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RELIABILITY OF STRESS EXERCISE TEST IN PATIENTS WITH PULMONARY ARTERIOVENOUS MALFORMATIONS

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ABSTRCT

Background: Pulmonary arteriovenous malformations lead a route for passing the emboli to the circulatory system and can be a reason for cerebrovascular accidents, attacks, and abscesses of the cerebral region.

Aim: To evaluate and assess the reproducibility, reliability, and efficacy of a 6-minute walk test and exercise stress test in subjects with pulmonary arteriovenous malformations. Also, to assess if these tests can be used at follow-up revaluation and can replace echocardiography and CT (non-contrast) in asymptomatic children.

Materials and Methods: In 20 subjects with PAVMs Exercise stress test and 6 minute walk test was done with continuous monitoring of ECG, heart rate, and oxygen saturation was done The study parameters were statistically evaluated and results were formulated regarding efficacy and reliability of 6 minute walk test and exercise stress test. They were baseline and after test heart rates and oxygen saturation. Differences in oxygen saturation recorded at baseline, and after test were also evaluated.

Results: Except for the difference in the oxygen saturation, all other parameters including heart rate and oxygen saturation (baseline and after test) showed significant reproducibility with the p-value of 0.7429 for 6 minute walk test. For the exercise stress test, all the parameters showed a statistically significant reproducibility p-value <0.005.

Conclusion: The study concludes that 6 minute walk test and exercise stress test are highly reproducible and can be used for follow-up revaluation replacing invasive techniques in subjects with pulmonary arteriovenous malformations.

Keywords: Pulmonary arteriovenous malformations, heart rate, oxygen saturation, exercise stress test, 6 minute walk test.

Keynote: The majority of subjects having pulmonary arteriovenous malformations have underlying Hereditary Hemorrhagic Telangiectasia which associate with arteriovenous malformations in different body parts including lungs, retina, liver, brain, and/or GIT.

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Introduction

Arteriovenous malformations can be found anywhere in the human body and pulmonary arteriovenous malformations (PAVMs) were first described as communications between arteries and veins which were abnormal and had thin walls (Churton-1987). These thin-wall vascular communications can rupture during dilations leading to pulmonary hemorrhage.[1] These pulmonary arteriovenous malformations are the shunts. These are located in the extra-cardiac region and helps bypass filtration in the lungs. These malformations lead a route for passing the emboli to the circulatory system and can be a reason for cerebrovascular accidents, attacks, and abscesses of the cerebral region.[2]

The majority of subjects having pulmonary arteriovenous malformations have underlying Hereditary Hemorrhagic Telangiectasia which is a genetic disorder with mutant genes of a protein and receptor. Subjects with Hereditary Hemorrhagic Telangiectasia can have arteriovenous malformations in different body parts including lungs, retina, liver, brain, and/or GIT.[3] Subjects with hereditary hemorrhagic telangiectasia should be investigated for pulmonary arteriovenous malformations and the opposite should also be considered. These malformations are the main reason for death in subjects with telangiectasia.[4]

Currently, the treatment strategies of PAVNs are targeted at preventing complexities including hemoptysis/ hemothorax, preventing paradoxical emboli formation, transcatheter embolization, and/or improvement of intolerance for exercise/dyspnea. Out of these transcatheter embolization is effective with lesser complications. These include ischemic attacks, angina, reperfusion, and pleurisy. However, these complications are seen in less than 2% of subjects with transcatheter embolization.[5]

The diagnosis is made with contrast echocardiography followed by multidetector CT (in positive echocardiography) with reconstruction using thin slices. These methods are considered reliable for adults, whereas, reliability of screening tests in children is still questionable.[6] Following transcatheter embolization, it is recommended to evaluate the subjects after 6 months followed by every 3 years to assess reperfusion and growth. These malformations can be simple involving one pulmonary branch, complex with more branches from more than one segmental artery involved, and diffuse involving whole segmental artery in one or both lung.[7]

With CT not able to judge deterioration and progression of disease the exercise stress test was evaluated. It was seen that stable exercise tests were seen in patients with no progression and deterioration by PAVMs. With the deterioration of symptoms and enlargement of malformations, fall in oxygen saturation during exercise and change in exercise test were seen.[8] Exercise stress testing is considered as a non-invasive method with high safety in PAVMs still the reliability and efficacy of 6 minute walk test and exercise stress test need to establish. Despite high risk in subjects of pulmonary arteriovenous malformations for cerebral abscess, transient ischemic attacks, stroke, hemoptysis, and/or hemothorax, patients may remain asymptomatic with no cyanosis or clubbing.[9]

Hence, the present trial was carried out to evaluate and assess the reproducibility, reliability, and efficacy of 6 minute walk test and exercise stress test in subjects with pulmonary arteriovenous malformations. Also, to assess if these tests can be used at follow-up revaluation and can replace echocardiography and CT (non-contrast) in asymptomatic children.

