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Sanal Flow Choking Leads to Aneurysm, Hemorrhagic Stroke and other Neurological Disorders in Earth and Human Spaceflight: New Perspective

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Abstract

Evidences are escalating on the diverse neurological disorders associated with COVID-19 pandemic. The theoretical discovery of Sanal flow choking is a paradigm shift in the diagnostic science of asymptomatic stroke causing neurological disorders in earth and at the microgravity condition (human spaceflight). A critical review has been carried out herein for correlating the phenomenon of Sanal flow choking (PMCID: PMC7267099) and hemorrhagic stroke. Herein, we show that when systolic to diastolic blood pressure ratio (BPR) reaches the lower critical hemorrhage index (LCHI) the internal flow choking and shock wave generation occurs in the downstream region of the vessels, with sudden expansion, divergence, bifurcation, stenosis and/or occlusion, leading to pressure overshoot causing brain hemorrhage and/or neurological disorders. The critical BPR for internal flow choking is uniquely regulating by the biofluid/blood heat capacity ratio (BHCR). The BHCR is well correlated with BPR and blood viscosity. The closed form analytical model reveals that the relatively high and the low blood viscosity are risk factors of internal flow choking causing aneurysm and hemorrhagic stroke. In vitro data shows that fresh blood samples of healthy subjects evaporate at a temperature range of 37°C-40°C (98.6°F-104°F) and generate carbon dioxide, nitrogen, and oxygen gases in the vessel. The single phase in silico results demonstrated the occurrence of Sanal flow choking and pressure overshoot causing memory effect (stroke history) leading to progressive neurological disorders. We concluded that disproportionate blood thinning medication increases the risk of flow choking causing hemorrhagic stroke. The risk of brain hemorrhage and various types of neurological disorders in COVID-19 patients and others in earth and microgravity environment could be diminished by concurrently lessening the viscosity of biofluid/blood and flow turbulence by increasing the thermal tolerance level in terms of BHCR and/or by decreasing the BPR. The effect of Sanal flow choking is more severe in blood vessels with divergent/bifurcation regions because it leads to the shock wave generation and the transient pressure overshoot causing irreversible neuronal damage forming the core of infarction. We concluded that, for a healthy life all subjects with high BPR inevitably has high BHCR for reducing the risk of the internal flow choking (biofluid/Sanal flow choking) triggering neurological disorders as results of infraction.

Keywords: BHCR • Biofluid choking • COVID-19 • Hemorrhagic stroke • Neurological disorders • Risk factors • Sanal flow choking

Introduction

Evidences are escalating on the diverse neurological disorders associated with COVID-19 pandemic. It is reported that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might be more likely to cause thrombotic vascular events, including stroke, than other coronavirus and seasonal infectious diseases [1]. The epidemiology of COVID-19 stated that the susceptibility of the coronavirus infection was found in all age people. Studies further reveal that elderly people with comorbidities are at risk for severe disease [1]. The reported incidence of cerebrovascular disease in patients testing positive for SARS-CoV-2 ranges from 1% to 6%, potentially equating to large numbers of individuals as the pandemic progresses in some countries [2,3]. The large vessel stroke and the increased incidence of cryptogenic stroke in multiple regions have been reported in COVID-19 patients [4,5]. Of late V.R.S.Kumar et al. [6-9] reported that hemorrhagic strokes in multiple regions of various blood vessels causing neurological disorders are due to internal flow choking (biofluid/Sanal flow choking). This is particularly true for astronauts/cosmonauts who experienced neurological disorders during human spaceflight and thereafter [10]. The internal flow choking could be negated by concurrently lessening the blood viscosity and flow turbulence in the circulatory system by the rising thermal tolerance level in terms of blood/biofluid heat capacity ratio (BHCR) or by decreasing the blood pressure ratio (BPR). In light of the theoretical discovery of the Sanal flow choking in cardiovascular system (CVS), a mini review has been carried out herein with a scope of basic science to clinical perspective. This review aims for understanding the causes and effects of flow choking and further establishing the possibilities of the Sanal flow choking in the circulatory system, which leads to aneurysm, hemorrhagic stroke and other neurological disorders in all subjects including the COVID-19 patients.

The blood circulatory system is an internal fluid flow loop with multiple branches, transport nutrients and oxygen to all cells in the body. The center of the circulatory system is the heart, which is accountable to pump blood through the complex network of viscoelastic vessels, viz., arteries, veins and capillaries. Blood flow in the circulatory system is typically laminar but due to its pulsatile nature makes possible the flow transition to turbulent. Furthermore, the variations in the biofluid/blood flow properties and vessel geometry due to the local and pathophysiological reasons, including seasonal effects, contribute for the transition from laminar flow to turbulent

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[9]. Of late (2021) V.R.S.Kumar et al. [6-8] reported conclusively that human blood is a compressible fluid with different degrees of the compressibility percentage because the specific volume (or density) of blood does change with temperature and/or pressure. Authors further reported that blood heat capacity ratio (BHCR) is an important parameter determining the thermal tolerance level [6-9]. BHCR can be estimated from the specific heat at the constant pressure (Cp) and specific heat at constant volume (Cv) of fresh blood samples of all subjects. The specific heat capacity depends on the number of degrees of freedom and each independent degree of freedom permits the particles to store thermal energy and as a result the BHCR will be always greater than one. It corroborates that blood is a compressible fluid and internal flow choking [6-8] in circulatory system could occur at a critical systolic to diastolic blood pressure ratio (BPR) irrespective of hypertension or hypotension.

