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Combination therapy to preserve residual insulin secretion in type 1 diabetes

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Introduction: Several mechanisms are involved in the pathogenetic process leading to insulin deficiency in Type 1 diabetes (T1D). Overwhelming insulin demand contributes to endoplasmatic reticulum stress, reduced function of the beta cells and increased sensitivity to a toxic immunologic milieu. Increased blood glucose, infections and obesity may contribute to a harmful inflammation. Autoimmunity, primary or secondary, then seems to add the ultimate blow. We therefore perform a pilot-trial where we combine beta cell protection, anti-inflammatory treatment and immune modulation.

Patients and design: 60 Patients 10-18 years old with T1D since <4 months, fasting C-peptide >0.12 nmol/l and GADA positive all get intensive insulin treatment and strict blood glucose control to decrease beta cell stress. In addition they are randomized in a double-blind trial into one of four arms: A. Day 1-90 Ibuprofen 400 mg/d + Vitamin D 2000 U/d Day 1-450 + GAD-alum 20 mikrogsc Day 15 and 45. B. The same as A but placebo instead of Ibuprofen. C. The same as C but 40 instead of 20 mikrog GAD-alum. D: Placebo.

Results: Only some patients have passed 6 month visit, but so far minimal treatment related adverse events. Several patients low insulin requirement and HbA1c within normal range (<43 mmol/mol). Data will be presented in Nov-2014.

Conclusion: Combination of several treatment modalities, which as single therapy have insufficient efficacy, may offer safe alternatives to preserve residual insulin secretion.

Biography

Johnny Ludvigsson, is a full Professor of Pediatrics, Linköping University. He performed the first immune intervention ever in T1D with plasmapheresis (*BMJ* 1983) which lead to the discovery of 64kD (*Nature* 1982), later shown to be GAD. He performed a number of different immune interventions both with GAD-alum (*NEJM* 2008, *NEJM* 2012) and AntiCD3 monoclonal antibodies (*Lancet* 2011). More than 430 scientific publications also on diabetic complications (*NEJM* 1994), and is the main tutor of >20 PhD students. He was the first pediatrician ever as Honorary member of EASD.

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