Materials and Methods

The study was carried out to evaluate and assess the reproducibility, reliability, and efficacy of 6 minute walk test and exercise stress test in subjects with pulmonary arteriovenous malformations. Also, to assess if these tests can be used at follow-up revaluation and can replace echocardiography and CT (non-contrast) in asymptomatic children.

The study was undertaken at…… from…….. to …….. and included 20 subjects who had pulmonary arteriovenous malformations and who had either undergone transcatheter embolotherapy or have to undergo transcatheter embolotherapy. All the subjects were asked to sign the informed consent. The Ethical committee approval was taken from the institution. The demographic characteristics were recorded and a physical examination was performed on all 20 subjects. Also, medical history, family history, and present disease were considered in detail while questioning the subjects.

Clubbing, telangiectasia, and cyanosis were looked for in the physical examination. Levels of the oxygen saturations were noted in a standing position. CT chest recorded during diagnosing the pulmonary arteriovenous malformations were taken. Contrast echocardiography, MRI, and pulmonary angiography records were taken wherever applicable and available. Genetic testing was done to evaluate the status of hereditary hemorrhagic telangiectasia. The presence of hereditary hemorrhagic telangiectasia with pulmonary arteriovenous malformation was recorded.

Every patient was asked to perform one exercise stress test then one 6 minute walk test after 30 minutes of exercise stress test followed by another 6 minute walk test after 30 minutes. Then again exercise stress test was performed, then two 6 minute walk tests at 30 minutes intervals. In total two exercise, stress tests, and two 6 minute walk tests were performed in a sequence of exercise stress tests, two 6 minute walk tests, and exercise stress tests. All the subjects had the stable clinical condition without any systemic disease and had AHA level 1. The medical help if needed was available during all the exercise periods.

6 minute walk test was done to assess functional capacity on a 30-meter long straight hallway without using any exercise equipment as suggested by the American Thoracic Society and AHA with continuous availability of medical help. Rest was allowed during the test whenever the subject wanted. However, no subject took the rest in between. Before the test, oxygen saturation and heart rate were noted and fatigue and dyspnea were also asked. At 6 minutes oxygen saturation and heart rates were recorded along with the total distance covered.

The exercise stress test was done as suggested by AHA (American Heart Society) in comfortable exercise clothes. The patients were fitted with 10 electrodes to receive continuous ECG tracing during the exercise. Before commencement of the exercise stress test heart rate (using ECG) and oxygen saturation levels (using oximeter) were noticed for all the subjects. Continuous monitoring of ECG, heart rate, and oxygen saturation were done throughout the exercise stress test with a 30-watt increase every 2 minutes. The exercise stress test was sopped when subjects breathe shortness, leg tiredness, and/or 85% of predicted heart rate was reached. After completion of test resistance of cycle, ergometry was reduced to 15 watts, and heart rate and oxygen saturation were re-recorded.

The study parameters were statistically evaluated and results were formulated regarding the efficacy and reliability of 6 minute walk test and exercise stress test. They were baseline and after test heart rates and oxygen saturation. Differences in oxygen saturation recorded at baseline, and after test were also evaluated. The data collected were subjected to statistical+-evaluation.

Results

The study was carried out to evaluate and assess the reproducibility, reliability, and efficacy of 6 minute walk test and exercise stress test in subjects with pulmonary arteriovenous malformations. Also, to assess if these tests can be used at follow-up revaluation and can replace echocardiography and CT (non-contrast) in asymptomatic children.

