Effect of Hydroxyurea Therapy on Growth Parameters in Older Children with Sickle Cell Disease

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Objectives:

Sickle cell disease (SCD) is prevalent in Oman. Around 6 % of Omanis are carriers of the gene for sickle cell anaemia, 2–3 % for β-thalassaemia. Growth impairment is a known complication of SCD. Previous studies demonstrated no deleterious effects of hydroxyurea (HU) on the growth of children with SCD. This study was done to explore the potential effects of HU on growth parameters of older children with SCD and correlate these changes with clinical improvement.

Methods:

A prospective study was conducted on 97 SCD patients started on HU at Sultan Qaboos University Hospital (SQUH), Oman. Weight, height, and BMI were collected at baseline, 6 and 18 months after start of HU. Anthropometric data were converted to Z scores and compared with World Health Organization (WHO) standards. Z scores were compared between SCD patients who received low dose to those who received high dose HU.

Comparison of Z-scores of different growth parameters before and after HU therapy.

	Z-score Before HU	**Follow up after HU**		Difference	P value
		Period	**Z-score**		
Weight for age (WAZ)	-1.54 (±1.41)*	6 months	-1.38 (±1.20)	+0.16 (±.79)	0.240
	-1.35 (±1.52)**	18 months	-1.33 (±1.21)	+0.02 (±.93)	0.934
Height for age (HAZ)	-1.51 (±1.05)	6 months	-1.51 (±1.03)	0.00 (±.44)	0.994
		18 months	-1.59 (±1.07)	- 0.07 (±.50)	0.200
BMI for age (BAZ)	-1.07 (±1.50)	6 months	-0.83 (±1.36)	+0.24 (±1.04)	0.044
		18 months	-0.81 (±1.34)	+0.26 (±1.04)	0.028

*: weight comparison between baseline and 6 months follow up was possible in 37 patients.
**: weight comparison between baseline and 18 months follow up was possible in 27 patients

Differences in height and BMI parameters change between SCD patients with low dose or high dose hydroxyurea, .

	Low dose hydroxyurea (n=36)		**High dose hydroxyurea (n=43)**		P value
Height for age:		**Difference, p value**		**Difference, p value**	
	-1.64 (±1.20)		-1.44 (±0.90)		0.464*
➢Before HU ➢6 M after HU	-1.55 (±1.20)	+0.10 (±0.34), p=0.092	-1.52 (±0.86)	-0.08 (±0.49), p=0.279	0.061**
➢18 M after HU	-1.66 (±1.26)	-0.01 (±0.45), p=0.867	-1.55 (±0.89)	-0.10 (±0.54), p=0.206	0.344**
BMI for age:		**Difference, p value**		**Difference, p value**	
➢Before HU	-0.83 (±1.54)		-1.27 (±1.42)		0.206*
➢6 M after HU	-0.52 (±1.58)	+0.31 (±1.04), p=0.078	-1.09 (±1.04)	+0.18 (±1.02), p=0.252	0.527**
➢18 M after HU	-0.39 (±1.55)	+0.44 (±1.04), p=0.014	-1.12 (±1.03)	+0.14 (±1.02), p=0.364	0.234**

Low dose hydroxyurea between 10-15.9 mg/kg/day
High dose hydroxyurea between 16-26 mg/kg/day

Results:

The initial Z scores of included SCD patients were lower than WHO norms for their age and sex. The follow up Z-scores at 6 and 18 months from starting HU did not change significantly for both weight and height parameters, however, BMI Z-scores improved significantly at both 6 and 18 months follow up after HU (p value 0.044 and 0.028 respectively). No significant changes were observed in weight or height Z scores in either low dose or high dose HU groups during the period of follow up. BMI Z score improved significantly at 18 months follow up for the low dose HU group (p=0.014) compared to non-significant change in high dose group. Patients with minimal or no clinical improvement in annual VOCs showed non-significant changes in height after HU therapy.

Conclusions:

Hydroxyurea therapy did not adversely affect nor improve the weight and height in older children with SCD even in those with significant clinical improvement. Although BMI Z scores improved at 18 months of low dose therapy, a longer follow up on a larger sample of patients is required.

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