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Acute triggers of myocardial infarction: A case-crossover study☆

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KEYWORDS

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Abstract *Background:* Acute myocardial infarction (AMI) is one of the most preventable non-communicable diseases in human. Identifying triggers of myocardial infarction (MI) and prevention ways of exposure-induced complications can reduce morbidity and mortality in people at risk.
Aim: The aim of this study was to identify the emotional, environmental, physical and chemical dimensions of acute triggers in patients with AMI.
Methods: This case-crossover study was conducted on 269 patients with AMI, hospitalized at two remedial centers in Rasht in 2015. The study samples were selected by convenient sampling method. Data were collected using researcher-made questionnaire through interviews. Hazard and control periods for each trigger and its effects on the development of MI were studied. The collected data were analyzed using descriptive and analytical statistical methods, Cochran test, and generalized estimating equation (GEE) model with logistics function default in SPSS version 21, and $p < 0.05$ was considered statistically significant.
Results: The results showed that quarrel ($P = 0.008$, OR = 2.01) and hearing the sudden news ($P = 0.001$, OR = 2.19) were the most common emotional triggers. Respiratory infections ($P = 0.0001$, OR = 6.78) and exposure to hot or cold weather ($P = 0.005$, OR = 2.19) were the most frequent environmental triggers. Doing heavy activities ($P = 0.005$, OR = 1.66) and sexual

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activities ($P = 0.003$, OR = 2.36) were among the most common physical triggers. High-fat foods consumption and overeating ($P = 0.0001$, OR = 3.79) were the most frequent chemical triggers of AMI.

Conclusion: It seems that given the importance of the triggers in the incidence of AMI, planning is necessary to train vulnerable individuals to reduce exposure to triggers.

1. Introduction

The cardiovascular diseases impose an enormous cost on country's health and therapeutic systems. However, they are among the most preventable non-communicable diseases in human beings.[1] Two kinds of factors are involved in developing heart diseases, the chronic and acute risk factors (ARFs).[2,3] ARFs engage by sympathetic or parasympathetic stimulation leading to vasoconstriction, prothrombotic or biomechanical activities, thrombosis plaque rupture and myocardial infarction (MI) or acute coronary syndrome.[4]

During 1980s, a relationship between sexual activity, insomnia, and MI was found, and it was estimated that 50% of acute myocardial infarction (AMI) can be triggered by external factors. A relationship between physical activities, anger, sexual activity, cocaine abuse, overeating and AMI incidence has been shown hours before its onset over recent two decades.[4] AMI may be triggered by several factors such as physical activities, stressful events, overeating and increased air pollution, and the importance and prevalence of each of these triggers are unclear.[5] A trigger is, in fact, an external stimulus that causes pathological changes, and there is a direct relationship between exposure to a stimulus and disease incidence happening during some hour period (some minutes to 24 h before acute coronary syndrome (ACS) onset). This time interval is known as "hazard period".[6,7] If there is a vulnerable atherosclerotic plaque, the trigger, through vasoconstriction and prothrombotic construction, causes the thrombosis plaque rupture and reduces the heart's electrical stability threshold, and increases sympathetic activity via the release of central mediators such as catecholamine leading to ventricular fibrillation and sudden cardiac death.[2,8] Acute triggers fall in four categories, including emotional, physical, environmental and chemical triggers.[8–14] Karek et al. reported deaths increase as 58% in Persian Gulf War in 1991 following Iraqi missile attacks on Israel and resulted in stresses caused by a combination of emotional and chemical triggers. Also, emotional stresses caused by September 11, 2001, attacks in New York showed that terrorist attacks-induced psychological stresses can trigger cardiovascular events resulted from the combination of environmental and emotional triggers.[8]

