High altitude exposure and ischemic stroke: A literature review

Esteban Ortíz-Prado [1,2] *Jeff F. Dunn* [3]

Abstract

Despite our understanding of stroke, the risk factors involved and its treatment and prevention, stroke remains the second leading cause of death among humans worldwide. Several risk factors have been associated with higher incidences of stroke, such as hypertension or diabetes, while non-traditional risk factors such as vitamin D deficiency or cardiac valvular thickness have recently been identified. The potential role of hypoxia or high altitude exposure as a risk factor has not been clearly established. This review includes the relationship between acute and chronic high altitude exposure and the possible development of ischemic stroke in high altitude populations. Several risk factors are identified in high altitude dwellers such as polycythemia, increased platelet adhesiveness and greater risk to develop vascular thrombosis. Other conditions such as dehydration, extreme cold and immobilization might lead to increased risk of ischemic stroke in newcomers. Taking into account the limited number of studies, it is argued that high altitude and chronic hypoxia may be risk factors for the development of ischemic stroke. The altitude associated with higher prevalence of ischemic stroke is not clear, but it appears that there is increased risk above 3000m.

Rev Fac Cien Med (Quito) 2011; 36: 63-70

1 *Research assistant. Department of Radiology; Mountain Medicine and High Altitude Physiology Program. Faculty of Medicine, University of Calgary. Calgary-Canada*
2 *Assistant professor of Human Physiology. Medicine School; Faculty of Health Sciences, University of the Americas. Quito-Ecuador.*
3 *Professor. Departments of Physiology and Pharmacology, and Clinical Neurosciences. Faculty of Medicine, University of Calgary. Calgary-Canada.*

Correspondence:
Esteban Ortíz; MD, MSc. Escuela de Medicina, Facultad de Ciencias de la Salud, Universidad de las Américas. Av. de los Granados y Colimes, esq. Quito-Ecuador.
E-mail:
e.ortiz@udlanet.ec

Keywords
High altitude, Hypoxia, Ischemic stroke, Polycythemia, Platelet adhesiveness, Thrombosis

Introduction

Although extensive research has been carried out to understand the pathophysiology, etiology, risk factors and management of stroke, the role of hypoxic exposure as a risk factor is uncertain. Probing the role of hypoxia will be valuable in understanding the mechanism of stroke induction and beneficial for developing countries which are located at high altitude [1-3]. Hypoxia in this case is defined as a reduction in the relative levels of oxygen (either inspired or at the level of substrate delivery). Tissues have a chronic and acute response to hypoxia that involve genetic responses on the one hand, and acute metabolic and physiological changes on the other. As a result, this review makes a distinction between those living at altitude vs. those visiting from lower regions. Although the literature in this area is sparse, there are key epidemiological reports available. In this review we discuss the epidemiological factors with stroke prevalence among various groups at high altitude and the impact of hypoxia on select risk factors.

Epidemiological overview

Establishment of epidemiological impact of high altitude hypoxia on the development of stroke is very hard because of the presence of multiple variables which are difficult to con-

trol, such as time duration of exposure, genetic adaptations and previous risk factors.

It has been anecdotally noted that ischemic stroke is more prevalent in high altitude populations, and several cases of ischemic or thrombotic events have been reported in the literature [4–8] as early as 1920; **table 1**.

More recent references have more controlled observations. In El Cusco-Peru (3380m) stroke was reported to have a crude prevalence rate of 6.47 per 1000, certainly higher compared to values reported in previous studies (3.6/1000 in Quiroga-Ecuador, 1.3/1000 in Kashmir-Pakistan and 1.74/1000 Santa Cruz-Bolivia) [17, 18]; **figure 1**.

