

ACS Prevention: “The Endothelial Way”

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Abstract

ACS (Acute coronary syndrome) is characterized by sudden development of anginal symptoms in less than 24 hours. The healthy endothelium allows normal coronary blood flow due to its anti-thrombotic properties. This property can be used to prevent ACS. Endothelial dysfunction has pivotal role in development of ACS. ATP (Adenosine tri phosphate) mismatch in the endothelial cells is the primary reason for endothelial dysfunction. Increased basal sympathetic discharge & sudden change in BMR (basal metabolic rate) produces ATP mismatch. Increased basal sympathetic discharge results from mental exhaustion, stress & is associated with fast desynchronized rhythm(beta) in EEG. Normalization of basal sympathetic discharge by reducing mental work, adequate sleep & avoidance of exposure to sudden environmental temperature change will prevent sudden BMR change & changes in ATP requirement. Both measures can prevent endothelial dysfunction & ACS. Substances like Amla (*Phyllanthus emblica*), and diet rich in nitric oxide also strengthens endothelium, is helpful in preventing ACS.

Keywords: Acute coronary syndrome; ATP metabolism; Basal sympathetic discharge; BMR; Endothelial dysfunction

Introduction

“The healthy endothelium takes care of the coronary blood flow & heart”

Acute Coronary Syndrome (ACS) is portrayed by the quick onset of symptoms or findings of Unstable Angina (USA), ST-Elevation Myocardial Infarction (STEMI), or Non-ST-Elevation Myocardial Infarction (Non-STEMI) in previously symptomless individuals, typically less than 24 hours i.e. a person is asymptomatic one day back and becomes symptomatic very next day [1]. Critical narrowing in coronary vessels becomes more critical abruptly due to a sudden severe endothelial dysfunction resulting in ACS. There is impaired vasodilation, rupture of atherosclerotic plaque in coronary vessels, and appearance of anginal symptoms. The healthy endothelium permits normal coronary blood flow has antithrombotic, antiplatelet & profibrinolytic properties & checks the formation of atherosclerotic plaques and ACS. This property of endothelium can be utilized to prevent ACS. Unhealthy endothelium/endothelial dysfunction has converse features. The normal functioning of endothelium requires adequate availability of cellular ATP (Adenosine triphosphate) [2-12].

Methods

A brief discussion is being done to summarize various factors leading to unhealthy endothelium & the preventive aspects of the related factors. Reference studies used for this purpose are [1-37].

This review has been divided into the following heads

Factors responsible for ACS & preventive strategy

Three main factors leading to endothelial dysfunction & ACS are the following-

- a) Atherosclerosis risk factors [13-17]
- b) Sudden severe endothelial dysfunction (superimposed increase in sympathetic discharge, over pre-existing high basal sympathetic discharge) [18-20]

- c) Sudden change in BMR (basal metabolic rate/ATP requirement)) [21-23]

The preventive strategy focuses on curbing these factors responsible for endothelial dysfunction/unhealthy endothelium & ACS.

Pathophysiology of ACS

Endothelial dysfunction is marked by the development of atherosclerotic plaques. Severe endothelial dysfunction results in ACS, when stable atheromatous plaques convert to unstable plaques, that rupture into the lumen of the coronary artery, causing a sudden reduction in blood flow to the heart. The inability of arteries and arterioles to dilate leads to anginal symptoms [6].

Factors responsible for ACS

- a) Atherosclerosis- multiple atherosclerosis risk factors lead to plaque formation (chronic process) & narrowing of coronary vessels. Atherosclerosis is a steady process therefore it doesn't explain the sudden instability of plaque, anginal symptoms & development of ACS symptoms in an asymptomatic person [13-17, 20].
- b) Sudden severe endothelial dysfunction due to a superimposed increase in sympathetic discharge, over pre-existing high basal sympathetic discharge e.g. diabetes & hypertension. Preexisting high basal sympathetic discharge continuously produces some endothelial dysfunction & leads to the development of atherosclerotic plaques [6, 18-20].
- c) Sudden change in BMR (basal metabolic rate)- sudden change in BMR alters ATP requirement quickly & results in endothelial dysfunction [21-23]. Factors 2 & 3 produce ATP mismatch at the endothelial cellular level & convert healthy endothelium into unhealthy endothelium/endothelial dysfunction & precipitate ACS. ATP is the primary energy source for all cellular activities. "ATP unavailability /mismatch is the critical end-point for cellular/endothelial dysfunction" [6,20-25].
- d) ATP & its relation to the Sirtuin 1 gene

The role of the anti-aging gene Sirtuin 1 is important to the endothelial dysfunction and ATP mismatch for the development of ACS. Sirtuin 1 is involved in the regulation of endothelial dysfunction and ATP production. ATP has been shown to regulate Sirtuin 1 activity. Sirtuin 1 is critical to neuron function with sleep, temperature (heat shock gene sirt 1) & stress. Sirtuin 1 activators versus inhibitors are relevant [26,27].

