Observational Study

Managing lipohypertrophy in your practice

Kavita Gupta[1], Sunil Gupta[2]

Lipohypertrophy (LH) is a frequent and preventable complication of insulin injection therapy and is seen in more than 50 % people with type 1diabetes. The prevalence of LH amongst type 1 diabetics in India is high. Despite increasing number of type 1 diabetes every year, the data of LH from South Asian developing countries like India is sporadic. Insulin absorption diminishes if injected at the site of LH. This increases the risk of hyperglycemia. Conversely, when the same dose of insulin is injected in the same subject at the site without LH, there is an increased risk of hypoglycemia.

[*J Indian Med Assoc* 2018; **116:** 41-3]

Key words **: Lipohypertrophy, hypoglycemia, glycemic variation, incorrect injection technique, poor site rotation, needle re-use, injection site examination.**

Lipohypertrophy (or "lipo") is a common complication of diabetes injections and appears as a thickened, rubbery swelling of tissue that can vary in texture from soft to firm[1].

Fig 1 — Lipohypertrophy

Injecting insulin at LH site may lead to inconsistent absorption of insulin, with the potential risk for poor, unpredictable glycemic control and unexplained hypoglycemia. Incorrect rotation of injection site, re-use of needles and long duration of diabetes have been proposed to be the predisposing factors for development of LH.

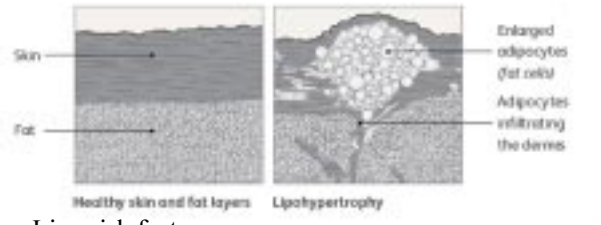
Fig 2 — Sites of Lipohypertrophy, Sunil's DCRC, Nagpur

Etiology:

There are two types of structural changes that occur as the results of lipo[2]:

Sunil's Diabetes Care'n' Research Centre, Nagpur 440010
[1]Diabetes Educator
[2] Diabetologist

- **Insulin absorption is less at the site of lipo vs normal tissue.**
- **It results glycemic variability and its complications.**
- **Its development is reduced by patient education, long acting insulin, injection site rotation with proper injection technique, avoiding needle reuse.**



Lipo risk factors are:

Three independent risk factors associated with the development of lipo are[3] :

- Longer duration of insulin therapy ($p < 0.001$)
- Incorrect injection site rotation ($p < 0.001$)
- Needle reuse ($p = 0.02$)

Clinical Implications :

Lipo can result in erratic insulin absorption[4]. In a euglycemic clamp study of 13 type 1 diabetes patients comparing insulin injection into lipo vs. normal tissue[5]:

Insulin absorption was reduced by up to **22%**

Post-prandial glucose levels were **≥26% higher**

In recent surveys comparing insulin-injecting patients with and without lipo, the presence of lipo was associated with:

- 0.55% higher HbA1c[3*]
- 10.1–15 IU/day higher insulin use[1,3]
- 33% higher rates of unexplained hypoglycemia[1†]
- 42% higher rates of glycemic variability[1‡]
- More frequent diabetic ketoacidosis[3]

*The ITQ polled 13,289 patients from 42 countries who had been injecting

insulin for <6 months or more. All differences from patients without lipo were significant at p<0.05[3].

[†]Unexplained hypoglycemia defined in the study as having a hypoglycemic episode one or more times a week in the absence of a definable precipitating event, such as a change in medication, diet or activity[1].

[‡]Glycemic variability was defined in the study as oscillations of blood glucose values from <60 mg/dL (3.3 mM/L) to >250 mg/dL (13.9 mM/L) at least three times a week in an unpredictable and unexplained fashion, and if there was evidence that such a pattern had been present for at least 6 months previously[1].

Prevention :

There are 3 key steps: suspect, detect, protect in managing lipo in your practice.

• Suspect :

The incidence of lipo is high, with up to 2/3 of patients who inject insulin having lipo present[1].

Lipo should be suspected in all patients who inject, especially in patients who are not properly rotating injection sites and who are reusing needles[3].

The incidence of lipo detected in studies can vary depending on the composition of the population. For example, in Blanco, 2013:[1], 76% Type-1 patients and 56.1% Type-2 patients had LH.

