

Erythropoiesis is not equally suppressed in transfused males and females with β -thalassemia major: are there clinical implications?

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Supplementary

Methods

All androgen deficient males routinely receive testosterone replacement at our centre. Our Hb reference ranges for males and females aged 13-55 are 130-180g/l and 120-160g/l, respectively. Each blood film was examined once.

Results

Assessment of genotype did not reveal a significant association with the indices of erythropoiesis (data not shown). Analyzer flagging (either for NRBCs and/or an abnormal reticulocyte pattern) occurred in 51% of all samples and was higher in males (62% vs 42%, $P = 0.041$), consistent with increased numbers of NRBCs and/or reticulocytes. To investigate if higher EPO levels in males could be attributable to the greater number of males with EMH, additional analyses were performed after excluding the 14 patients (11 males and 3 females) with EMH (Table 3). Analysis of the remaining 102 patients (40 males and 62 females) demonstrated that EPO remained significantly higher in males versus females (67mIU/ml (40-145) vs 52 (35-89); $P = 0.037$). Automated and manual NRBC remained higher for males compared to females in this analysis. There was no significant difference in EPO between splenectomised males ($n = 21$) and females ($n = 23$)(66 mIU/mL (41-97) vs 44 (30-68); $P = 0.11$) or non-splenectomised males ($n = 19$) and females ($n = 39$)(75mIU/ml (38-173) vs 57 (39-93); $P = 0.19$); however, the numbers in this sub-analysis may have been too small to detect a small difference.

Table 3. Summary and laboratory indices of pre-transfusion erythropoiesis for all patients without EMH.

Variable	Male n=40	Female n=62	P value
Age (years)	38.3 ± 9.8	38.4 ± 8.9	0.95
Weight (kg)	63.8 ± 9.2	55.8 ± 11.7	< 0.001
Height (cm)	165 ± 8.8	153 ± 8.2	< 0.001
Estimated annual transfused volume (l)	13.5 (13.5-13.5)	13.5 (10.1-13.5)	<0.001
Estimated annual transfused volume per kg (ml/kg)	204 (187-234)	225 (187-265)	0.103
Transfusion interval (weeks)	3.0 ± 0.7	3.1 ± 0.5	0.14
Estimated patient blood volume* (l)	4.33 ± 0.50	3.32 ± 0.53	< 0.001
Hemoglobin (g/l)	98 ± 10.4	99 ± 8.1	0.75
Ferritin (mcg/l)	759 (596-1139)	962 (630-1353)	0.21
Erythropoietin (mIU/ml)	67 (40-145)	52 (35-89)	0.037
Absolute automated reticulocyte count (10 ⁹ /l)	97 (32-148)	66 (31-127)	0.126
Absolute manual reticulocyte count (10 ⁹ /l)	32 (13-86)	37 (9-88)	0.95
Automated NRBC (number NRBC/100 WBC counted)	12 (0-37)	0.5 (0-20)	0.04
Manual NRBC (number NRBC/100 WBC counted)	16 (2-66)	2 (1-25)	0.013

Data are mean ± standard deviation or median (interquartile range). Transfused volumes are calculated on the assumption that each unit contains 260ml red cells (Australia Red Cross Blood Service red cell unit mean volume = 259 ± 23ml).¹⁵ *Calculated using Nadler's formula for total blood volume (TBV): men TBV (ml) = 604 + (367 x height³(m³)) + (32.2 x weight (kg)); women TBV = 183 + (356 x height³(m³)) + 33.1 x weight (kg).⁶