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Atmospheric variables and subarachnoid hemorrhage: narrative review

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Abstract

Background: Stroke is a neurological emergency that tends to be the first cause of death in many countries. Atmospheric variables are strongly associated with stroke, in which subarachnoid hemorrhage (SAH) has been associated in many studies to meteorological risk factors such as air pollution, air pressure, weather changes, and ambient temperature. These characteristics may influence the brain circulation and cause SAH, being diagnosed as idiopathic SAH or SAH with unknown cause.

Objective: The main objective of this review is to present the most relevant meteorological risk factors that may develop subarachnoid hemorrhage according to the current evidence that supports the strong association.

Conclusion: Brain vessel circulation may be influenced by atmospheric variables such as air pollution and weather changes, generating intrinsic changes in the intima of the vessels which leads to vasospasm and with comorbidities associated may develop SAH.

Keywords: Subarachnoid hemorrhage, Atmospheric variables, Brain vessels, Stroke

Introduction

Statistically, stroke has an incidence of 88.9 × 100000, being 85% ischemic stroke and 15% hemorrhage stroke [1]. A seasonal pattern as a risk factor for stroke has been observed in many studies. In a large meta-analysis of 72,694 patients, no direct relation was found between the occurrence of stroke and meteorological risk factors. However, in an observational cohort study which included 1535 patients with spontaneous subarachnoid hemorrhage admitted to the neurovascular center in the north of the Netherlands between 2000 and 2015, the atmospheric pressure variations like weather stations were significantly associated with SAH; the pressure variation on the second and third day before the stroke was independently correlated to a higher incidence of SAH (IRR 1.11; 95% CI, 1.00–1.23), which means the atmospheric pressure variations are strongly correlated to stroke [1, 2]. The principal objective of this review is to describe the most relevant information about atmospheric variables and SAH.

Methods

The searching was based on MeSH terms in PubMed and SCOPUS, looking for articles that may contribute to answer our question for searching: What are the meteorological risk factors for SAH? The require terms used were “meteorological risk factors “[All Fields] AND “subarachnoid hemorrhage” [All Fields] OR “SAH” [MeSH terms] OR “stroke” [All Fields] OR “stroke” [MeSH terms] AND (“favorable outcomes” [All Fields] OR “outcomes” [All Fields]) NOT (“pediatrics” [All fields] OR “child” [All Fields] OR "child [MeSH terms]) NOT ("death" [All Fields] OR "mortality" [MeSH terms]). Articles were retained for review in two cases, identifying the information in an attempt to generate hypotheses for future studies and contribute to the medical science according to answer every question about meteorological risk factors for SAH.

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Overview

Experimental and epidemiological studies have shown the direct association between air pollutants exposure and cardiovascular illnesses, such as hypertension [3]. Long-term exposure to pollutants may progress to brain vascular vasoconstriction and in vasospasm which is a risk factor for SAH, with reactive oxygen species (ROS) being the product between air pollutants and free electrons from vascular elastance. In an experimental study in rats published by Qinghua Sun et al., rats were exposed for 10 weeks to pollutants, and it was evidenced that the medial arterial pressure increased > 98 mmHg [4]. According to this study and other experimental and epidemiological studies, there is not enough evidence to conclude the association between air pollution and SAH. However, long-term exposure to pollutants is a risk factor for cardiovascular illnesses and stroke [5, 6].

Pollutants and incidence of SAH

Polluted effect is defined as the undesirable damage in the human body secondary to indoor and outdoor ambient air pollution [7]. There are six major air pollutants defined by the World Health Organization (WHO): ground-level ozone, carbon monoxide, sulfur oxide, nitrogen oxides, lead (Pb), and other pollutants of suspended materials; long-term exposure to these current air pollutants may lead to reduce the life expectancy [8], although this situation may be one of the reasons for unknown deaths associated with cardiovascular and lung diseases [8, 9]. Ground-level ozone (GLO) is the major constituent gas of the atmosphere, which is secondary to a chemical reaction between nitrogen oxides and volatile organic compounds. In the present, there is only evidence and cohort studies associated with respiratory tract diseases [7–9]. Carbon monoxide (CO) is produced by fossil fuel as in burning wood. The affinity of this pollutant to oxygen is 250 greater than oxygen, in which the toxicity of itself will depend according to the length of exposure. Sulfur dioxide (SO_2) is an important air pollutant emitted from natural volcanic activity and industrial process. Nitrogen oxides (NO_2) are emitted by traffic, motor engines, and lead or plumb (Pb) which are used in different industries; it is emitted from motor engines and petrol [7, 10].

