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## BACKGROUND

**Lipohypertrophy (LH)** is the most common local complication of insulin injection therapy, developing due to wrong injection techniques<sup>1</sup>. It also heavily affects the clinical outcomes, at least in patients in *multiple daily injections* (MDI):

- Mean prevalence is 38%,<sup>2</sup> but probably higher risk for DMT1 due to longer disease time and insulin dose
- Heavy effect on clinical outcomes [strong association with higher HbA1c, *total daily dose* (TDD)] and daily life (hypoglycemia and glycemic variability).<sup>3,4,5</sup>

With the increasing use of *continuous subcutaneous insulin infusion* (CSII), medical and nursing staff developed the opinion LH affects CSII therapy in the same way it does with MDI, although literature about pump therapy and LH is poor, and there is no accurate evaluation of its effect on therapeutic outcomes in these patients.

## AIMS

Evaluate the **prevalence** of LH within both **MDI** and **CSII** techniques, and try to recognize its influence, if any, on glycemic control and complications.

## METHODS

**115** patients with **DMT1** of age between **18 and 25** years were selected, due to their similar background: diagnosed in Turin's Pediatric Hospital, then undergone *transition* to our Center at the age of 18.

Anthropometric parameters were collected, along with data about glycemic control. The presence of LH was evaluated with a specific physical examination. A comparison of LH and healthy patients was performed for both therapeutic methods.

The collected data were studied with Shapiro-Wilk normality test, then compared using T-test, M-W or Chi squared test due to variables and group characteristics.

## INSULIN INJECTION THERAPY

25 patients out of 60 (**42%**) in MDI therapy resulted having at least one LH lesion.<sup>6</sup>

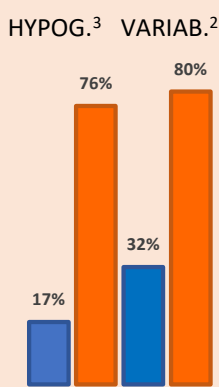
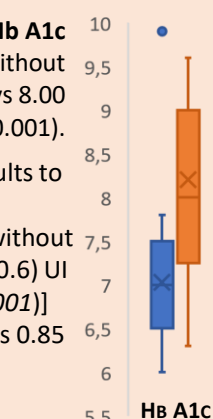
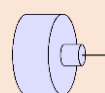
The *median*<sup>7</sup> **Hb A1c** level in patients without LH is 7.00 (1.0) vs 8.00 (1.8) with LH ( $p < 0.001$ ).

The mean **insulin use** results to be significantly lower for patients in MDI therapy without LH, for both **TDD** [38.9 ( $\pm 10.6$ ) UI vs 60.2 ( $\pm 13.9$ ) UI ( $p < 0.001$ )] and **UI/kg** [0.61 ( $\pm 0.17$ ) vs 0.85 ( $\pm 0.18$ ),  $p < 0.001$ ].

Patients with LH resulted having increased incidence of frequent unexplained **hypoglycemia**<sup>3</sup> episodes and marked glycemic **variability**.<sup>3</sup> Both differences resulted in  $p$ -value  $< 0.001$ , with OR of 15.3 and 13.5 respectively.

Correct injection **sites rotation** (3+) was achieved in 80% (LH-) vs 28% of patients ( $p < 0.001$ , OR 0.09).

**Needle length**  $\geq 5$  mm is linked with higher LH prevalence: 32% (LH+) vs 6% ( $p = 0.012$ , OR 7.7).



## INSULIN PUMP THERAPY

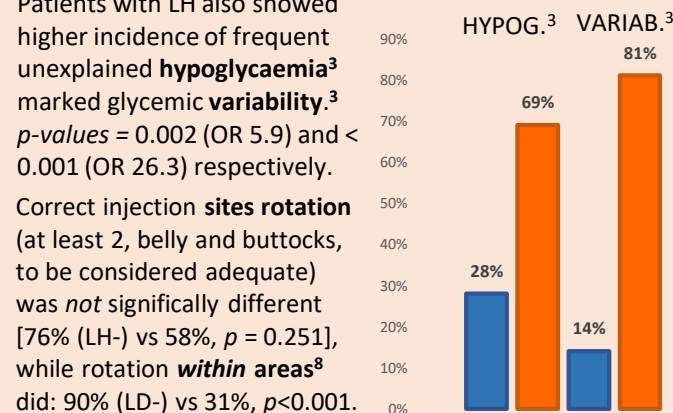
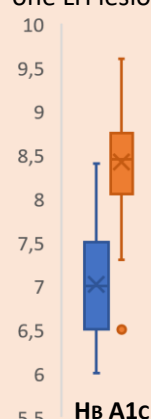
26 patients out of 55 (**47%**) in CSII therapy resulted having at least one LH lesion.<sup>6</sup>

The mean **Hb A1c** level in patients without LH is 6.98 (0.76) vs 8.42 (0.76) with LH ( $p < 0.001$ ).

The *median*<sup>7</sup> **insulin use** results to be significantly lower for patients in CSII therapy without LH, but less marked than with MDI: for **TDD**<sup>7</sup> [47.0 ( $\pm 15$ ) UI vs 58 ( $\pm 18$ ) UI ( $p$ -value  $< 0.001$ )] and **UI/kg**<sup>7</sup> [0.65 ( $\pm 0.16$ ) vs 0.86 ( $\pm 0.14$ ) ( $p < 0.001$ )].

Patients with LH also showed higher incidence of frequent unexplained **hypoglycaemia**<sup>3</sup> marked glycemic **variability**.<sup>3</sup>  $p$ -values = 0.002 (OR 5.9) and  $< 0.001$  (OR 26.3) respectively.

Correct injection **sites rotation** (at least 2, belly and buttocks, to be considered adequate) was *not* significantly different [76% (LH-) vs 58%,  $p = 0.251$ ], while rotation **within areas**<sup>8</sup> did: 90% (LD-) vs 31%,  $p < 0.001$ .



## CONCLUSIONS

The prevalence of lipohypertrophy in CSII and MDI patients is substantially **equal**. LH effect, together with injection technique mistakes, has heavy effect on glycemic control, insulin dose and complications, and it is quite important in both therapeutic methods.

The shortage of comfortable sites for CSII requires a new parameter in order to detect poor technique: rotation **within areas**<sup>8</sup> instead of *between areas*.

The increased insulin consumption in patients with LH is related to health care costs: for only 51 patients the extra charge is about **17.000 €**/year for insulin alone. LH is an old problem which need further and much modern investigation, suitable for the most recent therapeutic technologies.

1. Famulla S et al. *Diabetes Care* 2016 doi: 10.2337
2. Deng N et al. *J Diabetes Investig* 2017 doi: 10.1111
3. Blanco M et al. *Diabetes Metab* 2013 doi: 10.1016
4. Ji L et al. *Diabetes Technol Ther* 2017 doi: 10.1016
5. Grassi G et al. *J Clin Transl Endocrinol* 2014 10.1016
6. LH incidence: 42% (MDI) vs 47% CSII),  $p$ -value = 0.54
7. **Median (IQR)** is shown instead of *mean (DS)* because variables result to be not normally distributed.
8. Evaluated by the staff as correct if the injection point in the area is changed every time by 2-3 cm.



LH-



LH+