Traditionally hypertension is considered as the most prevalent risk factor for stroke. Stroke causes and the haemodynamic consequences are heterogeneous which make the management of blood pressure in stroke patient's complex necessitating an exact identification and meticulous delineation of therapeutic goals [7]. Until the theoretical discovery of the Sanal flow choking in the circulatory system there were no reliable conclusions to support whether hypertension or hypotension is more risk with regards to the hemorrhagic stroke and acute myocardial infarction [6-11]. The fact is that an asymptomatic stroke could occur in both hypertension and hypotension patient because the controlling parameter of this event is the BPR [6-11]. In brevity, attaining the critical BPR is considered as the risk factor for aneurysm and hemorrhagic stroke. At the threshold of the Sanal flow choking condition, a minor oscillation in BPR for both hyper and hypo subjects is likely to aggravate the risk of the brain hemorrhage in COVID-19 patients, which is corroborated with the clinical report presented by Razavi et al. [12] from Mazandaran University of Medical Science, Iran. The report [12] reveals the case of a 79 year old man with a history of fever and cough of 3 days duration. He was referred to the emergency department with acute loss of consciousness (heart rate 115 beats per minute; respiratory rate, 22 breaths per minute). At admission he was febrile (temperature 38.6°C) and his blood pressure was 140/65 mm Hg, which was found higher than the lower critical hemorrhage index (LCHI) causing the Sanal flow choking [6-9]. Note that there was no history of hypertension or anticoagulation therapy. Lung computed tomography revealed ground glass opacity in the left lower lobe, and brain computed tomography revealed a massive intracerebral haemorrhage (ICH) in the right hemisphere, accompanied by intraventricular and subarachnoid haemorrhage. Real time PCR of the oropharyngeal swab confirmed COVID-19 infection [12]. It is crystal clear from this case report that the aforesaid patient experiences gas embolism as his temperature exceeds 37°C, the evaporation temperature of blood of a healthy subject [6-8]. Additionally, the patient BPR was found higher (BPR=2.15) than the LCHI (critical BPR for flow choking) [6-8]. In such patients occurrence of the ICH due to the Sanal flow choking can be negated by increasing the BHCR and/or decreasing the BPR.

In light of the various clinical reports (catalogued and non-catalogued) and the recent discovery of internal flow choking in CVS [6-11], the classic definition of the hypertension causing cardiovascular risk is largely arbitrary (SBP ≥ 140 and/or DBP ≥ 90 mmHg). The prevailing ICH risk data remains challenging due to the fact that the internal flow choking could occur in both hypertension or hypotension subjects once the SBP/DBP ratio reaches the critical BPR. The internal flow choking could happen anywhere in CVS including capillaries, vasa vasorum and/or nanoscale vessels. Of late (2021) through the series of publications V.R.S.Kumar et al. [6-10] reported that cardiovascular risk can be negated by concurrently reducing blood viscosity and turbulence by increasing the blood heat capacity ratio (BHCR), which is an important parameter determining the thermal tolerance level of blood [6,7]. The ratio of Cp and Cv is defined as the BHCR.

V.R.S.Kumar et al. [6-9] reported conclusively that the high and low blood viscosity is risk factors of internal flow choking causing asymptomatic cardiovascular diseases. The over dose of blood thinning medication increases the Reynolds number, which increases the risk of flow choking. The fact is that while reducing blood viscosity the fluid flow turbulence increases as a result of an increase in Reynolds number, which leads to flow choking due to an increase in boundary layer blockage. Note that due to the large velocity gradient at the wall the frictional shear stress in a turbulent boundary layer is greater than in a purely laminar boundary layer. As a result, the boundary layer displacement thickness of the turbulent flow is higher than laminar flow. Therefore, for prohibiting the flow choking one should come up with a solution for meeting the conflicting requirements, viz., simultaneously decrease blood viscosity and turbulence. These conflicting requirements can be achieved by either increase BHCR and/or decrease BPR [1], which negates the risk of ICH due to the undesirable flow choking.

