Consensus Evidence-based Guidelines for Use of Insulin Pump Therapy in the Management of Diabetes as per Indian Clinical Practice

Jothydev Kesavadev*, Sunil M Jain**, A Muruganathan***, Ashok Kumar Das****

Abstract

The use of insulin pump in diabetes is likely to increase with recent advances in technology. Although the evidence for the superiority of pumps over multiple daily injections (MDI) is inconsistent, data from accumulating uncontrolled studies indicate greater reductions in glycated haemoglobin in patients switching to continuous subcutaneous insulin infusion (CSII) from MDI therapy. Due to the variability in insulin requirements and sensitivity to CSII pumps, hyperglycaemia in these patients is managed by endocrinologists using individualised therapy. A panel of experts reviewed the existing guidelines and framed recommendations specific to the clinical practice in Indian conditions for use of CSII pumps in the management of hyperglycaemia. Selection of right patient with basic education, motivation and learning skills are essential for successful implementation of CSII therapy with sophisticated programmes. Rapid acting insulin analogues with better pharmacokinetic and pharmacodynamic profile, physical and chemical stability and compatibility with most commercially available insulin pumps are preferred over regular insulin to achieve safe and stable glycaemic control. Further, educating pump users on proper use of CSII pumps, insulin dose adjustments, and handling of accessories are recommended in the current consensus guidelines. Practice of self-monitoring of blood glucose and glycated haemoglobin levels are essential to adjust insulin dosage for the management of diabetes. Use of CSII pumps in special patient populations should be carefully assessed and initiated by endocrinologist. The proposed guidelines can form a basis for use of CSII pumps in the management of hyperglycaemia in the Indian scenario.

Introduction

Burden of diabetes

The global rise in the number of people with diabetes is alarming with 8.26% prevalence and 5.09 million deaths due to diabetes in 2012.1 The corresponding numbers for prevalence and death due to diabetes in India are 9.09% and 1.06 million deaths, respectively due to diabetes in 2011.2 With the progressive nature of type 2 diabetes mellitus (T2DM) and continuous addition of new cases of diabetes, the number of people with diabetes complications and those requiring insulin for the management of hyperglycaemia also increases.

Insulin therapy in patients with diabetes

Insulin is the optimal therapy for the management of hyperglycaemia in patients with diabetes. The American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) position statement indicated insulin as second-line therapy for patients with uncontrolled diabetes (high levels of glycated haemoglobin) treated with metformin alone.3 The publication of Diabetes Control and Complications Trial (DCCT) results4 confirmed the benefits of intensified insulin therapy (IIT) in achieving good glycaemic control in patients with diabetes and thereby reducing the risk of complications. IIT usually involves administration of insulin either by multiple daily injections (MDI) of long acting insulin and short-acting insulin or using an external insulin delivery device such as continuous subcutaneous insulin infusion (CSII) pump.4

Continuous subcutaneous insulin infusion

CSII is the most sophisticated and precise insulin delivery method which uses a small programmable pump with a fine tube connected to a soft plastic cannula (introduced by needle), that goes into the subcutaneous tissue under the skin, often in the abdomen.5 The aim of CSII is to try to mimic endogenous insulin delivery profile more closely to the pattern of insulin delivery from pancreas, by providing continuously infused, low-volume basal insulin for fasting periods and delivery of increased rate boluses to cover meals.6,7 The insulin pump allows the user to programme many different basal rates of infusion depending on individual lifestyle. In addition, the user can programme the pump to deliver a bolus insulin dose (large dose of insulin) during meals to cover the excess demands of carbohydrate ingestion. Most pumps use rapid-acting insulin analogues (RAIAs) i.e. lispro, aspart and glulisine, as they have a rapid onset and shorter duration than regular human insulin (RHI).8

Advantages of CSII therapy

Insulin delivery via CSII pump is more consistent and precise in providing patient’s individual insulin requirements with low risk of severe hypoglycaemia than conventional delivery devices. Evidence from several studies indicate that CSII provides equal or better glycaemic control, lower hypoglycaemic episodes, better quality of life, improved psychosocial functioning and more flexibility with lifestyle when compared to MDI therapy.9,10 CSII should be indicated in patients to improve glycaemic control with a view to reducing the risk of long-term complications, reduce problems with hypoglycaemia, in particular for people with hypoglycaemic unawareness, and possibly prevent cognitive impairment in young children and improve health-related quality of life through more flexible lifestyles and activities.10 Moreover in patients with poor adherence associated with fear of MDI, CSII therapy may be considered an effective alternative to MDI.
Table 1: List of common indications and contraindications for insulin pump therapy in patients with diabetes

