Exploring The Potential Impact of Pharmaceutical Care Plan on High Sensitivity C-reactive Protein hsCrp in Post-Acute Coronary Syndrome Patients in Cardiac Rehabilitation Unit

eman casper[1], lamiaa el-wakeel[1], mohamed saleh[1], and manal el-hamamsy[1]

[1]Affiliation not available

May 5, 2020

Abstract

Objective: This study aimed to assess the impact of clinical pharmacist services addition to cardiac rehabilitation program, on high sensitivity C-reactive protein and echocardiographic parameters. Methods: The study was a prospective; randomized, controlled study. A total of 40 post-acute coronary syndrome (ACS) patients participating in cardiac rehabilitation program were randomly allocated to either the control group (n = 20) or the clinical pharmacist-provided services group (n = 20). High sensitivity C-reactive protein (hs-CRP) and echocardiographic parameters (left ventricular end systolic volume (LVESV), left ventricular end systolic volume (LVEDV) and ejection fraction (EF%) were compared between both groups at baseline and after 3 months. Results: After three months of follow-up, the intervention group showed a significant decrease in the percent change of hsCRP, LVESV and LVEDV compared to the control group. However, there was no statistical difference in the percent change of ejection fraction between both groups. Conclusion: Addition of clinical pharmacist services to cardiac rehabilitation program had resulted in marked decrease in hs-CRP, LVESV and LVEDV. Understanding the impact of the clinical pharmacist-provided services in post-ACS patients may encourage clinical implementation of this model in cardiac rehabilitation programs.

BACKGROUND:

One of the main causes of mortality worldwide is Coronary artery disease (CAD) [1].

In developing countries, cardiovascular diseases caused about eighty percent of deaths [2]. In 2014, CAD was responsible for about 23.14% of total deaths in Egypt[3].

Atherosclerosis is the underlying cause of CAD. Inflammation contributes to the process of atherosclerosis from the plaque formation till its rupture. Hence, biochemical markers of inflammation were investigated as noninvasive indicators of underlying atherosclerosis and as a success marker of therapeutic and preventive interventions.[4]

High sensitivity C-reactive protein (hs-CRP) is currently the best validated inflammatory biomarker. it has become as an independent predictor of vascular risk similar to systolic blood pressure ,even more, it was superior to non-HDL-C[5].

There has been a positive correlation between levels of hs-CRP, plaque ruptures risk and coronary artery remodeling grade[6]. Hence, hsCRP has been used clinically to detect that risk in both primary and secondary prevention settings[7].

Cardiac rehabilitation programs is a recommended intervention by the American College of Cardiology the American Heart Association in reducing coronary events and mortality in CAD patients[8].

Cardiac rehabilitation impact on inflammation was previously documented by the reduction of serum hs-CRP concentrations in CAD patients[9].

Despite their benefits, these programs are still underutilized. Although cardiac rehabilitation programs have significantly lowered CAD mortality, we are constantly searching for new modalities to further improve outcome and influence disease progression.

Whereas previous studies have repeatedly proved the favorable effects of clinical pharmacist interventions on outcomes of chronic diseases patients [10], none of these studies have evaluated the impact of clinical pharmacist services added to cardiac rehabilitation program on inflammatory marker , hs-CRP, in post-acute coronary syndrome (ACS) patients.

The aim of our study was to assess the impact of clinical pharmacist services addition to cardiac rehabilitation program, on inflammation and echo-cardiographic evidence.

METHODS:

The study was a prospective; randomized, controlled study. The study protocol was revised and approved by the research ethics committee for experimental and clinical studies at faculty of pharmacy, Ain Shams University, Cairo, Egypt on 11 February, 2015, number (49). The study was performed in accordance with the Declaration of Helsinki. Clinical Trail.gov registration No. NCT02922140. The study participants were recruited from cardiac rehabilitation unit. The included patients were (1) diagnosed with ACS by cardiologist;(2) followed-up at the cardiac rehabilitation unit; (3) 20–79 years of age; (4) able to perform regular physical activity according to patients' self-assessment and cardiologist judgment; (5) attending at least 12 exercise sessions of the cardiac rehabilitation exercise program and (6) reachable by telephone.