Sayed et al. [13] reported that post stroke cognitive impairment (PSCI) is a major source of disability, affecting up to two thirds of stroke survivors with no available therapeutic options. The condition remains understudied in preclinical models due to its delayed presentation. Although hypertension is a leading risk factor for dementia, how ischemic stroke contributes to this neurodegenerative condition was unknown until the discovery of the Sanal flow choking phenomenon, which occurs in both hypertension and hypotension subjects [6,7]. The scientific fact is that, NOT the blood pressure (BP) but the blood pressure ratio (BPR=SBP/DBP) is the controlling parameter of asymptomatic stroke. Hypertension was believed to be the most commonly occurring modifiable risk factor for stroke worldwide and was being increasingly recognized as a risk factor for the development of PSCI [14,15]. Chronic hypertension, particularly midlife high BP, has been associated with an increased risk for cognitive decline, vascular dementia and Alzheimer's disease [16]. One of the mechanisms by which hypertension was believed to contribute to the development of cognitive impairment was exposing the cerebral microvasculature to pulsatile pressure causing tearing of the brain vascular endothelium and smooth muscle cells leading to lipohyalinosis characterized by vessel wall thickening and a resultant reduction in luminal diameter and fibrinoid necrosis [17]. While pressure appears to clearly be a factor in the distribution of fibrinoid necrosis in human brains, the relative importance of pressure alone versus some additional humoral agent has been long debated by experimentalists studying diverse organs [18-20]. However, extensive studies have shown that abrupt, marked elevations of blood pressure alone can cause fibrinoid change in a matter of minutes [19]. William [18] strongly believed and implicated that blood pressure alone as the cause of fibrinoid degeneration. V.R.S.Kumar et al. [6-10] conjectured that the generation of multiple shock waves could occur in CVS due to the nano scale flow choking and streamtube flow choking [10,21], which leads to fibrinoid necrosis. Although the outcome gathered from the prevailing clinical and non-clinical studies add to the knowledge acquired on ICH, the fundamental cause of neurological disorder is still unknown to the scientific community. The recent theoretical discovery of the Sanal flow choking and the streamtube flow choking [6-10] sheds light on finding solutions for various neurological disorders as these concepts got incredible significance in biological sciences for predicting risk factors of aneurysm, arrhythmia, hemorrhagic stroke and acute heart failure.

A brain hemorrhage is a type of stroke and was believed to be caused by high blood pressure (hypertension), abnormally weak or dilated (aneurysm) blood vessels that leak, drug abuse, and trauma. It is caused by an artery in the brain bursting and causing localized bleeding in the surrounding tissues. Note that blood vessels in the brain circulatory system with sudden expansion, divergence or bifurcation regions without any apparent occlusions are more prone to hemorrhagic stroke due to the Sanal flow choking Figure 1 at a critical BPR, which is regulated by the BHCR. Brain arteriovenous malformations (AVMs) are abnormal connections of arteries and veins [22]. An AVM can develop anywhere in the body, but occurs most often in the brain. Brain AVMs are a leading cause of the hemorrhage in children and young adults, although they can cause other morbidities such as seizures, focal neurological deficits, and headaches. There is usually high flow through the feeding arteries, nidus, and draining veins, which may result in rupture and intracranial hemorrhage, the most severe complication

of an AVM. Clinically, brain AVMs are technically challenging and resource intensive to manage with the available therapeutic modalities and often require multi modal therapy. The factors influencing risk of hemorrhage associated with sporadic brain AVM is still poorly understood [9,22]. It has already been established that blood/biofluid is a compressible viscous fluid and internal flow choking can occur anywhere in CVS at a critical BPR causing hemorrhagic stroke and other neurological disorders [6-8].

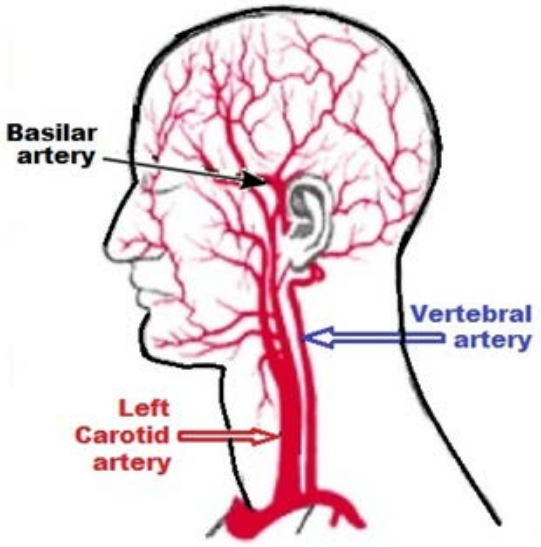

Figure 1. Highlighting various bifurcation regions in the brain circulatory system causing the Sanal flow choking and shock wave generation in vessels at a critical BPR leading to neurological disorders

Moyamoya is an unusual progressive cerebrovascular disease caused by blocked arteries that affect the flow of blood to the brain, which was originally termed in Japan. This term was coined because it results in a tangle of fragile blood vessels that resembles moyamoya (it means "puff of smoke") when viewed on an angiogram. Moyamoya can result in brain aneurysms and hemorrhage, transient ischemic attack (TIA, or "mini-stroke) or a major stroke. Moyamoya causes a narrowing or blockage of the carotid arteries where they enter the brain at the base of the skull (Figures 1 and 2). The body tries to compensate and restore blood flow by creating a network of tiny blood vessels that branch off from the arteries. Unfortunately, the newly formed blood vessels are fragile, and ineffective in restoring blood flow. These fragile vessels can rupture and bleed. The underlying cause of moyamoya was unknown, but it was thought to be linked to genetics and environmental triggers. In light of these clinical observations, the critical studies on the causes and effects of internal flow choking in CVS leading to various neurological disorders are of significance for the health care management. V.R.S.Kumar et al. [9] conjectured that Moyamoya disease is due to the internal flow choking and/or stream tube flow choking [9,21] causing the multiple shock wave generation followed by pressure overshoot causing the cell death in multiple regions of the vessels. Briefly, the concept of internal flow choking (biofluid/Sanal flow choking) in the blood circulatory system [9] provides an insight for the diagnosis, prognosis, treatment and prevention of various types of neurological disorders.