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any patient with type-1/type-2 diabetes on insulin therapy seeking improved quality of life</td>
<td>Psychiatric illness</td>
</tr>
<tr>
<td>Patients with diabetic complications (e.g., nephropathy, neuropathy)</td>
<td>Unwillingness to self-monitor</td>
</tr>
<tr>
<td>High insulin requirement</td>
<td>Lack of time and motive</td>
</tr>
<tr>
<td>Frequent episodes of severe hypoglycaemia with multiple daily injections (MDI) therapy</td>
<td>Cannot be trained on essential technical aspect of insulin pump therapy</td>
</tr>
<tr>
<td>Any patient requiring exogenous insulin therapy but not controlled with optimal MDI therapy</td>
<td></td>
</tr>
</tbody>
</table>

Statistics of CSII use

Insulin pump therapy in the management of hyperglycaemia has been used for more than three decades globally and more than a decade in India. An estimated 20% to 30% of patients with type 1 diabetes mellitus (T1DM) and less than 1% of insulin-treated patients with T2DM in the United States use insulin pumps. Globally, more than three lakh people with diabetes use CSII for the management of hyperglycaemia.

Existing guidelines

Existing guidelines on the management of hyperglycaemia using insulin pump therapy are provided by American Association of Diabetes Educators (AADE), American Association of Clinical Endocrinologists (AACE), National Institute for Health and Clinical Excellence (NICE), Scottish Intercollegiate Guidelines Network Guideline 116 (SIGN), Australian Diabetes Society and Indian specific guidelines (for the use of insulin pumps based on experience and cultural differences) by Kesavadev et al.

Rationale/need for India specific guidelines

Lack of evidence-based guidelines for the use of insulin pump in Indian scenario has prompted for development of this consensus evidence-based guidelines. The guidelines have been developed such that they are simple to use and universally applicable.

Scope of the current consensus guideline

Use of CSII is an appropriate alternative to patients with diabetes on MDI. The use of CSII system varies with the manufacturer and model used. The corresponding requirements for the management of hyperglycaemia also differ. The scope of the current review is to frame appropriate guidelines for the management of hyperglycaemia in patients with diabetes using CSII, broadly placed under: selection of patients for insulin pump therapy, insulin characteristics for pump therapy and general recommendations for use in Indian population, insulin pump therapy in special populations. The current consensus guidelines have been framed in consideration with the existing guidelines from AADE and AACE from United States, NICE and SIGN from United Kingdom, Australian Diabetes Society (ADS) from Australia, and suggested guidelines for use of insulin pumps in India, and justified for use in routine Indian clinical practice.

Methodology

A systematic review of literature from medical databases was conducted to provide the best possible evidence base for the recommendations. Existing guidelines, meta-analyses, systematic reviews and key cited articles relating to the medical condition were reviewed by a group of doctors, and recommendations relevant to Indian scenario were framed. The recommendations were discussed at the National Insulin Summit held in August 2013 by an expert panel of physicians, endocrinologists and key opinion leaders. At this summit, recommendations for each section of the guidelines, and overall recommendations were agreed upon. Where there was little or no evidence, the committee relied on experience, judgement and consensus to make their recommendations. The consensus document was drafted and circulated for further feedback from the participants and others who could not attend.

Grading system

The current consensus guidelines have been developed in accordance to the AACE protocol for standardised production of clinical practice guidelines. Recommendations are organised by topic and are assigned evidence level (EL) ratings on the basis of the quality of supporting evidence all of which have also been rated for strength. Recommendations are based on clinical importance and graded as A (strongly recommend), B (intermediate), C (weak) and D (not evidence-based), those are coupled by four intuitive levels of evidence: 1, 2, 3, 4. The evidence levels have been positioned on the basis of available evidence to be used for grading recommendations as follows.