A Brief Discussion About the Properties of Healthy & Unhealthy Endothelium

Healthy endothelium and its properties (antithrombotic nature/adequate ATP)

The healthy endothelium has adequate ATP for its functioning & receives a normal basal sympathetic discharge & normal ATP

metabolism (rate of ATP synthesis/breakdown, favoring seasonal requirements). The healthy endothelium thus carries out a crucial role in inhibiting thrombus formation, the platelet aggregation & has a profibrinolytic nature. It also maintains vascular tone according to the need for smooth blood flow in the coronary circulation [3,6,10,20,25].

Unhealthy endothelium and its properties (prothrombotic nature/ATP mismatch)

Unhealthy endothelium has ATP mismatch due to either receiving high basal sympathetic discharge or impaired ATP metabolism. (ATP production rate not favoring seasonal ATP requirement/BMR). There is a rift in the endothelial cell layer, entry of inflammatory cells, plaque rupture, impaired vasodilation & ACS [6-11].

Basal sympathetic discharge

A glimpse into its functions, origin, central connections, & clinical significance

"High basal sympathetic discharge- the principal reason for endothelial dysfunction" [6]

Definition & functions

Basal sympathetic discharge refers to the activity of the sympathetic nervous system at a basal rate and is associated with required ATP production at the cellular level. This discharge maintains normal blood pressure & heart rate. When its activity is increased basal discharge is said to be high. High basal sympathetic discharge is associated with ATP mismatch, endothelial dysfunction & ACS.

Central connections related to the origin of basal sympathetic discharge

Basal sympathetic discharge arises from the hypothalamus, (The highest center of the ANS is the hypothalamus) which in turn is influenced by various cortical areas i.e. the neocortex & cingulate gyrus & makes a physiological cortical-hypothalamic axis. The cortex, therefore has some indirect control/ modulating effect over the hypothalamus/sympathetic nervous system. Desynchronized cortical activity has poor physiological control over the hypothalamus & results in high basal sympathetic discharge [19,21,28-30].

Clinical significance

Various clinical conditions like mental stress, mental exhaustion & fast mental speed result in desynchronized cortical activity i.e. low voltage fast beta activity in EEG (electroencephalography) in an eye closure state. A spike response to the cold pressor test in SSR (sympathetic skin response) is suggestive of high basal sympathetic discharge [18,20,21,24,25].

Metabolic factors (BMR/basal metabolic rate)

Another important factor responsible for endothelial dysfunction is a sudden change in ATP requirement (BMR change).

ATP synthesis is directly proportionate to BMR. ATP metabolism (synthesis & breakdown) changes with season. ATP synthesis increases with the rise in BMR in winter & vice versa. Whenever there is a sudden change in BMR, due to a seasonal change (summer to winter, winter to extreme winter, winter to summer), or some dietary factor not suitable to the particular season, e.g. food that is hot in nature in the summer season & vice versa in the winter, there is ATP mismatch. Cells synthesize less ATP, & break more ATP to release energy in summer, on the contrary food that is hot in nature increases BMR, & ATP synthesis i.e. opposite to seasonal requirement, results in ATP mismatch & endothelial dysfunction & precipitates ACS [6, 20-24].

Prevention of ACS (keep endothelium healthy and prevent ACS)

Preventive aspects- Prevention of ACS requires a healthy endothelium (adequate ATP according to demand, no ATP mismatch) ACS is caused by two important factors one is high basal sympathetic discharge & two is ATP mismatch due to sudden BMR change. Preventive aspects require correction in both.

Correction in basal sympathetic discharge

Increased basal sympathetic discharge results from mental exhaustion/mental burn-out that results in a physiological depletion of neurotransmitters. Mental rest/adequate sleep helps in replenishing neurotransmitters. Stress results in desynchronized brain activity. Meditation, regular reading & writing synchronize the brain & result in normal basal sympathetic discharge & help in the prevention of ACS [6,21,25,28-32].

Metabolic Corrections

To keep synchronization with seasonal metabolism through

- a) Avoiding exposure to a sudden change in the environmental temperature
- b) Consumption of food favoring seasonal metabolism [6, 20, 21-23].
- c) The other methods that strengthen the endothelium & help in preventing ACS.
- d) Amla (*Phyllanthus emblica*) increases mitochondrial reserve capacity to increase ATP synthesis, & can be used in the diet [20,33-35].
- e) Food rich in nitric oxide strengthens endothelium [36].
- f) Aerobic exercises increase nitric oxide levels & support endothelium [37].

Conclusion & Suggestions

Healthy endothelium allows normal coronary blood flow. This property of endothelium can be utilized to prevent ACS i.e. To keep endothelium healthy and prevent ACS. Endothelial dysfunction due to ATP mismatch is the prime reason for the development of ACS. Two important reasons for ATP mismatch include, one increased basal sympathetic discharge resulting from mental exhaustion/

stress & two a sudden change in the BMR /metabolic change due to exposure to a sudden change in environmental temperature. Preventive strategy includes mental rest, adequate sleep & avoidance of sudden experience of changes in environmental temperature. The joint effort by an individual, employer level, the state level is required to prevent mental burn- out & ACS at a community level.

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