Internal Flow Choking: An Overview

Internal flow choking is a compressible fluid flow effect and a fluid dynamic condition in wall bounded systems associated with the venturi effect [9]. Internal flow choking occurs when sonic velocity is reached at the constriction section of any vessel (Figures 2a-2c). At the choked flow condition, the flow becomes independent from downstream conditions. In other words, internal flow choking occurs in CVS at a critical blood pressure ratio (SBP/DBP), which is governed by the BHCR (Eq.1).

$$BPR = \frac{SBP}{DBP} = \left(\frac{BHCR+1}{2}\right)^{BHCR/BHCR-1} \quad (1)$$

It is pertinent to note that if the blood vessel is having the shape of a convergent divergent (CD) nozzle due to occlusion, stenosis, vasospasm and/or the effect of boundary layer blockage (Figure 2) there are possibilities of the generation of shock waves and transient pressure overshoot in the downstream region of the vessel after attaining the internal flow choking condition, as dictated by Eq.1, as a result of supersonic flow development. Occlusion of the blood vessel causing internal flow choking may be due to atherosclerotic plaque, an embolised blood clot, necrosis or a foreign body presence. It is evident from Eq.1 that the critical BPR for internal flow choking is governed by the BHCR. There are two types of internal flow choking in CVS viz., biofluid choking and Sanal flow choking. Biofluid flow choking occurs in CVS due to the plaque induced CD nozzle flow effect and/or due to vasospasm (Figures 2 and 3) or any other type of occlusion. The Sanal flow choking phenomenon is established as the fluid throat induced internal flow choking due to the boundary layer formation owing to the compressible viscous flow effect [6-9]. The Sanal flow choking creates a physical situation of boundary layer blockage persuaded biofluid flow choking in the circulatory circuit at a critical systolic to diastolic blood pressure ratio (BPR) in all the subjects with and without any plaque (Figure 2c) and/or apparent occlusion.

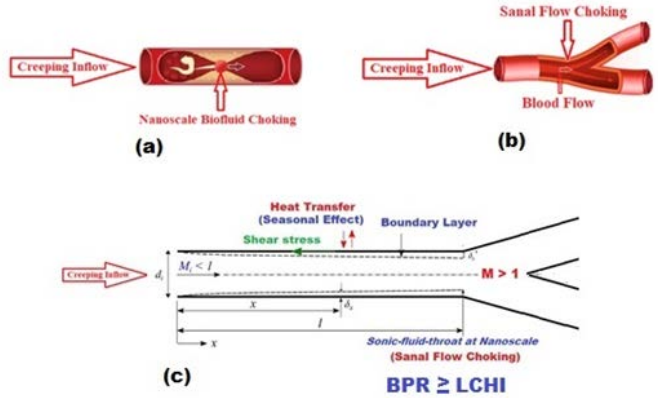

Figure 2. Demonstration of the internal flow choking in the cardiovascular system. (a) Nanoscale biofluid choking, (b) Sanal flow choking, (c) Idealized physical model of a vessel with bifurcation: Demonstration of the Sanal flow choking and supersonic flow development when BPR>LCHI

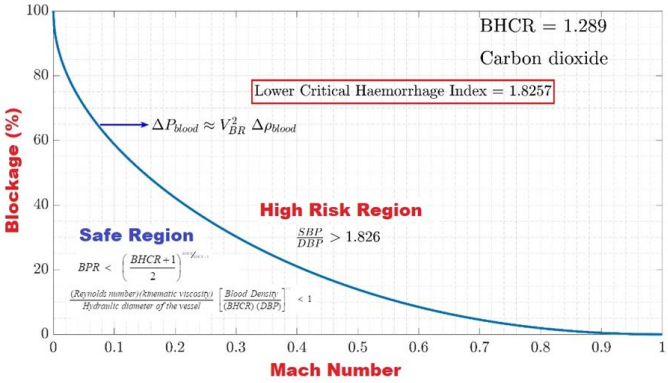

Figure 4. Analytical Methodology: Demonstrating the condition for prohibiting the internal flow choking in CVS causing asymptomatic stroke [8]

The nanoscale internal flow choking is a new theoretical concept in biological science [6-10]. As the pressure of the nanoscale biofluid/non continuum flows rises, average mean free path diminishes and thus, the Knudsen number lowers heading to a zero slip wall boundary condition with

compressible viscous flow effect, which increases the risk of cardiovascular diseases. Equation 1 tells us that low BPR, high BHCR or high thermal tolerance of blood reduces the risk of internal flow choking, which in turn reduces the possibilities of the shock wave generation and pressure overshoot causing asymptomatic cardiovascular diseases. At a critical BPR, the Sanal flow choking occurs anywhere in the CVS, including micro/nanoscale vessels with sudden expansion/divergence or bifurcation regions. At the threshold of the Sanal flow choking condition in viscoelastic vessels with sudden expansion or divergence/bifurcation, a minor oscillation of BPR, leads to transient supersonic flow development heading to the shock wave generation creating memory effect (stroke history or the cumulative development of cerebrovascular disease). The undesirable Sanal flow choking could occur at relatively high blood viscosity and low blood viscosity (due to high turbulence) in vessels without any occlusion Figures 1-3.

