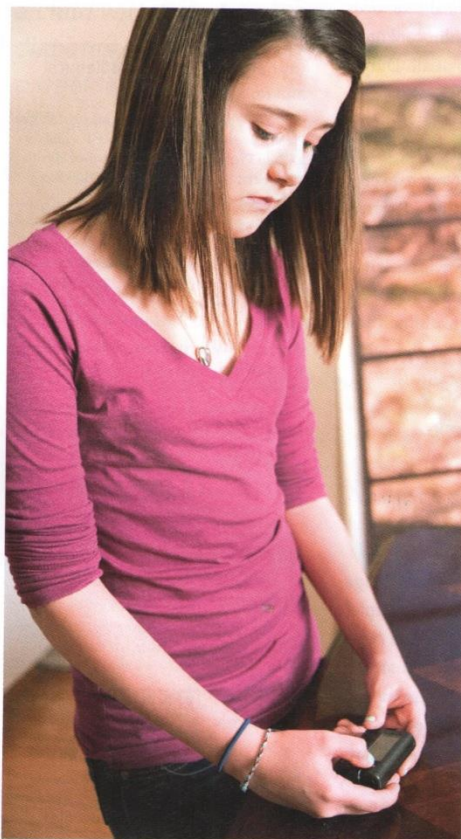


Debate – Insulin therapy: a matter of choice?



Type 1 diabetes accounts for approximately 10% of the total burden of diabetes in a population, but it is the most predominant form of the disease in younger age groups in most countries. Poor glucose control for the child living with diabetes ($HbA_{1c} > 7.0\%$) is linked to severe diabetic complications later in life and early death. The goal of best standard practice for type 1 diabetes care is to mimic physiological insulin replacement as closely as possible and to achieve this there are two main therapeutic approaches: multiple daily injection therapy (MDI) or insulin pump therapy. MDI is the accepted standard of care for maintaining near-normal blood glucose to reduce the risk of complications, but evidence is mounting that MDI does not deliver optimal glucose control as effectively as insulin pump therapy. Proponents of pump therapy maintain that long-term benefits far outweigh the costs (USD 7000 for device and a minimum of USD 2500 per year for supplies) because pump therapy improves HbA_{1c} values and reduces the number of serious complications, thereby making investment in pump programmes a cost effective proposition to consider in addressing the burden of diabetes.

To shed light on the controversy surrounding best care practice for children living with diabetes, *Diabetes Voice* invited two experts to contribute their opinions for or against supporting guidelines that require insulin pump therapy as first-line treatment in paediatric type 1 diabetes care.

What is important – insulin pump, multiple daily injections or improved access to treatment?

Kaushik Ramaiya

Type 1 diabetes, initially thought to be rare in Africa and other developing countries, has in the least quarter of the century become a major health challenge. It has been estimated that type 1 diabetes affects 19,000 people in the World's poorest countries¹ but due to the lack of reliable data on the disease in these countries, the true burden could be masked. The low prevalence of type 1 diabetes is a reflection of poor prognosis, low incidence and under diagnosis or misdiagnosis.² Also, type 1 diabetes is likely to be one of the lower priorities of respective ministries of health in developing countries taking into consideration its lower prevalence and high costs.

In Tanzania, the average annual cost of care for a patient with insulin requiring diabetes has been estimated as USD 229 of which two thirds was for purchase of insulin.³ In another study⁴ in Tanzania, about 50% of the patients considered their disease as a major physical and psychological challenge and the monthly cost for an average insulin treated patient equaled 26% of the minimal wage.

Most of the countries in sub-Saharan Africa already have a large burden of communicable disease such as HIV/AIDS, tuberculosis and malaria.⁵ With a large percentage of the population living below the poverty line, there are major challenges ahead in managing the 'double burden' of communicable and Non-communicable Diseases. The major barriers to access to care for patients with insulin requiring diabetes in Mozambique and Zambia⁶ were interrupted insulin supplies and unaffordable costs, lack

of standardisation of insulin syringes and interrupted supplies, the high costs and lack of consumables for diagnostic tools, a shortage of trained health care workers and the importance of traditional beliefs.

With the above background, offering insulin pump therapy to children and others with type 1 diabetes is a distant dream in the developing countries of sub-Saharan Africa. It could be affordable and accessible to the privileged few but for the majority the challenge is getting access to adequate multiple daily injections.

In order to achieve reasonable control of blood glucose in children aged less than 12 years old living with type 1 diabetes in the developing countries of sub-Saharan Africa, multiple daily injections is the way forward provided the challenges of ensuring access to insulin, syringes, monitoring tools and adequately trained health care providers can be overcome. Thankfully, there have been positive developments in improving this access to care for children with type 1 diabetes in these countries.

The International Diabetes Federation's (IDF) Life for a Child Programme has been instrumental in initiating improved access to care for children with type 1 diabetes in several countries of the Third World. The Programme has facilitated the supply of insulin, syringes, and monitoring tools and the training of health care providers and education for children and their care-givers.

Our experience for Tanzania - which is a beneficiary of the Life for a Child Programme has been variable. In spite of the provision of insulin, syringes, monitoring tools and adequately trained health care providers — paediatric endocrinologists, adult endocrinologists, clinical officers, nurses, diabetes educators and nutritionists — achieving the goal of HbA_{1c} of <7% has many challenges.

