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Original Research Article

Study of Plasma Free Fatty Acid and H_2S Along with Conventional Biochemical Parameters in Acute Coronary Syndrome with and without Diabetes Mellitus

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Abstract

Introduction: Acute coronary syndrome (ACS) is an umbrella term for situations where the blood supplied to the heart muscle is blocked. The FFAs is a major fuel in mammals besides glucose.

Aims: To find out whether any significant change of FFA (Free Fatty Acid) and H_2S (Hydrogen Sulphide) level occur in patients suffering from ACS. (Acute Coronary Syndrome).To finds out any difference in of FFA & H_2S level in Diabetic ACS in comparison to non-Diabetic ACS. To compare these two parameters with conventional biochemical parameters done in ACS, like Lipid Profile, and Lp(a).

Materials & Methods: The study was an observational, cross-sectional study conducted in the Department of Biochemistry in collaboration with the Department of Cardiology, NRS Medical College and Hospital, Kolkata. A total of 88 patients with Acute Coronary Syndrome were recruited during the study period from August 2017 to September 2018.

Result: One way ANOVA showed that there was significant difference in mean level of high density cholesterol of the patients of the three groups ($p<0.0001$). Tukey's test showed that the mean level of high density cholesterol of the controls was significantly higher than that of the other two groups ($p<0.01$).

Conclusion: We concluded that this study was under taken with the objective to find out whether any significant changes of level of FFA and H_2S in patients suffering from ACS with or without DM along with conventional biochemical parameters.

Keywords: Hydrogen Sulfide, Cardiovascular Risk, Metabolic dysregulation and Plasma Free Fatty Acids.

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Introduction

Acute coronary syndrome (ACS)is an umbrella term for situations where the blood supplied to the heart muscle is blocked. The blockage can be sudden and complete, or it can come and go – clot, break open, then clot again. In either case, the heart tissue is dying, even if it's just a few cells or a whole big section of the heart. More than seven million patients are reportedly diagnosed with AMI each year, 90% of myocardial infarctions are attributable to modifiable risk factors as smoking, dyslipidemia, hypertension and diabetes . Some studies have recently reported that STEMI patients with high glucose are related to adverse impact on survival, and the plasma FFAs concentration has been associated with lipid toxicity, apoptosis, and risk of diabetes mellitus and coronary heart disease. While it has been known for >40 years that elevation of plasma-free fatty acids (FFAs) occurs within 1 or 2 h of the onset of an acute coronary syndrome (ACS) and that the greater the increase in

plasma FFA the greater the incidence of serious ventricular arrhythmias, no account exists as to how this was discovered and developed.[1] Circulating FFAs are albumin-bound lipid molecules principally derived from adipose tissue lipolysis . The FFAs is a major fuel in mammals besides glucose. It is established that the excess supply of FFAs could suppress food intake and reduce hepatic glucose output. An overabundance of FFAs, due to exogenous lipid infusions or obesity, can lead to insulin resistance, vascular dysfunction, and myocardial dysfunction. Although most FFAs are bound to albumin, a small fraction is unbound FFA (FFAu); FFAu increases in the ischemic, under-perfused myocardium rapidly within 30 min, which is considered to be more sensitive in physiologic changes than bound FFAs.[2] Inflammation plays a critical role throughout the atherosclerotic stage in various vessels, ranging from fatty streak formation to cardiovascular events.

Plasma FFA compositions are dysregulated in CAD (coronary artery disease) patients, partly influenced by age and gene polymorphisms .More recently, the Quebec Cardiovascular Study showed that increased plasma FFA in healthy men predicted over a 5-year follow-up period the subsequent development of CHD.[3] Study aims to find out whether any significant change of FFA (Free Fatty Acid) and H_2S (Hydrogen Sulphide) level occur in patients suffering from ACS. (Acute Coronary Syndrome).

To finds out any difference in of FFA & H_2S level in Diabetic ACS in comparison to non-Diabetic ACS. To compare these two parameters with conventional biochemical parameters done in ACS, like Lipid Profile, and Lp(a).

Materials and Methods

Type of Study: Observational, cross sectional study.

