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Assessment of Carotid Baroreflex in Male Patients Suffering from Myocardial Infarction (MI)

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Abstract: Reports are available which suggest that depression of carotid baroreflex in Myocardial Infarction (MI) patients can occur. These patients are more subject to sudden death. The aim of the work presented here was to investigate carotid Baroreflex Sensitivity (BRS) in male patients after MI. Thus, in this study, we examined relation between decrease in BRS and duration of cardiac cycle in male MI patients. The study was performed on 15 infarcted male patients in the range of 40-70 years with the first cardiac attack and the same number of age matched healthy persons without any cardiac or pulmonary disease. the study was performed in both supine and seated positions. In order to estimate BRS, Neck Suction Devices (Eckberg Model) was used and electrocardiography (lead 2) was recorded continuously. Intensity of stimulation and duration of stimulation were 30 mm Hg and 30 sec, respectively. Duration of basic cardiac cycle in normal group in supine and seated positions was 0.8616+0.13 seconds and 0.8619+0.141 seconds respectively that increased to 0.9529+0.153 seconds and 0.9436+0.141 seconds after stimulation ($p<0.001$). duration of basic cardiac cycle in patients group in supine and seated position was 0.0717+0.127 and 0.8215+0.11 sec, respectively that increased to 0.9124+0.153 and 0.8767+0.15 sec after stimulation ($p<0.05$). When duration of basic cardiac cycle in supine and seated positions in patients was compared to healthy group, a different of 0.0511+0.011 ($p<0.001$) in supine and 0.032+0.011 ($p<0.001$) in seated position was observed. BRS significantly increased with age ($R = 0.736$: $p<0.001$ for control and $R = 0.66$: $p<0.05$ for patient group) in both groups and the differences were statistically significant. Adaptation in patients group was less compared to control group ($R = 0.9$, $p<0.001$ for control group and $r=0.673$, $p<0.01$ for patient group). This clinical study suggest that analysis of BRS in patients after MI can be important for prognosis and identifying MI patients at righ risk for sudden death merits careful examinations.

Key words: Carotid baroreflex, baroreflex sensitivity, neck suction device, myocardial infarction

INTRODUCTION

Today, solving the problem related to cardiovascular disease is one of the aims of medical researches in different communities. MI is one the severe disease that without any treatment, sudden death may occur. Autonomic regulation of heart diminishes due to MI and autonomic imbalance seems to play an important role in sudden death of heart (Gress *et al*., 1992). Low sensitivity of baroreflex in these patients in these patients due to decreasing of vagal tone. Decreasing of vagal effects on the heart can cause ischemia on the constancy of electrical statues of heart (Gress *et al*., 1992; Larovere *et al*., 1988) and is dangerous for patients. MI can change baroreflex function and decline the arterial baroreflex responses. In patients with MI, baroreceptor reflex of heart rate changes and R_R interval decreases in response of stimuli. Baroreceptors effects on heart are mainly through vagus. Decreasing of vagal tone can cause MI. Also, cardiac symphatic tone and oxygen usage increase in these patients that related to size of infracted area (Baskevfill *et al*., 1999; Jacob and Gillbert, 1998). It seems that Baroreflex Sensitivity (BRS) in MI patients can effective in prognosis of patients after MI (Gress *et al*., 1992; Eckberg, 1975).The aim of this study, was to assess of BRS in male patients with MI and correlation of BRS with age.

Important progress has been made in the risk stratification for both sudden and nonsudden cardiovascular deaths (Moss *et al*., 1979; Koike *et al*., 2006; Ruberman *et al*., 1981). However, identifying patients at a high risk for cardiovascular fibrillation

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remains elusive. Some of these patients have been identified (Schwartz *et al*., 1978; Zappa *et al*., 1977) but the underlying mechanisms, whether persistent electrical instability or major hemodynamic impairment, have not been clarified.