Pathology

Stroke is a medical emergency that tends to kill the patients in the worse scenario. The Stroke Guidelines 2018 update describe that every 40 s, someone around the world suffers a stroke, being economically devastating for the countries with patients who suffered [11]. Stroke is divided into two types: hemorrhage and ischemic; this classification includes a lot of complications for each one such as subarachnoid hemorrhage to the brain thrombus or embolus. There are many theories about atmospheric variables and subarachnoid hemorrhage; also, the brain vessels carry with itself and the atmospheric variables many changes [12].

Brain vessels with meteorological changes

First of all, it is important to understand the changes the brain vessels take with meteorological changes. The human brain receives 20% of the body's oxygen and glucose of cardiac output. Both are delivered to the central nervous system by cerebral blood flow (CBF) and transported across the blood-brain barrier (BBB) for neuron metabolism [13]. The balance of this particular organ is maintained by the cerebral vessel plasticity (CVP). Also, this CVP is obtained by a long vascular network; those are the arteries, arterioles, and capillaries [14]. This network supplies the brain with oxygen, energy, metabolites, and nutrients. In a normal situation, the brain vessels (BV) are highly sensitive to changes in the partial pressure of carbon dioxide in the arterial blood ($PaCO_2$); this is unique in the cerebrovasculature compared with peripheral circulation [13–15].

Role of $PaCO_2$

Elevations in $PaCO_2$ cause a decrease in cerebrovascular resistance and consequent increases in CBF; when this episode happens in patients with risk factors or comorbidities such as hypertension, diabetes, and Moya-Moya disease, the continuous elevation in CBF brings rupture of any brain vessel and causes hemorrhage secondary to vasospasm [16]. Also, the principal regulatory mechanism gets activated such as cerebral perfusion pressure and intracranial pressure (according to Monro-Kellie theory) [17]. The capacity of increased CBF and oxygen delivery exceeds metabolic demand and oxygen consumption by activated brain sites secondary to stress situations, thus providing a large gradient of nutrients to brain cells. However, when a hemorrhage episode occurs, the brain vessels lose its plasticity, decreasing the CBF; that is why many guidelines recommend the maintenance of the blood pressure [16, 18].

Despite the understanding of the vasospasm related to SAH, another study described the relationship between PCO_2 variability and SAH, determining the PCO_2 and partial pressure of arterial oxygen (PaO_2) have marked the influence on brain-blood flow and CVP. In this study, 26 adults volunteered, and 11 adults were analyzed between 7:00 and 12:00; the PCO_2 investigations there were marked variation in brain vessel tolerances to the extremes of both hypocapnia and hypercapnia; when hypocapnia was obtained, the blood in the brain vessels get alkaline which increases vasoconstriction measured with TCD, and when hypercapnia was obtained, the blood in the brain vessels get acidotic in which the CBF

increases and CPP gets high [19]. There are not many studies about arterial blood vessels related to brain vessel variability. Therefore, the incidence of SAH is strongly associated with PCO_2 variability, weather changes, and intrinsic endothelial injury [20].

Secondary brain injury and SAH

The main secondary brain injury after SAH is the three intertwined degenerative cascades adjacent to hematoma, including inflammation, red cell lysis, and iron deposition and thrombin production [21]. SAH is a special subtype of intracranial hemorrhage, which is caused by bleeding into the subarachnoid space, for a shortness of time period; cerebral vasospasm is the classic delayed neurological deterioration after an episode [22]. Intracerebral hemorrhage and SAH are conditions that are hard to explain physiopathologically; many theories explain these events with their predisposing factors. According to the pathogenesis of SAH and weather changes, it is important to understand the smooth muscle contraction and variability of PCO_2; vasospasm is prolonged cerebral arterial constriction caused by vascular smooth muscle contraction; the hemoglobin released caused by PCO_2 variability from the subarachnoid blood clots triggers the entry and release of calcium and subsequent activation of calcium and calmodulin-dependent myosin light chain kinase, which in turn leads to the phosphorylation of the myosin light chain and induces actin and myosin cross-linkage and mechanical shortening secondary to weather changes [21–23].

