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# Worldwide Injection Technique Questionnaire Study: Injecting Complications and the Role of the Professional

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## Abstract

From February 1, 2014, through June 30, 2015, 13,289 insulin-injecting patients from 423 centers in 42 countries participated in one of the largest surveys ever performed in diabetes. The first results of this survey are published elsewhere in this issue. Herein we report that the most common complication of injecting insulin is lipohypertrophy (LH), which was self-reported by 29.0% of patients and found by physical examination in 30.8% by health care professionals (HCPs). Patients with LH consumed a mean of 10.1 IU more insulin daily than patients without LH. Glycated hemoglobin levels averaged 0.55% higher in patients with vs without LH. Lipohypertrophy was associated with higher rates of unexplained hypoglycemia and glycemic variability as well as more frequent diabetic ketoacidosis, incorrect rotation of injection sites, use of smaller injection zones, longer duration of insulin use, and reuse of pen needles (each $P<.05$). Routine inspection of injection sites by the HCP was associated with lower glycated hemoglobin levels, less LH, and more correct injection site rotation. Patients were also more likely to rotate correctly if they received injection instructions from their HCP in the past 6 months. Fewer than 40% of patients claimed to have gotten such instructions in the past 6 months, and 10% said that they have never received training on how to inject correctly despite injecting for a mean of nearly 9 years. Use of these data should stimulate renewed commitment to optimizing insulin injection practices.


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In a separate article in this issue we introduce the worldwide Injection Technique Questionnaire (ITQ) survey.[1] That article describes the patient population and its injecting practices as well as survey methods, materials, centers, and participants. The present article addresses injection-related complications and the role of the health care professional (HCP).

## RESULTS

### Lipohypertrophy

To assess the presence of lipohypertrophy (LH), patients were asked: "Do you have any swelling or lumps under the skin at your usual injection sites that have been there for some time (weeks, months, or years)?" Overall, 29.0% answered yes. Nurses were asked to examine all the injection sites for LH both visually and by palpation. They found LH in 30.8% of patients; the frequencies by site and type of examination are shown in Table 1. The frequency of LH was relatively consistent across the 42 countries surveyed. Lipohypertrophy was seen almost twice as frequently in patients with type 1 diabetes mellitus (T1DM) as in those with type 2 diabetes mellitus (T2DM) and was virtually absent in patients with gestational diabetes, probably because of the very short time that such patients have been using insulin (data not shown).

Although there was a correlation between LH lesions that were visible and those that were palpated, it was not 100%. Table 2 presents data on this correlation in abdominal LH (the most frequent site used and consequently the one most frequently reported as having LH). Eighty-four percent of LH could be both seen and felt, but 14% could be felt but not seen. The same pattern is seen with the thigh, buttock, and arm (data not shown).

**TABLE 1. Findings From Visual and Palpation Examination by Nurses for Lipohypertrophy by Site**

| Injection site | Examination type | Lipohypertrophy found (%)[a] |
|---|---|---|
| Abdomen (n=7565) | Visual | 17.3 |
| | Palpation | 21.1 |
| Thigh (n=5425) | Visual | 9.8 |
| | Palpation | 11.2 |
| Buttock (n=2566) | Visual | 2.1 |
| | Palpation | 2.8 |
| Arm (n=4204) | Visual | 11.2 |
| | Palpation | 13.4 |

[a]Overall, the nurses found lipohypertrophy in 30.8% of patients.

When nurses found LH they were asked to measure the lesion along its longest axis. Results are shown in Supplemental Table 1 (available online at http://www.mayoclinicproceedings.org).[2] Lesions of LH varied from a mean of approximately 35 mm (in the arm) to approximately 50 mm (in the buttock), but there was considerable variability around these averages. When nurses found LH they asked the patient whether they were still injecting into it, and 44.0% said yes. Patients still injecting into LH were then asked how often they were doing so and why (Table 3).

Lipohypertrophy is associated with giving more injections per day, an earlier age at diagnosis of DM (especially in T1DM), and a longer number of years with DM and taking insulin (each $P<.05$). We found no association between the presence of LH and body mass index. Just less than one-third of those taking glucagon-like peptide-1 receptor agonists were found to have LH, but there was no association between LH and the duration of this therapy. It is unclear whether LH predated glucagon-like peptide-1 receptor agonist therapy.

**TABLE 2. Correlation Between Visible and Palpable Findings of Abdominal Lipohypertrophy[a]**

| | Visible (No. [%]) | |
|---|---|---|
| Palpable | No | Yes |
| No | 5112 | 23 (2) |
| Yes | 186 (14) | 1102 (84) |

[a]A total of 6423 patients' abdomens were examined. Percentages are based on the 1311 patients with lipohypertrophy.

**TABLE 3. Injections Into Lipohypertrophy**

| Parameter | Patients (%) |
|---|---|
| Frequency (n=1964) | |
| Every injection | 16.7 |
| Frequently (daily) | 39.5 |
| Occasionally (weekly) | 30.3 |
| Seldom (monthly) | 13.5 |
| Reason (n=1866) | |
| Convenient | 16.8 |
| Less painful | 22.1 |
| Just a habit | 34.7 |
| Do not know | 26.4 |

There was a strong association between the presence of LH and the total daily dose (TDD) of insulin (Table 4). A mean of 10.1 IU more insulin was consumed in the population with LH compared with those without LH. In patients with T2DM, this average TDD difference rose to 13.5 IU, whereas in patients with T1DM, the average TDD difference was 5.4 IU. These differences were similar in patients with LH who continued to inject into LH vs those who did not (Table 4).

Similar differences were seen for the various types of insulin: fast-acting analogues (mean of 4.4 IU more in patients with LH vs those without), basal analogues (mean of 1.5 IU more), and premixes (mean of 9.8 IU more) (all differences significant at $P<.05$). All currently used families of insulins were associated with LH (ie, there are no insulins that seem to protect the user from LH). However, it is not possible by the present data to determine whether any one type of insulin has higher risks.

The presence of LH was associated with higher glycated hemoglobin ($HbA_{1c}$) values,

**TABLE 4. TDD of Insulin as a Function of LH[a]**

| Parameter | TDD (IU), mean ± SD | Patients (No.) |
|---|---|---|
| LH present | | |
| Yes[b] | 55.2±33.0 | 2192 |
| No | 45.1±31.5 | 4889 |
| Total | 48.2±32.3 | 7081 |
| Injecting into LH | | |
| Yes[b] | 56.1±33.2 | 1644 |
| No | 47.1±32.2 | 2064 |
| Total | 51.1±32.9 | 3708 |

[a]LH = lipohypertrophy; TDD = total daily dose.
[b]Differences "Yes" vs "No"; significant at $P<.001$.