Studies suggest that the autonomic nervous system plays a critical role in triggering ventricular fibrillation (Schwartz *et al*., 1978; Malliani *et al*., 1980; Verrier and Lown, 1981; Schwartz and Stone, 1982). Vagal activation is generally viewed as protective (Verrier and Lown, 1980) while increased symphatetic activity predisposes the heart to ventricular fibrillation (Schwartz *et al*., 1976; Schwartz and Vanoli, 1981).

Changes in heart rate mediated by baroreceptor reflex can provide a meaningful way to assess autonomic neural control of the heart. Myocardial ischemia attenuates baroreflex control of heart rate in response to arterial pressure increases (Takeshita *et al*., 1980). Baroreflex function can be altered after MI, as drug-induced hypotension may not be associated with tachycardia (Malliani *et al*., 1980; Kelly *et al*., 1973).

MATERIALS AND METHODS

This case-control study was performed on 30 male subjects. Case group was 15 infarcted male patients in the range of 40-70 years old with the first cardiac attack that were hospitalized in cardiac unit of Shahid Madani Hospital in Tabriz city (Iran). For comparison, the control group was the same number of age matched healthy persons without any cardiac or pulmonary disease. This group was staffs of Medical Faculty of Tabriz University. Research protocol was performed in both supine and seated positions. One day before examination, test phases were explained to both groups. Neck Suction Device (Eckberg Model) was used for stimulating of baroreceptore (Eckberg, 1975). This device includes a suction pump that connected to neck chamber by means of a flexible tube. The suction pump can produce a negative pressure in chamber. There is a dimmer in the device that by altering of voltage, the negative pressure in range of 0 to −100 mm Hg can be produced. Negative pressure in front of neck pulls the sinus wall of carotid. Intensity and duration of stimulation were −30 mm Hg and 30 sec, respectively. The stimulation time was 20 sec. Electrocardiography (Lead 2) was recorded continuously. In order to elimination of respiratory effects on the heart, subjects did not breathe 5 sec after stimulation. For assessing of BRS, R_R interval mean was taken for each phase. Because, the sample size was less than 30 subjects for both groups, the non-paired and paired t-test was used for inter and intra groups, respectively. Linear regression was used by on way analysis of variance. Finally, analyzing of data was done by SPSS released 11 software program (WinXP). p-values less than 0.05 were statistically significant.

RESULTS

Results are available in Table 1, 2 and Fig 1, 2. Age mean was not different. In patients group and in supine position duration of cardiac cycle before and after stimulation were 0.8717±0.127 and 0.9214±0.153 sec, respectively. This different was statistically significant ($p<0.05$) but intensity was less than healthy subjects. In seated position (patients), duration of cardiac cycle

Table 1: Changing of R-R interval, before, during and after stimulation of baroreceptors in control and patient group in supine positions

	Control	Control	Stimulation	Stimulation	Stimulation	Stimulation	Stimulation	Stimulation	Stop	Stop	Stop
Control group	Breath	Breath holding	Breath holding	Breath holding	Breath	Breath	Breath	Breath holding	Breath holding	Breath holding	Breath
	1	2	1	2	1	2	3	1	1	2	1
R_R	0.849	0.8614	0.9529	0.9212	0.8937	0..884	0.8946	0.8836	0.8516	0.8733	0.8621
HR	70.67	69.65	62.96	65.12	67.13	67.87	67.06	67.9	70.48	68.7	69.59
SD	±0.12	±0.113	±0.12	±0.127	±0.1153	±0.118	±0.123	±0.11	±0.12	±0.135	±0.134
N	15	15	15	15	15	15	15	15	15	15	15
Df	14	14	14	14	14	14	14	14	14	14	14
T			12.77	5.30	3.56	2.33	3.86	2.07	1.06	0.81	0.05
P			<0.001	<0.001	0.003	0.035	0.002	0.055	0.12	0.21	0.93
Patient group											
	1	2	1	2	1	2	3	1	1	2	1
R_R	0.86	0.8717	0.9124	0.9	0.8936	0.8817	0.877	0.8734	0.8697	0.8713	0.8814
HR	69.17	98.83	65.76	66.66	67.14	68.05	68.41	68.69	68.98	68.86	67.86
SD	±0.12	±0.113	±0.12	±0.127	±0.1153	±0.118	±0.123	±0.11	±0.12	±0.135	±0.134
N	15	15	15	15	15	15	15	15	15	15	15
Df	14	14	14	14	14	14	14	14	14	14	14
T			2.73	1.93	1.08	0.54	0.32	0.11	0.12	0.20	0.073
P			0.02	0.02	0.11	0.31	0.45	0.43	0.56	0.41	0.92