The exclusion criteria were cognitive impairment, terminal illness, severe arrhythmia, systemic or cardiac inflammatory diseases, inability to communicate or incapacities hindering patients from medication administration at home.

A total of 40 post-ACS patients were randomly allocated to either the control group (n = 20) or the clinical pharmacist-provided services group (n = 20). The control participants received standard medical care by a cardiologist, while the intervention group received standard medical care plus clinical pharmacist-provided services. Details on standard medical care and clinical pharmacist-provided services have been previously published[11].

All patients participated in a 3-months cardiac rehabilitation (CR) program. It included two days/week supervised exercise sessions and educational talks.

The target heart rate was calculated according to Karvonen formula: [(maximal heart rate-resting heart rate*%exercise intensity) + resting heart rate]. The target heart rate was 40% of the maximal heart rate for the first month, 60% for the second month and 80% for the third month without dyspnea, pain, exhaustion or ST-segment depression¿2mm based on the initial exercise tolerance test using a modified Bruce protocol.

MEASURES

At baseline, patients' demographics and cardiovascular disease risk factors were recorded.

The following data were collected at baseline and after three months for all participants.

High sensitivity CRP Echocardiographic parameters: left ventricular ejection fraction (EF%), left ventricular end diastolic v

At baseline, there was no significant difference between the two groups in terms of patient demographics, risk factors for cardiovascular disease (hypertension, diabetes mellitus, smoking status, dyslipidemia, obesity or family history), hsCRP or echocardiographic parameters. Table 1 shows medications administered by both groups at baseline and after 3 months.

ENDOF STUDY EVALUATION:

The intervention group showed a significant decrease in the percent change of hsCRP compared to the control

group **(Table 2).**

The test group showed a highly significant decrease in the percent change of LVESV and LVEDV compared to the control group. There was no statistical difference in the percent change of ejection fraction between both groups **(Table 2).**

DISCUSSION:

The current study was undertaken to evaluate whether the addition of clinical pharmacist services to cardiac rehabilitation program versus cardiac rehabilitation program alone can influence the inflammatory marker high sensitivity C-reactive protein and echocardiographic parameters.

The current study demonstrated that the implementation of clinical pharmacist services in cardiac rehabilitation unit can improve the inflammatory status in post-ACS patients represented by a significant decrease in the level of hs-CRP in clinical pharmacist-provided services group versus the control group. The clinical pharmacist-provided services group also showed a significant decrease in the percent of change in LVESV and LVEDV compared to the control group. However, there was no statistically significant increase in the percent of change of ejection fraction.

The benefits of clinical pharmacist-provided services in chronic disease management have long been documented[10]. Clinical pharmacist can optimize drug adherence, adjust drug doses and promote drug therapy adherence. An important intervention of clinical pharmacist-provided services is to educate patients about their disease and drugs which might help improve the medication adherence. Hopefully, this evidence will encourage the incorporation of clinical pharmacist in cardiac rehabilitation programs. In our opinion, the addition of clinical pharmacist to the already present services of the cardiac rehabilitation including the exercise sessions may have a positive impact on the post-ACS patients' morbidity and mortality. Future studies are needed to confirm the current results.

CONCLUSION:

The addition of clinical pharmacist services to cardiac rehabilitation program had resulted in marked decrease in hs-CRP, LVESV and LVEDV. Future studies are required to confirm our results. Finally, future studies are needed to evaluate the impact of clinical pharmacist-provided services addition to cardiac rehabilitation program on CVD morbidity and mortality among post-ACS patients.

