1). For example, if a patient has been treated by MDI with glargine 30 U/d, and lispro 6 U before breakfast, 10 U at lunch and 10 U before dinner, then the initial basal rate with CSII could be 20 U/d or 0.8 U/h, with boluses at the same lispro dosage as before.

The basal rate may also be determined using the patient’s body weight in cases where the patient’s insulin needs are unknown. A conservative starting basal dose may be calculated using 0.22 U/kg body weight/d and dividing the result by 24 hours, to arrive at the number of units per hour (U/h). Up to four periods of basal rate variations are usually programmed to mimic physiological insulin secretion as closely as possible.

1.1.2. Prandial bolus

The prandial bolus is administered just before each meal or extra snack, provided that there is a period of at least 3 hours between boluses to avoid hypoglycaemic episodes due to insulin overlap. Initially, prandial bolus doses are kept the same as the rapid-acting analogue doses with MDI. However, when the patient has been treated with regular insulin, it is recommended to decrease the size of the preprandial
Glycaemic objectives are set independently of how insulin is administered—in other words, these targets are not specific to the insulin pump, but to the individual patient.

### 1.3. Algorithms for insulin dose adaptation

A number of methods can be used to adjust rapid-acting-analogue insulin doses in the pump: retroactive; immediate; anticipatory; and functional. A blood glucose diary or a computerized equivalent is a necessary tool for the patient and physician alike, as it can be used to analyze blood glucose results and adjust doses as necessary, and can also suggest modifications according to specific situations (such as sports activities, illness or a dinner party). The rules for dose adaptation vary according to the treatment centre. In general, however, there are two main strategies: conventional dose adaptation uses fixed doses that correspond to a fixed glucose quantity in each meal; functional or flexible insulin therapy (FIT) is described in *Flexibility of insulin therapy*.

#### 1.3.1. Basal rate adaptation (Table 1)

Nocturnal basal rates are adjusted according to glucose levels at 4am and at wake-up time (hours to be set by the patient). Basal rates during the day are set according to the fasting glycaemia before lunch and before dinner, and while fasting during the day (partial or total). It is advisable not to use more than these four basal-rate periods. When a significant increase results in a blood glucose level higher than the target range for two or three days during the preprandial period, the basal rate for that period of time needs to be increased by 0.1-0.2 U/h, depending on the previous basal rate (< or > 1.0 U/h, for example). On the other hand, on the day after a hypoglycaemic episode, the insulin basal rate should be decreased by 0.1-0.2 U/h, depending on the previous basal rate (< or > 1.0 U/h, for example), and the degree and severity of the hypoglycaemia. At home, the patient may be able to validate these basal rates during glucose-free or total fasting periods.

#### 1.3.2. Bolus adaptation according to carbohydrate intake

Boluses should be adapted according to the postprandial glucose value. It is advisable to take these measurements one or two hours after the start of a meal, which is usually when glucose levels peak in patients with diabetes [3].

In patients with a regularized carbohydrate intake at each meal, bolus doses can be increased by 10% if the postprandial glycaemia is greater than target levels for more than three days. However, if the postprandial blood glucose is below target or in hypoglycaemia, the insulin bolus should be decreased by 1-4 U the following day. In patients with flexible carbohydrate intakes, the bolus—or the ratio of carbohydrate units to insulin (see *Flexibility of in insulin therapy*)—should be adapted according to the postprandial glucose levels.

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**Table 1**

A method for determining the initial basal rate in a hospitalized patient

<table>
<thead>
<tr>
<th>1 Initial dose</th>
<th>Reduce basal insulin total daily dose by 10-20%, then divide by 24 to arrive at units per hour (U/h). Initially, only one basal rate is prescribed</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Separate the day into two parts if necessary</td>
<td>For fasting glycaemia, adjust the basal rate: 0 h to wake-up time (around 0700 h). For glycaemia before dinner (around 1900 h), adjust the basal rate: 0700 h to 0 h</td>
</tr>
<tr>
<td>3 If necessary, separate the day in four parts</td>
<td>For glycaemia at 0400 h: 0 h to 0400 h. For fasting glycaemia: 0400 h to wake-up time. For glycaemia before lunch (around 1200 h): 0800 h to lunch time. For glycaemia before dinner (around 2000 h): 1200 h to 0 h</td>
</tr>
<tr>
<td>4 Decrease each basal rate by 10% when the patient leaves hospital</td>
<td></td>
</tr>
<tr>
<td>5 At home</td>
<td>The patient can validate these basal rates through complete or glucose-free fasting periods.</td>
</tr>
</tbody>
</table>

Boluses of insulin analogues by 10-20%. Bolus calculation is estimated according to the carbohydrate amount in each meal, and these dosages may be flexible or not (see *Flexibility of insulin therapy*). Bolus doses must also take preprandial glycaemia into consideration. If it is above target, a corrective dose must be added to the bolus (see below). Preprandial bolus dosages need to be modified according to the blood glucose results obtained in the postprandial period (one or two hours after each meal).

### 1.2. Glycaemic targets

Insulin-dosing requires that the physician sets a range of glycaemic targets for each patient; for example, in a young patient without hypoglycaemic unawareness or unstable retinopathy, the targets could be as follows [3]:

| Fasting and preprandial blood glucose: 70-130 mg/dl |
| Postprandial blood glucose: < 180 mg/dl |

Postprandial glycaemia measurements should be taken one to two hours after the beginning of the meal, which is usually when glucose levels peak in patients with diabetes [3]. Patients should also be given an individualized target blood glucose range that may vary over time according to the clinical context (paediatric, pregnancy, hypoglycaemic unawareness). In cases of preproliferative retinopathy or with hypoglycaemia-unaware patients, safety targets should also be laid out, for example:

| Fasting and preprandial blood glucose: 100-150 mg/dl |
| Postprandial blood glucose: 150-250 mg/dl |

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The patient is considered to have an adequate bolus dose if the difference between the one-hour postprandial and preprandial blood glucose does not exceed 80 mg/dl (mean 40 mg/dl) [4].

