

Use of hydroxyurea from childhood to adult age in sickle cell disease: semen analysis

We read with interest the paper by Berthaut et al.¹, who studied the influence of hydroxyurea on sperm parameters and fertility of human males.

In that retrospective multicenter study, sperm parameters and fertility were evaluated in 44 adult patients. They suggested that a pre-treatment semen analysis be performed and sperm cryopreservation be offered to patients before Hydroxyurea treatment. In five patients, six semen samples were collected during Hydroxyurea treatment. The treatment duration varied from 2 to 10 years. No details on ages at the beginning of the treatment were given for these five patients. As the mean ages of their all forty-four patients was 25.8 years (range, 16-48 years), we could suppose that the treatment was initiated in adult patients.

We know that long term use of hydroxyurea has been largely performing in children with good outcomes on morbidity and survival.²⁻⁵ While exploring these improvements no fertility overviews were taken into account. But now a day, most of these children have reached adulthood, thus a fertility issue raised.

We investigated the effect of Hydroxyurea treatment on fertility when initiated during childhood in four patients since it was not possible to have semen for analysis at that age with their 11.2 years mean age (range, 8-16). Semen samples were analyzed according to WHO standards.⁶ Among our 4 patients (mean age 22.2 years, range 19-24 years), two experienced severe oligozoospermia and two azoospermia. The oligozoospermic patients had shorter treatment duration (8 and 9 years) than the azoospermic subjects, who had been on HU for 12 and 15 years respectively. They also had increased percentages of morphologically abnormal spermatozoa. Details of these four patients are given in Table 1.

The remaining questions are about the:

- quality of spermatogenesis, even after hydroxyurea removal, more than fifteen years after its early starting before puberty. Furthermore in patient who had never experienced normal spermatogenesis.
- organization of an informed counseling to be provided to parents on immature testicular tissue cryopreservation in children before HU initiation.
- alternative treatment if hydroxyurea removal is decided, with a view to semen cryopreservation when best values are obtained.

This study must therefore be extended to a larger cohort of patients to determine the real risk factors in order to ensure better management of male sickle cell disease patients receiving Hydroxyurea since childhood.

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Table 1. Main characteristics of patients and semen parameters.

Age at TTT (years)	TTT duration (years)	Semen parameters								
		Testicular volume index (cm ³)	Sexual abstinence (days)	Volume Ejaculate (mL)	Count x10 ⁶ /mL	Total sperm count	Progressive motility (%)	Normal 1 forms (%)	Vitality (%)	
1	16	8	17	5	0.8	2.48	1.98	4	5	72
2	10	9	7.12	5	2.7	0.6	1.63	50	0	60
3	11	12	6.12	5	1.8	0	0	-	-	-
4	8	15	5.59	2	1.8	0	0	-	-	-
Mean	11.25	11	8.95	4.25	1.78	0.77	0.9	27	2.5	66
Normal value			11-19		>2	>20		>50	>14	>75

TTT: treatment.