- • “1”: Meta-analysis of randomised controlled trials, randomised controlled trials
- • “2”: Meta-analysis of nonrandomised prospective or case-controlled trials, nonrandomised controlled trial, prospective cohort study, retrospective case-control study
- • “3”: Cross-sectional study, surveillance study (registries, surveys, epidemiologic study, retrospective chart review, mathematical modelling of database), consecutive case series, single case reports
- • “4”: No evidence (theory, opinion, consensus, review, or preclinical study)

Consensus Guidelines for Management of Hyperglycaemia with Insulin Pump Therapy

Selection of patients for insulin pump therapy

Insulin pump therapy should be considered for diabetes control, when the treatment goals and outcome measures are not met by intermittent insulin injection. However for successful implementation of pump therapy, both patient and providers must have the knowledge, skills, and resources to use this therapy safely and effectively. According to AACE, “the ideal CSII candidate would be a patient with T1DM or absolutely insulin-deficient T2DM who currently performs 4 or more insulin injections and 4 or more self-monitored blood glucose (SMBG) measurements daily and is motivated to achieve tighter blood glucose control, and is willing and intellectually and physically able to undergo the rigors of insulin pump therapy initiation and maintenance”. AACE guidelines do not recommend pump therapy in patients lacking the commitment or competence to perform basic diabetes self-management behaviours, while NICE guidelines do not recommend CSII therapy for the treatment of people with T2DM. It further suggests that CSII should be initiated only by a trained medical professional in centres with sufficient infrastructure. SIGN guidelines recommend the use of pump therapy in individual patients with T1DM or T2DM who experience recurring episodes of severe
pharmacodynamic (PK/PD) profiles resulting in physicochemical with hydrophobic surfaces, altering their pharmacokinetic/
exposed to changes in temperature, pH, agitation and contact
to suffer structural changes and molecular aggregation when
stability in a given delivery device. insulin molecules are known
characteristics of insulin (human and insulin analogues) and
Insulin characteristics for pump therapy
The efficacy of any insulin preparation depends on its
stability in a given delivery device. insulin molecules are known
to suffer structural changes and molecular aggregation when
exposed to changes in temperature, pH, agitation and contact
with hydrophobic surfaces, altering their pharmacokinetic/
pharmacodynamic (PK/PD) profiles resulting in physicochemical instability and inter and intra individual pharmacological
variation in glucose lowering effect. Physicochemical effects include formation of fibrils, precipitation of insulin, catheter
occlusions in CSII system, and formation of biologically inactive and potential immunogenic high molecular weight proteins (HMWP).
Thus, before initiating or switching to insulin pump therapy, one should consider pharmacokinetic profile, physicochemical stability of insulin, and pump compatibility.

There is a lack of evidence from existing guidelines on
selection of insulin type for use in pump therapy. The current recommendations were framed for the very first time, on the characteristics of insulin (human and insulin analogues) and pump material based on data reviewed from clinical trials, as well as the clinical judgement of the panel in the Indian scenario.

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Pharmacokinetics: Rate of absorption
Unlike RHI, which forms dimers and hexamers (upon aggregation), rapid-acting insulin analogues (RAIA) remain monomeric even at high concentrations, which enables improved absorption after subcutaneous injection. Moreover, rapid-acting insulin has the lowest intra-patient variability compared to intermediate or long-acting insulins. In a study comparing soluble insulin to insulin aspart, subcutaneous injections of insulin aspart was associated with more rapid onset of action and a shorter duration of action with lower intra-individual coefficient of variation compared to soluble insulin (19 ± 9 vs. 11 ± 5%; P = 0.018). Only a few PK/PD differences have been observed in studies that compared the absorption rate and glucose control of one (RAIA) with another. Canadian guidelines recommend use of RAIA (aspart or lispro) with CSII in adults with T1DM.

Physical and chemical stability
Although RHI is effective in lowering blood glucose, even before being administered it can undergo a series of chemical and covalent changes affecting the primary structure of insulin resulting in deterioration or formation of less potent molecule. Precipitation, fibrillation and occlusion of insulin often occur due to decomposition, undermining its compatibility for CSII pump use.

Insulin precipitation
The risk of catheter occlusion associated with isoelectric precipitation of insulin modifies the PK, causing a delayed onset and prolonged duration of action of precipitated insulin compared to dissolved insulin. Insulin precipitates in the acidic environment, and the point at which precipitation occurs depends on the isoelectric point of the individual insulin preparation. In a study comparing insulin aspart, insulin lispro, and buffered RHI with respect to resistance towards isoelectric insulin precipitation and the degree of isoelectric insulin precipitation, insulin aspart demonstrated the highest resistance to isoelectric precipitation, with 10% and 90% of precipitation occurring at lower pH (5.90 and 5.67) than for buffered RHI (6.18 and 5.95) and insulin lispro (6.41 and 6.30), respectively.

