



Role of Salvia Miltiorrhiza Root Extract (Danshen) in Evaluation of Hibernating/Viable Myocardium: An Evidence Based Study; Utilizing Nuclear Imaging Technique

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Abstract

Background: Complementary and Alternate medicine (CAM) is gaining popularity these days especially in management of chronic illnesses. Salvia Miltiorrhiza Root Extract (Danshen) is one such option for chronic heart diseases. In this study NO₃ and SMRE augmented resting scans were compared to see which one was superior in evaluating hibernating myocardium.

Methods: Total of 30 patients was included in this hospital based, interventional study. They had ejection fraction 30% or less, with history of myocardial infarction in past. Informed consent was taken. Each underwent 3 studies,

1. Resting scan.
2. NO₃ augmented resting scan (using standard protocol).
3. SMRE augmented scan, in which two capsules of SMRE were administered sublingually (in place of NO₃). 20 mCi of Tc-99m sestamibi was injected after 10 min, an hour prior to acquisition.

Results: Data interpretation was done by using 17 segments nuclear model. Scan interpretation was done by two independent observers. Out of total 30 patient who underwent NO₃ and SMRE resting scans, presence of viable myocardium was indicated in N=15 scans (50%), where N=8 (53.3%) showed improvement with SMRE alone, N=2 (13.3 %) had improvement with NO₃ alone and the rest N= 5 (33.3%) demonstrated viability with both SMRE and NO₃. Using Chi squared test, at P value < .05, SMRE came out to be better than NO₃, for assessment of viable myocardium.

Conclusion: SMRE can be utilized for diagnosis as well as management of hibernating Myocardium as it is clinically useful, safe as well as cost effective.

Keywords: Salvia Miltiorrhiza Root Extract; Danshen; Hibernating Myocardium; Viable myocardium; Tc-99m Sestamibi Resting Scan; Coronary Artery Disease; Complementary and Alternate Medicine

Abbreviations: SMRE: Salvia Miltiorrhiza Root Extract; NO₃: Nitrate; CAM: Complementary and Alternate Medicine; CAD: Coronary Artery Disease, BP: Blood pressure, LV: Left ventricle.

Introduction

Any patient with chronic CAD can have hibernating / viable myocardium. This is suggestive of a condition where

reduced coronary blood flow results in impaired contractility [1,2]. Condition is worth studying as LV function in viable myocardium could be partially or completely restored with successful and timely re-vascularization. Radionuclide perfusion imaging (MPI) is a useful diagnostic technique to demonstrate the extent of viability. It has been observed that all the major hemodynamic functions including nutrient and oxygen supply, in response to variations in demand, are conducted in microcirculation [3].

Salvia miltiorrhiza root extract (SMRE) is a natural herb, commonly used in the treatment of cardiovascular disorder. It has tanshinones which can inhibit platelet inhibition. Biological actions of the compounds isolated from SMRE has shown its potential effect of attenuating microcirculatory disturbances, including anti oxidation, inhibition of adhesion molecules, platelet aggregation inhibition, mast cell inhibition, inhibition of apoptosis, and amelioration of the injury of many target organs including heart [4-6].

Keeping in view these facts, this study was conducted to detect hibernating myocardium in patients with known CAD and we also compared the results of NO₃ augmented and SMRE augmented scan in order to find out the better imaging modality for assessment of viable myocardium.

Materials and Methods

It was a hospital based interventional study, conducted in Nuclear Cardiology Department, of Federal Government Polyclinic Hospital (FGPC), Islamabad, Pakistan. Inclusion Criteria for the study subjects were as under:

- Patients between 33-72 years of age, with history of CAD, with/without active cardiac complaints like chest pain or dyspnea.
- Patients with history of myocardial infarction in the past.
- Echocardiography showed EF 30% or less.

Subjects enrolled in the study after formal informed consent. All patients were referred from the Cardiology OPD after thorough history and complete physical examination. They were kept NPO on the day of study. Each underwent 3 studies:

- a) Resting scan.
- b) NO₃ augmented resting scan (using standard protocol).
- c) SMRE augmented scan, in which two capsules of SMRE were administered sublingually (replacing nitrate) rest of the protocol was same as in NO₃ augmented scan.

BP was recorded before and after NO₃ and SMRE administration. 20 mci (740MBq) of Tc-99m sestamibi was injected in each study and all 03 studies, in each case, were conducted on three separate days. Acquisition was done, for 15minutes, in each study, on Siemen's E.cam dual head Gamma Camera, one hour after isotope injection. A semi-quantitative interpretation was performed, using short axis and vertical long axis myocardial tomograms, utilizing 17 segments Nuclear Model. For each study 0-4 point scale perfusion defect interpretation was used [7] i.e. 0=Normal perfusion, 1=Equivocal, 2=Moderate decrease, 3=Severe decrease in radiotracer uptake, 4=absence of detectable radiotracer in the segment. Statistical inference was drawn using Chi squared test, considering P value as .05.

