A pan-European epidemiologic study of insulin injection technique in patients with diabetes

Kenneth Strauss*, Heidi De Gols, Irene Hannet, Tuula-Maria Partanen, Anders Frid

ABSTRACT

Aim. A large pan-European epidemiologic survey of insulin injection techniques was performed in order to determine the epidemiologic profile by centre, country and continent of major issues surrounding insulin injection.

Methods. European insulin-injecting, type 1 or 2 diabetes patients, using insulin for at least 6 months via an insulin pen or syringe; 22 sites in seven countries, 1002 patients in total, 51% female, 58% type 1.

Results. Nearly 70% of patients inject using a pinch-up and this practice is associated with improved HbA1c. Thirty per cent of patients reported having lipohypertrophy. Concurrent nurse evaluation found the prevalence to be 27%. Independent risk factors for lipohypertrophy were found to be failure by the patients to check injection sites regularly, failure to rotate sites and longer duration of DM. Less than 50% of patients reported that they were taught about lipohypertrophy. Needles were used 3.3 times on average in Europe, with wide variation by country. Male sex, type 1 diabetics, a high daily number of injections and the use of the 12.7 mm length needle were factors associated with high needle reuse. Needle reuse, even more than once, increased the risk of lipohypertrophy by 31%. Nearly half of patients dispose of their needles directly into the trash after protecting the needle (recapping or clipping). Alarmingly, 22% dispose directly into the trash without protection.

Conclusion. There is a considerable way to go in ensuring optimal insulin injection practices. The issues raised by this study must be addressed by focused and intensive HCP efforts. Copyright © 2002 John Wiley & Sons, Ltd.

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Introduction

Diabetes nurses and observant patients have long known that the technique of injection is critical to the successful use of insulin, but the medical community at large and most insulin-using patients remain woefully unaware of the importance of proper injection technique. Recent years have seen increased emphasis on intensive insulin therapy and on the critical role of blood glucose measurements, but few realize that correct insulin injection technique is as important to good glucose control as the type and dose of insulin delivered[1-5]. The incorrect choice of sites and techniques may modify insulin absorption parameters, leading to an uncoupling of maximum glucose load and peak insulin effect. This can lead to both unexpected hyperglycemia and an increased risk of nocturnal hypoglycemia[6-10].

The first *Insulin Injection Technique Workshop*, held in June 1997 in Strasbourg, brought together over 40 injection experts from across Europe and the world. This meeting and the paper that followed[11] highlighted large areas of uncertainty in the field and called for a large study to examine the way patients actually inject insulin. It was felt that without a sound epidemiologic foundation it would be impossible to evaluate the effectiveness of current teaching approaches or to make general recommendations for change.

An attendee at the Strasbourg meeting, Diabetes Nurse Specialist Tuula Maria Partanen, of Finland, developed and tested an anonymous, voluntary questionnaire covering all aspects of insulin injection techniques. This questionnaire consisted of an initial patient section (administered by an experienced diabetes nurse) followed by a section completed by a nurse after an actual injection was observed and a meticulous examination made of all injection sites.

The objectives of this study were to understand the epidemiologic profiles for the major insulin injection parameters, to determine the leading causes of variability in injection technique, their ranking and their interactions and to query the patients' perception of the injection process, the psychological barriers and the aids.

Methods

Subjects

Over 18 months, from October 1998 to March 2000, 1002 insulin-injecting type 1 and 2 diabetic patients from 22 centres in seven European countries participated in the study. (For the names of participating centres and investigators see the acknowl-

Kenneth Strauss*, Heidi De Gols, Irene Hannet, Medical Department, Becton Dickinson - Europe, Erembodegem, Belgium, Tuula-Maria Partanen, North-Savo Polytechnic, School of Social and Health Professions, Kuopio, Finland, Email address: tuula-maria.partanen@pspt.fi, Anders Frid, Department of Medicine, University Hospital of Lund, Lund, Sweden, Email address: dr.frid@telia.com

*Correspondence to: Kenneth Strauss, MD, 24 Denderstraat, POB 13, Erembodegem-Aalst, 9320 Belgium. Email address: Kenneth_Strauss@Europe.bd.com