Compliance with Ethical Standards

Disclosure of potential conflicts of interest: All authors declare no conflicts of interest

- **Disclosure of funding:** This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors
- **Research involving Human Participants and/or Animals:**

Ethical approval: "All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Faculty of pharmacy, Ain Shams university, Cairo, Egypt (49), Clinicaltrials.gov registration no. NCT02922140, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

Informed consent: "Informed consent was obtained from all individual participants included in the study."

REFERENCES:

1. Roger VL, Go AS, Lloyd-Jones DM, et al. Executive summary: heart disease and stroke statistics-2012 update: a report from the American Heart Association. *Circulation.* 2012;125(1):188-197.

2. Yusuf S, Rangarajan S, Teo K, et al. Cardiovascular risk and events in 17 low-, middle-, and high-income countries. *New England Journal of Medicine.*2014;371(9):818-827.

3. Fawzy MS, Toraih EA, Aly NM, Fakhr-Eldeen A, Badran DI, Hussein MH. Atherosclerotic and thrombotic genetic and environmental determinants in Egyptian coronary artery disease patients: a pilot study. *BMC Cardiovascular Disorders.* January 13 2017;17(1):26.

4. Morrow DA, Lemos JAd, Sabatine MS, et al. Clinical Relevance of C-Reactive Protein During Follow-Up of Patients With Acute Coronary Syndromes in the Aggrastat-to-Zocor Trial. *Circulation.* 2006;114(4):281-288.

5. Koenig W. High-sensitivity C-reactive protein and atherosclerotic disease: From improved risk prediction to risk-guided therapy. *International Journal of Cardiology.* 2013;168(6):5126-5134.

6. Ridker PM. A Test in Context: High-Sensitivity C-Reactive Protein. *Journal of the American College of Cardiology.* 2016/02/16/ 2016;67(6):712-723.

7. Silva D, Pais de Lacerda A. High-sensitivity C-reactive protein as a biomarker of risk in coronary artery disease. *Revista Portuguesa de Cardiologia (English Edition).* 2012/11/01/ 2012;31(11):733-745.

8. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes. *J Am Coll Cardiol.* 2014;64(24):e139-e228.

9. Jamshidpour B, Moghadam BA, Vasaghi-Gharamaleki B, Mirzaii-Dizgah I, Nejatian M. The effects of phase III cardiac rehabilitation in serum and salivary Hs-CRP and anthropometric measurements in patients with coronary artery disease.*J Contemp Dent Pract.* 2013;14(5):819-824.

10. Milfred-LaForest SK, Chow SL, DiDomenico RJ, et al. Clinical Pharmacy Services in Heart Failure: An Opinion Paper From the Heart Failure Society of America and American College of Clinical Pharmacy Cardiology Practice and Research Network. *Journal of cardiac failure.* 2013;19(5):354-369.

11. Casper EA, El Wakeel LM, Saleh MA, El-Hamamsy MH. Management of pharmacotherapy-related problems in acute coronary syndrome: role of clinical pharmacist in cardiac rehabilitation unit. *Basic & Clinical Pharmacology & Toxicology.* 2019;0(ja).

Table 1. Medications Administered by both Groups at baseline and After 3 months.

variable	variable	Test (n=20)	Test (n=20)	Control (n=20)	Control (n=20)
		No.	%	No.	%
Beta blockers (Bisoprolol 2.5mg)	Before	18	90	19	95
	After	19	95	18	90
ASpirin (75mg)	Before	20	100	20	100
	After	20	100	20	100
clopidogrel (75 mg)	Before	20	100	20	100
	After	20	100	19	95
ACEI/ARB (Enalapril 10mg)	Before	18	90	16	80
	After	20	100	18	90
Statins (Atorvastatin 80mg)	Before	19	95	20	100
	After	20	100	20	100

variable	variable	Test (n=20)	Test (n=20)	Control (n=20)	Control (n=20)
Sublingual nitrates (isosorbide dinitrate 5mg)	Before	4	20	6	30
	After	20	100	6	30
ACEI=Angiotensin converting enzyme inhibitor; ARB= Angiotensin receptor blocker	ACEI=Angiotensin converting enzyme inhibitor; ARB= Angiotensin receptor blocker	ACEI=Angiotensin converting enzyme inhibitor; ARB= Angiotensin receptor blocker	ACEI=Angiotensin converting enzyme inhibitor; ARB= Angiotensin receptor blocker	ACEI=Angiotensin converting enzyme inhibitor; ARB= Angiotensin receptor blocker	ACEI=Angiotensin converting enzyme inhibitor; ARB= Angiotensin receptor blocker

