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PROFILE OF PULMONARY FUNCTIONS IN PEDIATRIC PATIENTS OF SICKLE CELL DISEASE IN CENTRAL INDIA

Physiology

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ABSTRACT

The pulmonary dysfunctions due to sickle cell disease (SCD) are one of the leading cause of morbidity and mortality in pediatric age group specifically in central India (Chhattisgarh) which lies in Sickling belt. Obstructive and restrictive pulmonary changes develop in children with sickle cell disease, but reports conflict as to the type of change that predominates. This study conducted to evaluate pulmonary function tests in pediatric patients of SCD and to understand the pathophysiology & pattern of pulmonary functions. Total 75 patients from 10 to 14 year age were compared with 45 healthy controls. In the SCD group FVC, FEV1, PEF, FEF25%-75% and MVV were lower as compare to control groups in both sexes. Pulmonary function is abnormal in children with Hb-SS & AS. It is likely that abnormal pulmonary function reflects intrinsic lung disease in these patients and the mechanisms are more complex in this population than originally appreciated.

KEYWORDS

Sickle Cell Disease, Electrophoresis, Restrictive and obstructive lung disease.

INTRODUCTION:

Sickle cell anemia (SCA) is a genetic disorder in which adult hemoglobin (HbA) was mutated into sickle hemoglobin (HbS). The substitution of single nucleotide (GAG → GTG) change in the 6 codon of exon 1 of the B-globin chain[1] leads to replacement of valine for glutamic acid at 6thposition of the beta globin chain of hemoglobin causes Sickle hemoglobin (HbS). HbS having tendency to polymerize[2] in the de-oxy state, aggregates of such polymers are called tactoids. They distort the shape of RBCs to form sickle cells. The formation of irreversible sickled RBCs is the cause of the severe manifestations. It is characterized by acute vaso-occlusive episodes leading to adverse events such as acute pain, acute chest syndrome, multi-organ dysfunction, stroke, renal dysfunction& pulmonary dysfunctions.

The pulmonary dysfunctions due to sickle cell disease (SCD) are one of the leading cause of morbidity and mortality also in pediatric age group.[3]Clinical lung involvement is in the form of the acute chest syndrome (ACS), pulmonary hypertension (PH) & pulmonary fibrosis. Although hypoxemia and respiratory disease are risk factors for vaso-occlusive crisis in patients with sickle cell disease, the mechanisms remain unclear.[4] Obstructive and restrictive pulmonary changes develop in children with sickle cell disease, but reports conflict as to the type of change that predominates.[5] The pattern of lung function change across childhood in SCD is also not very clear. In view of the above observations, it was planned to study spirometric lung function tests in children above 10 years of age with sickle cell disorders to understand the pathophysiology, & pattern of pulmonary functions that came to J.L.N. Hospital and comparison with age, sex and ethnic matched controls was done.

METHODS:

The present study was conducted in the department of Pediatrics & Physiology at Pt. JNM Medical college and associated hospital, Raipur. Subjects included were sickle cell disorder patients attending the indoor and outdoor from November 2014 to December 2016. These subjects were evaluated for sickling Sodium Meta bisulphide Slide Test and positive test results were confirmed for Trait or Disease by performing Hemoglobin electrophoresis. A total of 75 cases of sickle cell disease from 10 to 14 year age were recruited and 45 normal healthy age, sex and ethnic matched control subjects were taken from general population. Subjects with history of any cardiac disease, chronic lung disease or disability, ACS and respiratory infection at least two weeks prior to spirometry were excluded from study. Included Subjects were divided into three groups:

Group A – Sickle Cell Disease cases (HbSS): Included 34 patients from 10 to 14 years of age.

Group B- Sickle Cell Trait cases (HbAS): Included 41 patients from 10 to 14 years of age.

Group C- Normal healthy subjects (HbAA): Included 45 healthy subjects matched with the cases with respect to age, sex.

After taking informed consent from parents and children for lung function tests detailed history, physical examination and laboratory investigations were carried out. The study was approved by institutional ethics committee.

LUNG FUNCTION TEST

Lung function test was recorded with the Spirometer DATOSPIR-70, a turbine based device model number-511-700-MU2, manufactured by SIBEL S.A. Barcelona (Spain). Each subject underwent spirometry and forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1),FEV1/FVC (FEV1%), peak expiratory flow (PEF), forced mid expiratory flow ($FEF_{25\%-75\%}$) and maximum voluntary ventilation (MVV) were recorded and interpreted according to guidelines for measurement of respiratory function of British Thoracic Society and the Association of Respiratory Technicians and Physiologists[6].

STATISTICAL ANALYSIS:

Each parameter was tested for distribution of data. Sociodemographic and Pulmonary functions data are presented as mean ± SD. Paired and un-paired 't' test were used as appropriate for the data by using SPSS software, version 15.

RESULT:

Total 74 patients of sickle cell anemia (41 HbAS and 34 HbSS) were included after following exclusion criteria. The diagnosis of sickle cell anemia was confirmed in the laboratory by performing Hemoglobin electrophoresis and consent is obtained for study. They were compared with 45 healthy, age and sex matched controls. The period of the study extended from November 2014 to December 2016. The study is approved by institutional ethics committee. All the cases and controls in the study were divided into 3 groups (Homozygous SS, Heterozygous AS and Healthy AA).