R-R interval in sec, HR (Heart Rate) in beat min^{-1}, SD = Standard Deviation, N = No. of subjects, df = Degree Freedom, T = t-test, P = p-value and NS = Non Significant

Table 2: Changing of R-R interval, before, during and after stimulation of baroreceptors in control and patient group in seated positions

	Control	Control	Stimulation	Stimulation	Stimulation	Stimulation	Stimulation	Stimulation	Stop	Stop	Stop
Control group	Breath	Breath holding	Breath holding	Breath holding	Breath	Breath	Breath	Breath holding	Breath holding	Breath holding	Breath
	1	2	1	2	1	2	3	1	1	2	1
R_R	0.847	0.8619	0.9426	0.9168	0.8587	0.8547	0.863	0.8588	0.8386	0.83	0.8409
HR	70.83	98.61	63.58	65.44	69.87	70.2	69.52	69.86	54.71	72.28	71.37
SD	0.1246	0.141	0.136	0.1411	0.116	0.1082	0.1095	0.123	0.141	0.136	0.13
N	15	15	15	15	15	15	15	15	15	15	15
Df	14	14	14	14	14	14	14	14	14	14	14
T			6.37	3.39	0.16	0.46	0.7	0.31	2.9	1.98	1.28
P			0.001	0.004	0.32	0.35	0.25	0.35	0.012	0.02	0.1
Patient group											
	1	2	1	2	1	2	3	1	1	2	1
R_R	0.835	0.8215	0.8767	0.8646	0.8467	0.8329	0.8344	0.8325	0.8325	0.8374	0.8367
HR	71.85	73.03	68.43	69.39	70.86	71.52	72.03	71.90	72.07	71.65	71.71
SD	0.1323	0.11	0.15	0.135	0.0132	0.131	0.126	0.124	0.114	0.124	0.116
N	15	15	15	15	15	15	15	15	15	15	15
df	14	14	14	14	14	14	14	14	14	14	14
T			2.71	2.44	4.51	0.98	0.61	0.68	0.7	0.97	1.1
P			0.02	0.05	0.15	0.2	0.3	0.3	0.25	0.3	0.1

R-R interval in sec, HR (Heart Rate) in beat min^{-1}, SD = Standard Deviation, N = No. of subjects, df = Degree Freedom, T = t-test, P = p-value and NS = Non Significant

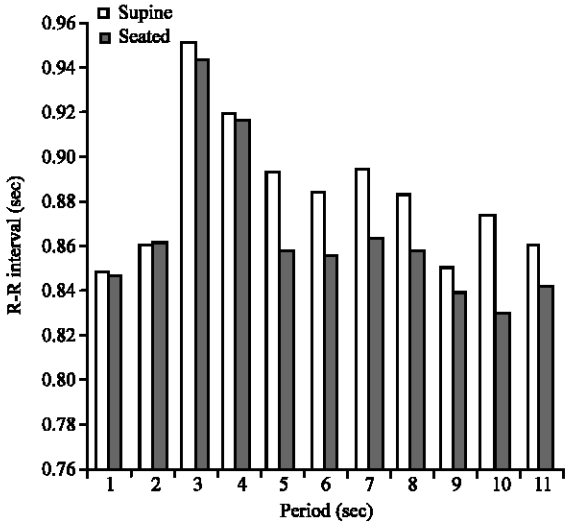

Fig. 1: Comparison of cardiac cycle in control group (seated and supine position)