The hospital based prevalence of Lipohypertrophy in 120 insulin injecting Type 1 and Type 2 patients with diabetes mellitus in India at Sunil's Diabetes Care and Research Centre, Nagpur also showed the prevalence of LH in 77.4% Type-1 and 36 % Type-2 patients with diabetes[9].

• Detect :

To detect lipo, it is important to examine your patients' injection sites4, to help you define skin appearance, lipo shape, size and texture.

Assessing lipo:Explain to your patients why lipo assessment and education are important for optimal diabetes management. Before you begin, remember to obtain written or verbal consent from your patients before examining them; they may be sensitive about exposing their injection sites. Explain what you are looking for and why it is important. Patients should be made to feel comfortable—the environment should be warm and the patient's privacy must be maintained at all times.

There are three steps to assessing lipo[4] :

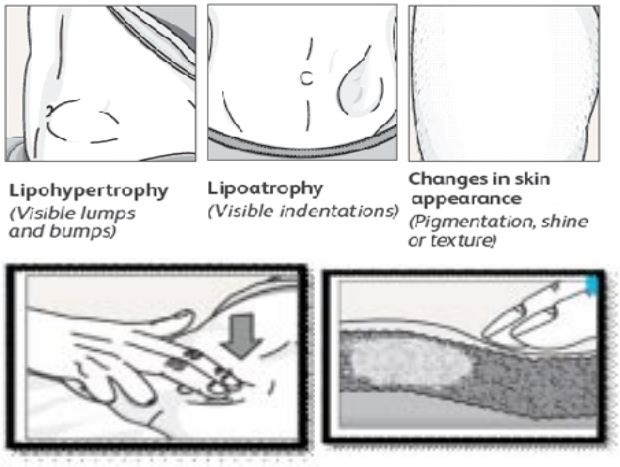
Visual inspection
Palpation
Recording

Sometimes lipo can be difficult to identify by visual inspection alone. When possible, palpating a patient's injection sites may help you identify lipo that you can't see[4].

Visual Inspection Steps :

(1) Ask your patient to expose their injection sites

(2) Carry out a visual examination of all visual sites, even uncommon sites your patients may use



(3) Use directional lighting to help illuminate the lipo

Palpation Steps[7] :

(1) Spread examination gel on the area; this will help facilitate the examination.

- Lipo may be more easily detected with your patient in different positions (lying down or sitting), and is often easier to detect if muscles are relaxed.
- Use two fingers, sweeping around the injection site.
- Use firm downward pressure, pushing deep into fat layer.

Recording Steps[4] :

(1) Mark the exact position of the lipo with a skin-safe marker (if your patient consents).

(2) Repeat palpation for all four injection sites. Mark and record all lipofor your patient's medical record.

(3) Teach your patient to identify lipo and healthy injection sites.

(4) Make a note to repeat the lipo inspection within one year. Sites should be examined at least once a year, or more frequently if lipo is already present[4].

• Protect :

44% of patients reported injecting into lipo[3]. Because insulin absorption into areas of lipohypertrophy is blunted, patients may be at risk of experiencing hypoglycemia when transitioning from injecting into lipo to healthy tissue due to improved insulin absorption. Advise your patients against continuing to inject into lipo, and work with them to titrate their insulin accordingly.

Use the Shortest Needle :

Ensure your patients are using the shortest needle length available, as per current recommendations published in Mayo Clinic Proceedings (4 mm pen needle and 6 mm insulin syringe needle). Shorter needles are more comfortable than longer needles. They also decrease the risk of accidental intramuscular injection, which may lead to hy-

poglycemia and glycemic variation[4].

Lipo usually regresses after stopping injections into affected sites. Explain to your patients that they may notice changes as early as 2 months, but it may take longer[4,8].

Always Inject with a New Needle :

Reusing needles has been associated with the development of lipo and injection pain[4].

Patients should understand that the risk of developing lipo increases the more a needle is reused[1].

