



COMPARISON OF FULL FAT MILK AND LEMON JUICE IN FACILITATION OF HEPATO-BILIARY CLEARANCE OF RADIOPHARMACEUTICAL ⁹⁹MTC-MIBI DURING MYOCARDIAL PERFUSION IMAGING

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ABSTRACT

BACKGROUND: Subdiaphragmatic activity observed during myocardial perfusion imaging (MPI) is a potential source of inducing artifacts during reconstruction of raw images. Present study was planned to assess which intervention (full fat milk or lemon juice) is better in reducing the subdiaphragmatic (SD) activity. This minimize the need of rest imaging in cases where stress imaging is normal, resulting in reducing unnecessary radiation exposure. We compared the effectiveness of lemon juice versus full fat milk in hepatobiliary clearance of radioactivity in patients undergoing myocardial perfusion imaging.

MATERIAL AND METHODS: It was a randomized controlled trial conducted at Nuclear Cardiology department, PIC, Lahore during April 2019 to October 2019 (Six months). A total of seventy (n=70) patients of both gender between age 25-75 years, referred for MPI for the evaluation of coronary artery disease were enrolled and randomized into two groups (full fat milk or lemon juice) by lottery method. The images obtained after 30 minutes were analyzed. At SD:C ratio of less than 1 was taken to be present and determined for assessing the effectiveness for two interventions.

RESULTS: Results of the present study demonstrates that effectiveness was found present in 57.1% (n=20/35) in milk group and it was 80.0% (n=28/35) in lemon juice group as per our operational definition (P=0.039). Effectiveness was found better among older males (P<0.05). No other significant difference was noted (p>0.05 in rest of variable subsets).

CONCLUSIONS: The effectiveness was significantly better in patients who took lemon juice as compared to those who took full fat milk after the administration of radiopharmaceutical.

KEY WORDS: Attenuation artifacts, Coronary artery disease, Myocardial perfusion imaging, SPECT

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INTRODUCTION

Radionuclide myocardial perfusion imaging (MPI) with single photon emission computed tomography (SPECT) is a minimally invasive imaging technique that is well established and has an important role in the assessment of coronary artery disease (CAD). The patients with diabetes, female gender and increasing age groups have more easy evaluation MPI. In modern nuclear medicine quantitative analysis of MPI is quite common and easily applied but the main limitation is presence of artifacts while using these softwares. Pervious reports have shown a sensitivity and specificity of 85-90% and 70-75% respectively in the evaluation of coronary artery disease using MPI studies conducted by Thallium 201 (99m) or Tc-sestamibi etc. One of the main reasons of relatively lower specificity of MPS is reporting equivocal perfusion defects as abnormal. This phenomenon is commonly observed due to attenuation and reconstruction artifacts. Extracardiac activity below diaphragm (sub-diaphragmatic activity) is a potential cause of inducing artifacts during reconstruction of the raw images. Different artifact picked during MPI studies have been evaluated in pervious studies and the effect of Lemon juice, water, and milk intake has been assessed which may lead to better image quality. Purbhoo et al showed that intake of milk and lemon juice reduced the infra cardiac artifact thereby improved the quality of MPI scan.¹¹ In an another study, Mousavie et al planned to see the effectiveness of lemon juice and milk on the secretion of liver and reduction of 99mTc-sestamibi radiopharmaceutical activity during myocardial perfusion imaging. The sub-diaphragmatic activity was assessed regarding the use of milk and lemon juice intake. They demonstrated that in patients who took full fat milk the subdiaphragmatic to heart ratio was < 1 in 8% ($n=2/25$) of patients while in patients who took lemon juice, the percentage was 36% ($n=9/25$) ($p=0.001$).

Subdiaphragmatic activity observed during MPI is a potential source of inducing artifacts during reconstruction of raw images. Nuclear cardiologists prefer subdiaphragmatic activity as low as possible in order to get high quality reconstructed images. Present study is planned to assess which intervention is better in achieving this objective i.e to reduce the subdiaphragmatic activity. This will on one hand help the nuclear cardiologist to report the scan with more confidence and on the other hand it shall minimize the need of rest imaging in cases where stress imaging is normal, which would

result in improvement in patients' convenience and reducing unnecessary radiation exposure.

The objective of this study was to compare effectiveness of lemon juice versus full fat milk in hepato-biliary clearance of radioactivity in patients undergoing myocardial perfusion imaging.