1.3.3. Correction of insulin doses

Preprandial additional or corrective insulin (bolus) doses are administered when blood glucose is outside of target range, according to blood glucose measures and total insulin dosages [5]. It is advisable to determine, for each patient, the dose required to reduce glycaemia by 100 mg/dl during the initial hospitalization. For a type 1 diabetic adult patient with a normal body mass index (BMI), such a required dose is approximately 2-3 U. When correction doses are required, it is necessary to adapt the corresponding dose—the basal rate or bolus—according to the time of the hyperglycaemia to prevent another similar episode during subsequent days.

If blood glucose is outside of the target range far from meal-times and/or during the night, the use of corrective boluses is not recommended due to the high risk of hypoglycaemic episodes, except in the case of ketosis (see Management and prevention of hypoglycaemia and ketosis: specific features of pump treatment).

1.3.4. During physical activity

At these times, the most important adaptation is to reduce the basal rate and apply the temporary basal rate available with all insulin pumps at least one hour before starting the exercise until one or two hours after stopping the activity. The basal rate should be lowered by around 30-50% (and sometimes more than 70%), depending on the duration and intensity of the exercise, and the patient’s level of fitness (Table 2). In cases of intense and immediate postprandial physical activity (such as swimming or intense physical activity), it is also suggested that the preprandial boluses be decreased. An alternative solution is to disconnect the insulin pump from the catheter, but only for a maximum of two hours.

Glycaemic control is recommended both before and after exercise. To avoid hypoglycaemic episodes, additional snacks should be ingested when the physical activity exceeds 30 minutes; an intake of 20 g/h of carbohydrates is usually recommended, whatever the insulin regimen. At the next meal, patients are then advised to increase their carbohydrate intake by 50-100%. For intense physical activity or training at the end of the day (just before or after dinner), a reduction in the basal rate during the nocturnal period is also recommended.

1.3.5. Other specific situations

In cases of acute illnesses, basal insulin requirements are usually increased. These higher basal rates should then be maintained or even further increased if food intake is reduced or halted. Under such conditions, rapid sugar ingestion is recommended as well as an appropriate reduction in insulin boluses.

1.4. Other advice

Troubleshooting guidelines for dose adaptation, protocols in case of severe hyperglycaemic episodes, ketonaemia or pump failure, and emergency phone numbers should be given to each patient in writing. If glycaemic deterioration occurs, the patient should know how to check for ketonaemia or ketonuria (see Management and prevention of hypoglycaemia and ketosis: specific features of pump treatment). Also, an ambulatory clinical visit may be scheduled for one month after starting CSII to check and verify how well the patient has understood the procedure and advice given.

To avoid insulin absorption problems, a new subcutaneous infusion site usually needs to be selected every three days, and the cartridge changed as necessary.

Blood glucose levels and insulin doses should be recorded on a flow chart and reviewed by the medical team every three to four months.

Patients should have at hand an at-home ‘survival kit’, comprising insulin pens (delivering fast- and long-acting insulin analogues) and needles in case of pump failure (with the appropriate replacement doses already calculated for the patient), and a glucagon kit.

1.5. Self-monitoring load glucose

This may need to be intensified for reasons related to both treatment efficacy and safety. In addition to preprandial levels, postprandial blood glucose levels also need to be monitored at
1.5 to 2 hours after a meal, or earlier, to allow adjustment of insulin doses if necessary, according to blood glucose, food intake and activity levels [6]. This is particularly necessary at the beginning of CSII therapy to determine the patient’s insulin/carbohydrate sensitivity with flexible insulin therapy (FIT). During the first month at least, blood glucose levels should be checked six times a day; subsequently, four or five capillary glucose tests should be done each day. A bedtime test of capillary glucose is also useful for checking metabolic control before the nocturnal period, when the risk of accidental interruption of insulin delivery is high. In a large number of studies and in clinical practice, nocturnal blood glucose tests performed between 2am and 4am were found to provide useful information for a more precise adjustment of the night-time basal rate. Patients treated with an external insulin pump are exposed to the well-known risk of the concomitant occurrence of unusual hyperglycaemia and symptoms considered by clinicians to suggest ketogenic decompensation that may warrant ketone-body determination. Defining this threshold of hyperglycaemia is, of necessity, arbitrary, and published reports have not proposed a consensus value for blood glucose (2.2-3 g.L⁻¹). However, for purposes of simplification, an unusual blood glucose > 2.50 g.L⁻¹ should prompt testing to detect ketone bodies in the urine or blood. In fact, it is recommended to check for ketone bodies once a day to detect any technical problems related to the device. The most appropriate time to do this is probably at bedtime [7].

1.6. Specific situations

1.6.1. In the paediatric population

In paediatric cases, patient selection is more a ‘family’ selection, as the family is a key component in the paediatric patient’s daily management and decision-making process. Patient and parental motivation is another key factor in the successful use of the pump. The first step is to provide comprehensive information on the advantages and limitations of pump therapy, the goals of such intensive therapy, and the need for at least four blood glucose tests a day, and to assess the feasibility, degree of support and disease awareness of the family, their expectations for the CSII treatment and the commitment to providing suitable follow-up. The parents of a young patient must be able to quickly respond in the event of an accidental disconnection. The decision time must be long enough to form an effective, voluntary partnership.