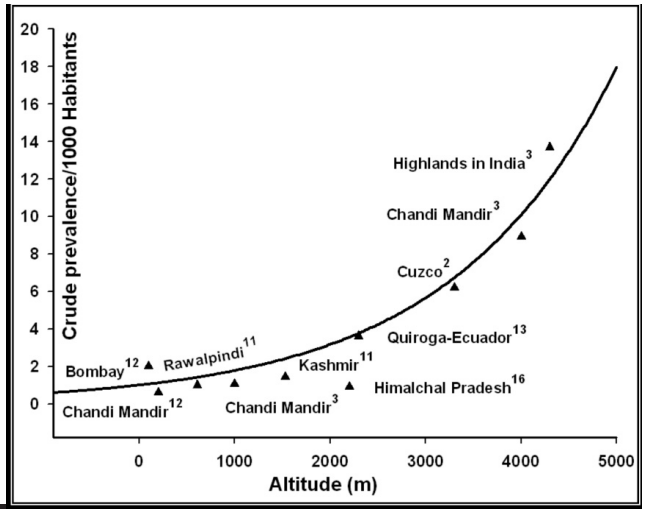

Figura 1. In this graph we show the relationship between high altitude and the prevalence of stroke in several cities around the globe

In India [3] the prevalence of stroke in soldiers living at 4200m was 13x higher (13.7/1000), compared with populations living at lower altitudes (1.05/1000). The length of exposure and polycythemia were described as the more important risk factors. It is important to note that this group of soldiers were healthy and relatively young (90% <45 years) which reduced the likelihood of other age related risk factors (just one soldier was reported to be a smoker).
In addition, the severity of ischemic stroke seems to be greater in the high altitude group. The presence of massive infarction areas (>50% of the affected hemisphere) were seen in almost 50% of the patients from the high altitude group which is significantly higher than the 14% reported from the low altitude control group [3].

In Pakistan, a relatively large study with 4000 subjects between the ages of 20-40 years, residing at >4571m studied the prevalence of stroke in high altitude populations [19]. All cases of stroke were included. During the same period 4000 subjects living in Rawalpindi (610m) were also observed as a race matched control group. They reported 10 positive cases of stroke at high altitude and just one case in the low altitude group. They concluded that living at high altitudes is associated with 10 times more risk of having a stroke, especially in young people between the ages of 20 and 40 years [19]. Granted the numbers of strokes are small, this study shows a marked difference in incidence between lowland and highland populations.

In 2001, Anand et al.[20] reported the most prevalent thrombotic complications caused

Table 1. Anecdotic stroke cases related with altitude reported in the literature

Date	Altitude (m)*	Clinical presentation	Author (year)
1895	4300	Right hemiparesis	Roverovsky (1896) [1]
1924	6000	Hemiparesis	Norton (1925) [5]
1943	6400	Dysphasia	Shipton (1943) [9]
1982	8200	Left hemiparesis	Clarke (1983) [10]
1983	6100	Semi-conscious	Asaji (1984) [11]
1986	7000 to 8000	Transient ischemic attack	Wohns (1986) [12]
1990	4800	Right hemiparesis	Sharma (1990) [13]
1994	4242	Right lat. Rectus palsy	Murdoch (1994) [7]
1997	7600	Right hemiparesis, radiological signs of edema	Basnyat (1997) [14]
2000	5800	Expressive aphasia, migraine	Dietz (2000) [15]
2002	5472	Anterior ischemic optic neuropathy	Bandyopadhyay(2002) [16]

by long term stay at high altitudes (3000 to 5000m). They found that the risk of ischemic stroke is 30x higher compared with lower altitude populations.

Al Tahan, Buchur et al. using a case-control study described the risk factors associated with stroke in Saudi Arabia among patients living at 620m vs. those living at >2000m. They reported that the frequency of thrombotic stroke at high altitude to be higher compared with the low altitude group (93.4% vs. 79.3%).
Cruz et al. [21] reported a crude stroke prevalence ratio of 3.6/1000 in the Andean village of Quiroga-Ecuador (2300m), which was higher compared with race-matched populations located at a lower altitude [18].

The elevation at which stroke starts to be more prevalent is hard to determine, however Mahajan et al. analyzed data from 100 patients admitted at a tertiary hospital in Himachal, Pradesh-India located at moderate altitude (2200m), and compared them with matched controls settled below 1000m. The prevalence of stroke in people residing at moderate altitudes was reported to be lower than those residing below 2000m. Although ischemic stroke was found to be more prevalent than hemorrhagic stroke, polycythemia was not found to be a significant risk factor in this population. This suggests that the altitude was not enough to cause acclimatization, thus, the onset of polycythemia and high hematocrit levels, two important risk factors associated with ischemic stroke [2, 3, 20].

