CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
http://doi.org/10.5281/zenodo.3262251

Available online at: http://www.iajps.com *Research Article*

A RESEARCH STUDY TO EXPLORE UNCOMMON OXIDATIVE STRESS MARKERS THIOL DISULPHIDE AMONG ACUTE MYOCARDIAL PATIENTS

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Article Received: April 2019 **Accepted:** May 2019 **Published:** June 2019

Abstract:

Objective: *The objective of the research was to find out uncommon oxidative stress indicators thiol disulphide in those patients having AMI (acute myocardial infarction).*

Material and Methods: *The mode of the research was controlled study carried out at Sir Ganga Ram Hospital, Lahore from December 2017 to May 2018. The research contains those patients having ST (AMI) elevation myocardial infarction as well as physically fit individuals. The selected individuals were divided into two groups and comparison of native and total thiol, tropine level and disulphide were carried out between the groups.*

Results: *Total numbers of individuals enrolled for research was one-hundred and twenty-eight, among them ninety-eight (76.5%) were AMI patients and thirty (23.43%) were controlled (healthy ones). The levels of disulphide were diminishing in AMI patients with respect to healthy individuals (P <0.001). In AMI patients the level of troponin is inversely proportional with disulphide along with total and native thiol levels.*

Conclusion: *In AMI patients, the total, as well as native thiol levels, are utilized as a unique oxidative stress indicator.*

Key Words: *AMI (Acute Myocardial Infarction), CAD (Coronary Artery Disease), Gama-Glutamyl Cysteine, STEMI (ST Elevation Myocardial Infarction).*

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Please cite this article in press Hanzala et al., ***A Research Study To Explore Uncommon Oxidative Stress Markers Thiol Disulphide Among Acute Myocardial Patients.,*** *Indo Am. J. P. Sci, 2019; 06[06].*

INTRODUCTION:

The balance between antioxidant as well as oxidant system is much significant for normal cellular and tissue structuring [1]. Unbalancing between antioxidant and oxidant system appears in the shape of oxidative stress [1 – 4]. The extravagant ROS (reactive oxygen species) production is the main factor of unbalancing. The other causes are ineffective reactive oxygen species removed through the antioxidant system. In above-mentioned case cardiovascular complications are increased because of damaging of several cellular and tissues structures [5]. Oxidative stress is sharply associated with the advancement and development of atherosclerosis. The CAD (coronary artery disease) are increased by plaque vulnerability increment in oxidative stress case [6, 7]. Alternately, a defensive role in opposition with oxidative stress was played by antioxidant mechanism [2, 4]. Thiol comprises of sulfhydryl class, and that is composed of sulfur as well as hydrogen items connected with a carbon atom. In the body, these thiol molecules are the most significant element of the anti-oxidant mechanism as well as perform a very important role in protecting cells from oxidative stress [1, 4]. The composition of albumin additionally on a lesser level, thiol of low molecular weight, along with cysteine (Cys), gama-glutamylcysteine, cysteinylglycine and glutathione [2]. The balancing of thiol disulphide is sustained as long as this group of proteins are oxidized by oxygen molecules and alterably transferred to disulphide bonds. In such cases, detoxification, enzymes activity control, antioxidant protection, apoptosis, adaptation, as well as cellular signals transduction system, the dynamic thiol disulphide, homeostasis which is currently defined oxidative stress indicator is very significant. The uncommon, as well as automated procedure, makes it probable to compute the level of thiol disulphide homeostasis accumulatively and one by one also. This stress to the maximum examination of the level of the thiol disulphide homeostasis [3 – 6, 8, 9]. The objective of the research was to find out uncommon oxidative stress indicators thiol disulphide in those patients having AMI (acute myocardial infarction) and correlate the finding with physically fit individuals (controls). The assessment of the association between troponin versus oxidative stress was also planned.

PATIENTS AND METHODS:

The mode of the research was controlled study carried out at Sir Ganga Ram Hospital, Lahore from December 2017 to May 2018. By utilizing facts, from that research and 1:2 formula was applied (one controlled to two patients) when recognized as (power = 0.90 and type 1 error = 0.05). The needed sample volume was twenty healthy persons and forty patients. The recommendation was achieved from an organizational ethic board along with informed written consent from every individual participant of research.