Evidence suggests that air pollution, time spent in a traffic jam, and temperature changes are among the environmental triggers of MI. Exposure to micro-pollutant with 2.5 μm is associated with the incidence of cardiovascular events and increases the risk of AMI.[4] Also, there is a relationship between respiratory infections[15] and seasonal temperature changes with the incidence of AMI.[16] Some studies have reported increased rates of hospitalization and mortality resulted from AMI in winter and the lowest hospitalization and death in summer. In a study conducted by Mohammadian, it was shown that the increase in AMI cases was not confirmed in cold seasons, and the results demonstrated that the incidence of AMI grew in spring season.[17] Physical triggers of AMI such as sexual activities and heavy exercises can play a role in AMI incidence. Despite the benefits of regular exercise, physical activities and exposure to acute factors such as sexual activities and psychological stress can trigger heart diseases.[13] Chemical triggers of AMI including eating high-fat foods, drinking coffee even a cup of it,[18] abusing alcohol, and smoking marijuana can cause heart diseases. According to official data provided by the Ministry of Health in IRAN 33–38% of deaths were caused by cardiovascular disease especially acute myocardial infarction.[9]

Therefore, given the importance of triggers effects on accelerating the process of sclerotic plaque rupture and the development of AMI, this study aimed to identify acute triggers in people with AMI and the relationship between acute risk factors and odds of AMI in patients at risk and to determine the most common type of trigger. By achieving these objectives, we can promote awareness of people at risk to prevent and reduce morbidity and mortality.

2. Methods

In this case-crossover, study triggers of AMI were examined at two remedial centers of Rasht. Rasht is the biggest city located in northern Iran with more than one million people. This city has a humid subtropical climate with relatively high temperatures in summer and rainfall coming from convectional thunderstorm activity and tropical cyclones in winter. The required sample size was determined as 269 based on results of Harrison's Principles of Internal Medicine, Lanky et al.'s study and the National Census of America.[20–22] In this study, each patient was his/her own control during the 24 h before the onset of symptoms and was compared with that at the time of a few days, few weeks, and few months before the onset of AMI. The first 24 h was considered as the hazard period. In addition to hazard period, another time interval, known as a control period, was considered to study the trigger effect. In this study, three control periods were used to study on triggers' effect with regard to their nature. This period was determined as one day, two days, and five days before AMI onset for triggers such as anger, quarrel, hearing sudden news, insomnia, watching sport games, sudden exposure to hot or cold weather, exposure to traffic jam, witnessing a car accident, doing heavy and sexual activities, eating high-fat foods and overeating, alcohol and drug abuse, and coffee or tea drinking, while this period was established as one week, two weeks, and more than four weeks before AMI onset for triggers such as respiratory infections and losing a job due to the chronic nature of the trigger. The control period was determined as one month, one to

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six months, and six to 12 months before AMI onset for loss of loved one trigger. According to previous studies that showed loss of loved ones living with a long-term effect on the incidence of myocardial infarction,[12] for this trigger the longest period of control time was considered. Cochran method was used to consider significant differences between triggers in the four time periods including one hazard period and three control periods. GEE method with logistic function default was applied in order to determine exposure to triggers and study incidence relative odds of AMI. Triggers were measured based on patient's exposure or non-exposure to a trigger. The unit for hazard period was an hour, and that for the control period was the day, week or month.

Patients were selected through convenience sampling, and they were enrolled based on medical records contents including changes in the electrocardiogram, laboratory findings, clinical symptoms, and AMI diagnosis by a cardiologist. The patient with STEMI and NSTEMI included in this study and unstable angina pectoris (UAP) were removed. Sampling was conducted over a period of 5 months, from September to February 2015. Inclusion criteria included patients' willing to participate in the interviews (having written informed consent), having appropriate consciousness, age over 18 years, and lack of memory disorder or psychosis. Data were collected using researcher-made questionnaire through the interview. Before data collection, a written informed consent was obtained from all patients. The questionnaire contained two parts: 1. demographic data and 2. triggers in four sections, and included 30 items, totally. The first part of the questionnaire contained 13 questions on demographic data such as gender, age, marital status, education, income, history of diabetes, hypertension, body mass index (BMI) based on the data recorded by the nurse on time of admission, cigarette smoking, alcohol and drugs abuse, drinking coffee or tea over three cups a day, and previous history of MI. The second part comprised of 17 questions to identify the acute triggers (emotional, environmental, physical, and chemical). This part was, in turn, divided into four sections. The first section contained the questions on identifying the emotional triggers including anger, insomnia, quarrel, hearing the sudden news, losing a job, the death of a loved one, excitement resulted from watching sports games and competitions and dramatic serials, and that exposure to these triggers was studied through calculating time interval. The second section composed of the questions on environmental triggers including long-term driving, exposure to traffic jam, witnessing a traffic accident or being involved in a driving accident, catching respiratory infections and exposure to hot or cold weather. The third section consisted of physical triggers including heavy and sexual activities, and the fourth section of the questionnaire included chemical triggers such as overeating, alcohol, and drugs abuse, and taking coffee or tea measures with a drunk cup of coffee or tea a day. The hazard and control period were evaluated for each trigger.

