INJECTION TECHNIQUE

IS IT IMPORTANT?

Anders Frid, Baveno 26 October 2014
Injection Technique: What Do We Know and What Do We Want to Know?

- What about insulin absorption from different sites? Are modern insulin analogues different from human insulins regarding absorption?

- In what tissue do we want to deposit insulin?

- What technique do we use to achieve that?

- Does depth of injection influence absorption?

- How thick is the skin?
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Christian Binder 1969:

• Soluble $^{131}$I-insulin (pig, U40) is absorbed faster from the abdomen compared to thigh with buttock in between.

NPH insulin

• Henriksen et al: Absorption of NPH (isophane) insulin in resting diabetic patients: evidence for subcutaneous injection in the thigh as the preferred site.

Absorption of Rapid-Acting Insulin Analogs

• No statistically significant difference between abdomen and thigh in time-to-peak.
• Peak is somewhat lower and effect more protracted in thigh.
Absorption of regular insulin and insulin lispro

Mean GIR versus time of all treatments (n = 12): Regular insulin (0.2 U/kg; A, insulin lispro (0.2 U/kg; B).

Absorption of insulin $^{125}$I-glargine after injection in arm, thigh and abdominal area

- ______ = arm
- ........ = thigh
- -------- = abdomen

Owens et al, Diabetes Care 23;6, June 2000
Injection site:

Injection site: ?

Injection site: ? Abdomen (pers. mess.)

Insulin Levemir

Injection site:

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Insulin Levemir

Injection site: thigh

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Absorption of Rapid-Acting Insulin Analogs

- No statistically significant difference in insulin absorption between fat and muscle tissue; however, only studied in resting muscle.
- There is a 10-fold increase in blood flow in the working muscle!
- International consensus is still to recommend subcutaneous (sc), ie, intralipomatous injection for rapid-acting insulins.
Insulin detemir, sc and im injection

Each mean profile based on data from 16 subjects
Note that at least two measurements must be available to calculate a mean concentration of Insulin Detemir. Thus at time points where there is one or no valid measurements no markings occur on the figure e.g. at time points later than 240 minutes for the i.v. adm. route

Novo Nordisk data on file
Early hypoglycaemia after accidental intramuscular injection of insulin glargine

B. Karges, B. O. Boehm* and W. Karges*

CT of thigh, normal-weight adult male
CT scan of abdomen, normal-weight male. White dots are contrast. 8 mm needle.
CT, abdominal area, female with DM2, BMI 28.0
Some Observations of Human Fat Tissue Distribution

Adult females
- Many have less than 8 mm of fat tissue laterally in the thigh
- All have more than 12 mm of fat tissue in the gluteal area
- Some may have less than 5 mm of fat tissue laterally in the abdominal area

Adult males
- A majority have less than 5 mm of fat tissue laterally in the thigh
- All have more than 12 mm of fat tissue in the gluteal area
- Many have less than 5 mm of fat tissue laterally in the abdominal area
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CT of thigh, normal-weight adult male
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Injection Depth and Insulin Absorption

Frid et al., Intraregional Differences in the Absorption of Unmodified Insulin from the Abdominal Wall. Diabetic Medicine 1992; 9; 236-239
Injection Depth and Insulin Absorption

- $^{125}$I-labelled short acting insulin was injected (5 units each patient)
- Radioactivity decreased by insulin absorption (in %)
- One defined injection site was chosen for each abdomen and thigh
- 2 injection depths, controlled by ultrasound:
  A) 3mm below the skin surface
  B) 2mm above the muscle facies

Injection Depth B) [from skin surface in mm]:
Abdomen  ♂ 9±2 / ♀ 15±3
Thigh      ♂ 7±1 / ♀ 14±3

Frid et al., Intraregional Differences in the Absorption of Unmodified Insulin from the Abdominal Wall_Diabetic Medicine 1992; 9; 236-239
Injection Depth and Insulin Absorption

No influence of the injection depth on the kinetics of insulin absorption has been shown in the study.
Influence of needle size for subcutaneous insulin administration on metabolic control and patient acceptance

