Original Article

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HEMODYNAMIC EFFECTS OF SIMPLE HAND PUMP EXERCISE SUPPLEMENTATION TO ADENOSINE STRESS PROTOCOL ON TC-99M SESTAMIBI IMAGING

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ABSTRACT

Objective: To find out the effect of simple hand pump exercise on standard adenosine stress technetium-99m sestamibi myocardial perfusion imaging in patients who were unable to perform on treadmill or bicycle ergometer.

Study Design: Prospective non-randomized controlled trial.

Place and Duration of Study: Department of Nuclear Cardiology, Armed Forces Institute of Cardiology / National Institute of Heart Diseases; Rawalpindi: Pakistan from 1st June 2014 to 31st Dec 2015.

Material and Methods: One hundred and forty-five consecutive patients who were physically unfit to perform exercise by their lower extremities were included in this study. These patients underwent adenosine Tc-99m sestamibi cardiac single photon emission computed tomography with exercise supplementation (AdenEx) protocol. Hemodynamic changes, electrocardiographic and scan findings were studied. These results were compared with a control group (Aden) which included 136 patients who underwent adenosine infusion alone.

Results: The mean age of AdenEx patients was 55 ± 13 years and that of the Aden group 57 ± 12 years. In AdenEx group heart rate increased to 37% as compared to 12% increase in Aden group. In AdenEx there was not a single incidence of hypotension as compared to Aden group where significant fall in systolic and diastolic blood pressure (millimeter of Mercury) from 140 ± 22 to 108±12 and 74 ± 16 to 50 ± 14 respectively. Chest discomfort, dyspnea, headache, jaw, neck and gastrointestinal symptoms were significantly less in AdenoEx group. The AdenEx group showed higher ECG sensitivity 6% vs 34%, respectively; $p = .003$).

Conclusion: By addition of simple hand pump exercise during adenosine infusion prevent fall in blood pressure, significantly increases heart rate, reducing side effects and increases ECG sensitivity. This protocol is best for patients who are unable to perform exercise by utilizing their lower extremities.

Keywords: Adenosine, Sestamibi, Hemodynamic changes, Hand pump exercise, Electrocardiogram.

INTRODUCTION

Stressed induced myocardial perfusion imaging is non-invasive functional cardiac imaging, widely utilized all over the world for the diagnosis as well as therapeutic management of patients with coronary artery disease[1]. Physical or pharmacological stress is induced as part of perfusion imaging. Adenosine is widely utilized for this pharmacological stress induction in physically fit or unfit patients. The adenosine being a powerful vasodilator has many limitations, including frequent side effects, lack of electrocardiogram (ECG) sensitivity and high tracer pooling particularly in splanchnic vasculature and liver[2-5].

Any type of physical activity redistributes the blood flow, towards the skeletal musculature and redistributes the injected radiopharmaceutical[6-8]. Studies have shown that the induction of exercise may help to overcome some of the important limitations of adenosine infusion alone[9-13]. The physical stress not only decreases the side effects of adenosine but also increases the sensitivity of ECG and tolerance by the patients[14-15]. No previous study has evaluated the effects of simple hand pump exercise during adenosine infusion. In our study only those patients are being included who could not perform other type of physical exercise. The primary objective of this

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study was to determine the hemodynamic changes by induction of hand pump exercise during adenosine infusion.

MATERIAL AND METHODS

fibrillation, LBBB or pacemaker were also included in Adeno group. Out of 145 patients AdenEx group, 95 (65%) were evaluated for diagnostic reasons and 55 (35%) for prognostic reasons. The baseline characteristics of the 2

Table-1: Demographic & Clinical characteristics of patients.

Variables	AdenEx (n = 145)	Aden(n = 136)	*p* value
Mean age (y)	55 ± 13	57 ± 12	0.22
Men(%)	87 (60%)	73 (54%)	0.39
Cardiac history	77 (52%)	65 (48%)	0.78
• Coronary disease	22 (15%)	16 (12%)	0.14
• Previous MI	17 (12%)	8 (9%)	0.13
• PTCA / stent	10 (7%)	11 (8%)	0.49
• Surgical revascularization			
Medications	78 (54%)	76 (56%)	0.21
• β-Blockers	45 (31%)	40 (29%)	0.35
• Calcium blockers	22 (15%)	20 (15%)	0.35
• Nitrates			

Table-2: Hemodynamic changes induced by Adenosine alone (Aden) or combined with exercise (AdenEx).