The success of pump therapy depends on a large extent on the skills and experience of the multidisciplinary paediatric team. The members of the team, especially the paediatrician and diabetes nurses, interact frequently with the patient and parents. They are also responsible for the initial individual educational programme about the treatment and for follow-up. An important issue is prevention of ketoacidosis and hypoglycaemic episodes especially during physical activity, which is not always adequately covered in children and adolescents [8].

The guidelines for switching from injections to CSII have been shown to be different for the paediatric population compared with adults, and prepubertal children in particular. A reduction (~20%) in total insulin dose is necessary on initiating pump therapy in pubertal, but not prepubertal, children [9,10]. In addition, although 50% of the daily insulin dose is given as basal rates, the occurrence of maximum basal rates is different between adults and children. Several paediatric studies, involving the use of fast-acting insulin analogues in pumps in prepubertal children, have shown a maximum basal rate from after dinner until midnight. In young children, a lower basal rate is required for the second part of the night. Nocturnal basal-rate adjustment is an essential instrument for reducing the risk of hypoglycaemia in diabetic children, especially in high-risk children aged <5 years [9]. The number of basal rates in this population is frequently reported to be two or three over 24 hours (early night, late night and daytime).

Paediatricians need to be aware of these specific factors to optimize the efficacy of CSII therapy. In children, small changes in bolus and basal rates are recommended to avoid fluctuations in blood glucose. Very small changes, such as 0.05 or 0.1 U/h for basal rates or boluses, can be accurately delivered by a pump-unlike pens and syringes-and are particularly suitable for very young children.

1.6.2. During pregnancy

Ideally, insulin pump therapy should be initiated prior to pregnancy to obtain near-normal glycaemia, thereby reducing the risk of spontaneous abortion and fetal malformations. Nevertheless, insulin pump therapy can be started during pregnancy in carefully selected patients. The criteria include patients who are highly compliant with capillary glucose testing (8 to 10 times a day), those who have failed to achieve acceptable control with MDI therapy and those who have asked to be treated with an insulin pump. These patients must also agree to monitor ketone bodies.

Insulin pump therapy should be initiated in specialist centres. The patient has to be well trained in pump use to spot any mechanical problems such as faulty placement of the insulin syringe or a kink in the infusion cannula that, if left unchecked, can interrupt insulin release and lead to hyperglycaemia or ketoacidosis. Hyperglycaemia, which is likely whenever pump infusion is interrupted, is particularly undesirable during pregnancy.

Although any type of pump may be used, insulin requirements are sometimes very high near the end of pregnancy so, in general, it is better to use a pump with a large capacity. Also, catheters should be long even for thin women, and it is better to use a tangential catheter rather than a straight one.
The abdominal wall should be avoided during pregnancy as insulin absorption becomes unpredictable with the progression of pregnancy, so alternative infusion sites need to be selected. Patients should change their pump catheter every 24 to 48 hours, and are instructed to change infusion site if they have two unexplained blood glucose levels >200 mg/dl.

Approximately 50-60% of the total dose is given as a basal insulin infusion, with the remaining insulin given as boluses prior to each meal. The basal rate is usually reduced while the patient is sleeping and in the early morning hours, but is increased as morning approaches. The remainder of the calculated insulin dosage is administered as boluses with the patient’s meals or snacks. However, protocols may vary during pregnancy, with a reduction of insulin requirements up to week 12 of pregnancy and an increase from then up to week 35 of gestation.

Programmable square-wave bolus doses are useful during pregnancy as it reduces the risk of glucose excursions and hyperglycaemia. The square-wave bolus can be administered at the start of a meal, but extended over several hours to reduce the hyperglycaemic peak after meals due to delayed gastric emptying in normal pregnancy as well as gastropathy.

During labour, the pump may be maintained with a single basal insulin infusion and strict glycaemia monitoring. After delivery and during the breastfeeding period, the patient’s requirements return to their prepregnancy levels except that the basal insulin infusion and boluses are decreased (by about 30%) to avoid hypoglycaemia.

Use of CSII during pregnancy requires skillful professional care especially by the obstetric staff, as well as careful selection of patients, meticulous patient monitoring and thorough patient education.

2. Management and prevention of hypoglycaemia and ketosis: specific features of pump treatment

2.1. Hypoglycaemia

Several studies suggest that the risk of moderate or severe hypoglycaemia is not increased by pump treatment [11-16]. There is, however, a specific risk of hypoglycaemia, or worsening of preexisting hypoglycaemia, related to the possibility of excess insulin infusion. However, experience has shown this risk to be more theoretical than actual, and it can be considerably reduced through proper patient education on the technical aspects of the pump, and by alarm and other safety features built into the pumps (Table 3).

Management of a hypoglycaemic episode during pump therapy is comparable to that used for a multiple-injection basal-bolus regimen [17,18]. In cases of severe hypoglycaemia and while awaiting specialized care by the medical team, disconnecting the pump may reduce the time spent in hypoglycaemia.