Place of Study: Department of Biochemistry in collaboration with the department of Cardiology, NRS Medical College and Hospital, Kolkata.

Study Duration: From August 2017 to September 2018

Sample Size: 88 acute coronary syndrome patients

Inclusion Criteria

- Patients of ACS diagnosed and confirmed by clinico-biochemical parameters.
- Thirty samples were collected from Non ACS person attending to Biochemistry Service Lab suffering from diseases other than Non ACS Cardiovascular Diseases of N.R.S. Medical College & . Hospital, Kolkata.

Exclusion Criteria: Patients having Cardiovascular disorder other than ACS.

Study Variables

- Age
- Sex
- Body Mass Index
- Smoking status
- History of hypertension or other comorbidities
- Presence of Diabetes Mellitus

Statistical Analysis: Data were entered into Excel and subsequently analyzed using SPSS and GraphPad Prism. Continuous variables were summarized as means with standard deviations, while categorical variables were presented as counts and percentages. Comparisons between independent groups were performed using two-sample t-tests, and paired t-tests were applied for correlated (paired) data. Categorical data were compared using chi-square tests, with Fisher's exact test applied when expected cell counts were small. A p-value of ≤ 0.05 was considered statistically significant.

Result

Table 1: Distribution of population of study

Group		Number	Percentage (%)
	Cases with T2DM	26	29.5
	Cases without T2DM	32	36.4
	Controls	30	34.1
	Total	88	100

Table 2: Comparison of mean level of H_2S, Level of FFA (M mol/mlnmol/ml), Level of LP(a) (mg/dl), Level of HbA1c , Level of Triglyceride (in mg/dl) and Level of total cholesterol (in mg/dl)of the patients of the three groups

Level of H_2S (M mol/mlnmol/ml)		Cases with T2DM	Cases without T2DM	Controls	Test Statistic((F2, 85))	p-value
	Mean ± s.d.	29.81±13.56	37.03±11.43	48.50±12.76	15.976	<0.0001
	Median	28.5	35	50.5		
	Range	Dec-63	17.00 - 60.00	20 - 72		
Level of FFA (M mol/mlnmol/ml)	Mean ± s.d.	210.62±152.41	209.67±53.97	193.06±78.35	12.238	<0.0001
	Median	178.845	198	154.765		
	Range	103.10 - 920.03	129 - 339	121.62 - 392.61		
Level of LP(a) (mg/dl)	Mean ± S.D.	45.73±32.31	37.09±30.78	7.61±9.66	16.849	<0.0001
	Median	31	25	3		
	Range	1 - 114	2.00 - 112.00	0.00 - 35.00		
Level of HbA1c	Mean ± s.d.	8.79±2.20	6.18±0.59	6.02±0.58	40.035	<0.0001*
	Median	8.15	6.1	6		
	Range	5.34 - 12.82	5.18 - 8.01	4.91 - 7.50		
Level of Triglyceride (in mg/dl)	Mean ± s.d.	204.73±92.18	181.28±65.55	102.27±25.21	19.421	<0.0001
	Median	211	170.5	98.5		
	Range	90 - 490	83.00 - 310.00	70 - 176		
Level of total cholesterol (in mg/dl)	Mean ± s.d.	198.00±42.06	162.41±38.99	134.43±34.22	19.105	<0.0001
	Median	190	163.5	123		
	Range	135 - 310	102.00 - 250.00	89 - 231		

Table 3: Comparison of mean level of high density cholesterol and Level of blood sugar (in mg/dl) of the patients of the three groups

Level of high density cholesterol (in mg/dl)		Cases with T2DM	Cases without T2DM	Controls	Test Statistic (F2, 85)	p-value
	Mean ± s.d.	40.50±12.22	41.91±7.44	46.00±6.95	11.905	<0.0001
	Median	41.5	42	46.5		
	Range	30 - 84	27.00 - 52.00	31 - 56		
Level of blood sugar (in mg/dl)	Mean ± s.d.	213.04±91.32	150.10±49.62	111.32±33.93	11.905	<0.0001
	Median	188.5	138	104		
	Range	101 - 487	78 - 304	69 - 220		