Table 2. High Sensitivity C-reactive Protein And Echocardiographic Parameters For Both Groups At Baseline And After 3 Months

Variable	Variable	Variable	Test (n=20)	Control (n=20)	*p*-value
hsCrp (mg/l)	Median (IQR)	Before	7.79 ([4.08,22.85])	7.39 ([2.62,21.17])	.4903 [a]
		After(%change)	-12.72 ([-39.17,29.62])	32.22 ([-26.69,133.6])	.0439 [a]
LVESV (ml)	Mean (SD)	Before	45.2 ([18.93])	47.25 ([19.7])	.739 [a]
	Median (IQR)	After (%change)	-7.69 ([-14.88, -5.06])	3.84 ([-5.38,10.48])	.0048 [b]
LVEDV (ml)	Mean (SD)	Before	95.8 ([23.93])	96.15 ([23.52])	.963 [a]
	Median (IQR)	After (%change)	-5.30 ([-17.36, -2.43])	1.30 ([-4.22,9.95])	.0087 [b]
EF%	Mean (SD)	Before	55.15 ([8.81])	54.05 ([12.93])	.7549 [a]
	Median (IQR)	After (%change)	2.487 ([-2.246,7.665])	1.02 ([-6.103,3.943])	.3872 [b]

Variable	Variable	Variable	Test (n=20)	Control (n=20)	*p*-value
hs-CRP=high sensitivity C reactive protein; LVESV=left ventricular end systolic volume; LVEDV=left ventricular end diastolic volume; EF%=ejection fraction. [a] Statistical test: Unpaired t-test, *P-value* > 0.05: non-significant. [b] Statistical test: Mann-Whitney test, *P-value* > 0.05: non-significant.	hs-CRP=high sensitivity C reactive protein; LVESV=left ventricular end systolic volume; LVEDV=left ventricular end diastolic volume; EF%=ejection fraction. [a] Statistical test: Unpaired t-test, *P-value* > 0.05: non-significant. [b] Statistical test: Mann-Whitney test, *P-value* > 0.05: non-significant.	hs-CRP=high sensitivity C reactive protein; LVESV=left ventricular end systolic volume; LVEDV=left ventricular end diastolic volume; EF%=ejection fraction. [a] Statistical test: Unpaired t-test, *P-value* > 0.05: non-significant. [b] Statistical test: Mann-Whitney test, *P-value* > 0.05: non-significant.	hs-CRP=high sensitivity C reactive protein; LVESV=left ventricular end systolic volume; LVEDV=left ventricular end diastolic volume; EF%=ejection fraction. [a] Statistical test: Unpaired t-test, *P-value* > 0.05: non-significant. [b] Statistical test: Mann-Whitney test, *P-value* > 0.05: non-significant.	hs-CRP=high sensitivity C reactive protein; LVESV=left ventricular end systolic volume; LVEDV=left ventricular end diastolic volume; EF%=ejection fraction. [a] Statistical test: Unpaired t-test, *P-value* > 0.05: non-significant. [b] Statistical test: Mann-Whitney test, *P-value* > 0.05: non-significant.	hs-CRP=high sensitivity C reactive protein; LVESV=left ventricular end systolic volume; LVEDV=left ventricular end diastolic volume; EF%=ejection fraction. [a] Statistical test: Unpaired t-test, *P-value* > 0.05: non-significant. [b] Statistical test: Mann-Whitney test, *P-value* > 0.05: non-significant.