The mean age, weight, height, blood pressure, respiratory rate and heart rate for male and females of heterozygous patients (AS) and homozygous patients was not significant different to that of control group. Table 1 shows the Spirometric values of the Heterozygous patients and controls. Mean FEV1 was lower in male patients as compared control (p=0.0301*). Mean FEF 25%-75% and MVV was significant less in both males (p=0.0001*, p=0.0283* respectively)& females (p=0.0118*, p=0.0028* respectively) patients as compared to controls. Table 2 shows the Spirometric values of the Homozygous patients and controls**.** Mean FVC &FEV1 was less in male patients as compared control (p=0.0289*, p=0.0129* respectively). Mean FEF 25%-75% and MVV was significant less in both males (p=0.0001*, p=0.0134* respectively) & females (p=0.0018*, p=0.0001* respectively) patients as compared to controls. The pulmonary function profile of the Homozygous was not significantly different from Heterozygous patients.

DISCUSSION:

Present study has been done in Chhattisgarh State which lies in the sickling belt[7] of India to understand the pathophysiology of pulmonary dysfunction in pediatric SCD patients. The limitation of the study was larger sample should be taken along with assessment of pulmonary hypertension. Sickle Cell Disease can affect many body systems, including the respiratory systems[8], which can impair lung function and functional capacity. As described above, Spirometric lung functions (FVC, FEV_1, PEF, $FEF_{25\%-75\%}$ and MVV) were performed to assess lung functions impairment in pediatric patients. In our study FVC, FEV_1, $FEF_{25\%-75\%}$ and MVV were lower in heterozygous and homozygous SCD male patients as compared to control groups where as $FEF_{25\%-75\%}$ and MVV were lower in heterozygous and homozygous SCD female patients as compared to control groups. Forced vital capacity (FVC) represents by lung dimension, compliance and respiratory muscle power whereas PEFR is determined by alveolar caliber, alveolar elastic recoil and respiratory muscle efforts[9]. So it may represent the early changes in the pulmonary functions in our patient population. There is no significant difference between the heterozygous and homozygous patients in either gender.

All the spirometric values are not significantly different between the groups can be explained with earlier studies which reported normal lung volumes and expiratory flows in children with SCD when compared with those of an appropriate control group as the mean age of our patient group was 13.33 years. Apart, studies reported that lung function abnormalities become more severe as age advances. Studies reported that as the disease advances there was deterioration of pulmonary functions was a prime contributor to mortality in SCD patients. Progressive decline in pulmonary function parameters can be explained from changes in lung compliance and microvascular occlusion developed due to repeated infections, thromboembolic episodes and severity of the attacks[10]. Interstitial lung disease, which is characterized by vascular remodeling and interstitial fibrosis, is a frequent complication of sickle cell anemia and further leads to restrictive, obstructive or mixed pattern of lung disease. Further studies are required to evaluate the effect of SCD on pattern of lung disease in pediatric population.

CONCLUSION:

Pulmonary function is abnormal in children with Hb-SS& AS. It is likely that abnormal pulmonary function reflects intrinsic lung disease in these patients and that the mechanisms are more complex in this population than originally appreciated. Greater understanding of the diagnostic utility of pulmonary function testing in this population is paramount as it could lead to a more comprehensive appraisal of the mechanisms responsible for pulmonary complication.

Table 1. Pulmonary function pattern of the Heterozygous sickle cell patients and controls

Parameters	Gender	Heterozygous (AS) n=41	Controls (AA) n= 45	PValue (0.05)*
FVC (Lit)	Male	2.50 ± 0.62	2.78 ± 0.93	NS
	Female	2.29 ± 0.55	2.36 ± 0.45	NS
FEV1 (Lit)	Male	1.90 ± 0.59	2.40 ± 0.85	0.0301*
	Female	1.86 ± 0.47	1.98 ± 0.44	NS
PEF (Lit / Sec)	Male	3.01 ± 1.47	3.62 ± 1.35	NS
	Female	3.15 ± 0.76	3.39 ± 0.60	NS
FEF 25%-75% (Lit/Sec.)	Male	2.07 ± 0.49	2.64 ± 1.22	0.0001*
	Female	2.18 ± 0.76	2.75 ± 0.64	0.0118*
MVV (Lit. / Min.)	Male	56.84 ± 17.20	72.09 ± 25.98	0.0283*
	Female	55.85 ± 14.08	69.44 ± 13.04	0.0024*

un-paired t-test. data presented as mean ± standard deviation, * p <0.05.

Table 2. Pulmonary function pattern of the Homozygous sickle cell patients and controls

Parameters	Gender	Homozygous (SS) n=34	Controls (AA) n= 45	pValue (0.05)*
FVC (Lit)	Male	2.22 ± 0.54	2.78 ± 0.93	0.0289*
	Female	2.25 ± 0.47	2.36 ± 0.45	NS
FEV1 (Lit)	Male	1.82 ± 0.46	2.40 ± 0.85	0.0129*
	Female	1.76 ± 0.36	1.98 ± 0.44	NS
PEF (Lit / Sec)	Male	2.85 ± 1.15	3.62 ± 1.35	NS
	Female	2.97 ± 0.67	3.39 ± 0.60	NS
FEF 25%-75% (Lit/Sec.)	Male	2.10 ± 0.50	2.64 ± 1.22	0.0001*
	Female	2.08 ± 0.55	2.75 ± 0.64	0.0018*
MVV (Lit. / Min.)	Male	54.53 ± 13.83	72.09 ± 25.98	0.0134*
	Female	52.67 ± 9.92	69.44 ± 13.04	0.0001*

un-paired t-test. data presented as mean ± standard deviation, * p <0.05.

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