ORTHOSTATIC HYPOTENSION PREDICTS THE EARLY MORBIDITY AND MORTALITY IN PATIENTS WITH ISCHEMIC HEART DISEASE IN CORONARY CARE UNIT

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ABSTRACT

Background: The mechanism by which the orthostatic hypotension and cardiac autonomic neuropathy increase cardiovascular morbidity and mortality remain to be settled. Some studies found exercise intolerance in patients with cardiac autonomic neuropathy with a reduced response in heart rate and blood pressure and decreased cardiac output during exercise. An association between cardiac autonomic neuropathy and QT prolongation has been shown.

Objective: To asses the role of the orthostatic hypotension in the development of the early cardiovascular complications in the patients of the coronary care unit.

Patients and method: In this a prospective observational follow up study, (50) patients with ischemic heart diseases were included. Blood pressure was measured with the standard mercury sphygmomanometer, the measurement in supine position was taken after at least 15 minutes of rest and the measurement in standing position was taken at the third minutes of standing, the orthostatic hypotension is said to be present when there was a sustained drop in systolic (≥ 20 mmHg) or diastolic (≥ 10 mmHg) blood pressure at the third minute of standing up.

Results: Out of twenty two patients with orthostatic hypotension fifteen patients developed cardiovascular complications and out of twenty eight patients without orthostatic hypotension five patients developed cardiovascular complications, this association is statistically significant

Conclusion: Orthostatic hypotension can be used as a prognostic marker for the development of early adverse outcomes in patients with acute coronary syndrome, thus it can be useful tool to screen the high risk patients in the coronary care unit.

Key words: orthostatic hypotension, complication of MI, IHD, DM.

Abbreviations:

ACE – I: angiotensin converting enzyme inhibitor
ARBs : angiotensin receptor blockers
OH : orthostatic hypotension

INTRODUCTION

Definition of orthostatic hypotension:

Orthostatic hypotension is defined as a sustained drop in systolic (≥ 20 mmHg) or diastolic (≥ 10 mmHg) blood pressure within 3 minutes of standing up."[1]"

Prevalence of orthostatic hypotension:

The prevalence of orthostatic hypotension varies substantially, depending on the methods used for detection and the groups being studied.

Most studies have been in selected population referred to a clinic for evaluation of syncope or dizziness in which prevalence estimates are relatively high > 30%. "2"Epidemiological data indicate that orthostatic hypotension has a prevalence of 4% to 33% in community dwelling elderly populations. "2, 3, 4"

Pathogenesis and causes of orthostatic hypotension:

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Symptomatic orthostatic hypotension is caused by a failure of the normal compensatory mechanism."[5"] The major compensations on assuming upright position are triggered by the drop in blood pressure in the carotid sinus and aortic arch .The heart rate increases, helping to maintain cardiac output .Relatively little vasoconstriction occur in the periphery, but there is prompt increase in the circulatory level of renin and aldosterone .The arterioles constrict helping to maintain the blood pressure."[6"]

Causes of orthostatic hypotension:

1-aging: **It has been suggested that orthostatic hypotension may be a normal consequence of aging[7"]; normal aging is associated with reduction in barorecepter sensitivity and decrease cardiac responsiveness to sympathetic stimulation. [7, 8"]**

2-medications: **many drugs can cause orthostatic hypotension, including diuretics (water pills) and other drugs that treat high blood pressure; heart medications, such as beta blockers; drugs for Parkinson's disease; tricyclic antidepressants; sildenafil (Viagra), particularly in combination with nitroglycerin; narcotics; and alcohol. Other prescription and over-the-counter medications may cause low blood pressure when taken in combination with medications used to treat high blood pressure.[9"]**

***3-heart problems*: some heart conditions that can lead to low blood pressure include extremely low heart rate (bradycardia), heart valve problems, heart attack and heart failure. These conditions may cause orthostatic hypotension because they prevent the body from being able to circulate enough blood.[9"']**

***4-diabetes*: untreated diabetes can cause dehydration by causing frequent urination. This can trigger orthostatic hypotension. In addition, diabetes can damage the nerves that help send signals regulating blood pressure.[9"]**

***5-nervous system disorders* , some diseases, such as Parkinson's disease, multiple system atrophy (Shy-Drager syndrome) and amyloidosis, can disrupt the body's normal blood pressure regulation system.[9"]**

Diabetes mellitus and orthostatic hypotension:

Individual with longstanding type 1 or 2 diabetes mellitus may develop sings of autonomic dysfunction involving the cholinergic, noradrenergic and peptidergic (peptides such as pancreatic polypeptides, substance P..etc) systems .The diabetes mellitus related autonomic neuropathy can involve multiple systems including cardiovascular, gastrointestinal, genitourinary, sudomotor and metabolic systems. Autonomic neuropathy affecting the cardiovascular systems causes a resting tachycardia and orthostatic hypotension. [10"]

Complications of orthostatic hypotension : [9"]

While mild forms of orthostatic hypotension may be a nuisance, more serious complications are possible, especially in older adults. These complications include:

1-Falls. Falling down as a result of fainting (syncope) is a common complication in people with orthostatic hypotension.