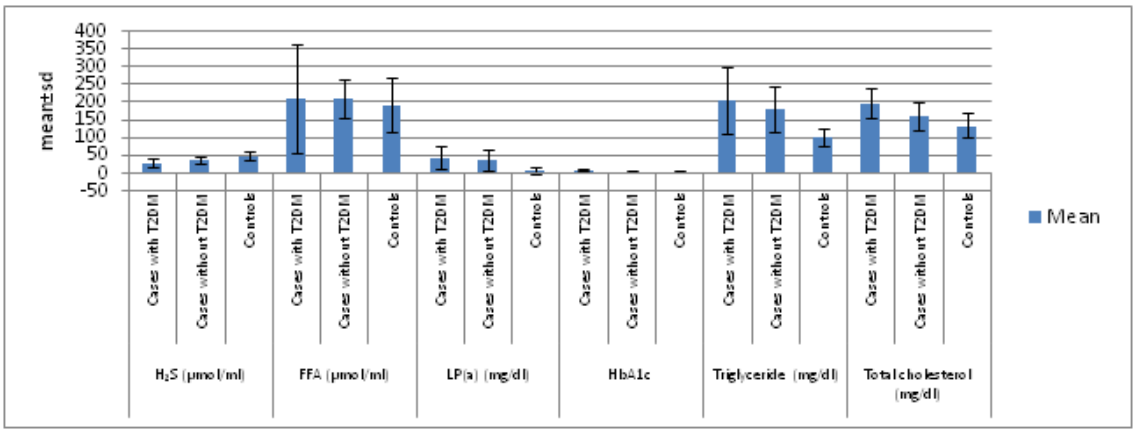

Figure 1: Comparison of mean level of H_2S, Level of FFA (M mol/mlnmol/ml), Level of LP(a) (mg/dl), Level of HbA1c , Level of Triglyceride (in mg/dl) and Level of total cholesterol (in mg/dl)of the patients of the three groups

Out of the 58 patients of ACS 26(29.5%) were with T2DM and rest 32(36.4%) were without T2DM. 30(34.1%) in the control group. One way ANOVA showed that there was significant difference in mean level of H_2S of the patients of the three groups ($p<0.0001$). Tukey's test showed that the mean level of H_2S of the cases with T2DM was significantly lower than that of the other two groups ($p<0.01$). One way ANOVA showed that there was significant difference in mean level of FFA of the patients of the three groups ($p<0.0001$). Tukeys test showed that the mean level of FFA of the cases with T2DM was significantly higher than that of the other two groups ($p<0.01$). One way ANOVA showed that there was significant difference in mean level of LP(a) of the patients of the three groups ($p<0.0001$). Tukey's test showed that the mean level of LP(a) of the cases with T2DM was significantly higher than that of the other two groups ($p<0.01$). One way ANOVA showed that there was significant difference in mean level of HbA1c of the patients of the three groups ($p<0.0001$). Tukey's test showed that the mean level of HbA1c of the cases with T2DM was significantly higher than that of the other two groups ($p<0.01$). One way ANOVA showed that there was significant difference in mean level of triglyceride of the patients of the three groups ($p<0.0001$). Tukey's test showed that the mean level of level of triglyceride of the cases with T2DM was significantly higher than that of the other two groups ($p<0.01$). One way ANOVA showed that there was significant difference in mean level of total cholesterol of the patients of the three groups ($p<0.0001$). Tukey's test showed that the mean level of total cholesterol of the cases with T2DM was significantly higher than that of the other two groups ($p<0.01$). One way ANOVA showed that there was significant difference in mean level of high-density cholesterol of the patients of the three groups ($p<0.0001$). Tukey's test showed that the mean level of high-density cholesterol of the controls was significantly higher than that of the other two groups ($p<0.01$). One way ANOVA showed that there was significant difference in mean level of blood sugar of the patients of the three groups ($p<0.0001$). Tukey's test showed that the mean level of blood sugar of the cases was significantly higher than that of the other two groups ($p<0.01$).