The shock wave can occur anywhere at any time in the supersonic flow when there is a flow compression due to stream tube effect or geometric effect or any other flow disturbance. Normal shock waves create very sharp transient pressure overshoot in CVS, which leads to bulging or tearing of vessels. The tearing (hemorrhagic stroke) or bulging of vessels (aneurysm) depends on the memory effect (stroke history) and relaxation modulus of the viscoelastic vessels. The memory effect depends on the strength of the shock wave and the associated occurrence of the transient pressure overshoot over the years due to frequent fluctuations in BPR, due to various reasons, causing periodic choking and unchoking fluid flow conditions. All these deliberations lead to establish herein that the internal flow choking is an undesirable phenomenon in CVS as it leads aneurysm, hemorrhagic stroke, moyamoya disease, myocardial infarction and other neurological disorders. The significant clinical aspect is that; the internal flow choking is uniquely regulated by the BHCR. Of late V.R.S.Kumar et al. [6] correlate the BHCR with BPR, blood viscosity (BV) and ejection fraction (EF) for establishing the concept of internal flow choking causing asymptomatic cardiovascular diseases for taking brilliant clinical decisions in case by case manner [23-37]. Stroke is one of the leading causes of morbidity and mortality worldwide. Stroke and myocardial infarction (MI) share some common risk factors and pathophysiological mechanisms [36]. Compared with the general population, stroke patients have an increased risk of death that notably results from acute heart failure [37]. There have been several reports in the scientific literature which suggest the linkage between cardiovascular disorders and neurological disorders particularly Alzheimer's disease and Parkinson disease [38]. V.R.S.Kumar et al. [6-10] reported conclusively through closed form analytical models that pathogenesis of all the asymptomatic disorders is due to the undesirable flow choking in the CVS over the years, which was unknown to medical science.

Methodology

The theoretical discovery of the Sanal flow choking [6-10] is a breakthrough in biological science, which creates a radical change in the diagnostic sciences of asymptomatic cardiovascular diseases because the various causes of the Sanal flow choking are complementing with all the established concepts in the medical sciences [8,9]. The concepts of Sanal flow choking is reviewed herein for highlighting pragmatic solutions for reducing the risk of internal flow choking leading to the shock wave generation causing asymptomatic cardiovascular diseases. Note that the boundary layer blockage (BLB) factor causing the Sanal flow choking would alter due to the blood viscosity variations as a consequence of the blood thinning medication and/or the seasonal effects [8,23]. Indeed, boundary layer blockage induced internal flow choking is more prone during the winter season than the summer season due to the higher blood viscosity at the relatively low blood temperature. It leads to say that the risks of internal flow choking leading to asymptomatic cardiovascular diseases would be high during the winter than in the summer season [6-11,23]. It is important to note that disproportionate blood thinning medication will increase the Reynolds number, which produces the high turbulence level creating enhanced boundary layer blockage (BLB) factor causing an early internal flow choking. Therefore, as stated earlier, we can establish herein that relatively high blood viscosity and low blood viscosity are risk factors for an early internal flow choking in cardiovascular system (CVS) causing asymptomatic cardiovascular diseases. Though the BHCR is the unique parameter controlling the phenomenon of flow choking, the physical situation of flow choking is influenced by other parameters too, viz., blood viscosity, density, Reynolds number, BPR, and stenosis (vessel geometry).

$$\frac{(Reynolds\ number)(kinematic\ viscosity)}{Hydraulic\ diameter\ of\ the\ vessel}\left[\frac{Blood\ \ Density}{(BHCR)\ (DBP)}\right]^{1/2} < 1$$

$$BPR < LCHI = \left(\frac{(BHCR)_{\substack{Evolved\ gases\\ with\ the\ lowest\ BHCR}} + 1}{2}\right)^{(BHCR)_{lowest}/(BHCR)_{lowest}-1}$$

$$UCHI = \left(\frac{(BHCR)_{blood} + 1}{2}\right)^{BHCR_{blood}/(BHCR)_{blood}-1}$$

Equation 2 is declaring the unchoked flow condition in the CVS, which could predict the cardiovascular risk for taking a conclusive clinical decision on each and every subject in all seasons. An accurate estimation of the parameters highlighted in Eq.2 is absolutely required for the future health care management of all subjects aiming for prohibiting asymptomatic cardiovascular diseases.