Although the above are not large studies, there is strong evidence that high altitude living both in sojourners and native populations is associated with an increased risk of ischemic stroke. We hypothesize that this risk is associated, in part, with high altitude acclimatization. The following discussion identifies risk factors associated with altitude that may contribute to this increased risk.

Risk factors at high altitude

In this section we described the prevalence of multiples stroke risk factors among newcomers or high altitude residents. Even thought the division between these two groups is difficult since just very few studies are available, we commented when needed and described in the following section and key points are summarized in **table 2**.

Polycythemia

Despite the advantages of increased blood carrying capacity at high altitudes, polycythemia also increases the risk of thrombus formation [11]. Polycythemia is probably the most important risk factor associated with ischemic stroke during high altitude exposure, either in newcomers or high altitude residents [2, 3, 22–25].

High hematocrit levels and polycythemia produces high blood viscosity and inadequate blood flow, which are both associated with thrombus formation [26]. These conditions, aggravated by the fact that hypoxia induces vascular endothelial damage and possible platelet aggregation, enhance the thrombotic processes [27], and in so doing are likely to increase the risk of developing stroke during high altitude exposure.

Thrombosis and embolism

During pathological conditions, thrombogenesis can cause severe and deleterious clinical manifestations. Some conditions, such as decreased physical activity [28, 29], increased hematocrit [30–33] or cold temperature [34, 35] have been associated with pathological thrombus formation.

The extremely low ambient temperature and the consequent peripheral vasoconstriction causes restriction of blood flow to the extremities. In addition, the physical inactivity and forced immobility, aggravated by progressive dehydration, might facilitate clot formation and causes arterial or venous thrombosis, especially in relatively newcomers (<10 months) populations [27].

High altitude exposure, has been linked per se with increased risk to develop arterial or venous thrombosis [28, 36, 37], which might lead into death [38]. This exposure has been associated with deleterious results especially in low altitude residents who visited high altitudes locations.

Long term stays in high altitude locations (>10 months) have been associated with 30 times higher risk of spontaneous vascular thrombosis in unacclimatized subjects [20, 39].

It may be that thrombosis is a relatively common complication after high and extreme altitude exposure. The exactly mechanism involved is not clear yet, however, the effects of hypoxia in platelet adhesiveness and polycythemia, facilitated by presence of different

Table 2. Clinical or environmental conditions affecting the prevalence of stroke during high altitude exposure.

RISK FACTORS	DURING HYPOXIA	RELEVANT COMMENTS
Polycythemia and high Hematocrit	Increased	The most important stroke risk factor found in high altitude populations, causing blood stasis, endothelial damage and reduce blood flow
Platelet adhesiveness	Increased	Higher adhesiveness, strong evidence supporting the fact that after acute exposure, platelets become "stickier"
Thrombosis and embolism	Increased	Higher prevalence of thrombotic related events at high altitude compared with matched control groups
Obesity	Increased?	Obesity is increased at high altitude populations??
Coagulation at high altitude	Unclear	Auto-induced cascade activation, especially in AMS, HAPE, HACE increased pro and anti coagulant factors
A-V shunting	Increased	It is theorized that increased systemic flow would increase the possible transfer or emboli through pulmonary shunts and a patent foramen ovale
Platelet count	Increased, normal or decreased	Unclear below 4500m increased above this elevation.
Hypertension	Reduced	Lower prevalence in high altitude populations, reflected with lower prevalence of hemorrhagic stroke
Physical activity	Reduced	It is hypothesized that more active life style is found amongst highlanders, since highlanders living at sea level gain weight
Diabetes mellitus type II	Reduced	Apparently lower prevalence of DMII at high altitude, despite the fact that obesity seems to be more prevalent
Atherosclerosis and lipid profiles	Reduced	Higher levels of HDL, lower prevalence of atherosclerosis, better lipid profiles, lower complications caused by atherosclerosis.

conditions such as cold or immobilization, are maybe responsible for such an increase in the risk of thrombosis and ischemic stroke during high altitude exposure, especially in non-acclimatized subjects.