The study included 20 subjects having both male and female with the mean age of 26.3 years and with the age range of 8 years to 67 years. The demographic characteristics of the study subjects are listed in table 1. The results showed that in a total of 20 subjects, there were 6 males and 14 females with mean oxygen saturation of 94.1 with the range of 67-100. The mean height and weight of study subjects were 1.7 (range-1.2-1.9 meters) meters and 65.2 kgs (range- 30-89kg) respectively. All the included subjects completed all the exercise stress tests and 6 minute walk tests.

The reproducibility and efficacy of 6 minute walk test were also evaluated in the present trial and the results are summarized in Table 2. The statistical significance was kept at the p-value of <0.05. Except for the difference in the difference of oxygen saturation, all other parameters including heart rate and oxygen saturation (baseline and after test) showed significant reproducibility with the p-value of 0.7429. The distance covered by study subjects during test1 and test 2 respectively was 470.9±83.9 m and 476.8±70.6 with a p-value of 0.8111. The baseline heart rates were 94.7±14.8 and 95.2±15.9 for the two respective tests. These heart rates respectively post-tests were 107.5±16.6 and 107.5±16.6 beats per minute (p-value=0.7557). The oxygen saturation level at baseline for the two tests were 94.1±7.6 and 95.5±7.3 (p-value=0.559) respectively. These values respectively post-test were 92.4±9.7 and 93.2±8.2 (p-value=0.7797).

Concerning the exercise stress test, the results showed that significant reproducibility was seen in all the parameters. The work during the exercise stress test was seen as 115.3±41.1 and 114.1±40.3 respectively (p-value=0.9262). Oxygen saturation as seen in two tests respectively at baseline was 94.5±6.5 and 94.3±6.8 with a p-value of 0.9247. These values respectively post-test were 91.7±9.7 and 92.3±9.3 (p-value=0.8248). These values were statistically significant. Similar results were seen about the heart rate where baseline values for two tests respectively were 90.7±15.6 and 90.9±14.9 beta per minutes (p=0.9671) and post-test values for heart rate were 158.8±15.5 and 157.7±15.7 beats per minutes (p-value=0.8247). All these values were statistically significant showing reproducibility of the exercise stress test (Table 3).

Discussion

The study was carried out on 20 subjects to evaluate and assess the reproducibility, reliability, and efficacy of 6 minute walk test and exercise stress test in subjects with pulmonary arteriovenous malformations. Also, to assess if these tests can be used at follow-up revaluation and can replace echocardiography and CT (non-contrast) in asymptomatic children. All 20-subjects completed both the 6 minute walk test and exercise stress test successfully. It was seen that both these tests were reliable and showed reproducibility in the study subjects. This was in agreement with the findings of Murphy J et al[10] in 2009 where authors have reported the stability

of exercise stress testing in subjects with pulmonary arteriovenous malformations and changes were only seen in subjects with disease progression and developing symptoms. In the present trial, the results of the 6 minute walk test and exercise stress test were comparable with more decrease in oxygen saturation with the exercise stress test which could be due to more oxygen consumption during the exercise than with the walk.

The study included 20 subjects having both male and female with the mean age of 26.3 years and with the age range of 8 years to 67 years. In a total of 20 subjects, there were 6 males and 14 females with mean oxygen saturation of 94.1 with the range of 67-100. The mean height and weight of study subjects were 1.7 (range-1.2-1.9 meters) meters and 65.2 kgs (range- 30-89kg) respectively. All the included subjects completed all the exercise stress tests and 6 minute walk tests. These parameters were following the parameters in the studies of Khalid SK et al[11] in 2008 and Pollak JS et al[12] in 2006 where authors used the comparable demographic characteristics as the present study.

The reproducibility and efficacy of 6 minute walk test were also evaluated in the present trial. The statistical significance was kept at the p-value of <0.05. Except for the difference in the difference of oxygen saturation, all other parameters including heart rate and oxygen saturation (baseline and after test) showed significant reproducibility with a p-value of 0.7429. The distance covered by study subjects during test1 and test 2 respectively was 470.9±83.9 m and 476.8±70.6 with a p-value of 0.8111. The baseline heart rates were 94.7±14.8 and 95.2±15.9 for the two respective tests. These heart rates respectively post-tests were 107.5±16.6 and 107.5±16.6 beats per minute (p-value=0.7557). The oxygen saturation level at baseline for the two tests were 94.1±7.6 and 95.5±7.3 (p-value=0.559) respectively. These values respectively post-test were 92.4±9.7 and 93.2±8.2 (p-value=0.7797). These findings were consistent with the findings by Li AM et al[13] in 2005 and Nixon PA et al[14] where authors have reported the reliability and reproducibility of the 6 minute walk test in subjects with hereditary hemorrhagic telangiectasia and pulmonary arteriovenous malformations.

