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Impact of Social Deprivation, Demographics and Centre on HbA1c Outcomes with Continuous Subcutaneous Insulin Infusion

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Novelty Statement
- Continuous subcutaneous insulin infusion (CSII) is often considered the 'gold standard' method of insulin replacement therapy for individual with Type 1 diabetes
- This is the first UK study to specifically report on the interaction of social deprivation, demographics and centre on pre-and post CSII HbA1c levels.
- Those with higher social deprivation and women had higher baseline HbA1c levels. However, the benefits of CSII therapy were not found to be associated with social deprivation or demographics, but only with pre-CSII HbA1c and centre.

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Conflict of interest*:*

ABSTRACT

Aims:

To assess the impact of social deprivation, demographics and centre on HbA1c outcomes with continuous subcutaneous insulin infusion (CSII) in adults with type 1 diabetes.

Methods:

Demographic data, postcode-derived English Index of Multiple Deprivation data and 12 month average HbA1c (mmol/mol) pre- and post-CSII were collated from three diabetes centres in the North West UK region, University Hospital of South Manchester (UHSM), Salford Royal Foundation Hospital (SRFT) and Manchester Royal Infirmary (MRI). Univariable and multivariable regression models explored relationships between demographics, Index of Multiple Deprivation , centre and HbA1c outcomes.

Results:

Data were available in 693 (78%) individuals (centres UHSM, SRFT & MRI: n=90, 112 and 491 respectively); 59% women; age at CSII start: median 39 (IQR 29.5-49.0) years; diabetes duration: 20 (11-29) years; Index of Multiple Deprivation: 15,193 (6,313-25,727). Overall HbA1c improved from 69 (8.5%) to 64 (8.0%) mmol/mol (median) within the first year of CSII. In multivariable analysis, higher pre-CSII HbA1c was significantly associated with higher deprivation (p=0.036), being female (p<0.001), and centre MRI (p=0.005). Following pre-CSII HbA1c adjustment, post-CSII HbA1c or HbA1c change were not related to demographic factors and deprivation, but remained significantly related to the centre; UHSM & SRFT had larger HbA1c reductions with CSII, compared to MRI (median -7.0 [-0.6%] vs. -6.0 [-0.55%] vs. -4.5 [-0.45%] mmol/mol p=0.005).

Conclusions:

Higher pre-CSII HbA1c levels were associated with higher deprivation and being female. CSII improves HbA1c irrespective of social deprivation and demographics. Significant differences in HbA1c improvements were still observed between centres. Further work is warranted to explain these differences and minimise variation in clinical outcomes with CSII.

Keywords: type 1 diabetes, continuous subcutaneous insulin infusion, insulin pump therapy

Insulin pump therapy, also known as continuous subcutaneous insulin infusion (CSII), is considered the 'gold standard' of insulin replacement therapy for people living with Type 1 diabetes (T1DM) (1). Use of CSII has been shown to improve overall glycaemic control, as measured by HbA1c, and reduce the burden of hypoglycaemia (2-4).

There is considerable variation in access to CSII in the United Kingdom (5). According to the National Insulin Pump audit of 2016/2017, the proportion of those with T1DM treated with CSII varies from less than 5% to more than 50% in participating centres. Notably, there is considerable variation in HbA1c levels achieved between individual centres, including the proportion of those with HbA1c below 7.5% (59 mmol/mol) (from 17% to 69%). Overall, approximately 15% of people living with type 1 diabetes in England are treated with CSII, but the proportions are lower in areas with higher deprivation (5).

Greater Manchester has a population of 2.8 million, with multi-ethnic and socially diverse groups. It is the first region in the UK to have a fully devolved health and social care budget, providing new opportunities to better serve the needs of the people living and working in the area (6). As recent national diabetes audits have shown variation of treatment target achieved, it is thus imperative to understand potential factors such as demographics and level of deprivation which may influence diabetes care and outcomes. Our objective was to compare and evaluate factors associated with changes in HbA1c levels within a year of starting CSII between the three hospitals in the region, accounting for demographics and deprivation measured with the postcode derived English Index of Multiple Deprivation.

Research Design and Methods

Setting: We conducted this study at three Greater Manchester hospitals – University Hospital of South Manchester (UHSM), Salford Royal Foundation Hospital (SRFT) and Manchester Diabetes Centre, Manchester Royal Infirmary (MRI).

Design: Retrospective observational cohort study.

Inclusion criteria: We included individuals initiated on CSII therapy between the years 2000 and 2015 who had paired HbA1c data.