Platelet count and platelet adhesiveness

Simulated high altitude exposure (>3000m) has been associated with increased platelet adhesiveness [40, 41], which may increase clotting and thrombosis formation [6, 28, 42].
The mechanism of this apparently higher adhesiveness is not totally understood [43, 44], however, stronger adhesiveness causes reduced blood flow in compromised vessels [45]. This, in turn, causes endothelial tone control failure which results in arterial vasospasm within the cerebral circulation [45].

The number of platelets circulating throughout the vessel and its adhesiveness are important variables. A higher platelet count with higher adhesiveness will facilitate clot and thrombus formation, which might lead to higher incidences of pathological states, such as thrombosis.

Hypobaric hypoxia has been associated with either a reduction the number of circulating platelets [46], increase [39, 47, 48] or no change [43]. However, a recent prospective cohort study found that platelet count is increased by 70% after 8 months of chronic hypoxia exposure above 3500m suggesting that chronic exposure will lead into acclimatization and therefore stronger adhesiveness [39].

Coagulation at high altitude

Hypercoagulability has been noted during high altitude acclimatization, and has been found to operate as an important risk factor for ischemic stroke [39, 49, 50].

However, Crosby et al, in 2003 reported the activation of the coagulation cascade, might not occur in a range of 3600m for unacclimatized subjects and 4600m in fully acclimatized human beings [51].

More recent studies have found a phased change in the coagulation cascade, rather than alterations in cofactors or proteins concentrations. Significant initial prothrombotic states, followed by a compensatory increased capillary fragility and increased bleeding time have been reported [52]. Increased levels of serum fibrinogen, higher levels of serum thromboplastin, β-thromboglobin and platelet factor IV were also reported during acute and chronic hypoxia [39, 44].
On the other hand, evidence of widespread intravascular clotting which is associated with and may result from reduced fibrinolytic activity with increased plasma fibrinogen, increased factors V, VIII and X, decreased factor XII, and increased platelet adhesiveness and platelet factor 3 and electrophoretic mobility of platelets reduced were reported [44, 53–55]. However, these results are in conflict with "Operation Everest II", where no changes in coagulation were shown at 8000m [56, 57].

We conclude that some pro-coagulation factors have been shown to be increased at high altitude, especially above certain elevation, however, the literature is still conflicting.

Arteriovenous shunting

Hypoxia may increase the risk of peripherally induced clots passing directly from the venous to the arterial system, thereby gaining access to the cerebral circulation. Acute hypoxia is known to increase shunt flow by over 50% in the lung [58]. The maximum diameter of these shunts remains to be determined but they are certainly over 50um, even during normoxia [59]. The existence of a patent foramen ovale is also being increasingly recognized as a risk factor for ischemic stroke [60].

It is worth considering that, since flow through such shunts would increase with increased cardiac output, the possibility of transfer of a venous embolus to the arterial system by this route would increase with altitude.

Atherosclerosis and lipids

The prevalence of atherosclerosis is hard to determine in high altitude populations, and its relationship with the development of ischemic stroke has never been reported. However, the presence of cardiovascular diseases at high altitude caused by atherosclerosis seems to be lower [61–63].

The relationship between this low prevalence of cardiovascular diseases, caused specifically by atherosclerosis, might be related to the fact that increased high density lipoproteins (HDL) are found in high altitude residents [1, 64, 65]. Higher levels of HDL are associated with a reduced risk of developing stroke [66–68]. A recent study found that serum leptin levels, a newly discovered risk factor of stroke [69, 70], seem to be lower among high altitude residents [64].

Lipid profiles seems to be better in high altitude populations, suggesting that other factors, such as hypoxia are more often the cause of the development of cerebrovascular diseases during high altitude exposure.

Conclusions

It is argued in this review that altitude exposure is associated with an increased risk of ischemic stroke in both residents and sojourners. This conclusion is supported by a range of epidemiological and observational studies, associating several risk factors with increased risk to developing ischemic stroke at altitude. These include 1) polycythemia, 2) stronger platelet adhesiveness, 3) increased levels of thromboplastin, 4) blood stasis aggravated by the presence of polycythemia, endothelial damage and hyperviscosity 5) prolonged immobility, 6) and increased chances of dehydration which are potential risk factors for the development of stroke. The altitude associated with higher prevalence of ischemic stroke is not clear, but it appears that there is increased risk above 3000m.

