VICIOUS ROLE OF HIGH CALORIE DIET ON ORGAN METABOLIC SYNDROME INDUCED THROMBOCYTE, LEUKOCYTE AND ERYTHROCYTE ALTERATIONS

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Abstract

Metabolic syndrome is growing globally amongst all aged people. There is escalation of different oxidative stress parameters, pro-inflammatory markers and pro-apoptotic markers which leads to vital organ metabolic syndrome. Hepatic and renal dysfunction due to intake of high calorie diet leads to decrease in platelet count. Likewise, during vital organ metabolic dysfunctions, there is increase in infiltration of leukocytes resulting in inflammation, while the erythrocyte count decreases, accompanied by increase in red blood cell distribution width. Potential therapy for the vital organ dysfunctions due to metabolic syndrome can be thrombolytic therapy and transfusion of erythrocytes or erythropoietin. People need to rethink about their lifestyles, dietary habits, physical activity and consumption of anti-oxidant foods containing green vegetables and fruits as well as Mediterranean diet to get rid from vital organ metabolic syndrome.

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Key words: metabolic syndrome, cerebral dysfunction, cardiometabolic diseases, hepatic malfunctions, renal disorders, blood cells

Introduction

The metabolic syndrome (MetS) is a “member of the family” of cardiometabolic diseases (CMD) such as atherosclerosis, hypertension, obesity and type 2 diabetes mellitus (T2DM), non-alcoholic fatty liver disease (NAFLD) and brain, ovary and kidney disorders being their “relatives” (1-6). Major risk factors for the development of MetS are high calories intake (in form of highly lipogenic and high carbohydrate foods) and decrease in physical activity due to sedentary lifestyle (7-8). Metabolic syndrome is increasing epidemically with multifactorial aetiologies and nearly 10% - 84% population around the world is suffering from MetS (3). Western pacific and developing countries are the most affected diabetic prevalent regions. According to International Diabetes Federation, around 4.8% of world population is suffering from diabetes and by 2030, this will increase to 7.26%. In developing countries around 80% of people are diabetic (9-10).

Unnecessary intake of high-caloric diets results in T2DM which causes unfavourable effects on the central nervous system such as progress of dementia due to negative affect function of the hippocampus (brain region critically involved in learning and memory) increases risk for the development of Alzheimer's disease, diabetic encephalopathies due to insulin resistance and brain atrophy (2-3). Microglia is the cell type which activates by the consumption of high calorie diets and activation of microglia releases pro-inflammatory cytokines (11-13). Hyper-caloric nourishing leads to amplified intra hepatic triglyceride subsidies to the expansion of NAFLD (14). Non-alcoholic fatty liver disease is concomitant with corpulence, that incorporate changing degrees of steatosis,

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hepatocellular damage, and fibrosis (15-16).

Along with its “classical” fat storage function, the adipose tissue today is considered as a dynamic para- and endocrine organ composed of adipocytes, stromal-vascular and immune cells (17, 18). There are three types of adipose tissues: white adipose tissues (WAT), brown adipose tissue (BAT) and beige adipose tissue. Due to urbanisation and industrialisation, and intake of high calorie diet increases accumulation of adipose tissue which causes hypertrophy and/or hyperplasia of adipocytes and down-regulates uncoupling protein-1 (UCP-1) thus thermogenesis will slump down (19-21). Activation of WAT leads to dysfunction in the secretion of adipokines, multifunctional signaling proteins (22-27). There is escalation of free fatty acids (FFA) and pro-inflammatory mediators like tumour necrosis factor- α (TNF- α) and interleukin-6 (IL-6), plasminogen activator inhibitor-1 (PAI-1) and C-reactive protein (3). Metabolic syndrome is associated with microvascular dysfunction due to activation of endothelial cells, leucocytes and platelets (28-31).

Oxidative stress escalates during intake of high calorie diet that mirrors an imbalance between the reactive oxidative free radicals and detoxification of responsive intermediates or to repair the subsequent harm (32). Dispute in the typical reduction and oxidation condition of cells results in increase in the generation of peroxides and free radicals that harm all constituents of the cell, including proteins, lipids, and DNA (33-34). Oxidative stress plays pivotal role in different CMD, since oxidation of LDL in the vascular endothelium is a precursor to develop atherosclerotic plaque and results in coronary artery disease (35-37).