### Table 3
Specific risks of hypoglycaemia and ketosis related to pump therapy

<table>
<thead>
<tr>
<th>Hypoglycaemia prolonged by persistent excess insulin infusion</th>
<th>Mechanism</th>
<th>Detection and/or prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump ‘runaway’ due to too much pressure in the reservoir</td>
<td>Theoretically impossible according to material technical specifications</td>
<td></td>
</tr>
<tr>
<td>Incorrect pump programming: excessively high basal rate; excessively high or supplemental bolus; time incorrectly adjusted; changed insulin concentration</td>
<td>Patient education (i.e. programming, checks); safety features: automatic pump cut-out; overinjection alarm; flow interruption and maximum bolus alerts; push-button lock; clear programming displays; history recall of last boluses delivered; ability to cancel bolus</td>
<td></td>
</tr>
<tr>
<td>Electronic or mechanical failure</td>
<td>Safety alerts, most frequently for SMBG and ketone-body detection</td>
<td></td>
</tr>
<tr>
<td>Empty reservoir</td>
<td>Safety alerts</td>
<td></td>
</tr>
<tr>
<td>Catheter occlusion</td>
<td>SMBG and ketone-body detection; delayed occlusion alert</td>
<td></td>
</tr>
<tr>
<td>Insulin leakage, air bubbles</td>
<td>SMBG and ketone-body detection (no alert)</td>
<td></td>
</tr>
</tbody>
</table>

SMBG, self-monitoring of blood glucose

2.1.1. Fine-tuning of insulin doses

The risk of hypoglycaemia is reduced by the exclusive and continuous administration of fast-acting insulin, and the number of possibilities offered by the pump for adjusting insulin doses. The basal rate can be modified every 30-60 minutes to maintain a near-perfect match to the patient’s insulin needs and variations throughout the day, and to keep blood glucose levels stable during interprandial periods, thereby allowing meals to be taken later than usual without major risk of hypoglycaemia. As basal rates can be adjusted to a precision of 0.05-0.10 U/h and boluses by 0.1-0.5 U, when the insulin is diluted, so even finer modifications can be made, thereby reducing the risk of hypoglycaemia both in adults with low daily needs and in children [9].

2.1.2. Temporary basal rates

Temporarily reducing the basal rate can prove useful for patients engaging in physical activity, especially unplanned activities. Ideally, the rate should be reduced (by 30-50%, depending on the type and intensity of the exercise) [18,19] at least one or two hours before the exercise as well as dur-
Routine testing for ketone bodies should be performed when excess carbohydrate intake. For this reason, patients should that, in itself, was likely to cause hyperglycaemia (such as later identified or treated insulin deficiency [25,26], fostered by cases of ketoacidosis during pump therapy are the result of a hyperglycaemia occurs, whatever the circumstances. Most each hyperglycaemic episode arising during pump therapy.

2.2.1. Identifying insulin deficiency

Customizing prandial insulin infusions allows patients to avoid certain types of hyperglycaemia that can occur at the end of the meal, such as when the meal lasts longer than expected or when the carbohydrate content is lower than expected. Any method can be considered as the number of boluses is not a problem for the patient. Part of the bolus can be administered at the beginning or halfway through a meal, and the remainder at the end of the meal or with dessert, or it can be taken with each course. Bolus infusion over an extended period (from 30 minutes to 8 hours with some pumps), and perhaps combined with an immediate bolus, can be a solution in this particular situation. This approach is especially useful for patients who have documented gastroparesis [21] or for those whose blood glucose decreases rapidly in the early postprandial phase to subsequently rise again [22].

2.2. Hyperglycaemia and ketosis

The risks of hyperglycaemia, ketosis and ketoacidosis specifically related to pump therapy are potentially higher than with MDI treatment [12,23]. If insulin infusion is stopped as a result of a technical problem with the infusion kit or improper use of the kit, this may lead to a deficiency of rapid-acting insulin [24] (Table 3). Thus, the prevention of ketoacidosis depends on early identification of an insulin deficiency, and the swift implementation of corrective measures and troubleshooting to determine the cause of the ketoacidosis. It also requires comprehensive patient education through an experienced centre.

2.2.2. Symptomatic correction of insulin deficiency

Once the insulin deficiency has been identified, it needs to be corrected by subcutaneous rapid-acting insulin analogue supplements. The first supplement is delivered using a prefilled pen. If the pump is to be used again, the cause of the problem has to be identified and resolved (the catheter changed, for example) before using it to deliver the supplemental insulin, which may lead to a delay in treatment. Supplements should be renewed every 2-3 hours until no more ketone bodies are present. The dosage of the insulin supplements will vary according to the levels of blood glucose and ketone bodies, and the usual practices of the medical team (Table 4) [30,31]. Should the patient fail to improve (worsening hyperglycaemia, continued presence of ketone bodies) following the administration of two insulin supplements, or the clinical signs of worsening appear (presence of confusion, vomiting), the patient or his family should contact the initiating centre to decide whether or not to continue with ambulatory treatment. This is especially necessary with ketonuria > + + or ketonaemia > 3 mmol/l, when the likelihood of diabetic ketoacidosis is particularly high [31,32].

2.2.3. Troubleshooting the cause of and correcting an insulin administration defect

The attempt to identify and correct the cause of glycaemic deterioration begins after the first insulin injection by pen, and involves a thorough check of the infusion kit, including inspection of the withdrawn catheter/cannula along with the infusion site. This inspection should first look for an obstruction or folding (by sending a bolus through the kit), and check that the cannula has not become dislodged. Pump therapy can be restarted once the catheter, reservoir and, if necessary, the
insulin have been changed (because of insulin denaturation and/or old cartridges). Over the next few hours, the patient may need supplemental insulin doses, which can be administered with the pump as boluses. Should the pump prove (or appear to be) the cause of the problem, the supplemental doses should be administered through multiple injections until the defective item has been replaced by the provider.

2.2.4. Precautionary measures: self-monitoring and the ‘survival kit’

Patients have to be able to identify and troubleshoot at an early stage, even before any alarm is triggered, any problems that might interrupt the administration of insulin. For this reason, they are advised to check their blood glucose at least four times a day (and sometimes more) and to carry with them at all times a self-monitoring kit (glucose meter, lancet, strips for testing for capillary blood glucose and ketone bodies), a rapid-acting-analogue insulin pen and needles. The recommendations of the paramedical ALFEDIAM, updated in 2007, insist upon these important aspects of patient monitoring [33].