Table 1: Number of subjects per European country

Country	Number of patients	Percent	Cumulative percent	Number of centers
Sweden	101	10.1	10.1	1
Belgium	66	6.6	16.7	1
Germany	258	25.7	42.4	6
France	178	17.8	60.2	4
Italy	149	14.9	75.0	3
Spain	129	12.9	87.9	3
UK	121	12.1	100.0	4
Total	1002	100.0		22

Table 2: Overall descriptive statistics

	N	Mean	Std. Deviation	Minimum	Maximum
Age (years)	998	46.9	18.4	13.00	89.00
Weight (kg)	995	75.0	15.8	40.00	168.00
Height (cm)	995	168.0	9.3	140.00	200.00
Body Mass Index*	994	26.5	5.2	15.79	62.46
Duration of diabetes (years)	993	14.7	10.6	0.40	58.00
Injections/day	992	3.3	1.2	1.00	8.00
Dose of Insulin (IU)/day	992	48.8	23.5	3.00	178.00
Times patient uses a single needle	812	3.3	3.1	1.00	11.00
HbA_{1c} according to patient	724	7.9	1.8	4.20	16.00
HbA_{1c} according to nurse	968	8.0	1.7	4.30	16.20
Glucose controls/day	335	3.4	1.3	1.00	8.00

*BMI=height (in meters)/(weight in kg)^2

edgements section at the end of the article.) Subjects were 13 years of age or over and had used insulin for at least 6 months. In order to eliminate selection bias subjects were accessioned to the study on a sequential basis, i.e. consecutive eligible and consenting patients entering the clinic were accessioned. Injections were performed with an insulin pen or syringe or both and participants gave verbal consent to participate. Becton Dickinson sponsored the study. No patient identifying information was made available to the sponsor and patients were informed that their care would not be affected in any way by their participation. They were not put at risk by the study and were not paid to participate. Ethics committee approval was obtained.

Questionnaire
Besides patient demographic information, the key insulin injection parameters queried by the questionnaire were the following.

Current practice: injection device and needle length, insulin type, number of injections/day, frequency of dosage adjustment, choice of injection site, use and characteristics of skin folds (pinch-up), needle entry angle, size of injecting zone, site rotation, disinfecting prior to injecting, dwell time of needle under the skin, site inspection by patient and professional, needle reuse, sharps disposal, injection through clothing.

Observed anomalies at injection sites: insulin reflux, bruising, lipoatrophy, lipohypertro-

phy, inflammation, induration, scarring.

Knowledge about injections: identity of teacher, themes covered in training, adequacy of coverage, desire for more knowledge.

Psychological perceptions of injections: ease of injection, pain, needle phobia, missed injections and reasons.

Glucose control: latest HbA_{1c}, knowledge about normal value for HbA_{1c}, frequency of fingersticks, use of glucose control results.

There were also a number of open-ended questions, which allowed the subjects to express opinions not covered in other parts of the questionnaire.

Validation
The questionnaire was first tested in 100 patients in two centres in Finland. Further validation studies were performed on another 100 patients in Lund, Sweden, in 1998, and once the questionnaire was fully validated the wider study was begun.

Analysis
SPSS software was used. Descriptive statistics, frequencies and rankings were obtained. Chi-squared analysis was performed where appropriate for contingency tables. Log-linear analysis and ANOVA were used for the analysis of individual parameters and multiple regression and correlation analysis were used for multiparametric analysis. Two-tailed tests were used in all analyses. Initially each of the 22 sites was analysed independently and only when the distributions of key demographic parameters (age, sex, BMI and duration of diabetes) were shown to be equivalent were sites pooled into country groupings. The same process was followed for each country grouping before pooling all the data into a total Europe database.