The questionnaire was given to 10 university faculty members to determine validity, and content validity index was obtained as 98.6%. Test-retest method was used for reliability. Since the answers to the questions were qualitative, kappa coefficient was used, and the consensus coefficient degree was determined as 1 indicating the patients' agreement in measurement. In this study, five patients were reluctant to participate, and one patient was excluded due to misdiagnosis. The collected data were then encoded and were analyzed using SPSS version 21. Demographic data were reviewed using descriptive statistics methods (frequency, mean, and standard deviation). Cochran test was used to examine triggers' significance in four time periods including one hazard period and three control periods, while GEE with logistics function default was applied to categorize triggers. Statistically, $P < 0.05$ was considered as significant.

This study was approved by the Ethics Committee of Guilan University of medical sciences with a code number of IR.GUMS.REC.1394.218.

3. Results

In the case-crossover study, 269 patients with AMI were studied for six months. The results showed that 62.8% and 37.2% of patients were male and female, respectively. Most of the patients were in the sixth decade of life 31.6%, with the low education level (primary level) of 38.3%, and 43.1% were low-income with 200–400 US dollars income per month. According to Table 1, 59.5% of patients had body mass index (BMI) above 25, and 43.9% had high blood pressure history and 36.4% suffered from diabetes.

There was a statistically significant difference between hazard and control periods of triggers in anger, insomnia, hearing sudden news, loss of loved ones, watching sport games, respiratory infections, exposure to sudden hot or cold weather, physical and sexual activities, overeating and high-fat foods consumption, and drinking tea in four time periods (Table 2). The most frequent emotional triggers were anger and insomnia, and the most common environmental, physical, and chemical triggers were respiratory tract infections, heavy activities, and drinking tea, respectively (Table 2).

Of emotional triggers, hearing the sudden news ($P = 0.001$, CI = 1.35–3.53), and quarrel ($P = 0.008$, CI = 1.19–3.38) were associated with a twofold increased odds of AMI, while the loss of loved one was related to very little odds (OR = 0.27, $P = 0.02$, CI = 0.08–0.84). Among the environ-

Table 1 Frequency of the underlying diseases history in the studied patients.

Study variable		Number	Percent
Diabetes history	Yes	98	36.4
	No	171	63.6
Hypertension history	Yes	118	43.9
	No	151	56.1
Overweight according to body mass index (BMI) > 25	Yes	160	59.5
	No	109	40.5
Cigarette smoking	Yes	101	37.5
	No	168	62.5
Alcohol abuse	Yes	22	8.2
	No	247	91.8
Opium or other drugs abuse	Yes	52	19.3
	No	217	80.7
Coffee or tea drinking > 3 cup per day	Yes	135	50.2
	No	134	49.8
myocardial infarction (MI) history	Yes	44	16.4
	No	225	83.6

Table 2 Triggers frequency and significance level of time periods.