Acknowledgements

This work was funded in part by an NIH RO1 EB002085 and the Canadian Institutes of Health Research FIN 79260.

Conflict of interest

None declared by authors.

References

1. Al-Huthi MA, Raja'a YA, Al-Noami M, Abdul Rahman AR. Prevalence of coronary risk factors, clinical presentation, and complications in acute coronary syndrome patients living at high vs. low altitudes in yemen. Med Gen Med 2006; 8: 28.
2. Jaillard AS, Hommel M, Mazetti P. Prevalence of stroke at high altitude (3380m) in Cuzco, a town of Peru. A population-based study. Stroke 1995; 26: 562 – 68.
3. Jha SK, Anand AC, Sharma V, Kumar N, Adya CM. Stroke at high altitude: Indian experience. High Alt Med Biol 2002; 3: 21 – 27.
4. Roverovsky V. The central asian expedition of capt. Roberovsky and lt. Kkozloff. Geogr J 1896; 8: 161.
5. Norton EF. The fight for Everest 1924. New York; 1925: 90 – 119.
6. Cucinell SA, Pitts CM. Thrombosis at mountain altitudes. Aviat Space Environ Med 1987; 58: 1109 – 11.
7. Murdoch DR. Lateral rectus palsy at high altitude. Journal of Wilderness Medicine 1994; 5: 179 – 81.
8. Grotta JC. Cerebral venous thrombosis - a new diagnosis in travel medicine. J Travel Med 1996; 3: 137.
9. Shipton E. Upon that mountain. London: Hodder and Stoughton; 1943: 129 – 30.
10. Clarke CRA. Cerebral infarction at extreme altitude. In: Hypoxia, Exercise and Altitude. Sutton JR, Houston CS, Jones NL; eds. New York: Liss; 1983: 453 – 54.
11. Song SY, Asaji T, Tanizaki Y, Fujimaki T, Matsutani M, Okeda R. Cerebral thrombosis at altitude: Its pathogenesis and the problems of prevention and treatment. Aviat Space Environ Med 1986; 57: 71 – 76.
12. Wohns RN. Transient ischemic attacks at high altitude. Crit Care Med 1986; 14: 517 – 18.
13. Sharma A, Sharma PD, Malhotra HS, Kaul J, Pal LS, Das Gupta DJ. Hemiplegia as a manifestation of acute mountain sickness. J Assoc Physicians India 1990; 38: 662 – 63.
14. Basnyat B. Seizure and hemiparesis at high-altitude outside the setting of acute mountain sickness. Wilderness Environ Med 1997; 8: 221 – 22.
15. Dietz TE, McKiel VH. Transient high altitude expressive aphasia. High Alt Med Biol 2000; 1: 207 – 11.
16. Bandyopadhyay S, Singh R, Gupta V, Gupta A. Anterior ischaemic optic neuropathy at high altitude. Indian J Ophthalmol 2002; 50: 324 – 25.
17. Saposnik G, Del Brutto OH. Stroke in South America: A systematic review of incidence, prevalence, and stroke subtypes. Stroke 2003; 34: 2103 – 07.
18. Heckmann JG, Kolominsky-Rabas PL, Heuschmann P, Erbguth FJ, Neundorfer B, Galeote J. Low incidence of stroke in the chiquitanos tribe in the bolivian lowlands. Stroke 2000; 31: 2266 – 70.
19. Niaz A, Nayyar S. Cerebrovascular stroke at high altitude. J Coll Physicians Surg Pak 2003; 13: 446 – 48.
20. Anand AC, Jha SK, Saha A, Sharma V, Adya CM. Thrombosis as a complication of extended stay at high altitude. Natl Med J India 2001; 14: 197 – 201.
21. Cruz ME, Schoenberg BS, Ruales J, Barberis P, Proano J, Bossano F, Sevilla F, Bolis CL. Pilot study to detect neurologic disease in Ecuador among a population with a high prevalence of endemic goiter. Neuroepidemiology 1985; 4: 108 – 16.
22. Mahajan SK, Kashyap R, Sood BR, Jaret P, Mokta J, Kaushik NK, Prashar BS. Stroke at moderate altitude. J Assoc Physicians India 2004; 52: 699 – 702.
23. Wang X, Wu T, Chen Q, Wei C, Zhao G. [Relationship between hematocrit (hct) and cardiac systolic time intervals (sti) in residents at 4300 m altitude]. Space Med Eng (Beijing) 1998; 11: 365 – 67.