### Table 4
Management of hyperglycaemia with ketosis

<table>
<thead>
<tr>
<th>Ketone bodies</th>
<th>Blood glucose (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine: 0 or trace</td>
<td>&lt; 250</td>
</tr>
<tr>
<td>Blood: &lt; 1 mmol/l</td>
<td>No change</td>
</tr>
<tr>
<td>Urine: +</td>
<td>0-5%</td>
</tr>
<tr>
<td>Blood: 1–1.4 mmol/l</td>
<td>5%</td>
</tr>
<tr>
<td>Urine: ++ or +++</td>
<td>10%</td>
</tr>
<tr>
<td>Blood: &gt; 1.5 mmol/l</td>
<td>15%</td>
</tr>
<tr>
<td>Urine: trace</td>
<td>0-10%</td>
</tr>
<tr>
<td>Blood: ≥ 0.5 mmol/l</td>
<td>15-20%</td>
</tr>
<tr>
<td>Urine: + or blood 0.8-1 mmol/l</td>
<td>4 U of insulin (3-5 U)</td>
</tr>
<tr>
<td>Urine: ++ or blood 1.6-2 mmol/l</td>
<td>8 U of insulin (6-10 U)</td>
</tr>
<tr>
<td>Urine: +++ or blood 2.4-3 mmol/l</td>
<td>12 U of insulin (9-15 U)</td>
</tr>
</tbody>
</table>

For hyperglycaemia > 250 mg/dl (protocol from Department of Diabetology, Rangueil Hospital, Toulouse)

<table>
<thead>
<tr>
<th>Ketone bodies</th>
<th>Diagnosis and management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine: 0</td>
<td>Normal</td>
</tr>
<tr>
<td>Blood: &lt; 0.3 mmol/l</td>
<td>Re-check blood glucose and set perfusion, ketone bodies after 2 h</td>
</tr>
<tr>
<td>Blood: 0.3-0.4 mmol/l</td>
<td>Suspect</td>
</tr>
<tr>
<td>Urine: ≥ trace</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Blood: ≥ 0.5 mmol/l</td>
<td>Supplemental doses of insulin every 2-3 h</td>
</tr>
</tbody>
</table>

3. General pump function and comparison of available insulin pumps in 2008

The goal of insulin pump therapy is to mimic the normal function of the pancreas as closely as possible. Nowadays, insulin pump technology is relatively well developed. Modern insulin pumps are about the size of a pager, and are able to administer rapid-acting insulin analogues to the majority of patients at precise basal and bolus rates to control blood glucose levels throughout the day and night. The newer pumps have even longer-lived batteries, and hold around twice as much insulin as did the older pumps. More specifically, the technical sophistication of these devices has made them much easier to use in young children. This review discusses how insulin pumps work, and the differences between bolus and basal rate delivery with the currently available models.

Subcutaneous insulin infusion (CSII) via an insulin pump helps to overcome the limitations of multiple daily injections (MDI) by imitating physiological insulin secretion. The two main components of insulin secretion are basal and prandial insulin secretion. The pump controls the infusion rates to create both basal and bolus profiles.

The benefits of CSII may vary according to the patients’ age. For adolescent insulin-pump users, they have the option to programme a slightly higher insulin infusion rate for the early morning hours to address a rise in blood glucose at that time. Elderly patients with longstanding type 1 diabetes who experience overnight hypoglycaemia can programme the pump to reduce the amount of basal insulin at night. Lifestyle benefits are a major advantage of insulin pump therapy in younger patients as they can programme several basal rates at different times throughout the day. They can also modify their insulin regimen by using a temporary basal rate during physical activity, depending upon the intensity and duration of the exercise. This is possible because of the unique ability of the latest insulin pumps to allow precise basal rates to be programmed and modified at different times of the day [34].

The pump user can also change the time-action profile of insulin boluses according to the expected type, size and duration of meals. This confers greater flexibility in meal timing and quantities. Thus, the modern insulin pump offers several technological features that facilitate fine-tuning of the daily insulin profile.

3.1. General pump function

3.1.1. Basal insulin rates

Treatment starts with a single basal rate that is monitored before any additional basal rates are programmed. An extensive glucose profile is important for counteracting the dawn phenomenon or identifying those patients who are prone to overnight hypoglycaemia. If readings are > 300 mg/dl, then
checking capillary blood glucose at bedtime, 12am, 3am and 6am, and adjusting the overnight basal rate, is recommended. Experience shows that adults often need an increase in basal rate in the dawn hours (from 4-9am) whereas children often need an earlier increase in basal rate. For basal rate adjustments during the day, it is recommended to check capillary blood glucose before mealtimes, and it may also be worth skipping a meal to check it every two hours over the following six hours. Additional adjustment to the daytime basal rate is necessary if capillary blood glucose is > 300 mg/dl. Most patients need no more than two or three basal rates per 24 hours or when initiating pump therapy during a stay in a hospital care unit (Fig. 1).

Lin, followed by a sustained administration and then a rapid decrease in insulin. It can provide adequate insulin coverage for patients enjoying an extended multiple-course meal or those who have slow gastric emptying due to gastroparesis. Pumps can also deliver a combined bolus, which is a standard bolus followed by an extended bolus. This is helpful for meals that contain rapidly absorbed nutrients followed by multiple courses. A dual-bolus profile also appears to be slightly better at mimicking physiological insulin secretion and reducing postprandial glucose excursions [22]. In that study, nine type 1 diabetic patients using CSII ate pizza, tiramisu and cake for four consecutive Saturdays, each time using a different type of bolus (Fig. 3).