Results

It was a hospital based interventional study, conducted in Nuclear Cardiology Department of Federal Government Polyclinic Hospital (FGPC), Islamabad, Pakistan. In this 03 months study, a total of 30 patients (22 males, 8 females), age 33-72 years (mean age 52.5 years) were included. All of them had history of myocardial infarction in past, and most of them had some typical cardiac symptoms as shown in Table 1.

No of Pt.	Age	Gender	Symptoms	Type of Myocardial Infarction
1	56	M	dyspnea	anteroseptal
2	53	M	yspnea	inferolateral
3	48	M	Chest pain	anteroseptal, inferolateral
4	70	F	dyspnea	anteroseptal
5	58	M	dyspnea	anterior wall
6	45	M	Chest pain	anteroseptal
7	38	M	No symptom	inferolateral
8	52	F	dyspnea	Inferior wall
9	33	M	Chest pain	anterior wall
10	70	M	No symptom	antero-apical
11	65	M	dyspnea	anteroseptal

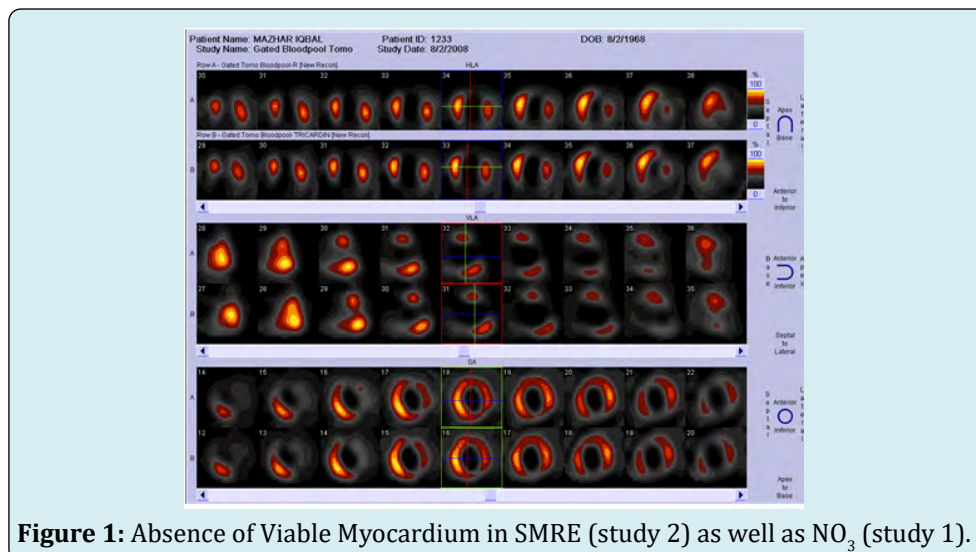
12	52	M	dyspnea	anteroseptal
13	76	M	dyspnea	inferolateral
14	58	M	dyspnea	anteroseptal, inferolateral
15	72	M	dyspnea	anteroseptal
16	62	F	Chest pain	inferolateral
17	54	M	dyspnea	inferolateral
18	47	M	dyspnea	anterior wall
19	60	F	No symptom	Inferior wall
20	58	M	Chest pain	anteroseptal
21	59	M	No symptom	inferior wall
22	67	M	dyspnea	inferolateral
23	64	F	dyspnea	anteroseptal
24	62	M	Chest pain	anteroseptal
25	49	F	Chest pain	anteroseptal, inferolateral
26	54	M	dyspnea	anterior wall
27	51	M	dyspnea	anteroseptal
28	63	F	Chest pain	anteroseptal, inferolateral
29	51	M	dyspnea	anterior wall
30	56	F	dyspnea	inferior wall

Table 1: Baseline data of Study Subjects Indicating Symptoms and Type of Infarct.

Visual analysis of scan results was done by two independent observers. Total of 30 patients were studied, in which 15 patients didn't show any viable myocardium, around the infarcted area. Presence of viable myocardium was noted in rest of the 15 patients.

Improvement in myocardial perfusion was declared on the basis of predefined 0-4 point scale. N=8 scans (53.3%)

showed improvement (presence of viable myocardium) with SMRE alone. N=2 (13.3%) had improvement with NO₃ alone and the rest N= 5 (33.3%) showed improved perfusion with both SMRE and NO₃. (Figure 1), shows a case, where SMRE as well as NO₃ augmented scan didn't show any evidence of viable myocardium surrounding the infarcted area, study one in the figure was conducted with NO₃ and study 2 was with SMRE, both studies showed no improvement in perfusion.