24. Winslow RM, Monge CC, Brown EG, Klein HG, Sarnquist F, Winslow NJ, McKneally SS. Effects of hemodilution on O2 transport in high-altitude polycythemia. J Appl Physiol 1985; 59: 1495 – 1502.

25. Kiyohara Y, Ueda K, Hasuo Y, Fujii I, Yanai T, Wada J, Kawano H, Shikata T, Omae T, Fujishima M. Hematocrit as a risk factor of cerebral infarction: Long-term prospective population survey in a japanese rural community. Stroke 1986; 17: 687 – 92.

26. Heath D, Reid Williams D. Transport and release of oxygen to the tissue. In: Heath D, Reid Williams D. High Altitude Medicine and Pathology. Oxford: Oxford University Press; 1995: 55 – 73.

27. Fujimaki T, Matsutani M, Asai A, Kohno T, Koike M. Cerebral venous thrombosis due to high-altitude polycythemia. Case report. J Neurosurg 1986; 64: 148 – 50.

28. Toff WD, Jones CI, Ford I, Pearse RJ, Watson HG, Watt SJ, Ross JA, Gradwell DP, Batchelor AJ, Abrams KR, Meijers JC, Goodall AH, Greaves M. Effect of hypobaric hypoxia, simulating conditions during long-haul air travel, on coagulation, fibrinolysis, platelet function, and endothelial activation. JAMA 2006; 295: 2251 – 61.

29. Hodkinson PD, Hunt BJ, Parmar K, Ernsting J. Is mild normobaric hypoxia a risk factor for venous thromboembolism? J Thromb Haemost 2003; 1: 2131 – 33.

30. Schobersberger W, Hoffmann G, Gunga HC. [Interaction of hypoxia and haemostasis - hypoxia as a prothrombotic factor at high altitude?]. Wien Med Wochenschr 2005; 155: 157 – 62.

31. Tewari SC, Jayaswal R, Kasthuri AS, Nath CS, Ohri VC. Excessive polycythaemia of high altitude. Pulmonary function studies including carbon monoxide diffusion capacity. J Assoc Physicians India 1991; 39: 453 – 55.

32. Kryger M, McCullough R, Doekel R, Collins D, Weil JV, Grover RF. Excessive polycythemia of high altitude: Role of ventilatory drive and lung disease. Am Rev Respir Dis 1978; 118: 659 – 66.

33. Berglund B. High-altitude training. Aspects of haematological adaptation. Sports Med 1992; 14: 289 – 303.

34. Blomback M, Kronlund P, Aberg B, Fatah K, Hansson LO, Egberg N, Moor E, Carlsson K. Pathologic fibrin formation and cold-induced clotting of membrane oxygenators during cardiopulmonary bypass. J Cardiothorac Vasc Anesth 1995; 9: 34 – 43.

35. Ikeda T, Yanaga K, Lebeau G, Higashi H, Kakizoe S, Starzl TE. Hemodynamic and biochemical changes during normothermic and hypothermic sanguinous perfusion of the porcine hepatic graft. Transplantation 1990; 50: 564 – 67.

36. Saito S, Tanaka SK. A case of cerebral sinus thrombosis developed during a high-altitude expedition to Gasherbrum I. Wilderness Environ Med 2003; 14: 226 – 30.

37. Baumgartner RW, Siegel AM, Hackett PH. Going high with preexisting neurological conditions. High Alt Med Biol 2007; 8: 108 – 16.

38. Dickinson J, Heath D, Gosney J, Williams D. Altitude-related deaths in seven trekkers in the Himalayas. Thorax 1983; 38: 646 – 56.

39. Kotwal J, Apte CV, Kotwal A, Mukherjee B, Jayaram J. High altitude: A hypercoagulable state: Results of a prospective cohort study. Thromb Res 2007; 120: 391 – 97.

40. Sharma SC, Balasubramanian V, Chadha KS. Platelet adhesiveness in permanent residents of high altitude. Thromb Haemost 1980; 42: 1508 – 12.