Apoptotic markers like caspases (categorised as initiator Caspase 2, Caspase 8-10) and executioner (Caspase 3, Caspase 6, 7) carry the apoptosis process through intrinsic and extrinsic pathways (38-39). When initiator caspases are enacted, they develop a chain response, actuating a few other killer caspases (40). Some studies have demonstrated that diet induced obesity increases caspase activation and adipocyte apoptosis (41). These changes are linked with increase in intrinsic and extrinsic pathways which are mitochondrial receptor intervened pathways of apoptosis (42). Restraint of adipocyte apoptosis can bring about another objective for the heftiness related metabolic entanglements (43-44).

Increased levels of saturated long chain fatty acids (LCFAs) activates caspase-2 results in cell death. Accumulation of LCFAs in non-adipose tissues have shown lipoapoptosis. LCFA-instigated lipoapoptosis influenced in numerous cell sorts, including hepatocytes, cardiomyocytes, proximal tubule cells in the kidney, and islet beta cells in the pancreas (45). Lipoapoptosis

has assumed critical part in the pathogenesis of a few metabolic infections, including NAFLD, T2DM and CMD (45). Lipoapoptosis shows trademark highlights of the characteristic apoptotic pathway which incorporates mitochondrial permeabilisation, cytochrome c discharge and effector caspase enactment (46-47). Upon actuation of cytochrome complex with apoptotic protease activating factor (apaf-1) bringing about the initiation of caspase – 9. This complex, named the apoptosome that separates and actuates the killer caspases (caspase-3 and 7). This enactment of caspase brings about the cellular demise (48-49).

Role of high calorie diet on oxidative stress and inflammatory dysfunction induced alteration of platelets

Platelets play an important role in inflammatory response which cross talk between platelets and other cells that participate in the inflammatory response is a more robust reaction of the microvasculature and other tissue components to inflammatory stimuli (50). Platelets add to provocative signs of various procedures that underlie the tissue injury (51). Platelet adhesion increases frequency of thrombosis in intense and interminable irritative conditions, actuates vascular endothelial cells and leucocytes in microvessels (52-53). Lipid mediators (e.g. platelet activating factor), cytokines like interferon- γ (IFN- γ), and ILs and chemokines are cases of mediators that can actuate platelets and assembly of platelet linkage atoms hold fast to whole microvasculature (54). The microvascular endothelial injury, described by impeded in vasodilatation of arterioles, leucocyte and platelet work in post-capillary venules, expanded oxidative anxiety (55).

Role of high calorie diet on vital organ dysfunctions induced alteration of platelets

Alzheimer's disease (AD) is most common problem with higher intake of calories and results in vascular injury. Besides atherosclerosis, inflammation is also the major culprit for neurodegenerative disorders (56). Platelet-induced chronic inflammation results in atherosclerosis and promotes plaque development. Mean platelet volume (MPV) and platelet count (PLC) can be estimated in various cerebral dysfunctions (57). Fundamental to the pathogenesis of occlusive blood vessel sickness is the enactment of platelets at locales of vascular damage by means of pathologically misrepresented and deregulated variants of the defensive systems associated with haemostasis (58). Mean platelet volume (MPV), the most usually utilised measure of platelet estimate, is a potential marker of platelet reactivity. Lifted MPV is related with extended platelet aggregation, extended thromboxane accumulation and β -thromboglobulin release. In addition, higher MPV is found in patients with

diabetes mellitus, hypertension, hypercholesterolemia, smoking, and corpulence (59). Real examinations exhibited that hoisted MPV was related with a higher rate of restenosis after coronary angioplasty (60). Evaluating MPV and platelet count data in patients with acute coronary syndrome had lower counts and larger platelet volumes in comparison to those with stable angina (61-62). Chronic liver disease refers to a long-term compulsive process of metabolic diseases, hepatotropic viruses, drug abuse and autoimmune disorders (63). Chronic liver disease results in decrease in production of thrombopoietin (TPO) which results in thrombocytopenia (64). Due to liver dysfunction, there is destruction of platelets from spleen (65). Thrombocytopenia aggravates hepatic destruction and contributes in different pathophysiological conditions of liver (66). Infusion of platelets assume a critical part in advancing liver recovery. In case of liver cirrhosis, NAFLD and NASH (non-alcoholic steatohepatitis), we can augment the platelet count using TPO-R agonists (46). Several studies showed the decrease of platelet count in renal failure (67-68). The decrease of platelet count and mild thrombocytopenia in patients with chronic renal failure (CRF) results in high risk of bleeding due to thrombocytopenia and platelet dysfunction (69-70).