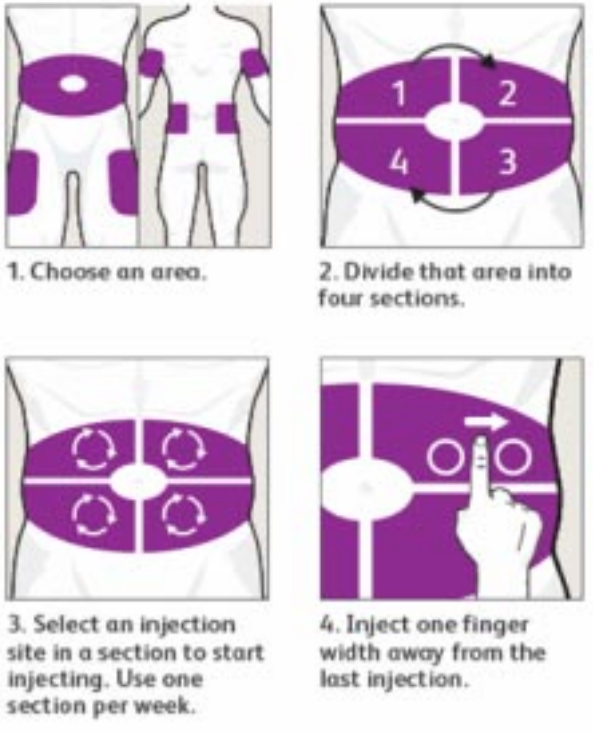
Number of times needle was used	Per cent increase in risk of developing lipo[1]
2	54%
3	76%
>6	85%

Baseline incidence of lipo in patients who used their needles once was 57%[1].

Rotate Injection Sites :

It is important that patients rotate both between and within their injection sites. Use of larger zones should be recommended.4 .Work closely with your patients to customize a site rotation plan that matches the number and frequency of injections they take.

Instruct Patients To[4] :



Impact of Management :

Patient education can help[3]. Proper injection technique can also help prevent lipos from forming[4].

After 3 months, targeted individualized training on proper injection technique, including site rotation, lipo avoidance and the switch to a 4 mm needle was associated with improved blood glucose control and reduced insulin consumption[6] :

HbA1c was reduced by	0.58% ($p < 0.05$)
Fasting blood glucose was reduced by	14.2 mg/dL ($p < 0.05$)
Total daily dose of insulin was reduced by	2 Units ($p < 0.05$)

Switching injections from lipo to normal tissue often requires a decrease in the dose of insulin injected[7].

- The change in dose varies from patient to patient and should be guided by frequent blood glucose measurements.
- Reductions often exceed 20% of their original dose.

Summary :

Lipohypertrophy (LH) is a frequent and preventable complication of insulin injection therapy.It is important to inspect injection sites and review proper injection technique with your patients at every visit[4]. Targeted individualized training on proper injection technique, including site rotation, lipo avoidance and the switch to a 4 mm needle was associated with improved blood glucose control and reduced insulin consumption in as early as 3 months.

References

1 Blanco M, Hernandez MT, Strauss KW, Amaya M — Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes. *Diabetes Metab* 2013; **39:** 445-53.
2 Fujikura J, Fujimoto M, Yasue S — Insulin-induced lipohypertrophy: Report of a case with histopathology. *Endocr J* 2005; **52:** 623-8.
3 Frid A, Hirsch L, Menchior A, Morel D, Strauss K — Worldwide injection technique questionnaire study: injecting complications and the role of the professional. *Mayo Clin Proc* 2016; **91:** 1224-30.
4 Frid AH, Kreugel G, Grassi G — New insulin delivery recommendations. *Mayo Clin Proc* 2016; **91:** 1231-55.
5 Famulla S, Hovelmann U, Fischer A — Insulin injection into lipohypertrophic tissue: blunted and more variable insulin absorption and action, and impaired post-prandial glucose control. *Diabetes Care* 2016; **39:** 1486-92.
6 Grassi G, Scuntero P, Trepiccioni R, Marubbi F, Strauss K — Optimizing insulin injection technique and its effect on blood glucose control. *J Clin & Trans Endocrinol* 2014; **1:** 145-50.
7 Frid AH, Kreugel G, Grassi G — New insulin delivery recommendations. *Mayo Clin Proc* 2016; **91:** Supplemental appendix 6.
8 Lipohypertrophy — Injections and lumpy skin. https://www.diabetes.co.uk/conditions/lipohypertrophy.html. Accessed January 18, 2017.
9 The hospital based prevalence of Lipohypertrophy in 120 insulin injecting Type 1 and Type 2 patients with diabetes mellitus at Sunil's Diabetes Care and Research Centre, Nagpur IDF 2015, Vancouver, Canada,Poster Discussion.