Intracerebral hemorrhage (ICH) and coronary heart disease (CHD) have the same pathological base, atherosclerosis, and similar risk factors causing internal flow choking. Significant difference exists in gender, age, smoking, hypertension, history of hypertension, drinking and glucose (GLU), history of diabetes mellitus and triglyceride (TG). It is evident from Eq.1 and 2 that a decrease in BHCR, DBP and the vessel diameter increases the risk of internal flow choking leading to cardiovascular risk, which is correlating with the existing clinical findings [6-10,23,33,34]. Equation 1 also reveals that an increase in systolic blood pressure (SBP) without altering the diastolic blood pressure (DBP) increases the possibilities of internal flow choking in CVS causing cardiovascular risk (CVR). Briefly, an increase in BPR increases the CVR. Equation 2 and Equation 3 are two independent and complementing conditions set for prohibiting the internal flow choking in the CVS. Note that nanoscale fluid flow system with apparently high risk blockage (Figure 2a) must always maintain the flow Mach number less than one as dictated by Eq.2 for negating the undesirable internal flow choking causing shock wave generation and pressure overshoot in the CVS leading to asymptomatic cardiovascular diseases. In such cases the flow Mach number can be retained always less than one by keeping BPR always less than the lower critical hemorrhage index (LCHI), which can be achieved by increasing the BHCR through drugs or otherwise. The impeccable analytical model (Eq.2) reveals that the usage of blood thinners without increasing the BHCR create high risk of bleeding and stroke. The fact is that the blood thinner decreases the viscosity and increases the Reynolds number, which augments the turbulence level causing an enhanced boundary layer blockage, which predisposes for an early flow choking. The flow turbulence enhances the deficit of energy in the type of friction, which increases the boundary layer blockage in the vessels and generates heat and augment the internal energy affecting a reduction in BHCR. Additionally, turbulence enhances the perfusion pressure essential to push the blood flow, which creates an early undesirable Sanal flow choking in the circulatory system.

In order to avoid the undesirable shock wave generation followed by transient pressure overshoot in CVS an unchoked fluid flow condition must be maintained throughout the circulatory system. It could be achieved by maintaining the BPR always lower than the lower critical hemorrhage index (LCHI), which is dictated by the lowest value of the BHCR (see Eq.3) of the evolved gases from blood or foreign gases entered in the CVS. Air can enter in veins and arteries during surgical procedures. It has been reported

that non meticulous brain surgeries result in an air embolism. Significant venous air embolism may develop acutely during the perioperative period due to a number of causes such as during head and neck surgery, spinal surgery, improper central venous and haemodialysis catheter handling, etc. The trend of using self-collapsible intravenous (IV) infusion bags instead of the conventional glass or plastic bottles has several advantages, one of them being protection against air embolism [35].

Note that BHCR of CO2 is lower than air, which creates an early internal flow choking. For instance, if CO2 is the dominant gas in the CVS it is mandatory to maintain BPR lower than 1.82, within the pathophysiological range of human temperature, for creating an unchoked flow condition for prohibiting the shock wave generation [6-9] causing asymptomatic cardiovascular diseases due to transient pressure overshoot. The fact is that at the choked flow condition the critical BPR is a unique function of BHCR. Briefly, the LCHI can be predicted (Eq.3) using the lowest value of the BHCR among the dominant gases present in the CVS of each subject (human being or animal). The upper critical hemorrhage index (UCHI) can be predicted (see Eq.4) from the specific heat of fresh blood at constant pressure (Cp) and the specific heat of fresh blood at constant volume (Cv) using the differential scanning calorimeter [6-10]. Figure 4 is demonstrating the condition for prohibiting the internal flow choking in CVS causing asymptomatic stroke [7,8].

In vitro data [6-10] shows that nitrogen (N2), oxygen (O2), and carbon dioxide (CO2) gases are predominant in fresh blood samples of the human being/Guinea pig at a temperature range of 37°C-40°C (98.6°F-104°F), which increases the risk of internal flow choking leading to the asymptomatic cardiovascular risk. It is evident from the reported results (Figure 5) that the possibilities of internal flow choking in the human being is higher than the animal (Guinea pig) under the same thermal loading condition as the BHCR of the dominant gas evolved in the animal is found consistently higher than the human being. As a result, the LCHI is higher for the healthy male Guinea pig as dictated by the Eq.3. The mass spectrum of N2 is reported higher in animal whereas in human being CO2 is found higher [6-10]. It indicates that the thermal tolerance level of the healthy Guinea pig is higher and the cardiovascular risk is lower than the human being under identical conditions. Therefore, increasing the thermal tolerance level in terms of BHCR of the human being is an important factor for reducing the risk of asymptomatic cardiovascular diseases caused by the shock waves as a result of internal flow choking. Figure 6 is demonstrating the percentage variations of evolved gases (viz., N2-m/z=28, O2-m/z=32, CO2-m/z=44), from blood samples of four different healthy human beings and one healthy male Guinea pig of four weeks old [8], during the hyphenated technique at a blood temperature of 40°C (104°F). The estimated UCHI of healthy human being of age 23-48 with the different blood group is presented in Table 1 as a pilot data.

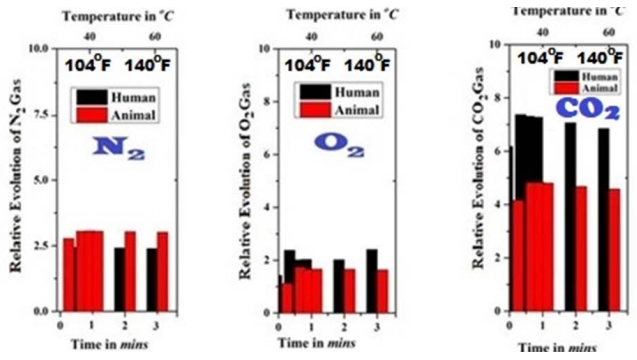

Figure 5. *In vitro* Methodology: Mass spectrum of N2, O2, and CO2 evolved as a function of both time and temperature [6].