2-Stroke. The swings in blood pressure with standing and sitting as a result of orthostatic hypotension can be a risk factor for stroke.

3-Mental impairment. Some research has indicated that orthostatic hypotension can damage parts of the brain, increasing the risk of some forms of dementia and other brain disorders.

Association between the cardiovascular complications and orthostatic hypotension:

The mechanism by which the orthostatic hypotension and cardiac autonomic neuropathy increase cardiovascular morbidity and mortality remain to be settled. One hypothesis involves impaired central control of respiration in patients with cardiac autonomic neuropathy [11"] , some studies found exercise intolerance in patients with

cardiac autonomic neuropathy with a reduced response in heart rate and blood pressure and decreased cardiac output during exercise [12,13,14] . An association between cardiac autonomic neuropathy and QT prolongation has been shown, with the latter condition being characterized by adverse cardiac events. [15, 16]

Early complications of ischemic heart diseases [17]

1-Recurrent chest pain:

When chest pain recurs after acute myocardial infarction, the diagnostic possibilities include post-infarction ischemia, pericarditis, infarct extension, and infarct expansion. [17]

2-Rhythm disturbances:

Acute myocardial infarction is associated with a proarrhythmic environment that includes heterogeneous myocardial ischemia, heightened adrenergic tone, intracellular electrolyte disturbance, lipolysis and free fatty acid production, and oxygen free radical production on recanalization. Arrhythmias thus are common early during acute myocardial infarction. Micro-re-entry is likely the most common electrophysiological mechanism of early phase arrhythmias, although enhanced automaticity and triggered activity also are observed in experimental models. [17]

3-Heart failure and Other low-output states:

Cardiac pump failure is the leading cause of circulatory failure and in-hospital death from acute myocardial infarction. Manifestations of circulatory failure can include a weak pulse, low blood pressure, cool extremities, a third heart sound, pulmonary congestion, oliguria, and obtundation. However, several distinct mechanisms, hemodynamic patterns, and clinical syndromes characterize the spectrum of circulatory failure in acute myocardial infarction. Each requires a specific approach to diagnosis, monitoring, and therapy. [17]

4-Mechanical complications:

Mechanical complications usually occur within the first weeks and account for approximately 15% of myocardial infarction-related deaths. Such complications include acute mitral valve regurgitation, ventricular septal defect and free wall rupture. [17]

5- Thromboembolic complications:

Thromboembolism has been described in approximately 10% of clinical series and 20% of autopsy series, a finding suggesting a high rate of undiagnosed events. Systemic arterial emboli (including cerebrovascular emboli) typically arise from an LV mural thrombus, whereas pulmonary emboli commonly arise from thrombi in leg veins. [17]

PATIENTS & METHODS

In this prospective observational follow up study, (50) patients with ischemic heart diseases were included. The diagnosis of ischemic heart diseases « myocardial infarction and angina » based on clinical and electrocardiographic findings. Thirty five patients were admitted to coronary care unit of Al - Sadr Teaching Hospital in Al - Najaf and (15) patients were admitted to coronary care unit of Ibn-Elbitar Teaching Hospital in Baghdad in the period from April 2006 to October 2007 . Twenty three patients had diabetes mellitus (based on WHO criteria for the diagnosis of diabetes mellitus).

Blood pressure was measured with the standard mercury sphygmomanometer, the measurement in supine position was taken after at least 15 minutes of rest and the measurement in standing position was taken at the third minutes of standing. Orthostatic hypotension is said to be present when there was a sustained drop in systolic (≥ 20 mmHg) or diastolic (≥ 10 mmHg) blood pressure at the third minute of standing up. On standing, participants were asked whether they were feeling any dizziness, faintness, or light – headedness and the procedure was aborted for safety reasons if necessary, this occurred very

infrequently. All patients were reviewed for smoking , antihypertensive drugs (β – blockers , ACE – I or ARB.s … etc) and for signs of peripheral neuropathy (by pin prick test , light touch and position sense) as a possible association with autonomic neuropathy . All patients were followed up daily for the development of the cardiovascular complications including heart failure , arrhythmias , shock , extension of their ischemia , others (mitral regurgitation , ventricular septal defect , thromboembolism and pericarditis) and death during the period of their admission in coronary care units with the maximum time of follow up was eight days .