Exclusion criteria: We excluded individuals whose CSII start date was unknown or those whose relevant pre/post-CSII data were unavailable.

Indication for CSII: In line with current national guidance, indications for CSII included poor glycaemic control, problems with hypoglycaemia, or glycaemic variability/erratic control.

Data collection: Demographic variables and HbA1c data were obtained from electronic medical records at individual centres. HbA1c data were collected from 12 months before and up to 12 months after initiation of CSII. The mean annual HbA1c (pre and post CSII) were used for all analysis. Typically, one to three HbA1c tests were available per patient before and after pump

start. We obtained the English Index of Multiple Deprivation 2015 for each participant's postcode from the Ministry of Housing, Communities and Local Government(7). The English Index of Multiple Deprivation is the official measure of relative deprivation for small areas in England and ranks these areas from 1 (most deprived area) to 32,844 (least deprived area).

CSII training: There were differences in pre-CSII structured education participation in all three centres. Approximately 84% and 53% of individuals in UHSM and SRFT respectively had completed the Dose Adjustment for Normal Eating (DAFNE) structured education course prior to starting CSII, whilst 20% in MRI had participated in a local structured education course. The remaining individuals in MRI received individualised training lasting 1 to 3 hours, which encompassed carbohydrate counting and other aspects of diabetes self-management, before commencing CSII therapy. In all three centres, a CSII training session lasting 3 to 4 hours, which included sick day rules and technical trouble shooting, was provided to all individuals. Established methods were applied to set initial basal rate settings (i.e. 70 to 80% of total daily dose on multiple daily injections, divided by 2).

Statistical analysis: Descriptive statistics were used to examine the demographics and HbA1c levels (raw and change), alongside boxplots. Differences between centres were tested via Fisher's exact tests (discrete data) and Kruskal Walis tests, with a post-hoc nemenyi test applied to analyse for differences between the three centres.

Univariable and multivariable regression models (full models alone) were utilised to assess relationships between individual outcomes: pre- and post-pump HbA1c, change in HbA1c and explanatory variables: age at pump start (years, standard and centred on the median), deprivation index (standard and centred on the median, scaled in units of 10^{-3}), gender (baseline female) and duration of diabetes at pump start (years, standard and centred on the median).

All p-values are two-tailed and values less than 0.05 were considered statistically significant. All analyses were conducted in R version 3.2.4 [R Core Team (2016). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.[URL: https://www.R-project.org/]

Results

Pre and post HbA1c data were available for 693 individuals (78%). Demographics and HBA1c data for the whole cohort and individual centres are shown in Table 1. Significant differences in gender and deprivation index were noted between the three centres. Although the spread of deprivation was wide across all three centres, median deprivation index was lowest (highest deprivation) in MRI. Overall, HbA1c improved from median 69 (IQR 61-80) to 64 (55-73) mmol/mol, (8.5% to 8.0%) within 1 year of CSII. The percentage of individuals with HbA1c level ≥ 69 mmol/mol (8.5%) reduced from 51.7% pre-CSII to 34.5% post-CSII. Patients with poorer glycaemic control at baseline showed larger HbA1c improvements compared to those with lower HbA1c levels (Supplemental Fig 1).

In a multivariable regression model combining deprivation index, age, duration of diabetes and gender, higher pre-CSII HbA1c levels were associated with higher levels of deprivation (p=0.011) and being female (p=0.001). However none of the demographic variables remained significant for post-CSII HbA1c or HbA1c change, when pre-pump HbA1c levels were adjusted for.

In the unadjusted analysis, significant differences were found between centres in pre and post HbA1c levels (Table 1). However the percentages of individuals achieving greater than 5 mmol/mol (0.5%) reduction in HbA1c were similar across centres (UHSM: 67.8% vs. SRFT: 64.3 vs. MRI: 63.7%, p=0.783).

Centres UHSM & SRFT were associated with lower pre-CSII HbA1c levels than MRI, even after adjusting for demographics and Index of Multiple Deprivation (p=0.015 and 0.012 respectively). Similarly, UHSM & SRFT demonstrated significantly lower post-CSII HbA1c levels (p=0.042 and 0.004 respectively) and greater change in HbA1c levels than MRI (median change -7.0 [-0.6%] vs. -6.0 [-0.55%] vs. -4.5 [-0.45%] respectively, p=0.005), even after adjusting for demographics, Index of Multiple Deprivation and pre-CSII HbA1c levels.

