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REVIEW ARTICLES

Cardiac syndrome X – a challenge for Cardiologist

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Abstract

Cardiac syndrome X is a multifactorial disorder. A triad of angina pectoris, positive exercise tolerance test (ETT) and angiographically normal epicardial coronary arteries, is called Cardiac syndrome X. Though the normal epicardial coronary arteries, patients present with debilitating chest pain which increases morbidity and poor quality of life. The particular cause of Cardiac syndrome X is still unknown. Many large trails are on going to detect exact pathogenesis of this condition. A multiple treatment regimens may reduce the morbidity and improve the quality of life of these patients.

Key words : Angina pectoris, exercise tolerance test.

Introduction

Cardiac syndrome X, a triad of angina pectoris, positive ETT and angiographically normal coronary arteries, is still a mystery to researchers as they have been trying to explore the cause for almost four decades. Patients suffer from debilitating chest pain which hampers quality of life but prognosis is better than other cardiovascular disease by drug therapy.[1]

Pathogenesis

There are many factors which may contribute to cardiovascular symptoms in Cardiac syndrome X patients, such as existence of underlying myocardial ischaemia, endothelial dysfunction, abnormal pain perception, hormonal imbalance and insulin resistance.

Myocardial ischaemia

Underlying myocardial ischaemia has been focused by researcher as a physiological cause of cardiac syndrome X. Patient who had abnormal vasodilator reserve showed a higher coronary resistance, a higher left ventricular end-diastolic pressure and reduced left ventricular ejection fraction during exercise compared with appropriate vasodilator reserve. Therefore myocardial ischaemia occurs in patients with angiographically normal coronaries.[2] Abnormalities of coronary microcirculation is another causal factor for myocardial ischaemia.[3] The vascular resistance after ischaemia was found to be consistently higher in cardiac syndrome X patients in a trial.[4] Phosphorus-31 nuclear magnetic resonance spectroscopy was used to demonstrate the existence of myocardial ischaemia by identifying metabolic and haemodynamic evidence of ischaemia in women with cardiac syndrome X.

In this case control study, Buchthal et al. demonstrated significant reduction in myocardial metabolite in 20% cases than control group.[5] But majority of patients with chest pain have no metabolic abnormality. So, myocardial ischaemia may be a factor in a few patients with syndrome X.

In another case control study, Cardiac magnetic resonance (CMR) was used to detect myocardial perfusion index. After injecting adenosine, myocardial perfusion index was increased in subendocardial and subepicardial layer in control group but only in subepicardial layer in cases. By this

way myocardial ischaemia was detected in cardiac syndrome X patients.[6]

Endothelial Function

Impaired endothelial function might be a cause of chest pain in cardiac syndrome X patients. Egashira et al. used intracoronary acetylcholine in a case control study which suggested impaired endothelial-dependent vasodilation in cases with syndrome X.[7]

Another case control study demonstrated that flow mediated vasodilatation was markly reduced in both cardiac syndrome X and coronary heart disease patients than that of normal controls.[8]

C-reactive protein (CRP) which is a marker for chronic inflammation increases with the development of vascular atherosclerosis. Ridker et al. found a relation of CRP with endothelialdysfunction.[9] Another author observed increased number of ischaemic episodes in cardiac syndrome X patients with high levels of C-reactive protein by 24 hours holter monitoring.[10]

Pain perception

Panting et al. found 90% of cardiac syndrome X patient experienced severe pain after using adenosine in their case control study by using CMR. On the other hand only 40% of control group reported some discomfort.[6] Pain threshold and tolerance were found to be lower in syndrome X group after giving external pain stimulus.[11] Eighty- one percent of cardiac syndrome X patients had pain during catheter manipulation in compare to patients with significant coronary artery. Only 6% experienced pain.[12]

Insulin resistance

Insulin resistance may have influences on endothelial dysfunction in cardiac syndrome X patients. In a case control study, it has been found that 40% reduction of glucose uptake in syndrome X patients than normal control group.[13] Dean et al. found that a glucose tolerance test provoked hyperinsulinaemia in cardiac syndrome X patients in compare to control group.[14] But in another study researchers found no difference in glucose uptake by insulin in between cases and controls.[15] So, it has not established that insulin resistance is a causal factor for syndrome X.

Hormonal changes in menopause

The prevalence of cardiac syndrome X is higher in menopausal women.[16] Changes in ovarian hormones during menopause may contribute to the pathogenesis of cardiac syndrome X patients. Other researchers found a relationship between syndrome X and oestrogen deficiency in postmenopausal and hysterectomised patients who had presented with cardiac syndrome X.[17] A group of investigator identified that hormone replacement therapy (HRT) decreased frequency angina pain in post menopausal cardiac syndrome X patients. 17b oestradiol was used as therapy in this study.[18]

Treatment of Cardiac syndrome X

Nitrates (sublingual, dermal and oral), Calcium channel blockers (diltizem, amlodipine, nifedipine etc.) and potassium channel openers (nicorandil) are frequently used to reduce pain in cardiac syndrome X. Investigators found that Nitrate is useful in controlling chest pain in about 50% cases of cardiac syndrome X patients in an observational study.

In another study 17- Beta-estradiol therapy was used to lessen angina in post menopausal women with cardiac syndrome X and this therapy showed good result.[18] Various hormone-replacement therapies have showed the reduction of angina frequency and severity, while others have shown little or no symptomatic effect. Many trials are on going to establish the efficacy of this therapy.

Calcium channel blocker (Nifedipine) was used in a observational study which evoked impaired coronary vasodilator response in cardiac syndrome X patients in compare to patients with coronary artery spasm.[19]

Atenolol had showed significant improvement of chest pain in cardiac syndrome X patients in comparison to Amlodipine and Nitrate in a double-blind crossover trial.[20]

Conclusion

Cardiac syndrome X patients suffer a lot which have no particular cause. Many researches are still in progress to identify the cause of this debilitating disorder. Traditional anti angina drugs are used to control the chest pain of these patients. Despite of poor quality of life long time prognosis is good in cardiac syndrome X patients.

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