

CIRCADIAN VARIATION IN THE ONSET OF ACUTE MYOCARDIAL INFRACTION IN KASHMIR

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Abstract : A prospective observational study of two hundred patients of acute myocardial infarction admitted in Accident & Emergency Department and the Coronary Care Unit of a premier hospital, Sher-e-Kashmir Institute of Medical Sciences, Srinagar, India was carried out to determine the time of onset of chest pain and whether onset of myocardial infarction " Occurs randomly or observes circadian variation in the frequency of its onset" 50% of the patients developed infarction between 4 am to 10 am with anterior ST elevation myocardial infarction in 50% Second peak of 22% was observed from 4 pm to 10 pm as compared to trough 100/0 between 10 pm to 4 am. 18% of myocardial infection occurred between 10 am to 4 pm. This study revealed variation in circadian rhythm in the onset of acute myocardial infarction and its complications. The pharmacological modulation of the physiological triggers can be tried to delay or prevent the occurrence of infarction.

INTRODUCTION

Myocardial infarction (MI) is the result of prolonged myocardial ischemia precipitated by an occlusive coronary thrombus in most cases, at the preexisting site of stenosis. Human body is a master computer with circadian rhythm, which are endogenously generated by self sustained oscillators called biological clocks -their relation being governed by Central Nervous System through suprachiasmatic nucleus of the hypothalamus region. Pineal gland has also been implicated in the control of circadian as well as circannual rhythm. The circadian rhythm study has numerous clinical implications in medical Science.

Cardiac disorders account for the vast majority of natural sudden deaths. In the United States, acute myocardial infarction develops suddenly in over 600,000 patients each year. These patients are either completely free of cardiac symptoms or have mildly symptomatic chronic stable angina pectoris¹. It is now well established that myocardial infarction is usually preceded by coronary thrombosis, which in turn is often superimposed on disrupted intima covering an atherosclerotic plaque^(2,3). Little is known about the events or circumstances that trigger these pathologic events or transform a chronic stable condition to an acute life threatening disease. The anatomic distribution of the occluded vessel, adequacy of collateral circulation and presence of additional stenotic lesion status determines the location and extent of infarction. However it is well established that onset of the pain of myocardial infarction has circadian periodicity, with a peak incidence between 6 am and 12 noon^(4,5,6). The rhythmic processes that drive the circadian rhythm are endogenously mediated and governed by suprachiasmatic nucleus of hypothalamus and pineal gland^(7,8) Various key physiological secretions like endogenous tissue plasminogen activator (tpa) activity, PAI-1 levels, plasma cortisol, plasma epinephrine and other parameters like heart rate, blood pressure and blood viscosity exhibit circadian variation. Existence of this marked circadian variation in these parameters including platelet aggregation in the morning and upon assuming upright posture may account for the observed circadian variation in the onset of Myocardial Infarction^(9,10)

MATERIAL AND METHODS

Two hundred consecutive patients of acute myocardial infarction with history of chest pain of more than 30 minutes duration, -cardiac by description with ECG showing characteristic changes of evolving myocardial infarction were included in the study. Enzyme studies were carried out for SGOT, SGPT, and CPK-MB estimation. Exact time of onset of events was recorded

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Following criteria satisfying the diagnosis for an acute evolving or recent myocardial infarction has been followed while conducting this study. Typical rise and gradual fall (troponins) or more rapid rise and fall (CK-MB) with at least One of the following, features (a) Ischemic symptoms; (b) Development of pathogenic Q waves on each reading; (c) ECG changes indicative of ischemia (ST -segment elevation or depression)

RESULTS

The results are tabulated in table 1 and table 2

Table 1: Distribution of patients according to onset of chest pain

Time of onset	No. of patients	Males	Females
4 am to 10am	100	76(38%)	24(12%)
10am to 4pm	36	24 (12%)	12(6%)
4pm to 10pm	44	40 (20%)	4(2%)
10pm to 4am	20	16(8%)	4(2%)

Table 2 : Temporal relationship of infarction type and death to time of onset of chest pain

Type of infarction	patients(n)	Time of onset of chest pain			
		4am to 10am	10am to 4pm	4pm to 10pm	4am to 10pm
Anterior wall MI	100	56	12	24	8
Inferior wall MI	0	40	16	16	8
Anteroseptal MI	16	4	4	4	4
Subendocardial	4	4			
Death	0				

DISCUSSION

Circadian variation in the frequency of myocardial infarction with morning resistance to thrombolytic therapy has been observed. Their may be an improvement in diagnosis and treatment of illness after understanding the role of circadian rhythm in the pathophysiology of acute myocardial infarction. Understanding of possible risk of atherosclerotic disease could improve the perception of pathophysiology of illness and increasing sensitivity to management.

Various studies have demonstrated a marked circadian periodicity in the time of onset of myocardial infarction with peak incidence between 6am to 12 noon. Master was the first to show the existence of periodicity in the occurrence of acute myocardial infarction (IOF) Subsequently isolated reports showed its peak occurrence in the morning hours ! The authors

observed that the peak in the onset of acute MI occurs in the morning hours (4 am to 10 am), which confirm the results of study conducted by Pells D' Alonzo¹¹.

Summary of similar results of various studies regarding time of onset of myocardial infarction pain were first published in 1983¹². The peak onset of pain was different in one study conducted by Dim troy¹³. In this study it peaked from 4pm to midnight with a second peak from 6 am to 8 am. A number of studies including Millis data reported a secondary peak in the late evening hours which the authors also confirmed. However, this peak was not present in summary findings of the World Health Organization report¹⁴. Other study from Sovelunivn showed peak incidence of chest pain occurring in the evening hours. He observed that these patients were usually young males and persons who preferred giving night duties. This probably reflects different processes involved in altering the circadian rhythm in this patient population from those causing myocardial infarction in the morning hours.

Most of the studies used subjective parameters to determine the time of onset of myocardial infarction ignoring the effect of sleep on minor episodes of pain and circadian rhythm in pain threshold.

Other studies were conducted using CK-MB elevation for considering that the myocardial infarction has occurred 4 hours before the initial elevation.

Numerous exogenous and endogenous daily rhythms have been found to have correlation with the variation in the onset of myocardial infarction. Among the exogenous daily rhythms, which bear direct correlation with the occurrence of MI, is physical and mental stress. Substantial increases in these daily rhythms occur after waking. Endogenous daily rhythms involve rise in cortisol and catecholamine levels during morning hours resulting in myocardial infarction operating through multiple mechanisms like, plaque rupture thrombosis, coronary vasoconstriction; and systemic vasoconstriction increasing the myocardial oxygen demand. Circadian variation in the tendency of the blood to clot is possibly related to decreased fibrinolytic activity of the blood and time dependent changes in the platelet activities¹⁵⁻¹⁸.

The onset of acute MI shows characteristic circadian variation, that is a definite morning peak related to biological rhythms and a vague nighttime peak related to socioeconomic factors.

The incidence of onset of myocardial infarction was found to be more frequent in the early morning hours and unaffected by geographical distribution as observed by other. Understanding the role of circadian variation in the path physiology of illness may lead to improvement in the perception and increasing sensitivity to diagnosis circadian variation has also been observed

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