Researcher divides the patients into three categories. Group one containing those patients having STEMI, 2nd group containing NSTEMI and nonspecific chest pain patients have placed in the third group. ST-elevation myocardial infarction was identified when patients presented indication of myocardial infarction constantly for thirty minutes along with > 1mm ST-segment elevation in two succeeding leads in subsequently verified by a rise in troponin i.e. evaluated the level of troponin indicates non-ST elevation myocardial infarction and existence of characteristics chest pain and remained for twenty minutes. Those patients who are hospitalized for medical examination and did not any common systemic complication as well as not used any drugs were chosen casually as a (control). Those individuals having a haematological irregulatory earlier stroke, cancer, intense level of renal complication, inflammatory, rheumatological diseases, reactive infection were not included in the research.

Acetylsalicylic acids of per oral of 300mg were given to every individual prior to coronary angiography at checkup time. If the patients have ST-elevation myocardial infarction, they were given 600mg of clopidogrel per oral. Moreover, in cases of non-ST elevation, myocardial infractions patients' 300mg clopidogrel per oral was given to those patients having age ≤ 75 years, and 75mg dipodgrel per oral was given to those patients having age greater than seventy-five years. The blood specimens of healthy individuals were achieved after a fasting interval of twelve hours in the morning as well as acute myocardial infarction patient's blood simple was taken at the time of admission in the emergency department. The blood sample of both the categories (healthy individuals/controls & patients) were put into a plain tube. After ten minutes centrifugation at 1500g, serum was apart and reserved at _80°c up to evaluation. The determination of thiol-disulphide homeostasis was performed as define earlier [10]. To frame independent operational thiol group reducibly disulphide bonds were initially reduce. Remaining reductant sodium borohydride was utilized as well as detached with formaldehyde and entire thiol categories along with lessened and native one were identified after 5,5 dithiobis reaction with the dynamic disulphide amount was given by half of the variation between native and total thiol. Moreover,

native thiol disulphide proportion was measured after the conclusion of native thiol and disulphide amount.

SPSS was utilized for data analysis. For correlation between patients and control category, Mann-Whitney u test was applied with the objective of comparability between three patients' categories and healthy individual group. Kruskal-walls one-way analysis of variance test was applied. Mann-Whitney u test was applied with the objective of comparability betweens groups with Bonferroni reformation for multiply comparison in the cases of the conclusion of statistical divergence among the category. Moreover, among patients categories association of troponin level were examined by utilizing Spearman rank correlation.

With the objective of descriptive statistic, median values, average and SD were used. The findings were recognized as statistically expressive at P<0.05.

RESULTS:

A total number of enrolled individuals for research are one-hundred and twenty-eight, among them ninety-eight were AMI (76.5%) patients. Whereas thirty (23.43%) were healthy individuals. The number of males and females among ninety-eight AMI patients were sixty (61.2%) and thirty-eight (38.8%) respectively. Similarly, the number of males and females among thirty healthy individuals are seventeen (56.6%) and thirteen (43.3%) respectively. The forty-three (43.8%) patients had ST-elevation myocardial infarction and thirty-five (35.7%) had non-ST elevation myocardial infarction and twenty (20.4%) patients had general chest pain among ninety-eight patients. The average age of the healthy individual as well as patients was (49.4±10.6) & (59.57±10.5) years respectively. In AMI patients, the level total thiol, native thiol as well as disulphide level were less with respect to healthy individuals (P < 0.001).

The variation was also expressive between the three subcategories of patients and control group. The total thiol, native thiol and disulphide level in the group of thirty healthy individuals were higher with respect to NSTEMI and STEMI subcategories (P< 0.05) however there was no expressive variation in the general pain group. Among ninety patients, the level of troponin is inversely proportional to the level of native thiol, total thiol and disulphide level.

Table – I: Disulphide, Native and Total Thiol Comparison (Group Wise)

Mean ± SD (Median)	Control (30)	Patient (98)	P-Value
Native Thiol	398.64 ± 82.43 403.4	274.43 ± 73.84 271.3	0.001
Total Thiol	439.21 ± 91.13 446.50	303.22 ± 814.31 294.95	
Disulphide	20.28 ± 6.30 22.23	12.38 ± 6.96 13.7	

Table – II: Disulphide, Native and Total Thiol Comparison among Various Patients Groups

Mean ± SD (Median)	Control (30)	STEMI (43)	NSTEMI (35)	Nonspecific (20)	P-Value
Native Thiol	398.64 ± 82.43	254.10 ± 79.75	258.73±51.50	340.09 ± 82.75	0.001
	403.4	261.4	265.8	369.65	
Total Thiol	439.21 ± 91.13	278.71 ± 86.89	283.51±53.18	384.37 ± 87.50	
	446.5	265.4	282.5	421.1	
Disulphide	20.28 ± 6.30	12.30 ± 6.66	12.39±3.56	22.14 ± 8.71	
	22.23	15.1	12.1	19.03	