	Baseline	1 min	2 mins	3 mins	4 mins	5 mins	6 mins	2 mins post stress	4 mins post stress
HR (bpm)									
• AdenEx	66 ± 12	74 ± 10	90 ± 11	106 ± 12	104 ±9	96±12	100±8	92±12	76±12
• Aden	70 ± 11	72 ± 10	80 ± 11	84 ± 12	80±9	80±12	78±8	74±12	77±12
Systolic BP (mmHg)									
• AdenEx	136±22	140±20	130±18	124±16	126±20	128±21	130±22	132±22	140±18
• Aden	140±22	136±18	120±18	110±16	112±20	108±21	108±22	123±22	130±18
Diastolic BP (mmHg)									
• AdenEx	84±12	80±12	70±12	62±12	66±12	64±12	66±12	66±12	66±12
• Aden	74±16	72±14	66±18	50±18	50±14	54±17	52±15	60±14	70±12

Heart rate beats per minute (HR bpm), Adenosine with hand pump exercise (AdenEx) Adenosine without exercise (Aden)

Table-3: Other symptoms/side effects observed.

	Baseline	One min	Two min	Three min	Four min	Five min	Six min	2 min post stress	4 min post stress
Flushing									
• **AdenEx**	-	-	25%	35%	40%	42%	46%	10%	4%
• **Aden**			29%	39	42%	54%	46%	12%	4%
Chest D									
• **AdenEx**			15%	20%	34%	30%	35%	5%	2%
• **Aden**	-	-	32	45%	38%	46%	46%	8%	6%
Dyspnea									
• **AdenEx**			22%	22%	23%	22%	24%	4%	1%
• **Aden**	-	-	26%	30%	40%	45%	46%	6%	2%

Chest discomfort (Chest D), Adenosine with hand pump exercise (AdenEx) Adenosine without exercise (Aden).

Patient population: A total of 281 patients, 145 in the AdenEx group and 136 in the Aden group, were included for final data analysis. All patients with resting ECG changes of atrial groups, including age, sex, cardiac history, and medications taken, were similar. All patients were asked to stop nicotine / caffeine intake for at least 24 hours before the examination.

Protocols for adenosine infusion and hand pump exercise supplementation: Myocardial perfusion studies were acquired by using one-day stress and rest protocols (Fig-1). All the procedure was explained to the patients. Intravenous line was secured by using 22-gauge cannula. Patients were made to sit on a sofa chair in semi recumbent position by adjusting the back with 12 lead ECG and blood pressure monitors attached. All baseline parameters like, heart rate, blood pressure, ECG were recorded on a designed sheet. A flexible rubber ball/pump (Fig-2) was given to the patient in free hand and was advised to start pumping. Adenosine infusion was started at a rate of 140 mcg/kg/min for 6 minutes and radiotracer Tc-99m sestamibi 8-12 mCi was injected at mid-way of this infusion. ECG, blood pressure and heart rate were recorded at every minute and continued till 3 minutes' post infusion. Any unwanted effect described by the patient was recorded. After the completion of stress, the patient was advised to take a glass of full cream milk.