3.1.2. Bolus insulin administration

Nowadays, insulin pumps are able to administer different types of boluses (Fig. 2). The standard insulin bolus has an immediate delivery followed by a decrease in insulin. However, some patients may be restricted by the time-action profile of fast-acting insulin analogues and may benefit from an extended bolus. This is characterized by a rapid rise of insulin, followed by a sustained administration and then a rapid decrease in insulin. It can provide adequate insulin coverage for patients enjoying an extended multiple-course meal or those who have slow gastric emptying due to gastroparesis. Pumps can also deliver a combined bolus, which is a standard bolus followed by an extended bolus. This is helpful for meals that contain rapidly absorbed nutrients followed by multiple courses. A dual-bolus profile also appears to be slightly better at mimicking physiological insulin secretion and reducing postprandial glucose excursions [22]. In that study, nine type 1 diabetic patients using CSII ate pizza, tiramisu and cake for four consecutive Saturdays, each time using a different type of bolus (Fig. 3).

A French multicentre randomized study comparing standard and dual-wave boluses is currently looking to determine whether or not a more ‘physiological’ bolus profile does indeed improve metabolic control in everyday life. Patients can customize their bolus regimens to their dietary intake and habits using FIT. The latest pumps have a built-in bolus calculator that determines the appropriate insulin dose: patients need only enter their blood glucose target, carbohydrate ratio and insulin-sensitivity factor. This function can reduce errors in calculation and decrease the number of correction boluses required.

3.2. Comparison of currently available insulin pumps

There are differences between insulin pumps, and it is important to examine these variations to help patients select the best pump for their treatment needs and lifestyle (Table 5). The final choice is important as the outlay for a new pump is only reimbursed by the French national health insurance system every four years.
### 3.2.1. Medtronic MiniMed Paradigm 515/715

The MiniMed Paradigm pump by Medtronic (Northridge, CA, USA) has a scroll bar on the display face to facilitate moving through the menus. The pump is able to deliver several types of insulin boluses, including a normal (immediate) bolus, an extended square-wave bolus and a combination of normal plus extended dual-wave bolus, depending on the type of meal and its timing. As part of FIT, patients can enter their carbohydrate intakes into the pump and the ‘Bolus Assistant’ will calculate the suggested insulin dose.

Paradigm can administer bolus rates from 0.1-25.0 U in 0.1-U increments and also has an audio bolus option. Basal rates can range from 0.05-35.0 U/h in 0.05-U/h increments. The pump also has a memory feature that allows the last 24 boluses, and the total insulin dose for the last 14 days, to be viewed on the pump display, while the last 90 days are

<table>
<thead>
<tr>
<th>Pump Type</th>
<th>Paradigm 515/715</th>
<th>ACCU-CHEK Spirit</th>
<th>Deltec Cozmo</th>
<th>IR-2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>Medtronic</td>
<td>Roche Diagnostics</td>
<td>Smiths Medical</td>
<td>Animas Novalab</td>
</tr>
<tr>
<td>Size (mm) (L x W x H)</td>
<td>515 (76 x 50 x 20)</td>
<td>81 x 20 x 55</td>
<td>88.9 x 19 x 50</td>
<td>74 x 19 x 51</td>
</tr>
<tr>
<td>Screen size (mm)</td>
<td>46 x 21</td>
<td>36 x 15</td>
<td>29 x 30</td>
<td>31 x 31</td>
</tr>
<tr>
<td>Weight (with battery and reservoir) (g)</td>
<td>100/108</td>
<td>110</td>
<td>94</td>
<td>98</td>
</tr>
<tr>
<td>Reservoir capacity (IU)</td>
<td>180/300</td>
<td>315</td>
<td>300</td>
<td>200</td>
</tr>
<tr>
<td>Catheter connection</td>
<td>Specific (Paradigm)</td>
<td>Standard (Luer lock)</td>
<td>Standard (Luer lock)</td>
<td>Standard (Luer lock)</td>
</tr>
<tr>
<td>Bolus rate amount</td>
<td>0.1-25.0 U (0.1-U increments)</td>
<td>0.1-25 U (0.1-U increments)</td>
<td>0.05-75 U (0.05-U increments)</td>
<td>0.05-35.0 U (0.05-U increments)</td>
</tr>
<tr>
<td>Bolus type*</td>
<td>N, E, D</td>
<td>N, E, D</td>
<td>N, E, D</td>
<td>N, E, D</td>
</tr>
<tr>
<td>Bolus ‘calculator’</td>
<td>Bolus Assistant</td>
<td>Bolus calculator on PDA</td>
<td>Bolus Wizard</td>
<td>Carb Smart</td>
</tr>
<tr>
<td>Flexible insulin therapy</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Basal rate range (U/h)</td>
<td>0.0-35 U/h (0.05 U/h increments)</td>
<td>0.0-20.0 U/h (0.1 U/h increments)</td>
<td>0.0-35 U/h (0.05 U/h increments)</td>
<td>0.0-35 U/h (0.025 U/h increments)</td>
</tr>
<tr>
<td>Number of basal rates per day</td>
<td>48</td>
<td>24 of 1 hour each</td>
<td>48</td>
<td>12</td>
</tr>
<tr>
<td>Basal delivery intervals</td>
<td>3-min, 0.005</td>
<td>15 min to 24 h</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Delivery accuracy</td>
<td>± 5%</td>
<td>± 5%</td>
<td>± 5%</td>
<td>± 5%</td>
</tr>
<tr>
<td>Memory: daily total insulin</td>
<td>Last 14 days on display, 90 days downloadable</td>
<td>Last 30 days on display, last 6000 events downloadable</td>
<td>4000 events</td>
<td>255 on display</td>
</tr>
<tr>
<td>Display format</td>
<td>Menu-driven</td>
<td>Icons and text</td>
<td>Menu-driven</td>
<td>Menu-driven</td>
</tr>
<tr>
<td>Display backlight</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Alert types</td>
<td>Beep or vibrate</td>
<td>Beep or vibrate</td>
<td>Beep or vibrate</td>
<td>Beep or vibrate</td>
</tr>
<tr>
<td>Occlusion alert</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Low-battery alert</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Low-reservoir alert</td>
<td>Yes for 30, 20, 10 U remaining</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Resistance in the water</td>
<td>Watertight</td>
<td>Watertight (up to 2.50 m depth and for 60 min)</td>
<td>Waterproof</td>
<td>Waterproof</td>
</tr>
<tr>
<td>Connection to PC</td>
<td>Yes</td>
<td>Yes</td>
<td>Palm OS (ezManager)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*N: Normal immediate bolus - E: Extended square-wave bolus - D: Dual-wave bolus
downloadable. Patients can use a wireless remote to operate the pump worn discreetly beneath their clothing. Alarms include infusion-line occlusion, low battery and low insulin reservoir. The Medtronic MiniMed pump has a watertight rating (IPX-8) up to a depth of 8 feet (2.44 m) for up to 30 minutes, and uses a standard AAA 1.5-V battery that keeps maintenance costs down and is convenient to replace. Other pumps require batteries that are less widely available. On the other hand, the Paradigm is the only pump that requires a specific catheter. Finally, the choice between the 515 and 715 models depends solely on the patient’s insulin daily needs, as the two models have different reservoir capacities. The newer 522/722 models can be integrated with Medtronic’s glucose sensors for real-time continuous glucose readings. However, these pumps are not yet reimbursable.