These challenges include lack of adherence, difficulties in the provision of patient education including their understanding of long term implications, lack of parental involvement in the management of their child and their reluctance to allow their child to carry out multiple blood glucose testing and multiple daily injections of insulin, and socio economic components such as lack of access to regular meals. Thus insulin injections are taken on an 'as and when required' basis.

It is therefore important to ensure that all the components of care (aetiology, pathophysiology, pharmacotherapy, nutrition and social and economic factors) are taken into consideration before taking a decision on what is suitable for each individual child. That is, the treatment of each child should be individualised so as to achieve the best control possible.

Benefits of the insulin pump are clear, but the pump is not for everyone

Emily G Moser and Satish K Garg

The ideal insulin delivery method for patients with type 1 diabetes remains a topic of debate, especially when it comes to young children, adolescents and young adults with type 1 diabetes. While there are advantages and disadvantages

to both multiple daily injections (MDI) of insulin and insulin pumps or continuous subcutaneous insulin infusion (CSII), the insulin pump should be considered an important option for insulin delivery in type 1 diabetes.

The insulin pump remains the most physiological system of insulin delivery available today. Functioning beta cells in the pancreas of a person without type 1 diabetes release a small amount of rapid-acting insulin to the liver continuously (referred to as basal insulin) with a bolus of rapid-acting insulin released with meals to maintain blood glucose levels throughout the day. An insulin pump delivers insulin in a similar manner by infusing a small amount of rapid-acting insulin subcutaneously without the use of long-acting insulin analogues. A bolus of rapid-acting insulin can be administered shortly before meals to mimic the physiological insulin bolus. The ultimate goal of insulin administration in patients with type 1 diabetes should be to imitate the physiological release of insulin, as done by the insulin pump.

The insulin pump has been shown by meta-analyses and several independent studies to decrease glycosylated haemoglobin (HbA_{1c}), total insulin dose, glycaemic variability and the incidence of severe hypoglycaemia when compared with MDI in patients with type 1 diabetes.^{7,8} However, the improvement in HbA_{1c} and reduction in hypoglycaemia is most significant in older individuals with a longer duration of diabetes and with a higher baseline HbA_{1c}.^{7,9} The insulin pump has higher patient satisfaction than MDI, possibly related to increased portability and improved ease of insulin dosing.^{10,11} Additionally, suspension of insulin infusion and sensitivity factors allow for improved control over insulin administration and modification of insulin dosing based on activity level, food intake and sickness.^{10,11}

Benefits of the insulin pump specifically for young children with type 1 diabetes include the ability to easily administer multiple insulin boluses without increased injections due to their high frequency and unpredictability of meal times and amounts, allowing for more accurate insulin dosing. Moreover, the insulin pump feature of predicting the amount of active insulin on board avoids 'insulin stacking' (injecting an insulin dose too soon after the previous dose thus increasing the risk of hypoglycaemia) as a result of frequent meals and frequent insulin dosing. Furthermore, the ability to apply multiple basal insulin rates and carbohydrate to insulin ratios are especially beneficial in children who frequently require differing insulin doses depending on

the time of the meal or snack.¹² Due to the pump's ease in ability to modify the administered insulin dose, the insulin pump may be preferred when total insulin dosing naturally increases as insulin resistance rises during puberty.

Despite clear benefits of insulin pump therapy, it may not be the best option for all patients with type 1 diabetes. Patients may not be willing to perform an adequate number of blood glucose measurements daily, possibly due to cost and time purposes, which is important for safety.¹³ In addition, the insulin pump has the theoretical increased risk of diabetic ketoacidosis (DKA) secondary to pump failure.¹⁰ However, several studies have shown similar rates of DKA in both MDI and insulin pump users. Lastly, the cost of the insulin pump is higher than MDI. Disadvantages specific to children using an insulin pump include a limited amount of available sites to place pump catheters and greater sensitivity to the adhesive used in the infusion sets.

The ideal method of insulin delivery and continuous glucose monitoring would be a closed-loop system in which the amount of insulin injected is modified by continuous glucose monitoring data of the current glucose value and trends in glucose levels. Several previous small, non-randomized clinical trials done in Europe utilising insulin pumps equipped with a Low Glucose Suspend (LGS) function have shown a significant decrease in hypoglycaemia without rebound hyperglycaemia or a change in HbA_{1c}.¹⁴ Two recently completed large, randomised clinical trials (both In-Clinic exercise-induced hypoglycaemia and In-Home) ASPIRE (Automation to Simulate Pancreatic Insulin Response) studies, have shown that a Low Glucose Suspend feature in sensor-augmented insulin pump therapy, the first step toward a closed-loop system, demonstrated a decrease in hypoglycaemia without a change in HbA_{1c}.¹⁵⁻¹⁶ Sensor-augmented insulin pumps equipped with LGS are available in Europe and many other parts of the world, but the LGS function has not been given FDA approval in the United States.

In conclusion, while MDI is a viable option for insulin delivery, we believe that the use of insulin pumps should be considered for patients with type 1 diabetes as it imitates the physiological release of insulin, decreases hypoglycaemia and HbA_{1c} and is a first step towards the ideal emerging diabetes management technology — a closed-loop system. Important consideration to individual situations should be given prior to determining the most appropriate insulin administration method for patients diagnosed with type 1 diabetes.

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