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POSTER ABSTRACTS

114.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Natural History and Clinical Outcomes of Patients with Sickle Cell Disease: The Burden of Avascular Necrosis in a British Cohort

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Background:
The UK "Natural History Study" is a real-world multi-site cohort study of adults living with sickle cell disorder. Since start of recruitment, data for 241 individuals has been validated: mean age 40.5 (std dev 13.9, range 8-79) with 149 (61.8%) female, and genotypes: HbSS (n = 156; 65%), HbSC (n = 73; 30%), HbS/beta(+) thal (n = 11; 5%) and HbSHPFH (n=1; 0.5%).
Avascular Necrosis (AVN) is a debilitating long-term orthopaedic complication of sickle cell disorder and in advanced stages leads to joint destruction and the need for orthopaedic surgery. The present survey looked at the baseline prevalence of AVN in our cohort in relation with clinical parameters.
Methods:
Patients were recruited after written informed consent by participating sites. Clinical history including the presence of AVN was defined as a diagnosis at the time of recruitment. Treatment history, admission rate, laboratory variables, steady state observations were assessed in univariate t-testing and logistic regression.
Results:
The prevalence of AVN in the cohort was 21% (50/241). 32 patients had prior orthopaedic surgery for AVN (64%). 38/156 HbSS patients (24%) were affected by AVN, of which 15 HbSS patients (40%) had more than one site of AVN involved. Of 73 HbSC patients, 11 had AVN (15%), 5 of whom had more than one site involved (45%). One patient with HbS/beta(+) had documented AVN. The one patient with HbS/HPFH did not have AVN.
The median age of patients with a diagnosis of AVN in the cohort was 45 (range 19-79) and 38 (range 18-79) for patients without AVN, respectively. The median age of first orthopaedic surgery was 37 years (range 20-74).
We looked in more depth whether clinical parameters were linked to prevalence of AVN in our cohort, see table 1. (HbS/beta(+) and HbS/HPFH not analysed separately).
Discussion:
The survey illustrates the burden of AVN in our cohort, with 1 in 5 patients affected. The true prevalence is most likely even higher because cases were only included if recorded in the patients' medical history; this also explains the high percentage (64%) of patients with AVN having had orthopaedic surgery. As can be expected, opiate use at home was significantly higher in patients with AVN (despite previous surgery), in particular among patients with HbSC. AVN was more prevalent in HbSS than other genotypes. There was a trend towards a higher prevalence of AVN in smokers than in non-smokers in the overall group (Odds ratio 2.43, 95%CI 0.90 - 6.53)
Within the limitations of the survey, there was a surprising lack of correlation between presence of AVN and disease parameters other than genotype which may be related to sample size. In the HbSS group, there was evidence of a lower haemolytic rate among patients affected by AVN, in keeping with previous reports. The use of hydroxycarbamide at the time of recruitment was not linked to the presence or absence of AVN. Also, HbF levels (regardless of whether patients were taking hydroxycarbamide or not) did not appear to affect the risk of having AVN.
Conclusion:
Our study prompts further research into prevention of AVN or reversal of early AVN. Traditional risk factors failed to identify those at risk, and longitudinal follow-up as well as biomarkers and genome-wide association studies may help understand the clinical variability of avascular necrosis in sickle cell disorder.

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Table 1. Characteristics of sickle cell patients with and without AVN.

	All Genotypes		HbSC		HbSS	
	No AVN	AVN	No AVN	AVN	No AVN	AVN
Smoking	12/191 (6%)	7/50 (14%)	5/62 (8%)	1/11 (9%)	6/118 (5%)	5/38 (13%)
Taking hydroxycarbamide	60/191 (31%)	20/50 (40%)	9/62 (15%)	2/11 (19%)	50/118 (42%)	17/38 (45%)
Hydroxycarbamide dose	15.9 mg/kg (SD 6.32)	15.8 mg/kg (SD 6.25)	14.3 mg/kg (SD 5.66)	12.9 mg/kg (SD 0.45)	16.4 mg/kg (SD 6.29)	16.2 mg/kg (SD 6.36)
Average Hb	98 g/L (SD 20.6)	96 g/L (SD 16.6)	116 g/L (SD 13.2)	117 g/L (SD 11.9)	89 g/L (SD 17.6)	91 g/L (SD 13.1)
Average HbF	5.5% (SD 5.53)	6.7% (SD 6.97)	2.1% (SD 1.80)	2.5% (SD 1.93)	6.8% (SD 6.07)	8.0% (SD 7.53)
Average reticulocytes *p=0.04	187.6 (SD 99.57)	169.6 (SD 88.29)	130.9 (SD 46.22)	120.6 (SD 56.74)	222.2 (SD 107.55)*	180.4 (SD 89.07)*
Average WBC	8.1 (SD 2.80)	7.1 (SD 2.28)	7.1 (SD 1.95)	6.3 (SD 1.09)	8.8 (SD 2.96)	7.3 (SD 2.48)
Average bilirubin *p=0.02	38.4 umol/l (SD 28.52)	32.7 umol/l (SD 36.87)	20.8 umol/l (SD 13.70)	23.2 umol/l (SD 19.99)	47.7* umol/l (SD 27.22)	35.4* umol/l (SD 25.79)
Number of severe painful episodes per person per year	0.48	0.34	0.27	nil	0.62	0.45
Opiate use at home *Odds Ratio 3.56 (1.79 – 7.07) ** Odds Ratio 13.68 (3.06 – 61.19) ***Odds Ratio 2.28 (1.03 – 5.07)	30/191 (16%)*	20/50 (40%)*	5/62 (8%)**	6/11 (55%)**	24/118 (20%)***	14/38 (37%)***

P-values (two-sample t-test) or 95%CI (Odds Ratio) are only given if statistically significant.

Figure 1

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