Personal statement on Continuous Subcutaneous Insulin Infusion

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Experience of the technology

I am the lead author of the original publication on CSII (Pickup et al BMJ 1978; i: 204-207), I set up the UK's first NHS-funded Insulin Pump Clinic, which remains one of the largest and where I am currently the Consultant in Charge. I have some 30 years clinical experience of management of people with diabetes by CSII, have published over 100 papers on CSII and lecture widely nationally and internationally on the topic.

Clinical use of CSII: our own practice and recent research results

We use insulin pump therapy at Guy's and St Thomas' Hospitals Trust for people with type 1 diabetes who have not achieved satisfactory glycaemic control using the best modern insulin treatment, a package of multiple daily insulin injections (MDI, including the use of insulin analogues), frequent blood glucose self monitoring and insulin dosage adjustment, dietary advice and structured patient education. The three main indications we use for insulin pump therapy are: (i) frequent unpredictable severe hypoglycaemia (as recommended in the NICE guidelines 2003), (ii) unpredictable swings in blood glucose which are often accompanied by a high HbA1c and episodes of biochemical hypoglycaemia, and (iii) a marked dawn phenomenon.

We have provided recent evidence to support the clinical effectiveness of CSII based on both our own practice (Pickup JC et al. Pract Diab Int 2005; 22: 10-14 and Pickup JC et al. Diab Metab Res Rev 2006; 22: 232-237) and a meta-analysis of recent trials. The meta-analysis we performed (unpublished, but reviewed in the Technology Assessment Report) considered 22 studies of long pump duration using modern pumps and insulins, and showed a four-fold reduction in severe hypoglycaemia during CSII compared to MDI (rate ratio 4.12 [CI 2.86-6.13]) and a significant average reduction in HbA1c of 0.62% (CI 0.47 to 0.78%). Most importantly, we found the biggest improvements in both HbA1c and hypoglycaemia reduction occurred in those who were worst controlled on MDI, seen in both metaregression of published trials and in individual patients in our own clinic. In an audit of insulin pump therapy at Guy's Hospital, for example, the reduction in HbA1c in the NICE-recommended group of hypoglycaemia-prone type 1 diabetic subjects was as much as 3% in those with an HbA1c of 11.0% on MDI, and the mean reduction in HbA1c was 1.5% (Pickup JC et al. Pract Diab Int 2005; 22: 10-14). This larger difference in HbA1c between MDI and CSII than seen in meta-analysis is because hypoglycaemia-prone subjects maintain a higher HbA1c on MDI than the general type 1 patient and thus improve more when treated by CSII (see below).

Thus, we have found that, when used in the target group of those uncontrolled on MDI, CSII is considerably more effective at reducing HbA1c than previously thought. Because this reduction occurs on the steep part of the curve relating microvascular risk to HbA1c, the clinical impact and cost effectiveness is also larger than previously recognised.

Patient reactions to CSII in our clinic

The patient experience is overwhelmingly positive in our view. A preliminary assessment we performed using a validated patient-centred quality of life questionnaire showed significant improvement vs. MDI (Pickup JC, Harris A J Diabetes Sci Technol 2007; 1: 394-399), but the formal quality of life assessment can undervalue individual responses. Many patients in our clinic have endured an extraordinary burden of hypoglycaemia on MDI - weekly ambulance calls, abandonment of their career, breakdown of marriages and fear of even going out of the house. It is a consistent comment from patients that pump therapy has not just improved control and reduced hypoglycaemia but changed their lives and made them feel 100% better. One repeatedly hears patients say that doctors fail to understand the human dimension of poor diabetes control – the impact on lives and well being.

The need for revised clinical indications by NICE

Our view is that the evidence base for the NICE 2003 guidelines for pump use in those with continued severe frequent hypoglycaemia on MDI has been robustly confirmed in both adults and children and should remain.

We strongly recommend that NICE consider two additional indications for a trial of CSII: those type 1 diabetic subjects with an elevated HbA1c and/or wide swings in blood glucose on best attempts with MDI and those with a marked dawn phenomenon during MDI. We have shown that the HbA1c achievable on MDI is significantly related to the blood glucose variability (Pickup JC Diab Metab Res Rev 2006; 22: 232-237), and that those with high variability maintain a high HbA1c to avoid hypoglycaemia. Such patients are markedly improved by switching to CSII because pump therapy reduces both within- and between-day blood glucose variability (Pickup JC Diab Metab Res Rev 2006; 22: 232-237. Since the introduction of MDI based on long-acting insulin analogues, lesser numbers of patients now have a large dawn increase in blood glucose level, but significant numbers of patients cannot reduce the pre-breakfast blood glucose level without precipitating nocturnal hypoglycaemia. We find such patients are improved on CSII because of the constant basal infusion and the ability to pre-programme changes in rate during the night. We feel this should be included by NICE as an indication for a trial of insulin pump therapy.

Our view on the protocol necessary for an insulin pump clinic

We believe that it is essential to employ a sequential approach. After an initial consultation with the doctor, patients at Guy's Hospital are entered into a pre-pump assessment programme run by a specialist diabetes nurse and dietitian and lasting some months. This programme has several functions: patients undergo renewed patient education to try and improve control on MDI, including carbohydrate counting and insulin dosage adjustment, they learn about and discuss pump therapy with the staff and consider options with friends and relatives at home. Staff are also able to assess the suitability of the patient for pump treatment during this time. A significant percentage (initially ~25%, but currently ~10%) of those referred enjoy improved control using MDI at the end of the assessment programme or decide not to proceed with CSII. Only those who have continued poor control on MDI are offered a trial of CSII. Using this screening

process, more than 95% of those started on CSII are improved and continue with pump treatment.