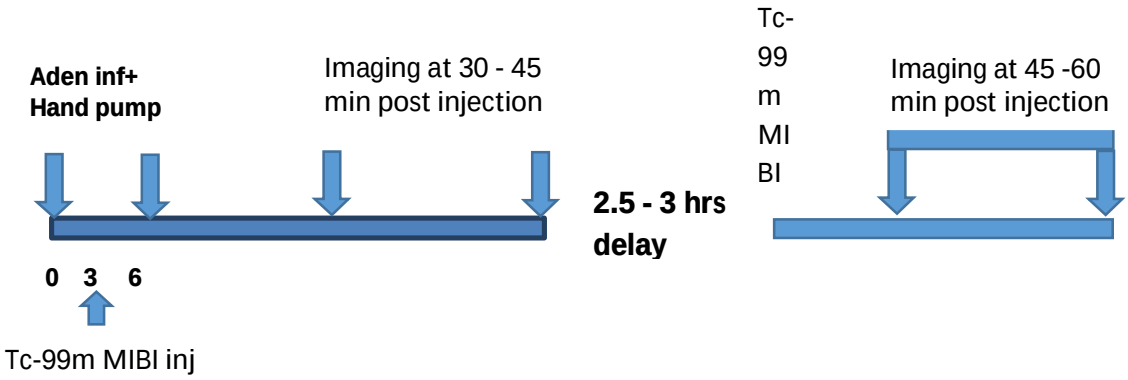

Figure-1: Adenosine stress first protocol with hand pump exercise.

Myocardial Imaging: Gated single photon emission computed tomography (SPECT) study was acquired on dual head dedicated cardiac gamma cameras Philips Adac CardioMD and Positron/IS2 Pulse CDC equipped with high resolution general purpose parallel-hole collimator at 45 min post injection. The acquisition parameters were based on guidelines and recommendations published by the American Society of Nuclear Cardiology16. The gated SPECT study was acquired in a step-and-shoot mode, using a non-circular orbit of 180°, starting at a 45° right anterior oblique angle and ending at a 45° left posterior oblique orientation for a total of 32 projections of 40 seconds duration each. The images were stored by using 64x64 matrix and were processed by means of a Butterworth filter with a frequency cutoff of 0.40 cycles/pixel and an order of 6.0 for image reconstruction. The processed images were displayed and analyzed by using Corridor 4DM (Segami) v5.1, Cedars-Sinai quantitative perfusion SPECT (QPS4) and quantitative gated SPECT (QGS4.0). The tomographic slices were analyzed systematically by, dividing the heart into 9 regions and further analyzed by using 20 segments polar map. The diagnosis of ischemia was based solely on qualitative and quantitative analysis.

Statistical Analysis: The data expressed as mean ± SD with two sample proportional analysis applied for determination of differences in the two groups. Comparison of different hemodynamic changes in same group was analyzed by applying paired Student t tests and unpaired Student t test was applied to analyzed these changes in different groups. A *p*-value equal to or less than .05 was considered significant.

RESULTS

Baseline characteristics are shown in table-1. Hemodynamic data during and after infusion like heart rate, systolic and diastolic blood pressure summarized in table-2. Some of the

major hemodynamic findings for both groups are elaborated below.

Tolerance to Hand pump Exercise and Hemodynamic Change: Hand pump exercise was well tolerated by most of the patients. 92% patients continued the hand pump for six minutes with 5 to 7 seconds rest intervals in case of tiredness. The peak heart rate achieved in AdenEx group was 106 ± 12 beats/min (table-2). This hand pump exercise also raised systolic blood pressure as compared to Aden group where, fall in blood pressure was observed. In 4% of Aden group patients there was severe fall in blood pressure (>50 mmHg fall in systolic and diastolic blood pressure). Symptomatic hypotension occurred in 11% of patients in the Aden group; however, it was not seen in other group (p = .02).

Flushing, chest discomfort, dyspnea, headache, jaw, neck and gastrointestinal symptoms were significantly less in stress group (table-3). First and 2nd degree heart block was observed in 2% of Aden group. In 8 (6%) patients of Adeno group there was transient asystole associated with severe breathlessness. Dizziness associated with diaphoresis and pallor without presyncope and syncope was a symptom in 7 (5%) patients.

Electrocardiographic Changes: The ECG changes were compared with scintigraphic findings by making scintigraphy results as gold standard. In Aden group ECG show 20 true positives, 50 true negatives, 66 false negatives, and 0 false positive results. In the AdenEx group ECG exhibit, 50 true positives, 45 true negatives, 30 false negatives, and 20 false positives trace. ECG sensitivity was improved in AdenEx group as compared to Aden group and it was 34% vs 15%, p = .006. No significant differences occurred between the Aden and AdenEx groups with regard to positive predictive values (100% vs 40%, respectively; p = .18) and negative predictive values (67% vs 62%, respectively; p = .50). Using the Fisher test, we found a real gain in the number of true-positive results detected in the exercise group (2 vs 12 patients, p = .002). Using the McNemar test, we observed that the probability of having a positive ECG result was lower than that of having a positive sestamibi result only in the Aden group; this same condition was not present in the AdenEx group.