Trigger type	Trigger	Exposure number/hazard period	Percent	Mean (h)	Standard deviation	Minimum time period (h)	Maximum time period (h)	Significance in four time periods
Emotional	Anger	86/269	32	4.99	5.50	0.08	24	0.003
	Insomnia	99/269	36.8	13.1	2.4	12	20	0.03
	Quarrel	46/269	17.1	4.71	4.85	0.08	12	0.0001
	Sudden news	58/269	21.6	5.78	5.01	0.08	12	0.0001
	Loss of loved one	4/269	1.5	1.9	2.9	0.5	7	0.002
	Watching sport games	8/269	3	5.17	4.80	0.5	12	0.049
Environmental	Exposure to traffic jams	32/269	11.9	6.7	6.46	0.5	24	0.24
	Witnessing car accidents	4/269	1.5	1	0	1	1	0.18
	Respiratory infections	88/269	32.7	3	2	1	6	0.0001
	Exposure to hot or cold weather	44/269	16.4	4	2.51	0	6	0.001
Physical	Physical activities	111/269	40	3	3	1	12	0.0001
	Sexual activities	41/269	15.2	7	5	0	12	0.0001
Chemical	Overeating & high-fat food consumption	89/269	33.1	5.71	4.94	0	20	0.0001
	Alcohol abuse	3/269	1.1	4	3	2	8	0.46
	Drugs abuse	44/269	16.4	5.45	4.25	0	13	0.20
	Drinking tea	163/269	60.6	4.12	4.18	0.016	14	0.0001

mental triggers, sudden exposure to hot or cold weather was associated with significantly increased odds of AMI. Respiratory infections increased the odds of AMI during the hazard period with OR = 6.7 (P = 0.0001, CI = 3.94–11.65), and sudden exposure to hot or cold weather was related to a raised odds of AMI with OR = 2.19 (P = 0.005, CI = 1.27–3.77). Of physical triggers, both heavy and sexual activities increased the odds of AMI. Heavy activities were associated with an increased odds of AMI with OR = 1.6 (P = 0.005, Cl = 1.16–2.37), and sexual activities increased the odds of AMI with OR = 2.3 (P = 0.003, CI = 1.33–4.19). Among the chemical triggers, overeating and high-fat foods consumption can heighten the odds of AMI with OR = 3.7 (P = 0.0001, CI = 2.41–5.96) (Table 3).

4. Discussion

This study was conducted to identify acute triggers of AMI, to prevent heart attack, and to increase awareness about MI in people at risk. The results of this study showed that emotional triggers: quarrel and hearing sudden news were associated with significantly twofold increased odds of AMI. In a study conducted by Masoumi, it was shown that hearing bad news caused a 6.9-fold rise in odds of AMI; hence, the current study is consistent with Masoumi one. Also, a quarrel in the study was related to twofold increased odds of AMI. Furthermore, Colombo stated that quarrel at work or home can increase the odds of AMI.[4] Here, acute psychological stress mechanism is a common factor. Despite a higher frequency of occurrence of anger and insomnia, they were not the predictive factors for AMI. Mostofsky and Penner reported that anger trigger was associated with 2.3-fold increased odds of AMI.[23] Bulkey indicated that anger trigger was related to 8.5-fold increased relative risk rate of AMI.[24] The results of this study contradict those of Mostofsky and Bulkey in the case of anger trigger. It seems that due to the lack of categories in the study and different interpretations of anger in various cultures, the contradiction emerges. Anger in Bulkey's study was divided into seven degrees, and anger with more than five degrees increased odds of AMI, while the only measure was the presence of anger trigger in this study. In a study performed by Clark, insomnia was associated with 1.69-fold increased odds of AMI,[25] which is incompatible with that in our study. The discrepancy could be due to differences in individual interpretation of insomnia. Also, the patient may not have enough accuracy to report insomnia period. In the case of loss of loved one, relative odds of AMI was low and had a conflict with Mostofsky[12] and Carey studies.[26] The discrepancy could be due to very limited exposure to the above-mentioned trigger and short-term hazard period in this study. In Carey and Mostofsky studies, the hazard period was considered as by one month, while this period was 24 h before the onset of AMI. In the case of losing a job and watching sports games, the results cannot be generalized due to very limited exposure.

Of environmental triggers, respiratory infections and exposure to hot and cold weather increased odds of AMI. The study found that respiratory infections were associated with 6.78-fold raised odds of AMI. Warren-Gash et al. reported that 1–3 days following respiratory infections onset caused 4.19-fold increased odd of AMI.[27] Corrales et al. showed that pneumonia was associated with fourfold raised odds of AMI.[15,28] Also, Colombo et al. noted that respiratory infections were related to 2.7-fold increased odds of AMI.[4] In the conducted study, exposure to hot and cold weather was among

Table 3 Types of triggers and each trigger's odds ratio for acute myocardial infarction (AMI)