For the exercise stress test, the results showed that significant reproducibility was seen in all the parameters. The work during the exercise stress test was seen as 115.3±41.1 and 114.1±40.3 respectively (p-value=0.9262). Oxygen saturation as seen in two tests respectively at baseline was 94.5±6.5 and 94.3±6.8 with a p-value of 0.9247. These values respectively post-test were 91.7±9.7 and 92.3±9.3 (p-value=0.8248). These values were statistically significant. Similar results were seen concerning the heart rate where baseline values for two tests respectively were 90.7±15.6 and 90.9±14.9 beta per minutes (p=0.9671) and post-test values for heart rate were 158.8±15.5 and 157.7±15.7 beats per minutes (p-value=0.8247). All these values were statistically significant showing reproducibility of the exercise stress test. Similar results were reported by Rhodes J et al[15] in 2010 and Gupta P t al[16] in 2002 where it was shown that the exercise stress test showed reliable and reproducible results in terms of heart rate and oxygen saturation in patients with pulmonary arteriovenous malformations.

The studies by Preston Dl et al[17] in 2007 and Cardis E et al[18] in 2007 have shown that the conventional radiographic techniques such as CT, MRI, pulmonary angiography, echocardiography, and multidetector CT expose the patients to high radiation doses which can, in turn, be harmful to the already suffering subjects. This shortcoming was overcome in the present study where relatively non-invasive methods with no harmful radiation exposures were used.

Conclusion

The present study concludes that 6 minute walk test and exercise stress test are highly reproducible and can be used for follow-up revaluation replacing invasive techniques in subjects with pulmonary arteriovenous malformations. Also, the harmful radiation exposure factor was eliminated using 6 minute walk test and exercise stress test. The present trial had few limitations including geographic area bias, uniform area population, smaller sample size, and short monitoring period. Hence, multi-institution longitudinal studies with a larger sample size and longer monitoring period are required to reach the definitive conclusion.

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S. No	Parameter	Number	Percentage
1.	Total Subjects	20	
2.	Mean Age	26.3 years	
3.	Age Range	8- 67 years	
4.	Sex		
a.	Males	6	30%
b.	Females	14	70%
5.	Oxygen saturation	94.1	
6.	Oxygen saturation Range	67-100	
7.	Height (in meters)	1.7 meters	
8.	Height Range	1.2-1.9	
9.	Weight (in kgs)	65.2	
10.	Weight Range	30-89	

Table 1: Demographic Characteristics of the study subjects

S. No	Parameter	6 min walk test 1 (Mean± S.D)	6 min walk test 2 (Mean± S.D)	p-value
1.	Distance Covered during the test (in meters)	470.9±83.9	476.8±70.6	0.8111
2.	Oxygen Saturation (at Baseline)	94.1±7.6	95.5±7.3	0.5559
3.	Oxygen Saturation	92.4±9.7	93.2±8.2	0.7797

	(post-test)			
4.	Heart Rate (at Baseline in beats per min)	94.7±14.8	95.2±15.9	0.9186
5.	Heart Rate (post-test in beats per min)	107.5±16.6	105.7±19.6	0.7557
6.	The difference in oxygen Saturation	1.6±3.2	1.3±2.5	0.7429

Table 2: 6-minute walk test parameters of the study subjects

S. No	Parameter	Exercise stress test 1 (Mean± S.D)	Exercise stress test 2 (Mean± S.D)	p-value
1.	Work during the exercise stress test (W)	115.3±41.1	114.1±40.3	0.9262
2.	Oxygen Saturation (at Baseline)	94.5±6.5	94.3±6.8	0.9247
3.	Oxygen Saturation (post-test)	91.7±9.7	92.3±9.3	0.8428
4.	Heart Rate (at Baseline in beats per min)	90.7±15.6	90.9±14.9	0.9671
5.	Heart Rate (post-test in beats per min)	158.8±15.5	157.7±15.7	0.8247
6.	The difference in oxygen Saturation	3.3±3.7	2.7±2.6	0.5565

Table 3: Exercise stress test parameters of the study subjects