G Kreugel,* HJM Beijer, MN Kerstens, JC ter Maaten, WJ Sluiter, BS Boot

**Conclusion:** For insulin injection, a 5mm needle length is associated with unchanged HbA$_{1c}$ levels, unchanged frequency or severity of hypoglycaemic events and less discomfort for patients compared with 8 or 12 mm needles. The use of 5 mm needles is as safe as 8 or 12 mm needles. Further research is advisable involving thin and obese patients using 5 mm needles, in order for shorter needles to be recommended as standard practice.
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Original article
Skin and subcutaneous adipose layer thickness in adults with diabetes at sites used for insulin injections: implications for needle length recommendations

Michael A. Gibney
Christina H. Arce
Karen J. Byron
Laurence J. Hirsch
BD (Becton, Dickinson and Company), Franklin Lakes, NJ, USA
What Insulins at What Injection Site?

• All insulins should normally be given sc
• Soluble human insulins in the abdominal area
• NPH-insulins in the thigh or gluteal area
• Rapid-acting insulin analogs in the abdomen, may be given elsewhere
• Insulin glargine in abdomen, thigh, or gluteal area (no studies), strictly sc
• Insulin detemir in the thigh (or gluteal area, no studies), strictly sc
• Premix insulins abdominal area in the morning; thigh or gluteal area in the afternoon/evening
So what about GLP-1 analogs?

• Calara F et al: …all injection sites yielded equivalent pharmacokinetic profiles strongly suggesting equivalent exenatide bioavailability after subcutaneous injection into the arm, thigh, or abdomen.

Kapitza et al:
Kapitza et al:

Journal of Clinical Pharmacology, 2011;51:951-955
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OF COURSE IT IS!
IS IT IMPORTANT?
TITAN

127 participants from Europe, Russia, USA, Canada, China, Taiwan, South Korea, Japan, Indonesia, The Philippines, India and Pakistan

10th - 13th September 2009

T. I. T. A. N
Third Injection Technique workshop in AthenNs
New injection recommendations for patients with diabetes

A. Frid\textsuperscript{a}, L. Hirsch\textsuperscript{b}, R. Gaspar\textsuperscript{c}, D. Hicks\textsuperscript{d}, G. Kreugel\textsuperscript{e}, J. Liersch\textsuperscript{f}, C. Letondeur\textsuperscript{g},

J.P. Sauvanet\textsuperscript{h}, N. Tubiana-Rufi\textsuperscript{i}, K. Strauss\textsuperscript{j,*}

\textsuperscript{a} Endocrinologist, Clinic of Endocrinology, Skåne University Hospital, Malmö, Sweden
\textsuperscript{b} Endocrinologist, Worldwide VP Medical Affairs, BD Diabetes Care, Franklin Lakes, New Jersey, USA
\textsuperscript{c} Diabetes Specialty Nurse, Diabetes Unit, University Hospital La Paz, Madrid, Spain
\textsuperscript{d} Diabetes Specialty Nurse, Diabetes Service, NHS Enfield Community Services, London, UK
\textsuperscript{e} Diabetes Specialty Nurse, Diabetes Unit, University Medical Center Groningen, The Netherlands
\textsuperscript{f} Diabetes Specialty Nurse, Diabetes-Schulungszentrum, Universitätsklinikum Giessen und Marburg, Germany
\textsuperscript{g} Diabetes Education Manager, BD Diabetes Care, Rungis, France
\textsuperscript{h} Endocrinologist, Internal Medicine Department, APHP Hôpital Saint-Louis, Paris, France
\textsuperscript{i} Pediatric Endocrinologist, Diabetes Department, APHP Hôpital Robert Debré, Paris, France
\textsuperscript{j} Endocrinologist, Global Medical Director, BD Diabetes Care, Erembodegem, Belgium
Needle length

- 4, 5 and 6 mm needles may be used by any patient including obese ones; they will provide equivalent glycaemic control compared to 8 mm and 12.7 mm needles (9,63,110,112,113) A1

- There is no evidence to date of significant leakage of insulin, increased pain, worsened diabetes management or other complications when using shorter (5-6 mm) needles. (9,63,110,114) A1
Lifting a skin fold

- Skin folds are essential when the distance from skin surface to the muscle is less than the length of the needle.
- Lifting a skin fold is an easy and effective means for ensuring SC injections.
- A proper skin fold is made with the thumb and index finger (possibly with the addition of the middle finger).
- Lifting the skin by using the whole hand risks lifting muscle with the SC tissue and can lead to IM injections.