Insulin pump risks and benefits: an analysis of the EASD/ADA joint statement

The European Association for the Study of Diabetes and the American Diabetes Association have recently published a joint statement on pump safety, adverse event reporting and research needs. Steve Chaplin here analyses their findings and their import for clinical practice.

In 1978, British diabetologists reported that continuous subcutaneous infusion of insulin from a battery-driven syringe pump improved or maintained blood glucose levels in 10 of 14 adults with diabetes. In five, the overall quality of glycaemic control was not improved due to hypoglycaemia but severe hypoglycaemia occurred only in a sixth participant. There were four technical failures, mainly due to accidental removal of the catheter.

Nearly 40 years later, it’s surprising to read that we can’t be sure failure rates are lower now than they were in the years following this first report. But that is the view of the EASD/ADA Diabetes Technology Working Group who have published a joint statement on pump safety, adverse event reporting and research needs (Diabetes Care 2015;38:716–22).2

Technology and use
The use of insulin pumps is increasing, mostly among people with type 1 diabetes, and pumps are increasingly sophisticated.

So far, the interests of patients, clinicians and developers have been aligned but the EASD/ADA statement suggests that shortcomings in regulatory oversight and post-marketing surveillance are causing uncertainty about safety and value for money.

It is not known how many pumps are currently in use. Some estimates suggest 0.75–1.0 million globally but this may be too low: when Medtronic recalled one of its devices in 2014, well over 700,000 pumps were affected. This uncertainty is important because, EASD/ADA say, it is difficult to estimate the rates of malfunction and user error when the denominator is unknown.

Pumps are devices
In the US, pumps are classified as ‘moderate risk’ devices (Class II) unless they have integrated continuous glucose monitoring, when they are ‘higher risk’ (Class III). Clinical studies are not required for Class II devices: manufacturers only have to show their pump is at least as safe and effective as one in clinical use and carry out small-scale studies to demonstrate that people can use it safely. Such bench testing, the EASD/ADA statement says, is insufficient because ‘From a clinical perspective, it is clear that daily use of devices containing electronic and moving parts in a wide variety of conditions poses considerable challenges to performance’. Class III devices require clinical trial data of safety and efficacy, though these studies focus on the safety of the algorithms and system functionality rather than clinical performance.

Safeguards in the EU are lower, where pumps are Class IIb devices certified by notified bodies. These agencies are allowed ‘considerable discretion’ in the nature of their evaluations. It is this system that allowed faulty breast implants and hip prostheses onto the market, prompting the EU Commission to tell them to – in effect – get their act together. National authorities are now obliged to share safety information via a common database but more fundamental change has been delayed.

Postmarketing surveillance
Adverse events associated with pumps can be reported to the regulatory authorities (the Food and Drug Administration in the US and, in Europe, national agencies) or to the manufacturer. The EU-wide European Database on Medical Devices (EUDAMED) is available to regulatory agencies but not to the public. The US Manufacturer and User Facility Device Experience (MAUDE) database therefore provides the data for the EASD/ADA to review.

Most reports in MAUDE come from users rather than physicians. Pumps that fail or malfunction are usually returned to the manufacturers and the outcome is not made public. These companies are responsible for identifying patterns of harm and are required to share safety data with the regulatory authorities, though each has its own internal procedures for assessing reports.

The value of public access to MAUDE, is, however, limited. The database can only be searched by pre-selected categories and it is difficult to refine results by clinically relevant filters such as pump model, demographic group or type of adverse event at different stages in the care process. Further, it is difficult to determine which component of the system – pump, user, infusion set – was to blame. As with any database of spontaneous reports, MAUDE can reveal safety signals but is not reliable enough to compare devices. EASD/ADA retrieved 24,066 records of pump-related events in 2013. These data included 19,564 reports for a pump from one of the smaller manufacturers but 718 for one of the most widely used pumps.

MAUDE and EUDAMED can be improved by making the process of event reporting more standardised, open and transparent – e.g. by better coding and clarity about the many small innovations to pump design. The FDA recently licensed a Class III pump with a requirement for additional postmarketing surveillance of all users. This, the EASD/ADA statement says, could be a model for monitoring all pumps.

Complaints and recalls
In the US, all publicly available information about a pump that has been returned to the manufacturer is included in MAUDE. That may not be much: a search for device-related recalls in a 12-year period identified 124 reports; these were duplicates of 10 discrete events. EASD/ADA therefore asked six manufacturers to
share the information they held; all said they would but, in the nine months before the statement appeared online, only three had done so and they confined their responses to a personal meeting, a conference call and a Powerpoint presentation. It was clear that primary data of the sort required for an independent review would not be forthcoming.

**Technical versus human**

The technical specifications of a pump can be impressive on paper but there’s little to show this translates to benefits for the user. Manufacturers have different terminology for programs that estimate bolus doses, making education and training more difficult. The speed at which a bolus dose is delivered varies between devices but little is known about the impact on metabolic control. It is unclear whether users or clinicians actually value these facilities.