Discussion

One of the most intriguing findings in current results that indeed merit further investigation is H2S, which was significantly lowered in the serum of DM patients with ACS. H_2S has been traditionally viewed as a toxic gas and less recognized as an endogenously generated biological mediator. It has recently been hypothesized that H_2S is the "third endogenous signalling gasotransmitter" alongside with nitric oxide (NO). Endogenous H_2S is generated in mammalian tissues by two pyridoxal-5′-phosphate-dependent enzymes, cystathionine-β-synthase (CBS) and cystathionine-γ–lyase (CSE). In the heart, endogenous H_2S is synthesized from L-cysteine via CSE [4]. H_2S can regulate heart contractility and protects the heart from ischemic injury. The mechanism underlying the vascular relaxant effect of H_2S are yet to be determined, although opening of ATP-sensitive K+ (KATP) channels in vascular smooth muscle cells (SMCs) could mediate for such effect H_2S was also found to promote angiogenesis and is anti-atherosclerotic in nature. During atherosclerosis, there is an increase in the formation of reactive oxygen species (ROS). H_2S can directly quench ROS with its strong reducing properties and inhibit ROS production. Within the atherosclerotic lesion, there is a massive proliferation of vascular SMCs. H_2S inhibits vascular SMCs proliferation and induces their apoptosis Foam cells formation from macrophages by oxidized LDL is critical for the initiation and progression of atherosclerotic lesions. H_2S was shown to inhibit the formation of foam cells. [5] [6] [7] [8].

There still remains some controversy over the cross talk between H_2S and NO. Coletta et al. reported that the deficiency in endothelial nitric oxide synthase (eNOS) prevented the ability of H_2S to induce angiogenesis, suggesting that NO is required for H_2S to have its vascular effects. In a recent study, exogenously administered H_2S increased eNOS activity and NO bioavailability. Once we better understand how these molecules work together, we can begin building therapeutics that maximize the benefits of both signaling molecules.[9] In the current study, quantitative determination of H_2S showed that H_2S was elevated in the serum of control group , compared to cases. Therefore, reduction of H_2S found in cases of ACS with DM our study could be interpreted in different ways, with an initial explanation being dysregulation endothelial function. These findings indicate that metabolite profiling techniques can develop a detailed picture of the metabolic changes that occur in response to the disease. Hence, they provide an opportunity to develop predictive biomarkers/parameter that will potentially allow for an earlier medical intervention.

According to the recent ESC/ACC guidelines, diagnosis of MI requires the rise and fall of biochemical markers together with other criteria like ischemic symptoms and ECG changes. The standard biomarkers of MI are CK-MB and cTn. However, studies reveal that these markers may not rise during reversible MI [10]. Further, recent studies have suggested that plasma FFA levels are increased in MI; thereby it is known to play an important role in the clinical diagnosis . Despite the success of cTn and CK-MB, there is still a need for the development of early markers that can reliably rule out ACS from the emergency room at presentation and also detect MI in the absence of irreversible myocardial injury. Further, several prospective and cross-sectional studies have revealed that plasma FFA has strong predictive value for CAD. However, there are very few Indian studies revealing the same. This study was designed to assess the value of plasma FFA as a predictive marker in CAD\ACS. Our study showed that the patients with ACS had significantly higher levels of plasma FFA when compared to control subjects. While comparing the conventional biochemical parameters with changes of H_2S and FFA level, it has been observed that all the biochemical parameters significantly increased in cases of ACS patients with DM except H_2S which was significantly reduced in patients of ACS with DM.

Conclusion

We concluded that this study was under taken with the objective to find out whether any significant changes of level of FFA and H_2S in patients suffering from ACS with or without DM along with conventional biochemical parameters. There is significant reduction of H_2S level in cases of ACS with DM. There is significant increase in FFA level in cases of ACS with DM. There is significant increase in Lp (a) level in cases of ACS with DM. HbA1c level is also significantly increased in ACS patients with DM. Cases with DM show increase in total cholesterol level. Cases with DM show increase in Triglyceride level. Control group shows good range of HDL level. ACS patients with or without DM along with non ACS control were underwent investigations. Marker metabolites were identified in the serum of ACS patients especially with DM, all of them are considered as potential parameters. These findings indicate that metabolite profiling techniques can develop a detailed picture of the metabolic changes that occur in response to the disease. Hence, they provide an opportunity to develop predictive parameters that will potentially allow for an earlier medical intervention.

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