Fibrillation and formation of high-molecular-weight proteins
In addition to isoelectric precipitation, the occlusion tendency of commercial insulin products could also be attributed to fibrin deposition and fibril formation. Structural changes in insulin molecule results in the formation of insoluble insulin fibrils as well as soluble HMWP and are of potential concern because of their impaired biological potency and immunogenic properties compared to the native molecule. In a study comparing the stability of insulin aspart and insulin glulisine, it was observed that physical stability against fibrillation was reduced for glulisine and contained twice the amount of biologically inactive and potential immunogenic HMWP when compared to aspart (0.8% vs. 0.4%). High stability of insulin aspart can be attributed to the stabilising effect of the insulin-related impurities (e.g., HMWP) formed in parallel. Although the same stabilizing effect was expected to be present for glulisine, the opposite effect or effects leading to a net reduction in physical stability of insulin glulisine may be attributed to the significant reduction in stability of the pumped glulisine samples (reservoir samples 170 for aspart vs. 70 for glulisine) and needles’ end (230 for aspart vs. 20 for glulisine) (Table 2).

Compatibility
“Pump compatibility” of an insulin analogue may be defined
as how an insulin analogue reacts to storage in an insulin pump and how the pump user reacts to using that insulin analogue in the pump. Occurrence of occlusion and treatment satisfaction are two measures to determine insulin pump compatibility. An in vitro study on the rates of early and late occlusion in standard CSII catheters, showed fewer occlusions with aspart in comparison with lispro or glulisine.\(^4^1\) In addition, a case study has reported that insulin lispro precipitates and occludes the catheter resulting in unpredictable glucose fluctuations. This was resolved when the treatment was changed to insulin aspart, indicating greater pump compatibility of aspart in terms of lower rates of catheter occlusions.\(^4^4\) Moreover, the recommended duration of time that aspart may be kept in the insulin pump reservoir when unused, is up to 6 days compared to 48 hours or less for lispro and glulisine.\(^4^5\) On the other hand, patients with TIDM treated with insulin aspart showed lower rates of dermal or subcutaneous irritations, felt less depressed, and had positive view of physical discomfort and pain associated with pump.\(^4^6\)

**Recommendations**

- Rapid-acting insulin analogues should be preferred over regular human insulin for use in insulin pumps (Grade A; EL 3).\(^4^7\)
- Current data suggest that insulin glulisine is least compatible and insulin aspart is most compatible in insulin pumps (Grade A; EL 3).\(^3^4,4^8\)

**Use of insulin pump therapy**

The aim of any diabetes treatment is to achieve strict glycaemic control in order to avoid long-term diabetes complications while reducing the frequency of hypoglycaemic episodes. Insulin therapy is an integral component of the treatment of many individuals with diabetes. CSII using an external pump offers both better blood glucose stability as compared to multiple daily injections (MDI) and broader flexibility with lower rates of severe hypoglycaemia.\(^4^9,5^0\) Studies comparing CSII with NPH-based MDI demonstrate improved outcomes with CSII.\(^5^1\) Researchers also found that CSII resulted in lower glycated haemoglobin (HbA1c) along with a statistically significant reduction in the frequency of both mild and severe hypoglycaemic events when compared with NPH-based MDI.\(^5^2\) Similarly, in studies comparing CSII and glargine-based MDI in young children with TIDM, CSII showed comparable glycaemic outcomes without increased risk of hypoglycaemia.\(^5^3,5^4\) Moreover, CSII appears to be a superior treatment option in patients unable to achieve desired glycaemic targets with MDI. A head-to-head randomised comparison of insulin analogue-based MDI regimens with CSII confirmed the view that pump therapy can achieve better glycaemic control compared with insulin analogue-based MDI.\(^5^5,5^6\)

