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The efficacy and reliability of biological markers in pediatric pulmonary hypertension

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Objective: The present study aims to determine the efficacy and reliability of serum markers such as brain natriuretic peptide (BNP), uric acid, troponin T, C-reactive protein, D-dimer, von Willebrand factor (vWF) and CA-125 in clinical assessment of pediatric pulmonary hypertension (PH).

Methods: This is a retrospective analysis of 40 children with PH in aspect of serum markers. The diagnosis of PH was made when mean pulmonary artery pressure was measured ≥ 25 mmHg by catheter angiography.

Results: Congenital heart diseases were the most frequently encountered etiological factor for PH during childhood. As functional class advanced, serum concentrations of BNP, troponin T and CA-125 increased significantly and six minute walk distance decreased significantly (Table 1). There was a significant and negative correlation between six minute walk test and each of the variables including serum BNP, CA-125 and vWF levels ($p=0.008$, $p=0.016$ and $p=0.019$ respectively). When compared with children receiving monotherapy for PH, the children who were on combination treatment had significantly shorter six minute walk distance ($p=0.044$) as well as significantly higher concentrations of BNP, troponin T and CA-125 (Table 2)

Conclusion: Serum markers including BNP, troponin T, vWF and CA-125 are related with six minute walk distance and functional class which reflect the severity of PH at pediatric age. The combination of these serum markers may stand for a simple, cheap and non-invasive tool for clinical workup of PH during childhood.

Keywords: biological marker; child; functional class; pulmonary hypertension

Table 1: Serum Markers and Six Minute Walk Distance with respect to Functional Classification

	Class 1 (n=2)	Class 2 (n=18)	Class 3 (n=17)	Class 4 (n=3)	P
BNP (mg/L)	90.0 \pm 42.4	513.5 \pm 468.7	1190.2 \pm 651.9	4666.7 \pm 1527.5	0.001 \dagger *
Uric acid (mg/dl)	3.4 \pm 0.4	4.6 \pm 2.3	5.9 \pm 2.3	7.0 \pm 1.0	0.124
Troponin T (ng/ml)	0.003 \pm 0.001	0.004 \pm 0.003	0.007 \pm 0.005	0.206 \pm 0.131	0.003 \dagger *
CRP (pg/ml)	2.3 \pm 1.0	4.3 \pm 3.5	2.7 \pm 1.9	4.9 \pm 3.4	0.717
D-dimer (ng/ml)	17.5 \pm 2.1	144.1 \pm 140.1	115.0 \pm 66.8	293.2 \pm 240.0	0.408
vWF(%)	108.0 \pm 10.0	113.4 \pm 30.0	117.3 \pm 26.0	143.3 \pm 15.3	0.360
CA-125 (IU/L)	19.3 \pm 10.9	22.6 \pm 9.2	25.4 \pm 21.2	215.1 \pm 150.7	0.005 \dagger *
6 MWD (m)	460.0 \pm 0.0	484.1 \pm 91.6	376.3 \pm 104.4	120.0 \pm 14.1	0.001 \dagger *

* $p<0.05$ was accepted to be statistically significant.

\dagger Statistically significant difference was detected between Class 1 and Class 4.

Table 2: Serum Markers and Six Minute Walk Distance with respect to Treatment Modality

Variables	Monotherapy (n=20)	Combination treatment (n=20)	P
Brain natriuretic peptide (mg/L)	511.6 \pm 490.5	556.0 \pm 432.1	0.046*
Uric acid (mg/dl)	5.2 \pm 2.5	5.2 \pm 2.1	0.990
Troponin T (ng/ml)	0.006 \pm 0.005	0.081 \pm 0.023	0.041*
C-reactive protein (pg/ml)	4.0 \pm 3.2	3.2 \pm 2.7	0.978
D-dimer (ng/ml)	133.5 \pm 111.9	135.5 \pm 104.4	0.361
Von Willebrand factor (%)	113.7 \pm 21.0	118.5 \pm 33.2	0.966
CA-125 (IU/L)	22.9 \pm 17.7	84.4 \pm 43.7	0.037*
Six minute walk distance (m)	405.0 \pm 118.8	294.7 \pm 145.8	0.044*

* $p<0.05$ was accepted to be statistically significant.