Table – III: Pairwise Groups Outcomes Comparison

	Group	Stemi	Nstemi	Nonsp
Native Thiol	Control	0.001	0.001	0.048
	Stemi		0.941	0.03
	Nstemi			0.013
Total Thiol	Control	0.001	0.001	0.019
	Stemi		0.988	0.011
	Nstemi			0.003
Disulphide	Control	0.004	0.001	0.681
	Stemi		0.747	0.011
	Nstemi			0.001

Table – IV: Relation of Troponin Levels

	r	P-Value
Native Thiol	-0.424	0.003
Total Thiol	-0.453	0.002
Disulphide	-0.48	0.001

DISCUSSION:

The prospective clinical research identified that total as well as native thiol level in the patient's category were lower as compared to the healthy one group. Moreover, the levels of disulphide ware also lower in the patient's category with respect to control category. There were important statistically variations between the category's groups. The results are too significant, thiol comprises of sulphydryl class and that is compared if sulfur and hydrogen atom and it execute very important role in oxidative stress protection in cells. The main target of reactive oxygen species in proteins are SH group of sulfur comprising of amino acid. Whenever in the uniform conditions with reactive oxygen species sulphydryl groups oxidize as well as formulate reversible disulphide bonds. However, organized disulphide bonds might again be lessened to thiol category via the cellular decreasing effects of few adverse oxidants and thiol disulphide homeostasis is reverse by this system. The deprivation of thiol category is the fundamental molecular system advancing to anatomical and operational developments in proteins [3, 5]. Formally thiol compounds having low molecular weight could generally be computed in the structure, thiol having low molecular weight, were just a little amount of the total thiol however albumin as well as other proteins having thiol made huge part of it. Consequently, in earlier researches it does not present total thiol as well as disulphide amount in the body [11, 12]. Erel & Neselioglu developed a totally computerized technique through which dynamic thiol disulphide was initially measured into 2014 [10]. The fresh research determined total, native as well as disulphide level in acute myocardial infarction patients by utilizing this technique which simple, secure, fast and cheaper procedure. Reversals in vitro researches presented that abnormal thiol disulphide homeostasis emerge in propagation or apoptosis at the cellular level [13, 14]. Uniformly in the earlier researches degenerative diseases, in addition to autoimmunity, cardiovascular complications persistent inflammation, persistent kidney diseases, and hyperglycemia have been presented to be related with oxidative stress as well as hazard of diabetic have been demonstrated [11]. In a fresh research, the patients have free diabetic have low level of native & total thiol [11]. These findings are similar to our findings. Since diabetic is a hazardous agent in coronary artery diseases, huge value should be given to the analysis of these outcomes.

Additional researches presented that thiol disulphide homeostasis dropped in HT patients with respect to the healthy group [4, 17]. The results assist our findings, hypertension is a hazardous agent for myocardial infarction just as diabetic, and furthermore, this specific case is significantly established on the facts lofty oxidative stress indicators play synergistically with the absolute hazardous cause of CAD. Additionally, oxidative stress with augmented without a break of atherosclerotic disease. [3, 5, 17, 18].

In additional research, the level of native and total thiol was established to be expressively low as well as disulphide level was superior in preeclampsia when correlated with salubrious, simple gestation.

One more fresh research displayed that thiol disulphide homeostasis was established to be disordered in trichloroethylene vulnerable workers [2]. Another research concludes that thiol disulphide homeostasis insurgent bowel disease patients as well as examine the association of disulphide thiol equalize with complication activity [12]. The researchers utilized this fresh technique, several stress causes for heart, just like ischemia, overload pressure and volume stress to the issue of myocardium through protein indications, variations in genes and the oxidative results. Oxidant interfaces with thiol and that's are main intercellular and extracellular molecular adverse oxidant [19]. The association between CAD and oxidative stress has captivated clinical concerns for an extended time and it has been presented that couple extravagant oxidative stress, as well as insufficient safeguard, can produce early assault of intense CAD. Formally, a number of researches have presented that oxidative stress produced CAD through a couple of extravagant oxidative stress and insufficient defense system [5, 7]. Anyhow there are just a few researches in the literature that examine thiol disulphide homeostasis as uncommon indicators of oxidative stress in myocardial infractions patients as well as correlate the findings with healthy individuals.

CONCLUSION:

Total as well as native thiol levels are computed comfortably as well as performed selectively via manual spectrophotometric assay and could be an important hazardous indicator in acute myocardial infarction patients while hospitalization.

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