Table 2 quantifies the covariate effects along with the adjusted overall HbA1c changes from baseline. Change in HbA1c levels post-CSII was significantly associated with baseline HbA1c and centre. The model suggests each one mmol/mol higher baseline HbA1c level is associated with a 0.45 mmol/mol greater lowering in post-CSII HbA1c level. This translates to a HbA1c lowering of 29 mmol/mol (4.8%) for a woman from MRI with a pre-CSII HbA1c of 120 mmol/mol (13.1%) when all other covariates are fixed at their sample median.

Out of the whole cohort 141 (20%) had undertaken the Dose Adjustment for Normal Eating (DAFNE) course prior to starting on CSII. Those with DAFNE training had lower pre-CSII HbA1c; 67 (58, 73) vs 70 (61, 81), p=0.001 [8.3% (7.5, 8.8) vs 8.6% (7.7, 9.6%)] and lower post-CSII HbA1c 60 (54, 68) vs 65 (56, 74), p<0.001 [7.6% (7.1, 8.4) vs 8.1% (7.3, 8.9], compared to those who had not done DAFNE. However once adjusted for pre-CSII HbA1c,

deprivation index and centre, participation in DAFNE was not associated with pre, post or change in HbA1c with CSII. (Data not shown).

Discussion

Our study shows that CSII improves HbA1c irrespective of social deprivation status and demographics, however variation in HbA1c outcomes exists between different diabetes centres. The majority of individuals at UHSM & SRFT had participated in a validated structured education programme (DAFNE) before starting CSII therapy. In the unadjusted analysis those who had done DAFNE had lower pre and post CSII HbA1c levels. However after adjusting for deprivation index, pre-CSII HbA1c and centre, participation in DAFNE was not associated with HbA1c differences. Overall improvements in HbA1c during our study are broadly in keeping with published literature from UK (2; 8) and elsewhere (9). Notably our data also confirms other studies which showed larger HbA1c improvements in individuals with higher pre-CSII HbA1c values (3). In our study the number of individuals using CSII was considerably larger at MRI than UHSM and SRFT. At MRI approximately 44% of adults with T1D are treated with CSII, in contrast to UHSM and SRFT where 18-20% are treated with CSII. This may be due to some differences in the interpretation of CSII entry criteria or patient selection even amongst neighbouring Trusts. Impact of any differential interpretation of entry criteria or patient selection on HbA1c outcomes remains unclear.

In a previous study of children and adolescents, a 500 patient higher centre size was associated with a 1.5 higher odds of CSII use in an analysis that adjusted for age, gender and diabetes duration. However, the authors of this paper found no correlation between the proportion of CSII users in each centre and HbA1c (r= -0.26, p=0.084).(10)

We also used National Diabetes Audit, Insulin Pump Report 2016-17 (5), to evaluate relationships between the number of CSII users at each centre and: a) mean achieved HbA1c; and b) the percentage of individuals with HbA1c below 7.5% (Report available at: https://digital.nhs.uk/data-and-information/publications/statistical/national-diabetes-audit/insulin-pump-report-2016-17). We found no relationship with number of CSII users and HbA1c outcomes.

Our study has several strengths, one of which being the first UK study to specifically report on the impact of social deprivation on pre- and post-CSII HbA1c levels. Those with higher social deprivation had notably higher baseline HbA1c levels. However the benefits of CSII therapy were not found to be associated with social deprivation, only with pre-CSII HbA1c and centre. Yearly-averaged pre- and post-CSII HbA1c levels were used to maximise precision in estimating change in glycaemic control. We included a large sample size with wide socio-economic status (Interquartile range of the Index of Multiple Deprivation from 6312 to 25727). Limitations and caveats include the observational nature of the study, lack of information about hypoglycaemia, ethnicity, psychological status, staffing ratios and number of contacts and clinic visits among pump users in the three centres.

In conclusion, higher pre-CSII HbA1c levels were associated with higher levels of deprivation and being female. We also found significant differences in HbA1c outcomes with

CSII between three neighbouring hospitals in Greater Manchester. These differences were not due to social deprivation or commonly measured demographics such as age, sex or duration of diabetes. Although the two centres with better outcomes had more patients who had undertaken structured education, there were no differences in HbA1c outcomes between those who had undertaken structured education vs. those who have not, after adjusting for deprivation index, pre-CSII HbA1c and centre. Further work is warranted to understand whether other unmeasured confounders, such as psychological factors may explain these differences. People with type 1 diabetes from deprived backgrounds should be provided with equal access to CSII; there should be more comparisons of outcomes between units providing CSII services.

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