MATERIALS AND METHODS:

It was a randomized controlled trial carried out at Department of Nuclear Cardiology, Punjab Institute of Cardiology (PIC), Lahore between April 2019 to October 2019 (six months) after approval from hospital ethical committee. Sample size was calculated by taking level of Significance 5%, power of test 80%, anticipated population proportion (full fat milk) 8%¹² and anticipated population proportion (lemon juice) 36%¹². The sample size came out to be 35 in each group (Total sample size $35+35=70$). Consecutive non probability technique was employed and all the patients (both gender, between age 25-75 years) who were referred for myocardial perfusion imaging for the assessment of coronary artery disease were enrolled into the study. An informed consent was obtained. All those patients with history of old MI, coronary artery bypass surgery, coronary angioplasty, cholecystectomy and patients with known left bundle branch block (evident on ECG), cardiomyopathies (evident on echocardiography), known hepato-biliary disease, known peptic ulcer disease and pregnant and lactating women were excluded from the study. Randomized two groups of enrolled patients were made by lottery method. Group A patients were advised to take an ordinary glass of lemon juice (approximately 100 ml lemon juice in 150 ml water =250 ml) and Group B patients were advised to take an ordinary glass of full fat milk (approximately 250 ml) ten minutes after the injection of radiopharmaceutical. Gated myocardial perfusion imaging was acquired 30 min after the injection of radiopharmaceutical using predefined acquisition parameters [single photon emission computed tomography, 64×64 matrix, 1.45 zoom, 25 seconds per view, 90° rotation detector head configuration, circular orbit, step and shoot mode] on a dual headed gamma camera equipped with high resolution collimator. The images were analyzed by two experienced Nuclear Cardiologists who were blinded to the clinical information. Hapato-biliary clearance was determined on visual and semi-quantitative analysis of the raw images. Two regions of interests (ROI) were drawn, one on the cardiac region and other on the subdiaphragmatic region over liver and gall



bladder. The ROI gave the total number of counts in that particular region. The subdiaphragmatic to cardiac ratio (SD:C) was determined by dividing the counts obtained from subdiaphragmatic ROI by the counts obtained from cardiac ROI. An SD:C < 1 was considered as effective hepato-biliary clearance assessed at 30 min of injection of radioactive material. The data was analyzed by SPSS version 22. Chi-square test was applied to compare the effectiveness in both groups. P-value of ≤0.05 was considered as significant.

RESULTS:

A total of seventy (n=70) patients, 35 in each group were finally analyzed. Gender and age distribution in both groups is shown in table 1. Comorbids (hypertension, diabetes, hyperlipidemia) status is presented in table 2. Mean SD:C ratio in milk group was 1.01 ± 0.37 SD and in lemon juice groups was 0.81 ± 0.36 SD both study groups. Effectiveness was observed in (n=20/35) in milk group and it was (n=28/35) in lemon juice group. The effectiveness was significantly better in patients who took lemon juice as compared to those who took full fat milk after the administration of radiopharmaceutical (80.0% versus 57.1% respectively, P=0.039, table 3). Effectiveness was found better among older aged males (P<0.05, table 4). No other significant difference was noted (p>0.05 in rest of cases).

Table 1: Gender and Age distribution in both groups

GENDER	GROUP	
	FULL FAT MILK	LEMON JUICE
MALES	11	7
	31.4%	20.0%
FEMALES	24	28
	68.6%	80.0%
TOTAL	35	35
	100.0%	100.0%
Age (Mean ± SD)	55.2 ± 11.2	49.2 ± 8.7

Table 2: Comorbids in study sample

COMORBIDS		GROUP		TOTAL
		FULL FAT MILK	LEMON JUICE	
HYPERTENSION	PRESENT	25	22	47
		71.4%	62.9%	67.1%
	ABSENT	10	13	23
		28.6%	37.1%	32.9%
DIABETES	PRESENT	12	11	23
		34.3%	31.4%	32.9%
	ABSENT	23	24	47
		65.7%	68.6%	67.1%
HYPERLIPIDEMIA	PRESENT	8	5	13
		22.9%	14.3%	18.6%
	ABSENT	27	30	57
		77.1%	85.7%	81.4%

Table 3: Effectiveness of treatment in both groups

EFFECTIVENESS	GROUP		P-VALUE CHI-SQUARE
	FULL FAT MILK	LEMON JUICE	
PRESENT	20	28	0.039
	57.1%	80.0%	
ABSENT	15	7	
	42.9%	20.0%	
TOTAL	35	35	
	100.0%	100.0%	
SD:C (Mean ± SD)	1.01 ± 0.37	0.81 ± 0.31	

Table 4: Effectiveness of treatment in both groups (stratification for confounding variables)

VARIABLES	EFFECTIVENESS	GROUP		TOTAL	P-VALUE CHI-SQUARE
		FULL FAT MILK	LEMON JUICE		
MALES	PRESENT	6	7	13	0.036
		54.5%	100.0%	72.2%	
	ABSENT	5	0	5	
		45.5%	.0%	27.8%	
FEMALES	PRESENT	14	21	35	0.202
		58.3%	75.0%	67.3%	
	ABSENT	10	7	17	
		41.7%	25.0%	32.7%	
25-50 YEARS	PRESENT	5	12	17	0.176
		41.7%	66.7%	56.7%	
	ABSENT	7	6	13	
		58.3%	33.3%	43.3%	
51-75 YEARS	PRESENT	15	16	31	0.030
		65.2%	94.1%	77.5%	
	ABSENT	8	1	9	
		34.8%	5.9%	22.5%	