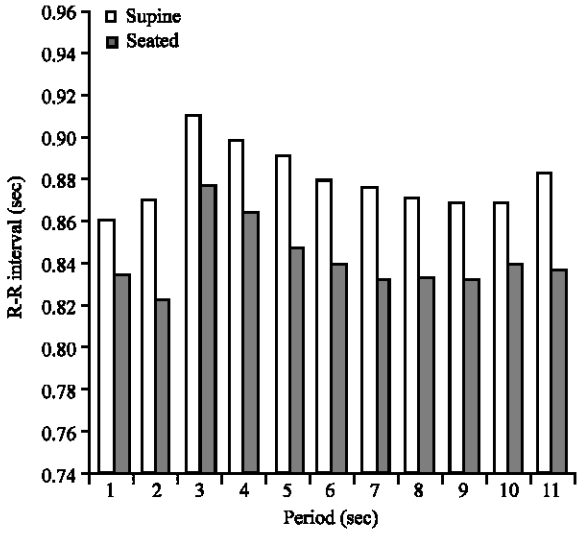

Fig. 2: Comparison of cardiac cycle in patient group (seated and supine position)

before and after stimulation was 0.8619±0.141 and 0.9439±0.136 sec, respectively. The differences was significant ($p<0.001$), but less than health subjects. Comparison of cardiac cycle duration between control group in both supine and seated position showed no differences but inpatients group, this differences was significant (Fig. 1, 2).Comparison of means in both groups were significant ($p<0.001$). There was no differences between Inferior and Anterior MI. Regression of BRS and age was significant ($p<0.001$), but this was little in patient group. Regression of BRS and time was statistically significant in both group ($p<0.01$ and $p<0.001$ for patient and control).

Tables showed that after stimulation of carotid, BRS increased in both groups and after stopping the stimulation, BRS decreased.

Figures show that R-R interval changing (in control subjects and in two positions) are less but in MI patients the changings are high. This shows that cardiac cycle alters in different positions in MI patients but in healthy subjects are stable.

DISCUSSION

This research was performed on patients with the first cardiac attack. Present results are consistent with

findings of others (Takeshita and Matsuguchi, 1980; Kelly *et al*., 1973; Minisi *et al*., 2003 ; Bennett and *et al*., 1980; La Rovere *et al*., 2002). Acute myocardial ischemia attenuated the baroreflex-mediated reduction in heart rate response to arterial pressure increases. The baroreflex slope reduces in ischemia (Takeshita and Matsuguchi, 1980). Indirect clinical evidence suggests that baroreflex function is impaired by MI. Heart rate response to negative pressure was attenuated in patient one year after MI and baroreflex slope reduces (Bennett *et al*., 1980). patients with the most advanced heart disease have the smallest heart rate reduction (Mircoli *et al*., 2002). In present study this observed after two months and it observed in patients that have the little change with stimulation.

There are different methods for stimulating of carotid baroreceptor in order to assessing of response. One of them is phenylepherin injection. In our study, Neck Suction Device (NSD). Eckberg Model, was used. (Eckberg, 1975). This method is not invasive and dangerous. In spite of other methods (such as Valsalva maneuver and phenylepherin injection), suction of neck wall not only cause optimal increasing of pressure in the vessels, but also has no side effects on the other systems. The phenyepherin injection has two inherent limitation. First, it treats R-R interval arterial pressure curve as a linear rather than a sigmoidal function. Therefore, arterial pressure elevations that occur within either the threshold or the saturation portions of the curve produce smaller calculated slope than do pressure changes confined to the linear portion of the curve. Second, drugs that increase arterial pressure by vascular smooth muscle excitation will also cause the smooth muscle layers that contain the pressure receptor units to contract, thereby altering the baroreceptor firing pattern or frequency (Eckberg, 1980).