The low usage of CSII in the UK; patient experiences of access to specialist services

It is well known that uptake of CSII in the UK is very low, probably no more than 1% of people with type 1 diabetes, compared to 25% in the USA and 10-20% in many European countries such Germany, the Netherlands and Israel. The experiences of patients referred to our clinic are informative as to the reasons for the UK's modest implementation of pump therapy. Our patients are registered with >40 PCTs, about 25% being referred from London, 25% from SE England (mainly Kent) and the remainder from around the UK; 25% have been started on CSII at another centre and referred for continued supervision at Guy's. This allows us a wide ranging view of attitudes to CSII amongst health care professionals and the difficulties of access around the country. The main problems seem to be poor knowledge of the effectiveness, safety and procedures of CSII by consultants, lack of a local CSII programme and team, usually due to competition for resources, and lack of a well-defined referral procedure for areas without local pump facilities.

About 50% of our referrals arise from a long-established link with consultants and PCTs in the Kent area and PCTs belonging to the SE London Insulin Pump Group who are themselves well informed about the indications for CSII but do not yet have a pump service in place. The remaining 50% of patients have often received little support for a trial of CSII from their local health care professionals, sometimes have encountered considerable opposition, and have consequently researched the value of pump therapy, located a pump clinic and asked for a referral from their GP entirely by themselves. Typical comments from patients are that their local consultant 'does not believe in pumps', or 'does not know anything about pumps' or thinks 'pumps are dangerous'.

It is clear that considerable education is necessary about the indications for CSII, and its possible benefits and restrictions. This extends beyond training courses in pump procedures which will be attended mainly by those with an interest in CSII, and the Appraisal Group may want to recommend how education on insulin pump therapy can be extended to the wider medical community.

Numbers likely to benefit from pump therapy

This is an important issue for the Appraisal group to consider because the 2003 NICE Guidance states that 'the proportion of people with type 1 diabetes who would be appropriate for and would take up insulin pump therapy would be of the order of 1% to 2% of the total'. The evidence base for choosing the figures of 1-2% was not presented and this limited range has been widely misunderstood and misinterpreted by commissioners of pump services, particularly in so far as it might justify a cap of 2% on the number of insulin pump users in an area.

I have presented elsewhere the evidence base for estimating the numbers of people with diabetes who might benefit from CSII on clinical grounds alone (excluding patient preference) (Pickup JC Diabetes Care 2006; 29: 1449-1452). The percentage of people with type 1 diabetes treated by MDI who are suffering from severe hypoglycaemia is at least 5%, those with markedly elevated HbA1c (say >9.0%), extreme blood glucose variability and unpredictable moderate hypoglycaemia ~15% and those with the dawn phenomenon ~5% of type 1 diabetic subjects. If we exclude patients unsuitable for insulin pump treatment because they are unable to perform pump procedures, are psychologically unsuitable or simply decline this treatment option and prefer MDI, a conservative estimate for those who ideally should be offered a trial of insulin pump therapy is thus about 15-20% of people with type 1 diabetes. This is similar to the percentage of patients that are already so treated in the USA and several European countries. However, as I have written before (Diabetes Care 2006; 29: 1449-52) 'I do not underestimate the organizational, financial, staffing and political challenges that that must be faced in meeting this target in many countries... Some countries may not be able to achieve this suggested level of pump usage in the near future for several reasons, but that should not influence our estimates of those who might be best treated by CSII on clinical grounds'.

The impact of new insulin analogues and patient education in our clinic

Because all of the patients referred to our Insulin Pump Clinic undergo structured patient education and transfer to MDI regimens based on glargine or detemir insulins before they are offered a trial of CSII, and only those who have continued poor control are considered for CSII, our clinic results confirm that a small but significant number of people with type 1 diabetes and very poor control are improved and managed by these measures alone, and do not need pump therapy (~10%). Equally, we confirm that new insulin analogues and education have not abolished the need for pump therapy, and the vast majority of those referred to the Insulin Pump Clinic remain poorly controlled until treated by CSII. Thus, the mean ± SD HbA1c in patients on isophane MDI was 9.0 ± 1.4%, vs. 9.1 ± 1.5% when they were treated in our pre-pump programme by glargine-based MDI, followed by an HbA1c of 7.2 ± 1.0% when switched to CSII.

This agrees with RCT evidence by others that neither structured patient education (DAFNE, BMJ 2002; 325: 746-56) nor glargine- or detemir-based MDI regimens (e.g. Diabetes Care 2004; 27: 1081-1087) reduce the frequency of severe hypoglycaemia in type 1 diabetes.

Improving implementation of NICE guidelines for CSII

My view is that supply of pump services via local DGH consultant diabetologists is insufficient in the UK. I favour, in addition, the setting up of regional centres of expertise in insulin pump therapy (and intensive insulin therapy) which in some areas will be the main suppliers. University hospitals would be natural starting bases, though not necessarily the only type of centre. Such centres should assess patients, start insulin pump therapy when appropriate and supervise ongoing care, but also take on the role of education for local GPs, hospital doctors, nurses and dietitians, through web sites, local meetings etc, defining the referral procedures in an area and perhaps go some way toward

countering ‘pump prejudice’. This model of pump centres has been well tested now as working within the context of the UK healthcare system.