Trigger type	Triggers	Odds ratio	Confidence interval of 95%		Significance level
			Minimum	Maximum	
Emotional	Anger	1.3	0.93	1.98	0.1
	Insomnia	1.1	0.8		0.4
	Quarrel	2	1.1	3.3	0.008
	Sudden bad news	2	1.3	3.5	0.001
	Loss loved one	0.27	0.08	0.8	0.02
	Watching sport games	2.7	0.7	10.3	0.1
Environmental	Long-term driving	1.2	0.7	2.1	0.4
	Witnessing a car accident or involving in it	2	0.36	11.9	0.4
	Severe respiratory infection	6.7	3.94	11.65	0.0001
	Exposure to hot or cold weather	2.1	1.27	3.77	0.005
Physical	Heavy activity	1.6	1.16	2.37	0.005
	Sexual activity	2.3	1.33	4.19	0.003
Chemical	Overeating & high-fat food consumption	3.7	2.41	5.96	0.0001
	Alcohol abuse	1.5	0.2	9	0.6
	Drugs abuse	1	0.6	1.6	0.8
	Drinking coffee or tea	1.3	0.99	1.96	0.05

the most important environmental trigger of developing AMI that was associated with 2.19-fold heightened odds of AMI. In a study done by Masoumi, it was expressed that exposure to cold weather was not AMI predictor[14]; it seems that difference in results is because of dissimilar weather conditions in Kerman and Guilan. Behaskaran in a study showed that temperatures above 20 °C can be associated with twofold increased odds of AMI.[29] In this study, the daily temperature was not recorded, and results of summer, autumn, and winter were studied; therefore, they cannot be generalized. Of physical triggers, both physical and sexual activities were AMI triggers and increased its odds. Sexual and heavy activities were related to 2.36- and 1.66-fold raised odds of MI, respectively. Masoumi et al. reported that sexual activities were associated with 3.4-fold heightened odds of AMI.[14] Also, Colombo showed that physical activities were related to 4.3-fold increased odds of MI.[4]

The most common chemical triggers for AMI were eating high-fat foods and overeating. In this study, overeating was associated with 3.7-fold increased odds of MI. Mitelman and Colombo introduced overeating as MI trigger, and Colombo indicated that overeating was related to sevenfold raised odds of MI.[4,8] There was no significant difference between tea, alcohol, and opium consumption among participants. Thus, these factors could not be AMI predictors. Mitelman and Mostofsky stated that alcohol abuse was associated with 2.3-fold heightened odds of ischemic stroke, but it has no effect on the incidence of MI, and this result is consistent with that of our study.[30] Moreover, Mitelman and Mostofsky showed that cocaine and marijuana abuse was related to 23.7- and 4.8-fold increased odds of MI, respectively.[8] There is a contradiction between the results of this study and those of Mostofsky one in terms of drug abuse and AMI trigger. This inconsistency derives from a common drug that is opium in our society, while Mostofsky worked on cocaine and marijuana having a different mechanism. Despite tea high consumption, no relationship between tea drinking and the incidence of AMI was observed. Likewise, no similar study showed a relationship between tea consumption and AMI incidence. Bylin et al. found that coffee drinking is an AMI trigger.[18] The results of our study were different from Bylin ones, which may be due to the difference in the type of beverage and the dissimilarity in the caffeine level in tea and coffee. Also, Nikpazhoh noted that there is no clear relationship between taking caffeine and heart diseases, and it appears that moderate consumption of coffee is not harmful to the heart. For some people having a particular sensitivity to caffeine, a physician may recommend that they avoid drinking coffee.[31]

5. Conclusion

This study showed that quarrel and hearing sudden news are among the most important triggers of AMI. It is essential that people at risk avoid exposure to stressful situations, and relaxation techniques to be taught to them. The study found that in addition to doing heavy activities, inactivity is an AMI trigger. Therefore, adjustments in daily activities and doing regular exercise are recommended to society's people. Furthermore, to avoid overeating, to treat respiratory infections at the proper time, and to reduce exposure to sudden hot or cold weather are recommended to prevent triggers' effects.

Conflict of interest

The authors declare they have no conflict of interest in the research domain.

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