Prevalence of diabetes among children treated with growth hormone in Israel

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Background: Growth hormone (GH) is a diabetogenic hormone. However, there is a lack of post GH treatment follow-up studies to detect possible late development of diabetes.

Aim: To determine the long term risk for diabetes in a cohort of children treated with recombinant human growth hormone (rhGH) in Israel, using data from the Israeli National Diabetes Register (INDR) for 2014 as a reference.

Methods: Between the years 1988 and 2009, 2,513 children under the age of nineteen were approved for GH treatment (mean age 9.2±3.7 years at GH approval and mean follow-up duration 12.1±5.3 years after GH approval). Out of these children 76.8% had IGHD (n=1,499; 59.8%) (**Table 1**). The patients were categorized to a low-risk category that included patients treated for isolated GH deficiency (IGHD) and small for gestational age (SGA) and a high-risk category that included patients treated for multiple pituitary hormone deficiency (mphd), chronic renal failure (CRF), Turner syndrome (TS) and Prader-Willi syndrome (PWS). This cohort was cross linked with the Israeli National Diabetes Register (INDR) for 2014 and prevalent cases with diabetes were identified. Due to the very small sample of individuals above age 30 in GH registry at 2014, we focused on children and young adults aged 10-29 years. The date of diabetes diagnosis, family history and type of diabetes are not available in the INDR. The expected number of patients with diabetes was calculated for each risk category using the diabetes prevalence rates in 2014 as a reference. Standardized prevalence ratios (SPRs) of diabetes were calculated for the age group 10-29 years.

Table 1: DM prevalence at 2014 (per 100) by indication categories for rhGH treatment among patients aged 10-29 years.

Indication for GH treatment	N	DM patients	Pre-existing DM
All	**2,513**	**23**	**4**
Low-risk group			
IGHD	1,499	7	2
SGA	427	2	1
High-risk group			
MPHD	151	4	1
CRF	203	5	0
PWS	40	1	0
TS	190	3	0
IGHD+CF	3	1	0

Abbreviations: IGHD: isolated GH deficiency; SGA: small for gestational age; MPHD: multiple pituitary hormone deficiency; PWS: Prader-Willi syndrome; TS: Turner syndrome; CRF: chronic renal failure; CF: cystic fibrosis.

Results: In 2014, a total of 23 patients aged 10-29 years were identified with diabetes. **Table 2** presents the SPRs of diabetes in GH treated children and young adults compared to the general population. In the low risk category there was no difference in the prevalence of diabetes compared to the general population (SPR 2.05, 95% CI 0.94-3.89). In the high risk category there was a significantly higher prevalence of diabetes (SPR 11.94, 95% CI 6.53-20.0) compared to the general population. When we excluded the four patients with pre-existing DM who had diabetes before the commencement of GH treatment, the excess SPRs in the high risk category was slightly attenuated.

Table 2: SPRs for DM for 2014 among patients aged 10-29, using the INDR reference rates for the same year

		Including patients with DM before GH treatment			Excluding patients with DM before GH treatment		
Age	**Prevalence rates INDR (%)**	**Observed cases**	**Expected cases**	**SPRs (95%CI)**	**Observed cases**	**Expected Cases**	**SPRs (95%CI)**
Low-risk group							
10-19	0.2	2	2.42	0.83 (0.10-2.99)	1	2.42	0.41 (0.01-2.31)
20-29	0.3	7	1.97	3.55 (1.43-7.30)	5	1.97	2.54 (0.83-5.93)
All		9	4.39	2.05 (0.94-3.89)	6	4.38	1.37 (0.50-2.98)
High-risk group							
10-19	0.2	4	0.91	4.93 (1.20-11.24)	3	0.91	3.30 (0.68-9.64)
20-29	0.3	10	0.26	38.25 (18.34-70.34)	10	0.26	38.8 (18.6-71.30)
All		14	1.17	11.94 (6.53-20.0)	13	1.17	11.14 (5.93-19.04)

Conclusion: Children with pre-existing risk factors for diabetes treated with GH have an increased prevalence of diabetes. It is advised to closely monitor blood glucose level during and after GH treatment especially in those children.