Table 1. Upper critical hemorrhage index of health subjects.

Specimen Reference	SBP/ DBP mm Hg	BPR	BHCR		UCHI	
			37.5°C	40°C	37.5°C	40°C
HM35A+	110/76	1.44	5.69	5.37	4.33	4.15
HM23A+	130/60	2.16	118.29	20.42	61.75	12.1
HM48B+	110/80	1.37	7.44	7.03	5.28	5.06
HM37O+	120/60	2	18.07	6.39	10.88	4.71

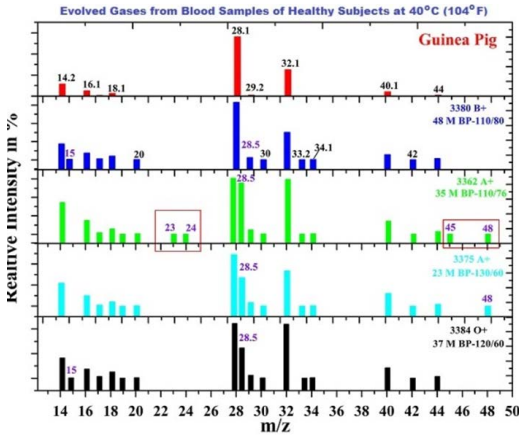

Figure 6. *In vitro* methodology: Demonstrating the percentage variations of evolved gases (viz., N2-m/z=28, O2m/z=32, CO2-m/z=44, Ar-m/z=40, an unknown composite gas-m/z=28.5) from blood samples of four different healthy human beings and one Guinea pig during the hyphenated technique at a blood temperature of 40°C (104°F) [8].

Over the decades, bio-medical researchers have been relying on in silico simulation to model and cognize the natural mechanisms behind the creation and evolution of hemodynamic disorders. It has been recognized that the wall shear stress exerted on the walls of the blood vessel due to the flow of blood/biofluid is one of the main pathogenic factors leading to the occurrence of such disorders. The magnitude and distribution of the wall shear stress in a blood vessel can provide an insight into the locations of possible aneurysm growth. In this review, as a proof of the concept of the Sanal flow choking, we are highlighting the single phase in silico results for demonstrating the shock wave generation followed by pressure overshoot in an idealized physical model of a blood vessel with divergent region with working fluid as gas [6] (Figure 7).

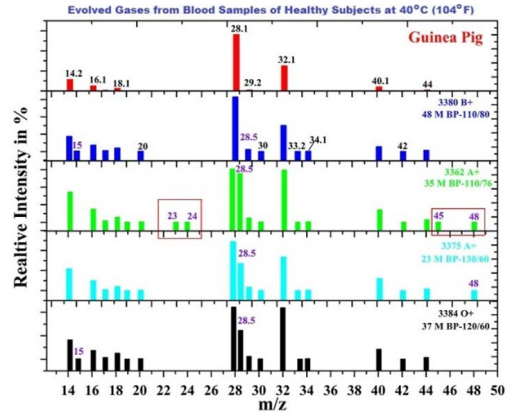

Figure 6. *In vitro* methodology: Demonstrating the percentage variations of evolved gases (viz., N2-m/z=28, O2m/z=32, CO2-m/z=44, Ar-m/z=40, an unknown composite gas-m/z=28.5) from blood samples of four different healthy human beings and one Guinea pig during the hyphenated technique at a blood temperature of 40°C (104°F) [8].

The in silico result presented in Figure 7 is clearly demonstrating the phenomenon of the Sanal flow choking and the shock waves generation at the subsonic inflow condition (creeping flow) leading to the transient pressure overshoots (stroke) in the downstream region of an artery with divergent port. Figure 7 provides the proof of the concept of fluid throat persuaded flow choking in the CVS. The closed form analytical prediction of the 3D blockage factor [11] at the sonic fluid throat location is a useful tool for the in vitro and in silico experiments in both the continuum and non-continuum flows with due consideration of heat transfer effects (real world fluid flow effect). Note that the phenomenon of Sanal flow choking is a paradigm shift in the diagnostic sciences of asymptomatic CVD. Therefore, development of a multi-phase, multispecies, viscoelastic fluid structural interactive in silico model capturing the memory effect (stroke history) is a meaningful objective for predicting a priori asymptomatic cardiovascular diseases with credibility [6-11]. Such an effort will be helpful for the diagnosis, prognosis, treatment and prevention of various neurological disorders of each and every subject with confidence.