Surely, however, it’s useful if a pump can prevent hypo- and hyper-glycaemia by using blood glucose measurement to correct the insulin dose? Manufacturers certainly claim this is an advantage but the EASD/ADA statement is sceptical, saying some users manage well without it and some providers won’t support these devices until they are backed by better evidence.

At least there is a requirement to use ‘human factors studies’ to determine whether regular pump users can use a device correctly. Such studies might cover understanding instructions, reading a display or inserting an infusion line in a clinical setting. The EASD/ADA welcome this but point out that it falls short of evaluating everyday use and more studies are needed to determine the needs of different user groups.

**Infusion systems**

Failure of the insulin infusion system (IIS) is potentially a serious hazard for pump users. Although little has been published on IIS failure, many of the records in MAUDE are associated with such events and they are the biggest cause of pump recalls. Occlusion, which appears to be associated with the frequency of changing the IIS, may be due to an interaction between the plastic of the IIS, the insulin formulation, the way insulin is pumped or the infusion site. Insulin absorption is impaired from sites of lipohypertrophy but little is known about the epidemiology of this problem, even though it is a familiar one among long-term users.

The pump and its IIS should therefore be considered as parts of one system rather than separate components, EASD/ADA state. Currently, regulatory authorities may code them separately or together and, because adverse events are assigned by product code, information about the IIS and a pump may be stored in different databases.

**Education and training**

Most of the adverse events in MAUDE are associated with user error or human factors rather than mechanical issues. Further, preventable events appear to be more common in non-specialised clinical settings. This suggests scope for reducing events by appropriate selection of candidates, education and training for users and health professionals, and ensuring that diabetes teams have enough staff with the right skill mix.

**Real world outcomes**

A US survey published in 1986 reported malfunctions in 25% of pumps, of which 29% were caused by drive failure and 14% by battery failure. We would expect modern devices to perform better but there’s not enough evidence to say for sure. Registry data from US centres show that patients with excellent glycaemic control are more likely to be pump users. One-year follow up shows that 4.4% of users discontinue pump use, most frequently due to discomfort with a ketoacidosis rate similar to that associated with multiple injections. This registry has close links to a patient networking site known as Glu (https://myglu.org) and both could...
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be further developed as sources of safety information. Sweden, Scotland, Germany and Austria all have diabetes registries from which data have been published but more could be done if the support were there, particularly on pump utilisation, choice of insulin and IIS, user outcomes and adverse events. One survey of 640 new pumps from four manufacturers identified defects in 36%, including failure (16%) and replacement due to mechanical defect (6.5%).

Such outcomes are clearly different from those reported in clinical trials. It’s not easy to organise large trials of devices that are frequently updated or replaced but it has been done and more funding is needed if clinically important questions are to be answered. These should be conducted by independent investigators.

Pump problems

A UK survey of 92 adults with type 1 diabetes who had been using a pump for at least six months (mean 3.3 years) found that problems are still common. See Figures 1, 2 and 3.

Summary

The EASD/ADA statement calls for a more rigorous and transparent climate in which pump safety can be evaluated. Based on the points summarised above, it has compiled a list of recommended actions in five areas: regulatory activity, the relationship between manufacturers and regulatory authorities, guidance and standards for health professionals, independent research and improved adverse event reporting. Full details are in the statement, which is freely available online.

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References

References are available online at www.practicaldiabetes.com.

INPUT’s comment on EASD/ADA advice

As a UK charity run by insulin pump users and their families, INPUT would welcome standardised post-market checks suggested in the recent EASD/ADA report. Clinically significant inaccuracies in insulin delivery at any point within the pump warranty make it unfit for purpose. Therefore pump users assume they are delivering accurately, and they comment on how reliable their pumps are as infrequently as do people comment on how well their banks process direct debits. Before a pump user considers inaccuracy, they may have to rule out many other factors that influence blood glucose levels.

Pump users must be alert to the potential of pump failure along with any other cause of rising blood glucose, such as illness or stress. Therefore the need to check blood glucose regularly (or use CGM) should be reinforced at each clinic visit. The pump training curriculum must include when to administer insulin by syringe. Pump trainers must be allowed time to be suitably trained and have adequate time to train new pump users, and clinics should have more than one pump-trained health care professional.

INPUT encourages pump users to contact the manufacturer (which usually provides a 24-hour helpline) rather than their care team (often an answerphone service even during office hours) with technical problems. Pump users should also report pump failure to the MHRA. However, many people have faced unreasonable barriers to pump therapy and are reluctant to risk being labelled as a complainer or a failure, fearful that the pump will be taken away without further dialogue.

Thousands of pump users and health care professionals bear testimony to the safety and efficacy of insulin pump therapy when used sensibly. As we progress towards fully automated insulin delivery, INPUT hopes manufacturers and clinicians will rise to the challenge of refining the safety of pump therapy so that treatment of type 1 diabetes can continue to improve, and even more people can meet their treatment and life goals.

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Reference

References