**Existing guidelines on CSII pump therapy**

Consensus statement endorsed by the ADA-EASD concluded that CSII (with proper support measures) is appropriate for children of all ages.\(^5^7\) AACE and ADS advocate the use of CSII over basal-bolus insulin therapy in patients with TIDM who are inadequately controlled with MDI.\(^5^8,5^9\) Similarly, NICE guidelines recommend insulin pump therapy as a treatment option for adults and children (≥ 12 years) with TIDM who are unable to achieve desired glycaemic targets with MDI therapy or whose HbA1c levels have remained high (8.5% or above) on MDI therapy despite a high level of care.\(^6^0\) The AAGE, Australian and Canadian guidelines strongly recommend the use of CSII therapy in patients with TIDM as part of an intensive diabetes management regimen to achieve glycaemic targets.\(^6^1,6^2\) Indian and SIGN guidelines also recommend CSII therapy in TIDM patients for better glycaemic control.\(^6^3,6^4\)

CSII is a convenient and effective alternative for patients with type 2 diabetes mellitus (T2DM) unable to achieve the ADA recommended HbA1c target of < 7% with MDI.\(^6^5,6^6\) AACE recommends insulin pump therapy for effective maintenance of glycaemic control in patients with T2DM requiring large doses of insulin. On the other hand, Indian guidelines advocate judicious use of insulin pumps in selected T2DM candidates for improved glycaemic control and reduced glycaemic excursions. However, NICE guidelines do not recommend use of CSII in patients with T2DM. Although available clinical evidence on CSII for T2DM is not yet consistent, large RCTs have consistently shown that CSII is equivalent to MDI, whereas smaller trials have concluded that CSII is superior.\(^6^7\)

In addition to the use of CSII pump for hyperglycaemia management, guidelines also press the need to take care of accessories used in the system. The AACE guidelines suggest that pump users must be prepared to trouble shoot problems related to pump operation, aware of insulin correction and adjustment formulas.\(^6^8\) Soft cannulas made of Teflon need to be changed every three days and those with steel cannulas every 2 days.\(^6^9,7^0\) Delay in change of cannulas can increase the risk of infection and other complications.\(^7^1\)

In view of the recommendations from existing guidelines, the expert panel has framed new set of generalised recommendations for use of insulin pump therapy for clinical practice specific to Indian population.

**General Recommendations for insulin pump therapy in Indian population**

- Patient selection is most important well-motivated patients keen to achieve good glycaemic control and interested in SMBG could benefit from insulin pump therapy, provided they can afford insulin therapy (Grade A; EL 4).\(^7^2\)
- Insulin pump therapy can be initiated in patients visiting out-patient department provided they have the mental and physical capacity to do so (Grade A; EL 4).\(^7^3\)
- Patient should be adequately educated on pump use, including aspects such as infusion set insertion technique and basic insulin dose adjustments at the beginning of the insulin pump therapy (Grade A; EL 3).\(^7^4\)
- Cannula of insulin pump should not be used beyond 72 hours and patients should be advised to change if they

### Table 2: Physical stability (fibrillation) and HMWPs, insulin aspart and insulin glulisine samples before, during, and after simulated pump use

<table>
<thead>
<tr>
<th>Flow rate, study duration</th>
<th>Physical stability against fibrillation (% relative to baseline)</th>
<th>HMWP (%) in the pumped sample</th>
<th>Flow rate, study duration</th>
<th>Physical stability against fibrillation (% relative to baseline)</th>
<th>HMWP (%) in the pumped sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin aspart</td>
<td></td>
<td></td>
<td>Insulin glulisine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.3 U/h, 10 days</td>
<td></td>
<td></td>
<td>0.3 U/h, 10 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reservoir</td>
<td>170</td>
<td>230</td>
<td>Reservoir</td>
<td>70</td>
<td>20</td>
</tr>
<tr>
<td>Needle’s end</td>
<td></td>
<td></td>
<td>Needle’s end</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HMWP (%) in the pumped sample</td>
<td>Baseline (day 0)</td>
<td>Day 4</td>
<td>HMWP (%) in the pumped sample</td>
<td>Baseline (day 0)</td>
<td>Day 4</td>
</tr>
<tr>
<td>Baseline (day 0)</td>
<td>0.2</td>
<td>0.3</td>
<td>Baseline (day 0)</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Day 4</td>
<td>0.3</td>
<td>0.8</td>
<td>Day 4</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Day 10</td>
<td>0.4</td>
<td>0.8</td>
<td>Day 10</td>
<td>0.4</td>
<td>0.8</td>
</tr>
</tbody>
</table>

All results are given as single determinations if nothing else is stated. Lag times measured by thioflavin T assay. Abbreviations: HMWP: High molecular weight proteins.
experience pain, irritation and/or inflammation (Grade A; EL 2).  