DISCUSSION:

Subdiaphragmatic activity observed during myocardial perfusion imaging (MPI) is a potential source of inducing artifacts during reconstruction of raw images. There are numerous reports in the literature, which examine the impact of drinking milk, water, and lemon juice on different subdiaphragmatic-related artifacts by using (99m) Tc-sestamibi MPI in order to determine a feasible method for improving the image quality.¹⁰⁻¹² Present study was planned to assess which intervention (full fat milk or lemon juice) is better in achieving this objective i.e to reduce the subdiaphragmatic activity. Results of the present study showed that effectiveness was found present in 57.1% (n=20/35) in milk group and it was 80.0% (n=28/35) in lemon juice group as per our operational definition (P=0.039). Effectiveness was found better among older males (P<0.05). No other significant difference was noted (p>0.05 in rest of cases). Cherng et al. suggested that intake of lemon juice which rich in acid increases the production secretin which leads to increase hepatobiliary clearance of bile. He also suggested that intake of 250ml diluted lemon juice approximately 10 min after tetrofosmin injection on rest and stress MPI may lead to better image acquisition. This may be due to rapid clear-



ance of tetrofosmin through liver, which may lead to decreased extra-cardiac, notably hepatic, interfering activities.¹⁶ Our results are comparable with other studies as well. In a recent study, Mousavie et al also studied the effect of milk and lemon juice intake during myocardial perfusion scan. They demonstrated that in patients who took full fat milk the subdiaphragmatic to heart ratio was < 1 in 8% ($n=2/25$) of patients while in patients who took lemon juice, the percentage was 36% ($n=9/25$) ($p=0.001$). Malhotra G also conducted the study of 33 patients including 26 males and 7 females. The patients were asked take to 250ml of lime drink and images were take 5 mins after the intake of lime juice. Quantitative assessment of counts in the inferior wall of myocardium (M) to those in adjacent abdomen (A) was performed on both pre- and postintervention studies by drawing an ROI of about 50 ± 5 pixels. M/A ratios were analyzed. All patients underwent myocardial perfusion single photon emission computed tomography. It was reported that the inferior wall of the myocardium was better seen, and sub diaphragmatic activity was minimal. The M/A ratio was significantly better in the post intervention group, viz. 2.19 ± 0.71 in the anterior and 2.07 ± 0.70 in the LAO 45 views as compared with those of pre intervention values of 1.50 ± 0.59 in the anterior and 1.41 ± 0.49 in the LAO 45 views, respectively ($P < 0.001$). They concluded that giving lime drink during MPI scan significantly reduces the artifact and lead to better evaluation of inferior wall of the myocardium. This method also reduces the time to conduct the study. Haghigatafshar M tried to provide an alternative method for patients who cannot take fatty foods to increase the transit of radiotracer from the liver. 100 patients were randomized into 4 groups to take 200 cc of lemon juice, 200 cc of pomegranate juice, 200 cc of secanjabin, and 100 mg of fatty meal, 10 min after injection of 20

mCi ^{99m}Tc -MIBI, respectively in groups A, B, C, and D. The study was conducted in both rest and stress imaging at 30 and 50 min post-injection. Results showed that both rest and stress imaging at min 30 and 50, A and D groups had significantly higher H/L ratio than groups B and C. Comparing the images of groups in both rest and stress protocol at minutes 30 and 50, A and D groups had significantly higher H/L ratio at 50 minutes in comparison with 30 minutes. It was recommended that intake of lemon juice and fatty meals during MPI scan may reduced extra-cardiac activity. Similarly Purbhoo et al assessed the effect of intake of lemon juice and full fat milk. His suggested that intake of these substances reduced infra-cardiac activity and lead to better image quality. The visual and quantitative data favored the intake of both milk and lemon juice.¹¹

In summary, subdiaphragmatic radioactivity during myocardial perfusion imaging with Technetium labeled tracers brings additional challenge while interpreting the myocardial perfusion imaging. It is wise to judiciously use all the available tools to avoid that interfering activity and to use better filter options during reconstruction of those raw images. Several authors have examined three different drinks including water, milk, and lemon juice and concluded that milk and lemon juice had significantly lowered interfering activity than plain water. In patients who refused to take diluted lemon juice and fatty foods have relatively lower image quality as compared to those who ingested fatty foods and lemon juice. So it may be a simple method to improve the image quality during MPI scan.

CONCLUSIONS:

The effectiveness was significantly better in patients who took lemon juice as compared to those who took full fat milk after the administration of radiopharmaceutical.



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