(Figures 2 & 3) demonstrate cases where viable myocardium was demonstrated by SMRE augmented scan, but not with

NO_3 . Study 1 in the figure was conducted with NO_3 and study 2 with SMRE.

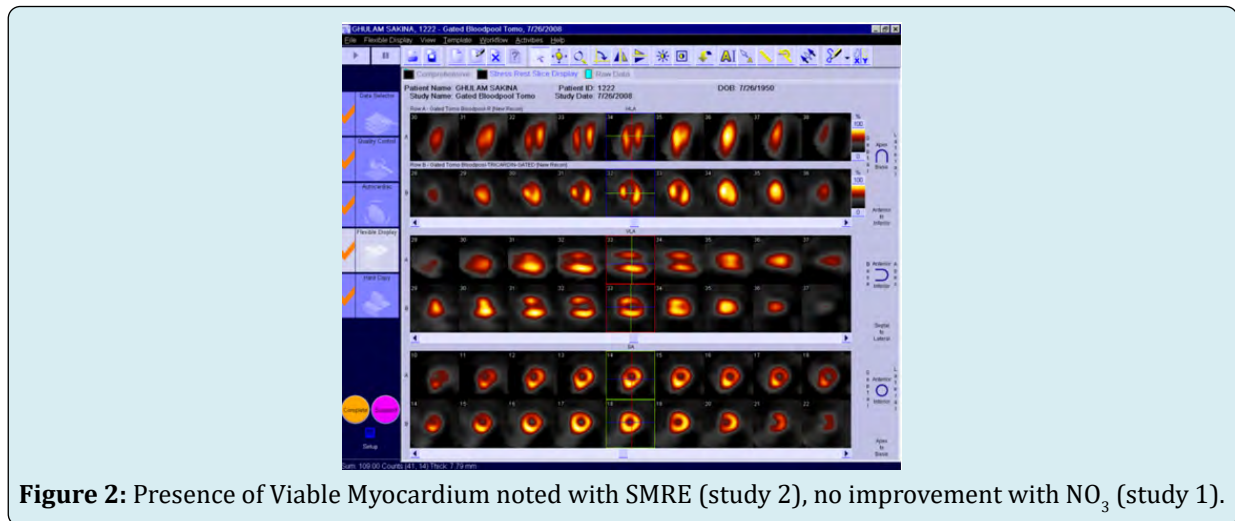


Figure 2: Presence of Viable Myocardium noted with SMRE (study 2), no improvement with NO_3 (study 1).

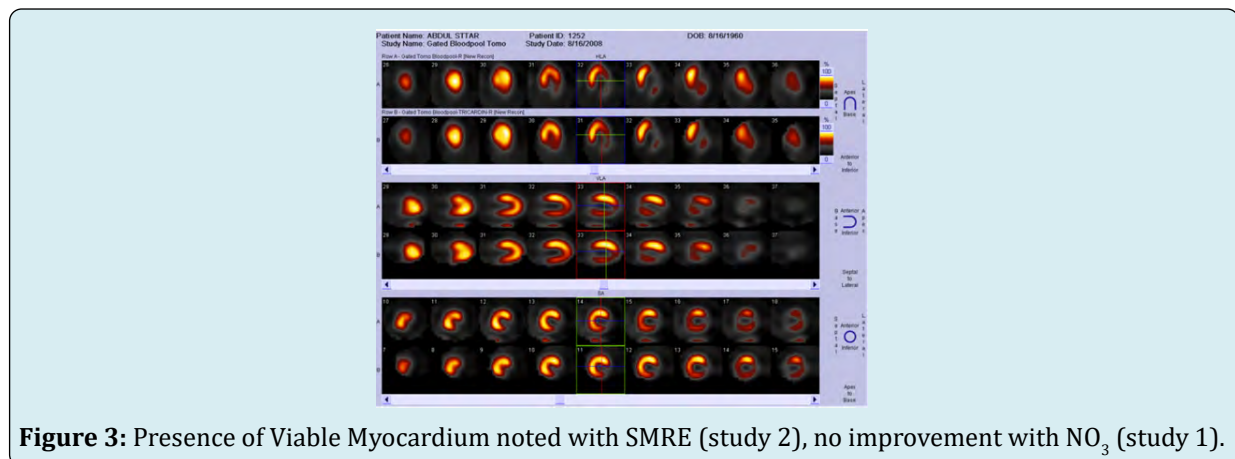


Figure 3: Presence of Viable Myocardium noted with SMRE (study 2), no improvement with NO_3 (study 1).

Our null hypothesis was that “there is no difference between NO_3 and SMRE when used in viability study”. The chi-square statistic was 7.2. The p-value came out to be .00729.