Results
Table 1 presents the contributions by country to the study. The percentages from each country correspond roughly to the proportion of that country's population to the total European population. Of the 22 centres approximately one-third ($n = 8$) were specialist diabetes clinics, one-third ($n = 7$) were community care centres and one-third ($n = 7$) were general practice centres. Half ($n = 11$) were urban and the other half were town or sub-urban. Table 2 shows the descriptive statistics of the patient population. Four hundred and ninety-one subjects were male (49.2%). The age distribution was bi-modal because

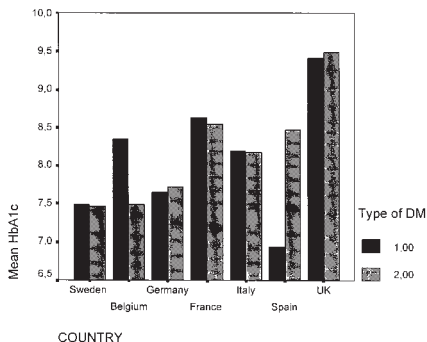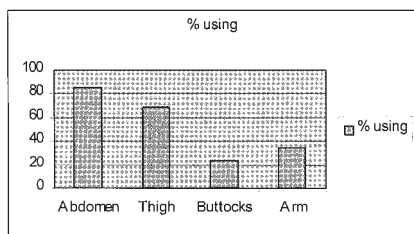**Figure 1.** HbA$_{1c}$ values by country as a function of type of diabetes.

Figure 2. Number of injections per day by country.

Figure 3. Percentage of patients using various injection sites; numbers add to more than 100% because of use of multiple sites.
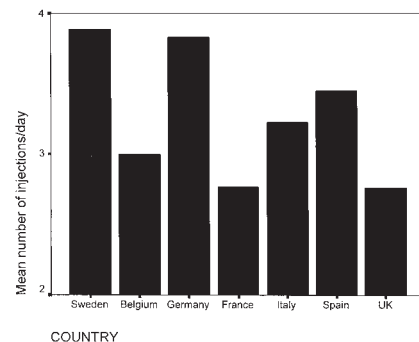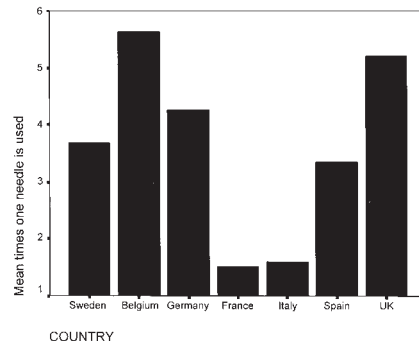

Figure 4. Relationship between the number of times a single needle is used to the presence of lipodystrophy for the two most common needles used, the 8 and 12.7 mm.

number of glucose controls performed/day (p = 0.384), rotation of injection sites (p = 0.584), injecting perpendicularly into abdomen (p = 0.375) or not pinching up in the thigh (p = 0.890), but it was highly significantly associated with (p = 0.0001) adjusting insulin doses. Patients who adjusted their own insulin doses tended to have lower HbA$_{1c}$ values, and the more frequent the adjustment the lower the HbA$_{1c}$. Sixty-two per cent of patients reported seeing bruising at the site of injection, 30% reported fatty swelling at the site of injection consistent with lipohypertrophy and 27% of patients had lipohypertrophy confirmed by nurse examination. Only 38% reported rotating injection sites each time they injected regular insulin. The presence of lipohypertrophy was not found to be significantly related to the length of needle (p = 0.390), the presence of brusing at the site of injection (p = 0.330), the sex of the patient (p = 0.797), the use or not of a pinch-up (p = 0.302), the angle of injection (p = 0.218), disinfecting the skin before injecting (p = 0.360) or the length of time the needle is left in the skin (p = 0.128).

Needle reuse is more prevalent amongst 12.7 mm needle users than amongst 8 mm users (Figure 4), but in both groups those who reuse needles more frequently are more likely to have lipos than those who do so less frequently. The number of times a single needle is used varied widely by country (Figure 5), with France and Italy having the lowest rates and Belgium and the UK the highest. Since the time of this study, pen needles have become available on prescription in the UK, and this may have affected the rate of needle reuse. Males reused needles significantly (p = 0.003) more frequently than females, and type 1 patients more than type 2s (p = 0.020). A possible explanation for the latter may be the increased number of injec-