Role of endothelial injury

Endothelial injury causes auto-oxidation of the oxyhemoglobin contained in blood clots encasing cerebral arteries producing methemoglobin and superoxide anion radicals, which in turn leads to lipid peroxidation. Harmful hydroxyl radicals and lipid peroxides permeate the vessel wall and injure the endothelial and smooth muscle cells [24]. Damage to the endothelium, in particular, is thought to lay a key role in the establishment of vasospasm; the synthesis of endothelial nitric oxide (NO) causes an important vasodilatation and regulation of vascular tone; in any case, endothelial injury causes decreased availability of the simple molecule NO and may contribute to the continuous vasospasm secondary to the weather variability. Also, a disbalance occurs between both the regulator tone molecules (NO and endothelin-1); endothelin-1 (ET-1) is the predominant isoform of endothelin and has the greatest role in vasoconstriction, losing the tone regulation of the brain vessels and CVP causing SAH [24, 25].

Ambient temperature on the incidence of SAH

Physiologically, $PaCO_2$ variability is highly sensitive for brain perfusion. Temperature ambient or weather effect is defined as the temperature of the surrounding air, and as such, it is modified by humidity [26]. In many studies, the temperature exposure in patients with risk factors to stroke has been established [27, 28]. The combination of humidity level, high and low temperature, or both is related to the incidence of SAH. Ambient temperature is measured at or near airport monitoring stations; this association has been studied in the daily or monthly mean; elevation in $PaCO_2$ causes a decrease in cerebrovascular resistance and consequent increases in cerebral blood flow (CBF), and hypocapnia causes increases in cerebrovascular resistance and decreases in CBF, in which the $PaCO_2$ sensibility in the brain is unique compared to the peripheral vasculature. Short-term temperature effects are defined as the hot and cold weather short-term effect by 1 °C increase or 1 °C decrease in temperature in a time frame [29]. Therefore, in a recent systematic review and meta-analysis which studied the short-term of ambient temperature and the risk for stroke, in which 20 articles were analyzed, among the studies that took morbidity as the outcome, a positive relationship was not found between temperature changes and stroke, which means that regardless of the weather short-term effect, the occurrence of stroke will be the same for hot and cold temperatures [27]. Furthermore, in a large multicentric study in China, both cold and hot temperatures were associated with increased risk of stroke mortality, where the potential effect of cold weather may last more than 2 weeks, compared to hot weather effects which were more immediate [30]. However, the physiologically plausible association exists between temperature conditions and stroke risk. In a large meta-analysis of 476,511 patients, it was concluded that lower temperature is significantly associated with the risk of intracerebral hemorrhage, but to define the relationship between weather short-term effect and ischemic stroke and subarachnoid hemorrhage, the study results are still being inconsistent [31].

Conclusions

There are many theories about meteorological risk factors for SAH; according to this review, there is a strong association between atmospheric pressure, ambient temperature, and climate changes. However, the first risk factor for SAH is hypertension, increasing the risk for cerebral vasospasm. It is well known that for many patients with hypertension and associated comorbidities in winter and windy seasons, the risk for stroke is high. As a medical emergency and with a high risk of death, knowing the risk factors for prevention and promotion is essential for any doctor in the field. Nevertheless, it would need more studies to identify idiopathic SAH, regardless of the knowledge of meteorological

risk factors, and what would be the first cause in those patients with idiopathic SAH.

Authors' contributions
Concepts: HEV, LP, LRM, AA; Design: LP, LRM, AA; Definition of intellectual content: HEV, LP, LRM, AA; Literature search: HEV, LP, LRM, AA; Data acquisition: NA; Data analysis: NA; Statistical analysis: NA; Manuscript preparation: HEV, LP, LRM, AA; Manuscript editing: HEV, LP, LRM, AA; Manuscript review: HEV, LP, LRM, AA. The author(s) read and approved the final manuscript.

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