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General review

Cerebral venous thrombosis at high altitude: A systematic review



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INFO ARTICLE

Article history:

Received 19 July 2016

Received in revised form

5 November 2016

Accepted 28 November 2016

Available online 27 December 2016

Keywords:

Cerebral venous thrombosis

High altitude

Thrombophilia

Risk factors

Mountain

Hypercoagulable state

ABSTRACT

Background and objective. – High altitude may be a factor associated with cerebral venous thrombosis (CVT). As our knowledge of CVT at high altitude is limited, it was decided to pool such information from the available case studies to determine whether high altitude can predispose to CVT.

Methods. – A systematic review of the literature was performed for cases reporting CVT at high altitude. Searches of the PubMed database (up to July 2016) were performed for publications, using 'cerebral venous thrombosis' and 'high altitude' as keywords. Cross-referencing was also done to complete the search.

Results. – Ultimately, 13 articles were included in our systematic review. The population consisted of 17 patients, predominately male (14/17), with a mean age of 32 (range: 19–47) years. Altitude range was 3000–8200 m. Nine patients stayed at high altitude for > 2 weeks; the duration of high altitude stay was unknown for the remainder. A hypercoagulable state was found in nine patients: secondary polycythemia in five; protein C deficiency in one; protein S deficiency in one; and factor V Leiden mutations in two. No comorbidities were found in any of these patients.

Conclusion. – Long-term stays at high altitude in association with a hypercoagulable state – in particular, congenital or acquired thrombophilia – appears to predispose to CVT. The

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<http://dx.doi.org/10.1016/j.neurol.2016.11.004>

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association of CVT with a single exposure to high altitude seems low, but the risk cannot as yet be specifically estimated.

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1. Introduction

High altitude may be an associated condition for cerebral venous thrombosis (CVT), but little is known of CVT at high altitude [1]. At sea level, the common risk factors for CVT include: inherited thrombophilia (factor V Leiden mutation, protein C and S deficiency); acquired prothrombotic state (pregnancy, puerperium or postoperative period); systemic disease (Behçet syndrome, systemic lupus erythematosus); neoplasia; oral contraceptives; and local causes [2]. A prothrombotic risk factor or a direct cause is identified in about 85% of patients with CVT, and a precipitating factor can cause sinus thrombosis in those with a genetically increased risk [3]. In addition, hyperhomocysteinemia is a strong, independent risk factor for CVT and found in 27–43% of patients with CVT [4].

The risk of CVT at particular locations in association with high altitude is unknown. CVT has been reported in people who climb to high altitudes ranging from 2500 to 5500 m. Volume depletion and polycythemia are thought to be possible mechanisms for CVT at high altitudes [5]. However, when a climber has a coagulation disorder (such as protein C deficiency, fibrinolytic enzyme deficiency or antiphospholipid antibody syndrome), sinus thrombosis can develop even at moderate altitudes of 1500–2200 m [6]. Nevertheless, the exact prevalence of CVT at high altitudes is not known, probably because the majority of events involving severe headache at high altitude are interpreted as acute mountain sickness (AMS) or high-altitude cerebral edema (HACE), and brain imaging is not routinely performed [7].

A recent study of patients in the Himalayas suggests that high altitude may constitute an associated condition for CVT as well as ischemic stroke, particularly in patients with polycythemia [8]. The International Climbing and Mountaineering Federation (UIAA) has published recommendations concerning cerebrovascular diseases at high altitude and, in particular, for ischemic stroke, transient ischemic attacks (TIAs) and hemorrhagic strokes, but these guidelines do not examine CVT at high altitude [9]. Also, only a few case reports of possible severe arterial stroke at high altitude in healthy people have been reported in the literature. One study [10] suggested a higher relative risk of stroke (RR: 10, $P < 0.05$) in high-altitude residents living above 4500 m compared with those living at 600 m above sea level.

To determine whether high altitude represents a factor associated with the occurrence of CVT, it was decided to perform a systematic review of the literature reporting cases of CVT at high altitude.

2. Methods

The present study was performed according to the recommendations of the Preferred Reporting Items for Systematic

Reviews and Meta-Analyses (PRISMA) statement (see Appendix A) [11]. The PubMed database was searched for articles in English (up to July 2016), using the terms ‘cerebral venous thrombosis’ and ‘high altitude’ as key words. Lists of references (cross-referencing) were also examined to identify relevant studies to complete the search. All full-text published articles were selected, and two authors (C.Z. and M.P.) independently assessed cases for inclusion. Any disagreements were resolved by discussion with a third author (D.R.). All studies evaluating CVT at high altitude were screened, with selection of only those reports containing data on demographic information, altitude, period of stay at altitude, clinical features and diagnostic methods. Unpublished articles, case reports and case series with missing data were excluded (Fig. 1).

3. Results

A total of 20 articles pertaining to CVT at high altitude were screened, with 13 ultimately included [6,8,12–22] in this systematic review (Table 1). The final population consisted of 17 patients, predominately male (14/17), with a mean age of 32 (range: 19–47) years. All patients had climbed to an altitude range of 3000–8200 m. Nine patients were at high altitude for > 2 weeks [8,14,19–22], whereas the duration of high-altitude stay was unknown for the others.

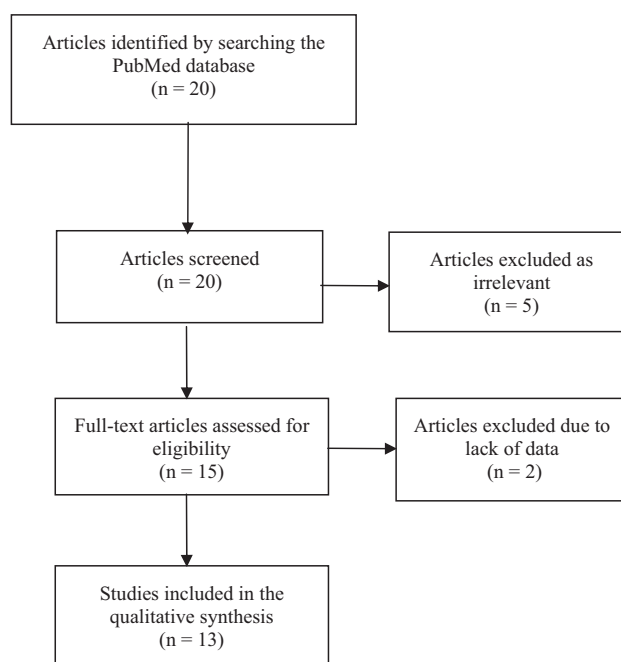


Fig. 1 – Flow diagram of our systematic literature review for the association of cerebral venous thrombosis (CVT) with high altitudes.

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