of the mixture of type 1 and 2 patients. There were 562 type 1 patients (58% of total), with a mean age of 36.3 years (SD 15.4), and 404 type 2 patients, with a mean age of 61.8 years (SD 10.3). HbA$_{1c}$ did not differ as a function of type of diabetes; country breakdowns are shown in Figure 1. The average number of injections given in this study was 3.3/day (SD 1.1). Figure 2 shows three main groupings by country: approximately four injections/day were the average in Sweden and Germany, approximately three injections/day in Belgium, Italy and Spain and between 2.5 and 3 injections/day in France and the UK. Nineteen per cent of patients used syringes, 64% insulin pens and 15% both devices. Four per cent of subjects use the 5 mm needle, 5.5% the 6 mm needle, 55% the 8 mm needle and 36% the 12.7 mm needle. The most commonly used injection site was the abdomen, followed by the thigh (Figure 3). Use of the buttocks (by 222 patients out of 967 total) was associated with lower HbA$_{1c}$ values (p = 0.050). When asked, 69.4% of patients claim to pinch a skin fold when they inject. Nurse observation found that 73% of patients asked to perform an injection used a skin fold. Three out of four patients pinch in Sweden, Germany and Spain, two out of three patients in France, Italy and UK and
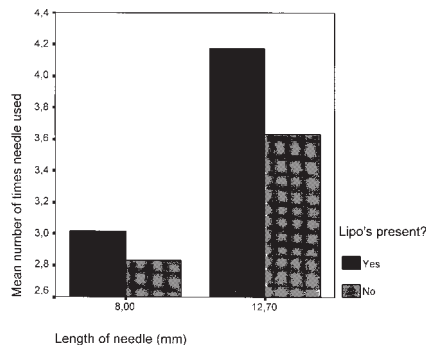
one out of two patients pinch in Belgium. Patients who pinch up had lower HbA$_{1c}$ values than those who do not pinch, 7.9 versus 8.2; p = 0.032). There was a significant relationship (p = 0.001) between leaving the pen needle in longer and a lower HbA$_{1c}$. Over 10 seconds seemed to be the ideal dwell time. Patients who regularly inspect their injection sites have significantly (p = 0.03) lower HbA$_{1c}$ values. HbA$_{1c}$ was not significantly related to

Figure 5. Needle use by country.

Figure 6. Needle reuse as a function of the length of the needle.
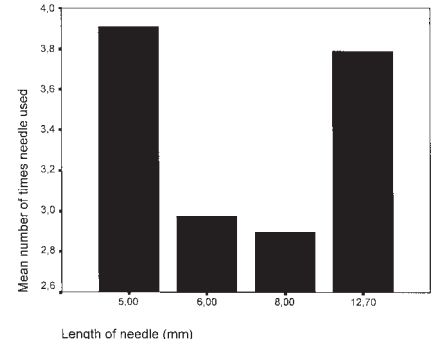
Table 3: Needle use, one time vs. more than once

Number of times needle used	Number of patients	Percentage patients
1	410	40.9%
>1	592	59.1%
TOTAL	1002	100.0%

tions given per day by type 1s. Needles are reused more often by patients who use the shortest (5 mm) and longest (12.7 mm) needles (Figure 6), although the former represented only a small fraction (4%) of the total needle count in this study. Needle length, in this study, was not related to bruising at the site of injection (p = 0.304) or to injection pain (p = 0.398).

Table 3 gives the overall breakdown of patients who use the needle only once versus those who use it more than once; 40.9% of European patients use a needle only once and then discard it; 59.1% use it more than once. A significant number of patients use the same insulin needle more than 10 times. There is a strong tendency (p = 0.067) for patients who reuse needles to have *more* lipohypertrophic lesions than those who use the needle only once. The risk of lipohypertrophy rises as the mean number of needle uses increases. Although lipohypertrophy is sometimes found in persons who do not reuse needles, there is a 31% increased risk of having lipohypertrophy if one reuses.

The link between lipohypertrophy and needle reuse was looked at in sub-groups, to determine whether there were special populations at risk. Pen users have a tendency to use the same needle more times than syringe users. Patients who use pens and reuse needles have a higher risk (p = 0.058) of having lipohypertrophy. Although lipohypertrophy is sometimes present in pen users who do not reuse, there is a 44% increased risk of lipohypertrophy for pen users if they reuse needles. Patients were asked to estimate the size of their injection area. Those who inject into small zones (5 cm by 4 cm or one-quarter the size of a postcard) and reuse needles have a much higher risk (p = 0.0001) of having lipohypertrophy, nearly threefold greater, than if they did not reuse. Patients are often taught to rotate their injection sites regularly, but this study found that only 38% did. Those who do not rotate their injection sites and reuse needles have a 43% greater risk (p = 0.088) of having lipohypertrophy than those who use a needle only once.