3.2.2. Roche Diagnostics/Disetronic ACCU-CHEK Spirit
Disetronic Medical Systems (Burgdorf, Switzerland) makes the D-TRON and H-TRON lines of pumps, and the latest ACCU-CHEK Spirit model. These pumps use icons on their display rather than menus. They have the largest insulin-reservoir capacity, holding 315 U of insulin. The D-TRON is the first insulin pump to use a prefilled insulin cartridge rather than a disposable cartridge that requires manual refilling by the patient. This is a convenience feature that some patients may well appreciate. The two Disetronic pumps can also deliver an extended bolus, and have backlit enhanced memory features and alarms that can be set on vibration mode. The ACCU-CHEK Spirit is the first pump able to communicate with a PDA (personal digital assistant) to help the patient target the insulin dose. It also has the IPX-8 standard waterproof rating up to a depth of 2.5 m for up to 60 minutes.

3.2.3. Animas Novalab IR-2020
Among the newer insulin pump companies in the American marketplace is the Animas Corporation (Frazer, PA, USA). The IR-2020 Pump incorporates some novel features, including a menu-driven display, a backlight and an audio bolus option for rapid administration of boluses without having to look at the display screen. The pump can administer small bolus amounts of 0.05-35.0 U in 0.05-U increments as well as extended boluses. One particular feature of the 2020 is insulin delivery in ‘pulses’ at 3-minute intervals and in amounts as tiny as 0.005 U. However, whether this feature, which mimics pancreatic secretion, has any clinical benefit in terms of metabolic control has yet to be established. The pump also has an excellent memory, able to store and display the last 600 boluses, and the total 24-hour insulin doses over the last 120 days. Its alarm systems include infusion-line occlusion, low battery and low insulin reservoir. The Animas pump has the IPX-8 standard waterproof rating, which may be an important feature for those who indulge in water sports.

3.2.4. Deltec Cozmo
Cozmo (Smiths Medical, St. Paul, MN, USA) is the smallest pump on the market, which may be something that many patients, especially women, will appreciate, and is also waterproof (up to 2.4 m for 330 minutes, or 3 minutes at 3.6 m). A new insert system is now available. This model also has a useful option that reminds the user to test for capillary blood glucose after meals, and can also verify whether or not the last bolus was delivered (considering the normal time of insulin bolus delivery is from one day to the next).

3.3. Conclusions and future directions

Given the current major progress in insulin pump technology, it is not surprising that glucose sensors will soon also be built into these devices [such as the Medtronic MiniMed RT (for real-time)]. At present, patients are still responsible for testing and interpreting their own blood glucose trends, and for modifying their basal insulin rates and boluses accordingly. Nevertheless, insulin pump therapy appears to be evolving towards a closed-loop system. As continuous glucose sensors are developed, they will soon be able to provide information to the insulin pump. Automatic—or, more likely, semi-automatic—inulin dose adjustments can then be made based on these measurements and on other individualized parameters derived from the patient’s previous glucose trends.

4. Flexibility of insulin therapy

Functional or flexible insulin therapy (FIT) represents a form of intensified insulin therapy that enables basal and prandial insulin needs to be managed separately through a basal-bolus or basal-prandial regimen. Such an FIT regimen was carried out initially with two injections of Ultratard (ultralente) and three injections of regular insulin 30 minutes before each meal or, even better, as intramuscular injections [35]. These injections have now been replaced by rapid- and slow-acting analogues delivered through a pump. A major advantage of this method is that patients can enjoy total freedom with regard to meal timings. The preprandial insulin dose is determined according to the amount of carbohydrates to be consumed. Patients need to learn how to calculate the amount of carbohydrates in their meals. If a blood glucose level is high, the patient can bring it back to within the target range using supplemental doses of fast-acting insulin analogues. All of these adjustments can be made using algorithms individually tailored to the given patient. FIT is a highly sophisticated learning process that allows the patient to become more fully knowledgeable about the system and to have better control over it through self-adaptation of the individualized algorithms based on acquired experience. Furthermore, despite the freedom of this method, no glycaemic deterioration has been reported [36].
Is pump therapy compatible with FIT? Several studies show that it is [37-40], and one, carried out in children, goes so far as to suggest that the pump is the most suitable tool for FIT [41]. Pump therapy has the dual advantage of offering a flexible approach to both prandial needs and basal rates (Tables 6 and 7).