- Once patient is comfortable with insulin pump therapy, advanced pump therapy education including different bolus types, carbohydrate counting and use of advanced pump menu should be discussed (Grade A; EL 4).

- Importance of SMBG should be emphasised to the pump users at every visit (Grade A; EL 3).

- Patients undergoing pump therapy, should have their HbA1c monitored every 3 months and should be regularly followed up (Grade A; EL 4).

- If HbA1c levels go beyond age specified targets, insulin dose should be adjusted until desired glycaemic targets are achieved (Grade A; EL 4).

- Individual/group training sessions should emphasize to keep the patient in follow up and monitor the progress in management of diabetes (Grade B; EL 4).

- Currently, oral anti-diabetic drugs (OADs) do not have a role as an adjunct along with insulin pump. Wherever required Metformin/insulin sensitisers may be considered when encountering high insulin resistance. However, it is emphasised that there is no role for OADs like sulphonylureas, dipeptidyl peptidase-IV inhibitors, meglitinides and others (Grade A; EL 4).

### Insulin pump therapy in special population

#### Hospitalised patients

In hospitalised patients, hyperglycaemia is often associated with worst outcomes including mortality. Moreover, perioperative hyperglycaemic episodes was found to increase the risk of postoperative mortality, cardiovascular, respiratory, neurologic, and infectious morbidity in surgical patients. Insulin, given either intravenously as continuous infusion or subcutaneously, is currently the only available agent for effective control of glycaemia in patients admitted to critical or non-critical care settings, respectively. With increasing use of CSII pump for hyperglycaemia management, health institutions can allow their staff are familiar with its use.

#### Carbohydrate count

In addition to the use of CSII pumps, focus on in-patient nutrition is also essential. In order to ensure effective glycaemic management, a consistent carbohydrate meal-planning system should be followed in patients with diabetes admitted to hospital. It involves counting total amount of carbohydrate offered rather than specific calorie content at each meal. In general, most patients receive a total of 1500–2000 calories per day (12–15 carbohydrate servings), obtained from whole grains, fruits, vegetables, and low-fat milk with restricted amounts of sucrose-containing foods. The AACE guidelines recommend patient’s knowledge on basic and advanced carbohydrate-counting skills. Use of consistent carbohydrate meal plans would facilitate matching the prandial insulin dose to the amount of carbohydrate consumed in people with diabetes. Although there is no evidence supporting consistent carbohydrate meal plans in pump users, it must be considered for beneficial effects in the management of diabetes. Based on the existing guidelines and clinical judgement, the panel framed recommendations according to Indian context for appropriate and safe use of CSII pumps in management of hyperglycaemia in patients admitted to critical and non-critical care settings of hospital.

#### Recommendations

- CSII is not recommended in critically ill patients or in settings with inability to manage insulin pump by the treating hospital staff (Grade A; EL 4).

- CSII is recommended to continue in non-critically ill patients if the patient can manage the use of insulin pump himself or has trained assistance for the same (Grade A; EL 3).

### Pump therapy in pregnant women with T1DM

In pregnant women with T1DM, CSII may be preferred over MDI therapy for similar or better glycaemic control that reduces the risk of spontaneous abortions and foetal malformations. CSII offers several advantages to pregnant woman with diabetes which includes: easier treatment of morning sickness and hyperemesis gravidarum, fewer glycaemic excursions and hypoglycaemic events, easier treatment of the dawn phenomenon and improved glycaemic management in the postpartum period when insulin requirements may fluctuate. In a retrospective observational study including 64 pregnant women with T1DM, treatment with CSII was associated with greater reduction in HbA1c level during first (CSII: 0.9% vs. MDI: 0.46%), second (CSII: 1.58% vs. MDI: 0.78%) and third trimester (CSII: 1.74% vs. MDI: 1.09%) of pregnancy compared to MDI treated patients. Moreover, the rate of abortion, preterm labour, caesarean section and hypoglycaemia in new born were less in CSII treated group compared to MDI treated group. In addition, Apgar score was significantly (P < 0.05) higher in CSII treated group compared to MDI treated group. Based on this evidence, it could be suggested that greater flexibility of CSII leads to better compliance and improved quality of life in patients during and after pregnancy and appears to be safe for use in pregnancy.