41. Chatterji JC, Ohri VC, Das BK, Chadha KS, Akhtar M, Bhatacharji P, Tewari SC, Behl A. Platelet count, platelet aggregation and fibrinogen levels following acute induction to high altitude (3200 and 3771 metres). Thromb Res 1982; 26: 177 – 82.

42. Sharma SC, Vijayan GP, Suri ML, Seth HN. Platelet adhesiveness in young patients with ischaemic stroke. J Clin Pathol 1977; 30: 649 – 52.

43. Sharma SC. Platelet count and adhesiveness on induction to high altitude by air and road. Int J Biometeorol 1982; 26: 219 – 24.

44. Singh I, Chohan IS. Blood coagulation changes at high altitude predisposing to pulmonary hypertension. Br Heart J 1972; 34: 611 – 17.

45. Hackett PH. High altitude and common medical conditions. In: Hornbein TF, Schoene RB, eds. High altitude: An exploration of human adaptation. In the series: Lung Biology in Health and Disease, (Claude Lenfant, series editor). New York: Dekker 2001, vol 161: 839 – 85.

46. Birks JW, Klassen LW, Gurney CW. Hypoxia-induced thrombocytopenia in mice. J Lab Clin Med 1975; 86: 230 – 38.

47. Simon-Schnass I, Korniszewski L. The influence of vitamin E on rheological parameters in high altitude mountaineers. Int J Vitam Nutr Res 1990; 60: 26 – 34.

48. Hudson JG, Bowen AL, Navia P, Rios-Dalenz J, Pollard AJ, Williams D, Heath D. The effect of high altitude on platelet counts, thrombopoietin and erythropoietin levels in young bolivian airmen visiting the Andes. Int J Biometeorol 1999; 43: 85 – 90.

49. Maher JT, Levine PH, Cymerman A. Human coagulation abnormalities during acute exposure to hypobaric hypoxia. J Appl Physiol 1976; 41: 702 – 07.

50. Nakanishi K, Tajima F, Nakata Y, Osada H, Sugiyama K, Maruta H, Kawai T, Suzuki M, Torikata C. Hypercoagulable state in a hypobaric, hypoxic environment causes non-bacterial thrombotic endocarditis in rats. J Pathol 1997; 181: 338 – 46.

51. Crosby A, Talbot NP, Harrison P, Keeling D, Robbins PA. Relation between acute hypoxia and activation of coagulation in human beings. Lancet 2003; 361: 2207 – 08.

52. Doughty HA, Beardmore C. Bleeding time at altitude. J R Soc Med. 1994; 87: 317 – 19.

53. Singh I, Chohan IS. Adverse changes in fibrinolysis, blood coagulation and platelet function in high altitude pulmonary oedema and their role in its pathogenesis. Int J Biometeorol 1974; 18: 33 – 45.

54. Singh I, Chohan IS. Reversal of abnormal fibrinolytic activity, blood coagulation factors and platelet function in high-altitude pulmonary oedema with frusemide. Int J Biometeorol 1973; 17: 73 – 81.

55. Singh I, Chohan IS. Abnormalities of blood coagulation at high altitude. Int J Biometeorol 1972; 16: 283 – 97.

56. Reeves JT, Groves BM, Cymerman A, Sutton JR, Wagner PD, Turkevich D, Houston CS. Operation Everest II: Cardiac filling pressures during cycle exercise at sea level. Respir Physiol 1990; 80: 147 – 54.

57. Andrew M, O'Brodovich H, Sutton J. Operation everest II: Coagulation system during prolonged decompression to 282 torr. J Appl Physiol 1987; 63: 1262 – 67.

58. Charan NB, Lakshminarayan S, Albert RK, Kirk W, Butler J. Hypoxia and hypercarbia increase bronchial blood flow through bronchopulmonary anastomoses in anesthetized dogs. Am Rev Respir Dis 1986; 134: 89 – 92.

59. Lovering AT, Stickland MK, Kelso AJ, Eldridge MW. Direct demonstration of 25- and 50-microm arteriovenous pathways in healthy human and baboon lungs. Am J Physiol Heart Circ Physiol 2007; 292: H1777 – 81.

