

24 HOUR CYTOKINE VARIABILITY IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

G Hagan, M Southwood, E Soon, C Treacy, D Taboada, G Deboeck, K Sheares, D Jenkins, J Pepke-Zaba, N Morrell, Papworth Hospital, UK

Objectives

Recent research has focused on the significance of inflammatory cytokines (in particular interleukins (IL)6,8,10 and TNF α) in CTEPH. We sought to examine daily variability of these cytokines in stable CTEPH patients.

Methods

Blood was collected between 8am-12pm on two successive days in 21 treatment naïve CTEPH patients admitted for elective investigations and 11 healthy controls. Patients with inflammatory conditions were excluded. Cytokine levels were analysed using high sensitivity human cytokine multiplex immunoassay . Intra-class correlation coefficients (ICC) and 95% limits of agreement (LOA) for inflammatory cytokines (Bland-Altman analysis) were obtained. Non-normal values were log transformed.

Results

Demographics are displayed in table 1 and results in table 2.

Table 1

Characteristic	CTEPH	Control
N	21	11
Male	9 (42.9%)	3(27.3%)
Age (Mean +/- SD)	60.38 +/- 14.83	43 +/- 7.5
NYHA Class (I/II/III/IV)	0/7/14/0 (0%/33%/66%/0%)	
Classification of CTEPH (Proximal/Distal/Residual PH >1 year post PEA)	14/5/2 (66.6%/23.8%/9.5%)	
Mean pulmonary artery pressure (mmHg) (Mean +/- SD)	43.62 +/- 11.34	
Mean cardiac index (L/min/m ²) (Fick)	1.88 +/- 0.42	

Table 2

	IL6	IL8	IL10	TNFα
Median with IQR (pg/ml)				
<i>CTEPH</i>	3.54 (0.75 – 5.43)	3.22 (2.47 – 4.11)	7.05 (5.14 – 15.09)	3.57 (2.46 – 4.02)
<i>Control</i>	0.34 (0.06 – 1.82)	1.99 (1.32 – 2.88)	8.94 (2.6 – 10.34)	1.67 (0.92 – 2.48)
ICC (0-1)				
<i>CTEPH</i>	0.54	0.75	0.68	0.72
<i>Control</i>	0.85	0.92	0.92	0.92
Normal distribution?	No	Yes	No	No
95% LOA (pg/ml)				
<i>CTEPH</i>		-1.68 to +2.38		
<i>Control</i>		-0.81 to +1.37		
Antilog of 95% LOA (ratios)				
<i>CTEPH</i>	0.08 to 14.75		0.38 to 3.43	0.50 to 3.27
<i>Control</i>	0.48 to 2.5		0.71 to 1.54	0.7 to 1.59

For non-normal values, the antilogs of the 95% LOAs represent the ratios of the value that samples may lie between 95% of the time. So for IL10, a value may lie between 0.38 to 3.43 times the previous day's value 95% of the time.

Conclusions

Levels of inflammatory cytokines in CTEPH patients show variability over a 24 hour period, even when taken at the same time of day in relation to planned investigations, that is greater than controls. This has to be taken into account in studies examining changes in these cytokines in CTEPH. In particular, IL-6 exhibits large within-patient variability in comparison to ILs 8, 10 and TNF α ; this is consistent with knowledge of cytokine variability in left heart failure(1).

References

1. Dibbs et al, J. Am. Coll. Cardiol, 33:1935-1942 (1999).