Imaging Results: There was no significant difference in the scan findings in both groups. There was reversible ischemia in 59% of the AdenEx group and 56% in Aden group. (59% vs 56%; p = .72). Out of 145 AdenEx patients 51 have normal study, 85 have reversible ischemia in single or multiple vessels territories, 6 have reverse redistribution and 3 have fixed perfusion defect. On the other hand, in aden group 77 have reversible ischemia, 50 show normal perfusion study, 5 having reverse redistribution and 4 showed fixed perfusion defects (table-5).

Figure-2: Rubber ball and pumping device for hand pump exercise.

DISCUSSION

There is a long list of side effects related to adenosine stress test, starting from simple flushing to arrhythmias. To reduce the number and intensity of these side effects without compromising the stress, many protocols were published and are in practice. In this study we

added simple hand pump exercise (continuous hand pumping of a rubber ball) (Fig-2) during the adenosine infusion. The major effects of this simple exercise were positive hemodynamic responses. It prevented the hypotension, diverted the patient concentration and prevented the heart block and asystole. Moreover, there was significant reduction of other adverse effects like, flushing, chest discomfort, headache, throat, neck and jaw discomforts. This simple measure during adenosine infusion increased the ECG sensitivity.

Comparison of our findings with those in the literature: The patients who could perform physical stress either by treadmill or bicycle ergometer, these combination protocols definitely give better outcome. However, in patients who are unable to perform physical stress, the hand pump exercise is the best alternate option. Many published studies used a combined protocol involved some form of exercise other than the hand pump[9-11,17,18]. Treadmill, bicycle ergometer has some peculiarities because the patient has to perform maximum physical stress apart from vasodilator effects of adenosine. Increase in heart rate together with vasodilatation is being achieved by this combination of physical as well as pharmacological stress[19-20]. The only important aspect of this combination is that when the tracer should be injected? Different published studies have shown the different timings of radiotracer injection. In our study we used the six minutes' adenosine infusion protocol and radiotracer was injected at midway of the infusion without any alteration of standard protocol.

Other studies, using different combined protocols, started exercise with the initiation of the adenosine infusion or after it had already been concluded[12,21-23]. The same beneficial effects can be obtained with exercise supplementation to adenosine, including a reduction in side effects and arrhythmias and improvement in the target-to-background ratio[24-25].

On the basis of our findings and the data available in the literature, addition of some kind of physical stress to vasodilator infusion improves image quality, reduction of unwanted effects with minimal efforts. By induction of some kind of physical stress may help the clinicians to identify patients who are considered to be non-responders to adenosine alone. This factor increases the diagnostic yield and helps to identify the more abnormally perfused areas in the left ventricular myocardium. The ECG changes also helpful in diagnosis of ischemia together with the imaging[19,26].

CONCLUSION

We demonstrated a significant difference in hemodynamic by introducing simple compression of elastic ball (hand pump exercise) in patients who were unable to perform any intense exercise like treadmill during pharmacological stress with adenosine. The patient's intentions were diverted to pumping elastic ball and hemodynamic changes significantly reduced the side effects of adenosine. The level of this stress performed prevented hypotension and increased ECG sensitivity. Exercise supplementation should be used in patients undergoing dipyridamole perfusion imaging whenever feasible.

Limitation of Study

Although the baseline characteristics age, sex, cardiac history, and medications are similar in both the groups (table-1), but it could be more evident and truly assessed if both protocol would be applied on same patient.

CONFLICT OF INTEREST

This study has no conflict of interest to declare. Abstract and results of this study were accepted and presented in an oral presentationat the International conference on Medical Education, organised by Association for Excellence in Medical Education(AEME) and held on 07th-09th March 2014 at University of Health Sciences(UHS) Lahore, Pakistan. No funding was received from any agency or institution.

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