60. Drighil A, El Mosalami H, Elbadaoui N, Chraibi S, Bennis A. Patent foramen ovale: A new disease? Int J Cardiol 2007; 122: 1 – 9.

61. Ramos A KH, Muro M, Arias-Stellaj. Patología del hombre nativo de las grandes alturas. Investigación de las causas de muerte de 300 autopsias. Bol Of Sanit Panam 1967; 62: 496 – 502.

62. Mirrakhimov MM, Rafibekova Zh S, Dzhumagulova AS, Meimanaliev TS, Murataliev TM, Shatemirova KK. Prevalence and clinical peculiarities of essential hypertension in a population living at high altitude. Cor Vasa 1985; 27: 23 – 28.

63. Sun SF. Epidemiology of hypertension on the tibetan plateau. Hum Biol 1986; 58: 507 – 15.

64. Cabrera de Leon A, Gonzalez DA, Mendez LI, Aguirre-Jaime A, del Cristo Rodriguez Perez M, Coello SD, Trujillo IC. Leptin and altitude in the cardiovascular diseases. Obes Res 2004; 12: 1492 – 98.

65. Santos JL, Perez-Bravo F, Carrasco E, Calvillan M, Albala C. Low prevalence of type 2 diabetes despite a high average body mass index in the Aymara natives from Chile. Nutrition 2001; 17: 305 – 09.

66. Amarenco P, Labreuche J, Touboul PJ. High-density lipoprotein-cholesterol and risk of stroke and carotid atherosclerosis: A systematic review. Atherosclerosis 2008; 196: 489 – 96.

67. Barter P. HDL: A recipe for longevity. Atheroscler Suppl 2004; 5: 25 – 31.

68. Yatsuya H, Tamakoshi K, Hattori H, Otsuka R, Wada K, Zhang H, Mabuchi T, Ishikawa M, Murata C, Yoshida T, Kondo T, Toyoshima H. Serum phospholipid transfer protein mass as a possible protective factor for coronary heart diseases. Circ J 2004; 68: 11 – 16.

69. Bodary PF. Links between adipose tissue and thrombosis in the mouse. Arterioscler Thromb Vasc Biol 2007; 27: 2284 – 91.

70. Wannamethee SG, Tchernova J, Whincup P, Lowe GD, Kelly A, Rumley A, Wallace AM, Sattar N. Plasma leptin: Associations with metabolic, inflammatory and haemostatic risk factors for cardiovascular disease. Atherosclerosis 2007; 191: 418 – 26.

Exposición a las grandes alturas y accidente cerebrovascular isquémico: Revisión de la literatura

Ortíz-Prado E, Dunn JF.
Rev Fac Cien Med (Quito) 2011; 36: 63 – 70.

Resumen

Palabras clave
Grandes alturas, Hipoxia, Accidente cerebrovascular isquémico, Poliglobulia, Adhesividad plaquetaria, Trombosis.

A pesar de nuestra comprensión de los factores de riesgo, tratamiento y prevención del accidente cerebrovascular, éste sigue siendo la segunda causa de muerte entre los seres humanos en todo el mundo. Varios factores de riesgo se han asociado con una mayor incidencia del accidente cerebrovascular, incluyendo la hipertensión arterial y la diabetes mellitus tipo 2, mientras que los factores de riesgo no tradicionales, tales como: la deficiencia de vitamina D o el engrosamiento valvular cardiaco que recientemente han sido identificados. El papel potencial de la hipoxia o la exposición a grandes alturas como factores de riesgo no se han establecido claramente. Esta revisión analiza la relación entre la exposición aguda y crónica a las grandes alturas y el posible desarrollo de accidente cerebrovascular isquémico.
En las poblaciones residentes en grandes alturas varios factores de riesgo están presentes, tales como: policitemia, aumento en la adhesividad de las plaquetas y un mayor riesgo de trombosis vascular. Otras condiciones como: la deshidratación, el frío extremo y la inmovilización, pueden conducir a un incremento en el riesgo para desarrollar un evento isquémico en los recién llegados a esas regiones. La altitud asociada con una mayor prevalencia del accidente cerebrovascular isquémico no está bien definida, pero parece que existe un mayor riesgo por encima de los 3000 metros.