Discussion

Although the diagnostic sciences have been advanced significantly over the decades [32-60], until the theoretical discovery of the Sanal flow choking, the real occurrence of the asymptomatic cardiovascular disease was poorly understood, largely for the reason that it was an under diagnosis condition [9]. In this review we show that the fundamental cause of aneurysm, hemorrhagic stroke and various asymptomatic neurological disorders are due to the internal flow choking following by the shock wave generation and pressure overshoot. Our conclusion is corroborated with the available clinical data [6-10,23,33,34]. The concept of Sanal flow choking is demonstrated through analytical, in vitro and in silico results. This review leads to say that a vaccination or a single drug, or a companion drug along with the traditional blood thinning drugs capable to reduce simultaneously the blood viscosity and flow turbulence could reduce the risk of asymptomatic CVD. New drug, for prohibiting the internal flow choking, must be capable to increase the BHCR and/or decrease the BPR. We recognized through this comprehensive review that the Sanal flow choking is the fundamental cause of asymptomatic cardiovascular diseases and/or the neurological disorders. The effect of Sanal flow choking is more severe in blood vessels with divergent/bifurcation regions because it leads to the shock wave generation and the transient pressure overshoot causing irreversible neuronal damage forming the core of infarction. Now the precipitating factor for the plaque rupture has come to the foreground. We concluded that the Sanal flow choking could occur anywhere in the circulatory circuit with gas embolism when BPR reaches LCHI. The boundary layer blockage factor depends on the BHCR, flow Mach number, biofluid viscosity and turbulence, which could alter due to seasonal changes, variations in lipoprotein and other contributing factors. The greater the reduction in low density lipoprotein (LDL) cholesterol, the lower the risk of stroke. The shock wave due to the Sanal flow choking could disrupt an atherosclerotic plaque or coronary artery wall. In a nutshell, the discovery of the biofluid/Sanal flow choking is a paradigm shift in the diagnostic sciences of neurological disorders.

Conclusion

In vitro study shows that nitrogen (N2), oxygen (O2), and carbon dioxide (CO2) gases are predominant in fresh blood samples of healthy subjects at a temperature range of 37°C-40°C (98.6°F-104°F), which enhances the possibilities of internal flow choking leading to pressure overshoot and cell death. This physical situation is more dangerous in COVID-19 patients, which could lead to stroke epidemic. We observed through in vitro study that, CO2, the gas with the lowest heat capacity ratio (HCR), is relatively and consistently higher in the healthy males than the healthy male Guinea pig of four weeks old. It reveals that as a preventive measure for all subjects with a low BHCR, including patients who are taking blood thinning medication, must maintain their BPR always less than 1.82, as dictated by Eq.3, for reducing the risk of asymptomatic CVD.

We concluded that a single anticoagulant drug capable to suppress the turbulence level and enhance the BHCR or a companion medicine along with the traditional blood thinning medications is predestined for meeting the conflicting requirements (i.e., decrease viscosity and turbulence simultaneously) of all the subjects for reducing the risk of asymptomatic hemorrhage and acute heart failure. In high risk subjects, (i.e., BPR is very close to the LCHI), a slight oscillation in the BPR predisposes to the choking and the unchoking phenomena, which could lead to arrhythmia and memory effect. Briefly, this study sheds light for exploring new avenues in biological science for discovering new blood thinning drugs for reducing the risk of internal flow choking causing asymptomatic cardiovascular diseases. The cardiovascular treatment should be targeted based on blood pressure ratio (BPR), instead of blood pressure levels alone, in chronic CVD patients. We concluded that the risk of internal flow choking heading to asymptomatic cardiovascular diseases could be decreased by concurrently reducing blood viscosity and turbulence by enhancing the BHCR and/or reducing the BPR.

The discovery of Sanal flow choking phenomena calls for continuous ambulatory blood pressure (BP) and thermal level monitoring in high risk patients in the diagnosis and preventive management of asymptomatic cardiovascular diseases. The continuous blood pressure and thermal level measurement could be done in a more pragmatic way by using a wearable BP monitor with the temperature sensor in the modern form of a wristwatch. Note that the Sanal flow choking is more susceptible at microgravity condition due to altered variations of blood viscosity, turbulence and the BPR. The effects of microgravity on the brain have received attention in relation to a syndrome involving optic disc edema and elevated intracranial pressure (ICP) in astronauts returning from the International Space Station (ISS). NASA coined the phrase “Visual Impairment and Intracranial Pressure (VIIP) syndrome” to describe this constellation of signs and symptoms [51-60]. The fact is that the microgravity environment decreases plasma volume and increases the hematocrit compared with the situation on the earth surface, which increases the relative viscosity of blood casing an early Sanal flow choking. We concluded that for a healthy life all subjects (human being/animals) in the earth and in the outer space with high BPR necessarily have high BHCR. We recommend all astronauts/cosmonauts should wear ambulatory blood pressure and thermal level monitoring devices similar to a wristwatch throughout the space travel for the diagnosis, prognosis and prevention of internal flow choking leading to asymptomatic cardiovascular disease including neurological disorders. We concluded that designing the precise blood thinning regimen is vital for attaining the desired therapeutic efficacy and negating undesirable flow choking leading to asymptomatic CVD. For a healthy life all subjects with high BPR inevitably have high BHCR for reducing the risk of the internal flow choking (biofluid/Sanal flow choking) triggering neurological disorders as results of infraction due to the shock wave generation and transient pressure overshoot.

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Conflict of interest

The authors declare no conflict of interest in every sphere.

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