Virtually all patients perform injections at home, but a surprisingly high percentage inject in private locations such as toilets (53.8%) or at work (32.2%). Nearly 70% of patients indicate the need to learn more about insulin injection, a remarkable percentage considering the mean duration of diabetes in this population was 14.7 years. Less than 60% of patients state that certain key themes were covered in their training: prevention of lipodystrophy, mixing insulins, needle length, use of back-up syringes (in the event of pen failure) and the safe disposal of used needles. Figure 7 shows disposal practices overall. Forty-seven per cent of patients dispose of their sharps in the trash after protecting the tip (recapping or clipping off the tip). Shockingly, 22% admit throwing their sharps away into the trash or flushing them without protecting the tip.
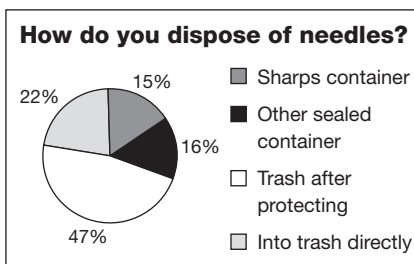
Discussion

This paper reports on the largest epidemiologic survey of insulin injection technique yet published. Over a thousand insulin injecting patients across Europe were surveyed in a randomized fashion and then examined by trained diabetes nurses.

Injection technique and glucose control

The use of a pinch-up has been recommended by experts in the injection of insulin. The First Insulin Injection Technique Workshop in Strasbourg[11] issued the following recommendation:

Figure 7. Disposal practices for the contaminated needles.

How do you dispose of needles?

- 15%
- 22%
- 16%
- 47%

- Sharps container
- Other sealed container
- Trash after protecting
- Into trash directly

For everyday use in most patients, *subcutaneous* rather than intramuscular, intraperitoneal or intradermal injection of insulin is preferred. Recent research has allowed direct visualisations of insulin as it is injected into tissue (CT, US). *Pinching up the skin* is one method that has been documented by CT scan and ultrasonography to increases the chance of subcutaneous injection. If one performs a pinch up it should be made with 2 fingers (thumb and index). The fold should be maintained throughout the injection, and 5-10 seconds afterwards, before removing the needle.[11]

Our study found that nearly 70% of patients inject using a pinch-up and that pinching up is associated with improved HbA_{1c}. Leaving the pen needle in longer was also associated with improved HbA_{1c}, possibly because this allows more time for insulin to diffuse into SQ tissues. A dwell time of over 10 seconds appeared to be optimal. Use of the buttocks as an injection site is also associated with improved HbA_{1c}, although it is practiced by fewer than 25% of patients in this survey.

Injection technique and lipodystrophy

Lipohypertrophy (often known by patients as a 'lipo') is described as a benign tumour-like swelling of the fatty tissue often seen at injection sites of insulin-administering diabetic subjects (up to 25% of insulin injecting diabetics in various studies)[12-18]. Lipos can rarely appear as shiny, firm areas on younger skin but typically are movable soft tissue lesions similar to lipomas. They vary greatly in size and are often felt more easily than seen. The etiology of these fatty lumps is not completely understood, but it is believed that, in susceptible subjects, an 'incorrect' injection technique may facilitate their occurrence.

Recent studies in children[12] and adults[14] demonstrated that lipos can be made to decrease in size by systematic and appropriate rotation of injection sites. In these studies significant size reduction (30-50%) of the lipos was achieved in 3 months. In addition HbA_{1c} values were also found to improve significantly and this improvement seemed to be correlated with the extent of lipo size reduction. Other studies[13,15] have shown that insulin absorption from lipodystrophic tissue is erratic, resulting in poorer glucose control. Lipos may also be responsible for significant insulin 'over-usage' or 'wastage', since

appropriate rotation schemes not only reduce the size of lipos but allow the patient to reduce their daily insulin consumption by up to 50%[19].

