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EFFECT OF STATINS ON CRP, IL6 AND MORTALITY IN COVID POSITIVE PATIENTS

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ABSTRACT

The present study draws special attention to find the effect of statins on CRP, IL6 and mortality in COVID infected patients. This study shows dramatic downward trend in the following inflammatory parameters mainly CRP, IL6 and mortality in COVID positive patients.

KEYWORDS: CRP, IL6.

INTRODUCTION

SARS-CoV-2

At the end of December 2019, an outbreak of atypical pneumonia was described in Wuhan city of China. A virus named "Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2)" was identified as the causative agent1,2. The rapid expansion of COVID-19 was declared as pandemic by The World Health Organization (WHO).

The current corona virus disease (COVID-19) pandemic, caused by severe acute respiratory corona virus 2 (SARS-CoV-2), creates major health problem across the globe, in spite of the availability of vaccines (3).

The presentation of the disease occurs in the form of mild, moderate or severe illness. Majority of the patients are either asymptomatic carrier who despite being without symptoms have the potential to be infectious to others coming in close contact, or have a mild influenza-like illness which cannot be differentiated from a simple upper respiratory tract infection. However hospitalization of patients depends on the severity of disease.

STATINS

Statins comprises of various groups which are used to lower lipids. They are used for the primary and secondary prevention of coronary heart disease in patient with dislipidemias. These agents act by inhibiting HMG.CoA reductase. They occupy a portion of binding site of HMG.CoA, blocking access of this substrate to the active site on the enzyme (4). There are various studies suggesting that statin use is associated with lower rate of intensive care unit or deaths in patients with covid-19(5). Statins are known inhibitors of the MYD88 pathway, which result in inflimation, and have been reported to stabilize MYD88 levels. In SARS-CoV and MERS.CoV there occurred disrelation of MYD88 resulting in inflammation.

AIMS AND OBJECTIVES

To assess the effect of statins on CRP, IL6 and Mortality in covid positive patients.

PARTICIPANTS: In this study 70 patients were admitted who were covid positive above the age of 20 yrs and mean age was 44 yrs. The study was done in two groups

GROUP 1: Effect of statins in covid positive patients with abnormal lipid profile, they were 20 in number

GROUP 2: Effect of statins in covid positive patients with normal lipid profile, they were 50 in number

INVESTIGATIONS: The following investigations to be done for the present study were stated as under:

1. C- REACTIVE PROTEIN
2. INTERLUIKIN 6
3. LIPID PROFILE
4. RT.PCR
5. HRCT CHEST

The following parameters were obtained during this study before starting statin therapy
Distribution of lipid profile in study patients

		Range	Group 1		Group 2		p-value
			N	Percent	N	Percent	
CHOL	High	250mg/dL to 300mg/dL	20	100	0	0	0.00
	Normal	50-200mg/dL	0	0	50	100	0.00
	Total		20		50		
TG	High	260mg/dL	20	100	0	0	0.00
	Normal	50-200mg/dL	0	0	50	100	0.00
	Total		20		50		
HDL	High	140mg/dL	20	100	0	0	0.00
	Normal	30-90mg/dL	0	0	50	100	0.00
	Total		20		50		
LDL	High	>150mg/dL	20	100	0	0	0.00
	Normal	<100mg/dL	0	0	50	100	0.00
	Total		20		50		

C REACTIVE PROTIEN AND INTERLUKIN6 BEFORE STARTING STATIN THERAPY

		Range	Group 1		Group 2		p-value
			N	Percentage	N	Percentage	
CRP	Negative	Less than 5mg/L	0	0	0	0	-
	Positive	6-10mg/L	20	100	50	100	0.034
IL6	Negative	0.00- 7.0mg/L	0	0	0	0	-
	Positive	More than 7mg/L	20	100	50	100	0.026

PARAMETERS AFTER STARTING STATIN THERAPY,STATINS TAKEN FOR TWO TO THREE WEEKS
Distribution of lipid profile in study patients

		Range	Group 1		Group 2		p-value
			N	Percent	N	Percent	
CHOL	High	250mg/dL to 300mg/dL	05	25	0	0	0.00
	Normal	50-200mg/dL	15	75	50	100	0.052
	Total		20	100	50	100	
TG	High	260mg/dL	06	30	0	0	0.00
	Normal	50-200mg/dL	14	70	50	100	0.028
	Total		20		50	100	
HDL	High	140mg/dL	15	75	0	0	0.00
	Normal	30-90mg/dL	05	25	50	100	0.024
	Total		20	100	50	100	
LDL	High	>150mg/dL	05	25	0	0	0.00
	Normal	<100mg/dL	15	75	50	100	0.36
	Total		20	100	50	100	