For safety purpose, the AACE guidelines suggest using low dose NPH during the night in this population, since basal insulin is not used in CSII pumps. This further ensures no lack of insulin in the circulation, even if the needle dislodges during overnight period (AACE 2010). Based on the existing guidelines and clinical evidence, the panel framed recommendations for appropriate and safe use of CSII pumps for the management of hyperglycaemia in pregnant women with T1DM.

#### Recommendation

- CSII gives better glycaemic control and outcome in pregnant women with type 1 diabetes compared to MDI treatment (Grade A; EL 2).

### Summary

CSII pump offers both better glucose stability and broader flexibility and freedom resulting in a better quality of life for the patient. The current consensus guidelines were developed from existing guidelines to promote optimal use of CSII pumps (Table 3) in the Indian context and to make it an integral part of diabetes management. However, in the framework of evidence based medicine, the benefits of this approach should be proven in clinical practice through appropriately designed clinical studies. We hope that use of CSII gains more attention in India and becomes an integral part of diabetes management. However, evidence-based clinical studies from India on benefits of CSII pumps over MDI in terms of influence on glucose and HbA1c levels, glycaemic variability and effect on weight control and/or hypoglycaemia are required to further their use in insulin users.
Table 3: Comparison of consensus recommendations with existing guidelines for use of CSII pump therapy in the management of hyperglycaemia

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Consensus guideline</th>
<th>AACE-ADA</th>
<th>AADE</th>
<th>Kesavadev et al.</th>
<th>NICE</th>
<th>SIGN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appropriate patient</td>
<td>All patients requiring better exogenous insulin therapy in whom glycaemic targets are not achieved with MDI therapy; experiencing frequent episodes of severe hypoglycaemia; Patients on insulin therapy who can afford; motivated for improved QoL; with high insulin requirement; with diabetes related complication; women with diabetes during pregnancy</td>
<td>Patients with T1DM and T2DM: ‘dawn phenomenon’, T1DM: extreme insulin sensitivity; T2DM: severe insulin resistance; C-peptide positive but suboptimal control on MDI, erratic lifestyle</td>
<td>Contraindicated in patients lacking the commitment or competence to perform basic diabetes self-management behaviours</td>
<td>Motivated for improved QoL</td>
<td>Patients motivated for improved QoL</td>
<td>In patients with very low basal insulin requirements</td>
</tr>
<tr>
<td>Insulin characteristics for pump therapy</td>
<td>RAIA preferred over RHI; insulin aspart is most compatible and insulin glulisine least compatible Not recommended in critically ill patients/settings where hospital staff are unable to manage*; Recommended in non-critically ill patients if patient/staff can manage insulin pump #</td>
<td>-</td>
<td>RAIA used in CSII pumps</td>
<td>Regular insulin or RAIA</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pump therapy in hospitalised patients</td>
<td>Use, if adequate glycaemic control not achieved with optimal use of MDI</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Pump therapy in pregnant women with T1DM</td>
<td>Use RAIA in pregnant women with T1DM with defined protocol; Safe and effective in pregnant women with T2DM</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
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</tbody>
</table>

General recommendations for insulin pump therapy by current consensus guideline (Adapted from all)

- Select motivated patients keen to achieve good glycaemic control and interested in SMBG
- Initiate in OPD patients with mental and physical capacity
- Educate pump patients on CSII pump insertion and insulin dose adjustments at the first use
- Cannula replaced every 72 hours, change if pain or irritation and inflammation
- Once comfortable start advanced pump therapy by education on bolus types, counting of carbohydrate and advanced pump menu, progress in glycaemic control
- Monitor HbA1c levels and SMBG; If HbA1c > target, adjust insulin dose

*Also suggested by ADA position statement; # also recommended by Endocrine Society guidelines

Abbreviations: AACE: American Association of Clinical Endocrinologists; ADA: American Diabetes Association; AADE: American Association of Diabetes Educators; NICE: National Institute for Health and Clinical Excellence; SIGN: Scottish Intercollegiate Guidelines Network; T1DM: Type 1 diabetes mellitus; T2DM: Type 2 diabetes mellitus; QoL: Quality of life; RHI: Regular human insulin; HbA1c: Glycated haemoglobin; RAIA: Rapid acting insulin analogues; SMBG: Self-monitoring of blood glucose; CSII: Continuous subcutaneous insulin infusion; MDI: Multiple daily injections; BG: Blood glucose; OPD: Outpatient department

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