Breath holding in the end of expiration has no effect on heart rate (Larovere *et al*., 1988; Eckberg, 1975). Stimulation of arterial baroreceptors decreases of stroke volume in left ventricle and by this way; blood pressure and heart rate are modulated.

Present results showed that, control of blood pressure is suppressed in MI patients. The cause of this isn't clear, but there are three probable mechanisms.

First, carotid baroreflex sensitivity in healthy subjects is due to discharging of vagal nerve and increased cardiac responsibility to vagal input (Gress *et al*., 1992) that is damaged by vagotomy but isn't altered by symphatetic blockage (Barney, 1988).

Second, in Mi, a part of heart has necrosis, so this area does not contract and the shape of heart has been changed. Also, declined contraction can decrease the velocity of arterial pressure that affect carotid sinus discharging and aortic nerves (Eckberg and Slehgt, 1992).

Third, there are afferent sensory receptors in heart that has been damaged in necrosis area. Cardiac compliance and receptors activities have been decreased (Mancia and Gress, 1995; Peter *et al*., 1988).

It seems that diminished BRS reflects the decreased vagal activity and increased symphatetic effects. This sensitivity is related to releasing of Epinephrine (Rundquist *et al*., 1997; Billman *et al*., 1982).

Although reflex alternations in baroreflex function may be important during acute myocardial ische- mia, they probably contribute very little to the changes after MI. Thehemodynamicconsequences of MI may contribute more to baroreflex slope reduction. MI decreases the upstroke velocity of systolic arterial pressure (Bishop *et al*., 1974) which is an important determinant of carotid sinus nerve activity (Kirchheim, 1976) and the baroreceptor reflex.Alterations in upstroke velocity may therefore, contribute significantly to the reduction of baroreflex slope after MI (Eckberg and Sleght, 1992; Donilowicz *et al*., 2004; Schwartz and Wolf, 1978; Randall *et al*., 1979; Scher *et al*., 1972).

Present results demonstrate that the capability of reflexly decreasing heart rate in response to increases in arterial pressure is markedly reduced after MI.

Baroreflexes and sudden death: BRS for both groups were different, which immediately suggested a difference in the autonomic control of the heart in these groups. A strict relationship between baroreceptor reflexes and vulnerability to ventricular fibrillation is logical on the basis of current knowledge. A steep baroreflex slope in response to an increase in blood pressure reflects primarily the activation of vagal efferent nerve fibers (Eckberg, 1980) coupled, to some extent, with reduced sympathetic efferent activity. Thus, healthy subjects seem to have a greater capability to reflexly increase their vagal tone than the MI patients (Donilowicz *et al*., 2004; Schwartz and Wolf, 1978; Randall *et al*., 1979; Scher *et al*., 1972).

The enhanced vagal tone decreases susceptibility to ventricular fibrillation. The vagal activation can oppose the decrease in the ventricular fibrillation threshold induced by sympathetic stimulation (Kolman *et al*., 1975). Moreover, the vagal stimulation antagonizes the increases in ventricular vulnerability associated with either coronary occlusion (Lown and Verrier, 1978) or psychological stress (Verrier, 1980). The association between high sympathetic activity and increased vulnerability to ventricular fibrillation is well established (Verrier and Lown, 1981). Thus, the analysis of the autonomic reflexes induced by baroreceptor activation allows for the identification of patients that are either more or less vulnerable to ventricular fibrillation triggered by acute myocardial ischemia (Eckberg and Sleght, 1992).

Clinical application: In the present study, patients followed 3 months. Two patients had re-MI. the BRS of these patients showed the lowest BRS. Decreased BRS cause re-MI and ventricle fibrillation (Gress *et al*., 1992; Larovere *et al*., 1988). Present results and other researches confirms that (Eckberg, 1975) assessing of BRS in MI patients is necessary (Eckberg and Sleght, 1992). Baroreflex testing can be used to predict the results of interaction between vagal and sympathetic reflexes. Identifying MI patients at high risk for sudden death by their cardiac autonomic response to changes in blood pressure merits careful examination.

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