C-REACTIVE PROTIEN AND INTERLUKIN 6 AFTER STARTING STATIN THERAPY(2-3 weeks)

		Range	Group 1		Group 2		p-value
			N	Percentage	N	Percentage	
CRP	Negative	Less than 5mg/L	15	75	48	96	0.042
	Positive	6-10mg/L	05	25	02	04	0.236
IL6	Negative	0.00- 7.0mg/L	16	80	45	90	0.621
	Positive	More than 7mg/L	04	20	05	10	0.054

DISCUSSIONS

Covid-19 is nowadays a measure health issue in whole world causing a lot of morbidity and mortality. Various modalities are done and have been in progress to stop its transmission, progression and its adverse effects on human life. There are various studies done that shows a beneficial effect of statins over the inflammatory markers and mortality thus reducing the chances of cytokine storm in covid positive hospitalized patients. Following studies are supporting the use of statin in covid positive patients and its effects on inflammatory markers like, CRP, IL6 and on mortality.

Claire Arnaud et al (24-03-2005) These results concluded that statins reduce IL-6–induced CRP production directly in hepatocytes via inhibition of protein geranylgeranylation. We further show that statins act via inhibition of STAT3 phosphorylation. These findings furnish new evidence for direct antiinflammatory properties of statins and provide new mechanistic insight into their clinical benefits.

C-reactive protein (CRP), mainly produced by hepatocytes in response to interleukin-6 (IL-6), is a powerful independent predictor of future cardiovascular events. In this study, we demonstrate that statins reduce IL-6–induced CRP production directly in hepatocytes. This effect is mimicked by an inhibitor of the geranylgeranyltransferase and we further demonstrate that statins act via reduction of STAT3 phosphorylation.

F. Montecucco(March 2009) concluded that The treatment with simvastatin or atorvastatin decreased CRP-induced release of CCL2, CCL3 and CCL4. In addition, both statins reduced CRP-induced intercellular adhesion molecule (ICAM-1) up-regulation, but had no effects on CD11b and CD18. Treatments with 1 μM simvastatin or atorvastatin significantly inhibited monocyte migration in response to CRP. CD32 and CD64 (CRP receptors) expression on monocytes was not affected by statins. Statin-induced inhibition of CRP-mediated chemokine secretion, ICAM-1 up-regulation and migration occurred through the inhibition of extracellular signal-regulated kinase (ERK) 1/2. Treatment with L-mevalonate or farnesylpyrophosphate, but not geranylgeranyl-pyrophosphate reversed the statin-induced effect on CRP-mediated functions and ERK 1/2 phosphorylation, confirming that statins blocked CRP-induced ERK 1/2 phosphorylation through the inhibition of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase.

Winfried März et al (10-2016) concluded that statins may lower C-reactive protein levels by interfering with the generation and/or release of C-reactive protein in the liver rather than by modulating inflammatory processes in the vessel wall.

A study done by Ahmad Fariz Malvi Zamzam Zein et al (30 June 2021) shows Statin potentially improved outcome in patients with COVID-19.

Carlos Diaz-Arocutipa et al (2021-08-04) showed that statins were independently associated with a significant reduction in mortality. Subgroup analyses showed that only chronic use of statins significantly reduced mortality according to the adjusted models.

Prateek Lohia (10 July 2021) concluded that Inpatient statin use was associated with significant reduction in mortality among COVID-19 patients especially those with DM. These findings support the pursuit of randomized clinical trials and inpatient statin use appears safe among COVID-19 patients.

SUMMERY AND CONCLUSION

The present study was conducted in postgraduate department of medicine, in government medical college Srinagar, over a period of 21 days to asses effect of statins over the inflammatory markers mainly IL-6, CRP and Mortality in covid positive hospitalized patients. This study shows drastic downward trend in inflammatory markers and mortality among covid positive hospitalized patients.

- The mean age of patients in our study was 44.
- There were 20% females and 80% males.
- This study also shows more improvement in inflammatory markers in covid positive female patients as compared to male positive patients.
- In this study statins were used for the duration of 2 to 3 weeks, after these inflammatory markers were reduced and there was a mortality benefit.

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