Though the exact causes of lipos are unknown, the predisposing conditions are clearly trauma to the skin and SQ tissue, which is repeated in time and place in the presence of insulin[20-24]. We cannot control the increase in the dose of insulin, nor the increased number of injections that accompany intensive therapy, but we can diminish the trauma to the skin and SQ tissue (by avoiding excessive reuse of needles) and we can decrease the exposure to place and time by careful site rotation.

Thirty per cent of patients in this study reporting having lipohypertrophy at any one of their injection sites. Nurse evaluation found the prevalence to be 27%. There is a strong tendency to more lipohypertrophy in patients who engage in some kind of needle reuse (use needle more than once) than in those who never reuse. Certain sub-groups seem especially vulnerable to lipohypertrophy if they reuse needles: patients who use insulin pens, patients who inject into small injection zones and patients who fail to rotate sites of injections on a regular basis. Although it is not possible to avoid all lipohypertrophy, this study supports the advice that for each insulin injection patients should change to an area that is lipo-free, change to a fresh site for every injection and change to a new needle with every shot. At the time of this study, three of the authors were employees of BD, a manufacturer of needles and main sponsor of the study. We are only too aware of the potential for conflict of interest in the above conclusion, and have done our best to eliminate this bias. We also invite others to perform similar studies in order that these conclusions might be challenged and validated.

Surprisingly only 38% of patients in this study rotated sites each time they injected rapid-acting insulin. The known value of a rotation scheme and the relatively low percentage of patients who practice rotation clearly highlight an important educational opportunity for those of us taking care of insulin-injecting diabetic patients. Less than 50% of patients reported they had been taught about effective means for preventing these unsightly and deleterious lesions. It should be emphasized that simply telling patients to rotate sites is not enough. They must be given an organized scheme[12,14] in order to plot a personal strategy for rotation and must be warned against blood sugar variations. Health care workers must check injection sites regularly and intervene appropriately before these lesions appear or enlarge.

Injection technique and needle reuse

Needles were used an average of 3.3 times throughout Europe, but there were wide country to country variations, with France and Italy having the lowest reuse rates. This fact seemed to be related to the instructions given by nurses in these countries not to reuse needles. Needle reuse was associated with male sex, type 1 diabetes, a high daily number of injections and the use of the 5 or 12.7 mm needle. The association of needle reuse with the presence of lipohypertrophy should give pause to those who actively endorse such practices.

Injection technique and sharps disposal

Forty-seven per cent of patients dispose of their syringe or pen needle directly into the trash after protecting the needle by recapping or clipping. Alarmingly, 22% dispose of needles without even this minimum precaution. This is clearly a public health hazard, which is under-appreciated at present. Forty per cent of patients reported receiving no instruction on the safe disposal of used sharps, suggesting that education is an appropriate first step in addressing this problem. It is clear as well that more convenient means of safe disposal should be provided to patients.

Conclusions

This initial survey of insulin injection technique in Europe should be considered a pilot study. Despite the high degree of agreement in the results from site to site and across regions in Europe there is some degree of risk in drawing conclusions for an entire continent or even for a single country from samples of only a few hundred subjects. More extensive studies are clearly needed, and patient populations not specifically targetted here (e.g. pediatrics, geriatric populations and gestational diabetics) should be the subjects of separate studies. Nevertheless, this survey has revealed sobering deviations from optimal injection practice and should provide the impetus for renewed and more innovative educational approaches, as well as pointing the way towards technology- and product-oriented solutions. The willingness is certainly there: more than 70% of patients indicate their need for more injection knowledge.

Keypoints
- Nearly 70% of European patients inject into a pinched skin fold and this practice is associated with lower HbA1c values.
- 30% of patients reported having lipohypertrophy. Subsequent nurse evaluation confirmed this prevalence. Less than 50% of patients reported that they were taught about lipohypertrophy.
- Independent risk factors for lipohypertrophy were found to be failure by patients to check injection sites regularly, failure to rotate sites and longer duration of DM.
- Needles were used 3.3 times on average in Europe, with wide by country variation. Needle reuse, even >1 time, increased the risk of lipohypertrophy by 31%.
- Nearly half of patients dispose of their needles directly into the rubbish after protecting the needle (recapping or clipping). But 22% dispose directly into the rubbish without protection.

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