So the results were statistically significant at $P < .05$ and we had to reject our null hypothesis concluding that SMRE was better than NO_3 for assessment of viable myocardium. Moreover no fall in systolic BP was noted with SMRE, which were a known side effect and a limitation with NO_3 augmented imaging technique.

Discussion

Cardiovascular disease is one of the leading causes of mortality worldwide [8]. It is often accompanied by major risk factors like hypertension, hyperlipidemia, diabetes and obesity that is why usually multi drug regimen is required

for management of CAD [9], in addition complementary and alternate medicine is gaining popularity owing to their minimal unwanted side effects [10]. According to an estimate 4–61% in Africa and Asia of cardiac patients, in Africa and Asia, take traditional medicines usually in combination with allopathic medicines [11].

Salvia miltiorrhiza root (Danshen) has been used quite commonly alone or with conventional drugs, by patients with angina pectoris and myocardial infarction, especially in Asia for its cardiovascular benefits as it contains both hydrophilic phenolic acids and lipophilic tanshinones, which are believed to be responsible for its therapeutic efficacy [12]. Around one hundred components are found in SMRE that can cause coronary vasodilatation, suppress thromboxane formation, inhibit platelet adhesion and aggregation, and scavenge free radicals [13–15].

Keeping in view the known actions of SMRE; in this study we tried to explore the role of SMRE in evaluation of hibernating myocardium and also compared the results of NO₃ augmented and SMRE augmented scan to find out which one is the better modality. It was a hospital based interventional study, in which a total of 30 patients, 22 males and 8 females were included. Each one had a history of myocardial infarction, as shown in table 1, with ejection fraction less than 30% on echocardiography. Each patient underwent 03 studies, a resting scan, Nitrate scan and SMRE scan. TC 99m-NO₃ augmented resting scan is well known diagnostic entity to evaluate hibernating myocardium.

We for the first time used SMRE for this purpose, keeping in mind, its already documented pharmacological effects. A meta-analysis of sixty randomized clinical trials showed that Danshen oral pill, consisting of *S. miltiorrhiza*, *Dryobalanops camphora* and *Panax notoginseng* showed much better efficacy compared to isosorbide dinitrate [16].

Results showed that out of total 30 patients, 15 didn't demonstrate any viable/ hibernating myocardium i.e. neither with NO₃ nor with SMRE scans, as shown in figure 1, whereas in the remaining 15; 08 patients (53.3%) showed improvement with SMRE alone, i.e. only with SMRE and not with NO₃, as shown in figure 2. Only 02 cases (13.3%) showed improvement with NO₃ alone, one of those cases is shown in Figure 3, and the remaining 05 patients (33.3%) showed improved perfusion in both SMRE and NO₃ augmented scans.

In this new scientific era, everyone is more interested in evidence based medicine that is why utility and positivity of SMRE in nuclear scan shouldn't be ignored. Moreover when statistical inference was drawn, SMRE augmented resting scan came out to be better diagnostic modality than NO₃ scan.

A fact that is worth mentioning here is absence of any significant side effects of this naturally occurring gift. All nitrates are notorious for their blood pressure lowering effect [17,18], but here; as we observed in the study, this herb didn't have any of such harm full effects, a fact already document in many previously done studies [19].

Though sample size in this study was not that big, but for future we definitely recommend another study using SMRE as a diagnostic tool for assessing hibernating myocardium. Also SMRE should be considered as therapeutic strategy to manage patient with chronic heart disease, as SMRE not only improves micro vascular circulation [13], but also it didn't show hypotension like side effects. Studies have shown that hypotension in people with heart failure and chronic heart disease is an indicator of poor prognosis and hinders the therapeutic management [18].

Like every treatment regimen, SMRE did show few side effects e.g. potentiation of anticoagulation of warfarin in three case reports [20-22] and a clinical study [23], but generally it was found to be quite a safe natural herb, to be utilized in patients with chronic heart disease for diagnostic as well as therapeutic purposes. At the end, one fact that is worth mentioning is that, it is a naturally occurring herb, which is much less costly than many of the allopathic medicines being used for management of chronic heart disease.

As cardiovascular illnesses are one of the most important problems globally and its incidence is increasing rapidly year by year, even in poor and developing countries [8]. The aim of the health professionals should be to find out management regimens which are not only clinically effective but also cost effective and this study supports SMRE to be one of such treatment options. So in view of the results achieved in this study we strongly recommend that more evidence based studies should be conducted with SMRE, with larger sample size, so that this natural gift of nature should be better utilized.

Conclusion

Salvia Miltiorrhiza Root Extract can be utilized in diagnosis as well as management of hibernating Myocardium, being safe and cost effective; it can be of great benefit in poor and developing countries.

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