Role of high calorie diet on vital organ malfunctions induced alteration of leukocytes

White blood cells (WBC) count will increase in patients having trauma due to decrease in blood supply (71). The leukocyte count is a marker of inflammation. Leukocytosis is an independent predictor of cardiovascular dysfunctions like stable angina, unstable angina and myocardial infarction (72-73). Elevation of eosinophil, neutrophil, and monocyte checks anticipate the rate of chronic heart disease. Leukocytosis influences chronic heart disease that intercedes aggravation, make proteolytic and oxidative harm to the endothelial cells, instigate hypercoagulability, and advances infarct development (74-76). The most astounding neutrophil accumulation is the indicator for early atherosclerosis (vascular brokenness) perceived cardiovascular risk factors; like dyslipidemia (77). White blood cells will elevate in patients who are suffering from chest pain and early coronary artery disease. Leukocyte count is key marker even if individual have lower risk of atherosclerotic disease (78--79). Ischemia and hypoxia to liver results in cellular death that results in apoptosis and necrosis. There will be generation of ROS which increases kupffer cells and increases infiltration of leucocytes are the key marker of inflammation (80-81). Neutrophil-inferred myeloperoxidase can improve macrophage cytotoxicity and incite neutrophil actuation in a NASH (82). Neutrophil-to-lymphocyte ratio is greater in NASH and related fibrosis (83). Neutrophils will in-

crease because of oxidative stress and decreased phagocytic limit. Pro-inflammatory mediators such as TNF- α , IL-1, IL-8 and lipid peroxidation products results in neutrophil extravasation into the hepatic parenchyma (84-86). In acute kidney injury and acute tubular necrosis, there is increase in leukocyte infiltration (87-88). There is escalation of leukocyte attachment particles like intercellular adhesion molecule 1, and P and E-selectin on endothelial cells during cellular injury (89). Leukocytes infiltration results in increase in NADPH oxidase activity and increases superoxide anion generation in acute kidney injury (90, 91).

Role of high calorie diet on vital organ impairments induced alteration of erythrocytes

Increase intake of high calorie diet results in hypoxia that leads to global cerebral ischemia and T2DM induced Alzheimer's disease, this is due to impairment of red blood cells (RBC) (92). Transfusion of RBC helps to mitigate the hypoxia induced cerebral injury (93-94). There is significant increase in RDW which predicts vascular ischemia (95). Erythropoiesis is significantly impacted by numerous inflammatory cytokines, oxidative stress, dyslipidemia and expanded RBC turnover in various cardiovascular disorders for example, patients with stable coronary artery disease (95-96). In contrast to the inflammatory markers and oxidative stress, RDW provides valuable information concerning prognosis in patients with coronary artery disease (79). Hepatic injury decreases formation of folic acid and vitamin B12, results in decrease in absorption of iron and decreases haemoglobin (Hb) level. Exogenous administration of vitamin B9 and B12 helps to increase Hb level (97).

Conclusion

Potential therapy for the vital organ dysfunctions due to MetS can be thrombolytic therapy and transfusion of erythrocytes or erythropoietin. Some naturally available plants will helps to increase platelet count, anti-atherogenicity, and increases erythropoiesis during vital organ MetS.

Intake of *Tinospora cordifolia*, *Carica papaya*, *Beta vulgaris* and *Chinese gooseberry* will help to increase platelet count that mitigate hepatic and renal disorders. *Tinospora cordifolia* and *Chinese gooseberry* are also anti-atherogenic by reducing the low density lipoprotein and increasing high density lipoprotein levels. *Beta vulgaris* helps to release nitrate which can be useful in platelet reactivity and restenosis and beneficial in myocardial infarction. *Carica papaya* and *Beta vulgaris* also helps in erythropoiesis.

We need to rethink about our lifestyles, dietary habits, physical activity and consumption of anti-oxidant foods containing green vegetables and fruits as well as Mediterranean diet to get rid from vital organ MetS.

Conflict of interest

The authors declare no conflict of interest.

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