The latest insulin pumps are designed for direct FIT operation. The patient’s parameters, such as supplemental insulin doses and units per portion, can be programmed into most pumps. Blood glucose and the number of carbohydrate portions for each meal can also be entered, and the total bolus automatically calculated and proposed to the patient: for example, a patient may need 2 U/20 g of carbohydrate, and his supplemental dose is 3 U to reduce blood glucose by 100 mg/dl. Before a meal, if his blood glucose level is 200 mg/dl and he plans to eat three portions (for example, 100 g of potatoes, 40 g of bread and 1 orange), then his bolus will be 2 U x 3 portions = 6 U, and the supplemental dose of 3 U makes a total bolus of 9 U (6 U + 3 U). However, the patient could just enter his blood glucose of 200 mg/dl into the pump along with the number of carbohydrate portions in his meal (which has different names according to the pump)—in this case, three portions. The 9-U dose will then automatically be proposed to the patient, who can choose to accept it or change it. The use of this option differs from one pump to another, and is optional. In real life, however, this method is often not used by patients as it may appear to be too complicated or the patient simply lacks the necessary information.

4.1.2. Do proteins need to be counted?
Postprandial glycaemia does not differ whatever the meal’s protein content, although blood glucose rises considerably more at night after a patient has had a protein-rich meal compared with a meal containing little protein [42]. The proposed explanation is that the increase in nocturnal glucagonaemia has been stimulated by the protein-rich meal [43]. It may be advisable to administer a dual-wave bolus, delivered over several hours, if a meal is protein-rich. Algorithms for this are currently being validated.

4.1.3. Multiple boluses
FIT allows the patient to vary the number of meals he would like. If the patient is under MDI therapy, this can involve a large number of injections, which can be uncomfortable. In contrast, it is easier to administer repeated prandial doses in the form of boluses.

4.1.4. Bolus before or after the meal?
Patients prefer injecting prandial insulin after a meal as it is then easier to calculate the portions of ingested carbohydrate. One study, involving 860 type 1 diabetics, compared the effects on blood glucose control of administering glulisine, a fast-acting insulin analogue, both before and after a meal [44]. HbA1c was moderately increased by 0.2%, while postprandial blood glucose levels were less well controlled. An insulin pump allows patients to get around this difficulty by splitting the bolus into two parts, delivering a minimal dose at the start of the meal and the remainder afterwards. However, this approach needs further investigation before any definitive conclusions can be made.

4.2. Basal rates
4.2.1. Freedom in meal timing
Basal insulin control is more flexible when insulin is administered continuously over a 24-hour period, and the pump method has less variability of action than multiple injections [45]. With a basal-bolus insulin regimen, is it possible to vary mealtimes without drawbacks? The question seems somewhat incongruous now, but this was a major issue back in the days...
when meal timings and content had to be strictly adhered to. Chantelau et al. carried out detailed studies of the glycaemic profiles of 10 type 1 diabetic patients treated with portable pumps under either a strict regime or a ‘freer’ one. Their results showed that a variation of 90 minutes in meal timings had no effect on basic blood glucose levels [38].

4.2.2. Validation of basal rates

Apart from the information it provides and greater flexibility in meal timing (especially when factoring in religious considerations), fasting can validate the selected basal rate(s). Nevertheless, a number of questions remain, such as the choice between total fasting or carbohydrate fasting (and then whether or not protein intake needs to be compensated for by minimal doses of fast-acting insulin), and between a 24- or 36-hour fast [46]. The hyperglycaemia-inducing action of proteins suggests that total fasting (or partial if necessary) is preferable. Fasting provides the answers to three questions: Is the dawn phenomenon properly compensated for (morning fast)? Is afternoon blood-glucose control appropriate (lunch-time fast)? Is the basal rate during the first part of the night correct (dinnertime fast)? This means that the insulin pump is an ideal tool for FIT in diabetic patients (Table 7). Current pump designs offer features that appear to aid FIT, although their actual worth remains to be validated.

Conflicts of interest: Nathalie Jeandidier carried out clinical trial as main clinical investigator for Lilly and Sanofi-Aventis.

Jean-Pierre Riveline has no conflict of interest.

Nadia Tubiana-Rufi and Anne Vambergue have not declared any conflicts of interest.

Bogdan Catargi has no conflict of interest.

Vincent Melki carried out clinical trials as co-investigator for Medtronic. He attended conferences organized by Abbott as contributor and by Abbott and Medtronic Inc. as audience member.

Guillaume Charpentier has no conflict of interest.

Bruno Guerci has no conflict of interest.

References


Appendix

This article is a collaborative work by the following authors, each of whom has been responsible for writing a specific part of this report:

Part 1: Nathalie Jeandidier, Jean-Pierre Riveline, Nadia Tubiana-Rufi, Anne Vambergue and Bruno Guerci

Part 2: Vincent Melki and Bruno Guerci

Part 3: Bogdan Catargi

Part 4: Jean-Pierre Riveline and Guillaume Charpentier.