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UK lipohypertrophy interventional study

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ABSTRACT

Introduction: Lipohypertrophy (LH) is one of the most common complications of insulin therapy. We conducted a prospective study in 18 UK centres to assess the impact of a targeted LH intervention on a range of clinical, biological and socio-economic parameters.
Methods: Seventy-five insulin-injecting patients were recruited randomly and were followed prospectively for 3–6 months, with results compared to baseline values. Interventions included the use of an intensive education program and a switch to a 4 mm pen needle.
Results: At all injection sites LH decreased significantly by the end of the study, either disappearing completely or shrinking by approximately 50% from its original diameter. Injections into LH decreased by more than 75% by the end. Most patients were not correctly rotating injection sites at the beginning but by the end most were, by a 5-fold margin. Only 1/3 of our subjects used the 4 mm needle at the beginning of the study, however, virtually all did by study end. The mean HbA1c improved by more than 4 mmol/L and there were significantly lower levels of unexpected hypoglycaemia and glucose variability. Total daily doses of insulin dropped by an average of 5.6 IU by study end.
Conclusions: We believe the impressive clinical improvements seen with training to prevent LH can be achieved by wide adoption of the interventions outlined in this study.

1. Introduction

Performing insulin injections correctly and consistently is challenging. A number of large international surveys have shown that patients requiring insulin often do not perform injections properly, even after years of practice [1–4]. Recently new recommendations for optimizing insulin delivery have been agreed and published [5–7]. These recommendations urge patients and professionals to address each of the key injection parameters at the beginning of insulin therapy as well as at least annually thereafter. In the UK, a group of diabetes nurse specialists has created FIT (Forum for Injection

Abbreviations: BMI, Body Mass Index; CRF, Clinical Report Form; FIT, Forum for Injection Technique; FITTER, Forum for Injection Technique and Therapy: Expert Recommendations; GCP, Good Clinical Practice; HbA1c, Glycated hemoglobin; IM, Intramuscular; ITQ, Injection Technique Questionnaire; IU, International Unit (of insulin); LH, Lipohypertrophy; NHS, National Health Service (UK); PN, Pen Needle; SC, Subcutaneous; SD, Standard Deviation; T1DM, Type 1 diabetes; T2DM, Type 2 diabetes; TDD, Total Daily Dose (of insulin); TITAN, Third Injection Technique workshop in AtheNs; UK, United Kingdom

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Technique), dedicated to improving this practice. FIT has issued recommendations which have been widely accepted as the gold standard throughout the UK, but the effectiveness of these guidelines has not been tested in everyday clinical practice until our study.

One of the main concerns of FIT was to decrease the most common complication of insulin therapy, lipohypertrophy (LH). LH is a swelling and/or induration of fat tissue which results from improper injection techniques. In prevalence studies LH has been found to be very common, affecting up to two-thirds of insulin injectors [8,9]. Vardar [10] identified three independent risk factors for LH: Duration of insulin use, with longer use associated with more LH ($p = 0.001$); Site rotation, with a failure to correctly rotate associated with higher LH risk ($p = 0.004$); Changing needles, with needle reuse also associated with LH ($p = 0.004$). Two other studies have identified similar factors [8,11].

When injections are given into LH, insulin is absorbed more slowly or with greater variability, reaches lower peak levels and has weaker glucose-lowering effects [12–17]. Patients injecting into LH find that their glucose values often rise, become more variable or are more erratic. To compensate, patients often inject higher and higher doses of insulin, which can worsen glycaemic variability as well as waste money. When they switch back from LH to normal tissue these effects reverse, but they must often lower their insulin doses to avoid hypoglycaemia [8,9,18,19].

We conducted an audit of 18 UK centres which implemented the FIT guidelines to assess the impact on LH as well as on a range of clinical, biological and socio-economic parameters.

2. Methods

In 18 real life settings throughout the UK (see Appendix A) we provided state-of-the-art injection technique training for 75 adult patients who inject insulin. This training included the use of an intensive education program (specified later) and a switch to a 4 mm pen needle (PN) (BD MicroFine Ultra™ with Pentapoint™, BD, Oxford, UK). Study nurses were trained in the best injection technique practices and in the appropriate use of injecting products, tools and materials. Patients were recruited randomly and were followed prospectively. Their outcomes at 3–6 months were compared to baseline values. This variable follow-up time was linked to clinic visit intervals in the UK, which vary between 3 and 6 months.

The primary objective of the study was to assess insulin usage, as measured by total daily dose (TDD), before and after the intervention. The secondary objective was to evaluate its impact on HbA1c; tertiary objectives were to assess effects on glycaemic variability, unexpected hypoglycaemia and various other disease burden parameters.

Study nurses were trained in optimal injection technique; LH detection, treatment and prevention; and the use of LH-specific tools and materials. The educational programme for nurses consisted of face-to-face training by Clinical Experts, mandatory completion and 'pass' of the E4H/FIT eLearning Programme[20] and demonstration of competency standards to the level of FIT UK [21], TREND UK [22] and TITAN [6].

The specific topics covered in the day-long programme consisted of:

1. How to accurately assess injection technique and identify patient technique errors.
2. Anatomy of Skin, Subcutaneous (SC) tissue and Muscle.
3. Assessing Intramuscular Injection Risk.
4. Optimal injection technique.
5. LH prevalence, pathogenesis, clinical and socioeconomic burden.
6. How to detect LH using live patient models, video demonstration and hands-on technique.
7. LH prevention – including correct rotation, grids and the effects of needle reuse.
8. Efficacious care and follow-up for patients with LH, including measurements in mm of LH lesions.
9. Optimal pen needle choice.

The tools in the training kit were the:

1. Think Lipo education slide deck.
2. Think Lipo Infographics.
3. FIT Unexplained Hypoglycaemia and Glycaemic Variation Wheel.
4. E4H/FIT eLearning.
5. LH detection kit—including gel, skin safe pen and body map.
6. New rotation grids and support materials.
7. Rotation Grid FAQ.
8. LH formation animation.
9. LH detection video.

Subject identity was kept confidential at all times and the study was conducted according to Good Clinical Practice and the Helsinki Accords. The study was organized in cooperation with BD (Becton, Dickinson & Co., Oxford, UK). BD associates did the initial training and distributed Clinical Report Forms (CRF) to centres and collected them once they were filled out. BD played no role in discussions with patients or the completion of forms. No participant identifying information was made available to BD. Ethics committee approval, though not required for such an audit, was nevertheless obtained whenever specifically requested by a centre and/or by local regulators. The participating centres and clinical trainers are listed in the Appendix A.

SPSS™ software (IBM, Armonk, NY, USA) was used by one of the author (KS) to perform the data analysis. Descriptive statistics, frequencies and rankings were calculated. Chi-squared analysis was performed where appropriate for contingency tables. Log linear analysis and ANOVA were used for the analysis of individual parameters and logistical regression and correlation analysis were used for multi-parametric analysis. In the regression model as each new variable was added there was a check to see if any other variable(s) could be deleted without appreciably increasing the residual sum of squares. The threshold for staying in the model was a $p < 0.05$. Two-tailed tests were used in all analyses except for TDD, for which it was felt appropriate, based on earlier studies [8,9], to use a one-tail test.