Statistical study: **The statistical analyses were based on Chi – square and t – tests with a p – value of 0.05 or less was considered statistically significant.**

RESULTS

Fifty patients with ischemic heart diseases aged between (28 – 93) years (mean 56 ± 13.5), (27) patients (54 %) were males and (23)

patients (46 %) were females , out of those (50) patients , (23) patients (46 %) were diabetics , (22) patients (44 %) had orthostatic hypotension (mean age 61±13.8) and (28) patients (56 %) had no orthostatic hypotension (mean age 51±11.5). (table 1)

Out of the (22) patients with orthostatic hypotension,(15) patients (68.2%) developed different cardiovascular complications and seven patients (31.8%) passed in uneventful course during their admission in coronary care unit , while out of (28) patients without orthostatic hypotension , five patients (17.9%) developed different cardiovascular complications and (23) patients (82.1%) passed in uneventful course during their admission in coronary care unit , statistically there was a significant effect of orthostatic hypotension on the development of the complication.

(p < *0.05)*. (table 2)

When we studied the combined effects of the orthostatic hypotension and diabetes mellitus on the development of the cardiovascular complications, statistically there was no extra risk of diabetes and orthostatic hypotension over the orthostatic hypotension alone on the development of the cardiovascular complications.

(p – value > 0.05) (table 3).

The incidence of the different cardiovascular complications, rhythm disorders, heart failure, shock, extension of preexisting ischemia, death and others (mitral regurgitation, ventricular septal defect, thromboembolism and pericarditis) were more frequent in patients with orthostatic hypotension than those without orthostatic hypotension (18 vs. 8) and statistically significant (p – value < 0.05). (table 4).

DISCUSSION

Orthostatic hypotension was an important and common problem in the coronary care unit patients (44%) especially in elderly (34%) and diabetic patients (28 %). Age is one of the most important factors in the aetiology of orthostatic hypotension, next coming factors are the antihypertensive drugs and diabetic autonomic neuropathy while sex had limited role. Some authors claimed smoking, but found no significant effect on orthostatic hypotension. "[18]" However in this study , the presence of the orthostatic hypotension increased with the age , we did not find significant effect of age and antihypertensive drugs probably due to small number of patients and that all patients were in complete bed rest that might play a role in orthostatic hypotension .

In the present study, we found significant relation between orthostatic hypotension and appearance of cardiovascular complications and death, during the follow up period of (2 – 8 days) in the coronary care unit.

Many researchers studied the relation ship between the orthostatic hypotension

and the morbidity and mortality both in elderly and young patients and in diabetics and non – diabetics and all found significant effect of orthostatic hypotension. Heikkil and K.E.Juhani (2004) concluded that diabetics with orthostatic hypotension carry a high risk vascular death. "18" In our study we did not observe the interaction between the orthostatic hypotension and diabetes mellitus for the increment of the morbidity and mortality, similar results had been observed by Kamal H. et al "19" suggesting that diabetes mellitus increased the mortality through the orthostatic hypotension and associated autonomic neuropathy.

The mechanism by which the orthostatic hypotension increases the cardiovascular morbidity and mortality is probably related to the associated autonomic dysfunction that leads to reduce response in heart rate and blood pressure and decrease in the cardiac output during exercise. Another factor is the association between the cardiac autonomic neuropathy and prolongation of QT interval, which lead to adverse cardiac events. "15, 16"

The limitations of our study were: the small number of the patients, short time of follow up and the need for other tests to detect signs of autonomic dysfunction and this may be due to the short time of the study, limited facilities and serious state of the patient.

CONCLUSION

Orthostatic hypotension can be used as a prognostic marker for the development of early adverse outcomes in patients with acute coronary syndrome, thus it can be useful tool to screen the high risk patients in the coronary care unit.

Tables

Table1: Factors which are affecting the orthostatic hypotension.

Characteristics		Patients without orthostatic hypotension N = 28 (56%)	Patients with orthostatic hypotension N = 22(44%)
Age	<50	7	5
	>50	21	17
Sex	Male	16	11
	Female	12	11
Diabetes mellitus		9	14
Peripheral neuropathy		4	11
Smoking		17	13
Antihypertensive Drugs	B- blocker	9	10
	ACE– I ARB.s	6	10

P > 0.05

Table2: The relation between the orthostatic hypotension and the cardiovascular complications

Patients	Complicated patients	Uncomplicated patients
Patients with orthostatic hypotension N=22	15 (68.2%)	7 (31.8%)
Patients without orthostatic hypotension N=28	5 (17.9%)	23 (82.1%)

P <0.05

Table 3: The effects of orthostatic hypotension and diabetes mellitus on the complications

Patients	Complicated Patients	Uncomplicated patients
Diabetic patients with orthostatic hypotension N= 14	10 (71.4%)	4 (28.6%)
Diabetic patients without orthostatic hypotension N= 9	6 (66.7%)	3 (33.3%)

P > 0.05

Table 4: Occurrence of different complications in relation to orthostatic hypotension

Complications	Patients with orthostatic hypotension	Patients without orthostatic hypotension
Rhythm disorders	4	0
Heart failure	7	4
Shock	1	1
Extension of ischemia	1	0
Others*	2	2
Death	3	1
Total	18	8

P < 0.05

*** mitral regurgitation, ventricular septal defect, thromboembolism and pericarditis.**

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