Detecting Cognitive Impairment at High Altitudes as a Means to Diagnose Acute Mountain Sickness

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Abstract

Objective: Acute mountain sickness effects trekkers traveling at high altitude. Currently there is no gold standard to diagnose acute mountain sickness, though the Lake Louise Score (LLS) is commonly used for assessment. As executive functioning is also impaired with hypoxia, a screening tool based on the Quick Mild Cognitive Impairment Screen (Qmci) was used and compared to the LLS as a potential new tool for objective testing.

Methods: Fluent adult English speaking subjects visiting the Himalayan Rescue Association Aid Posts in Manang, Nepal at 11,548ft (3520m) and Thorong Phedi, Nepal at 14,927ft (4550m) were recruited into the study. Subjects were administered the LLS and a slightly modified version Qmci (eQmci). Scores from the two surveys were compared.

Results: The LLS was compared to the eQmci using the Pearson and Spearman correlation coefficient. There were 27 (30%) subjects that met criteria for AMS based on the LLS and 13 subjects that met criteria for mild cognitive impairment based on the eQmci (14%). There was poor correlation between the eQmci score and the LLS.

Discussion: There was not a clear correlation between scoring systems for acute mountain sickness and cognitive impairment. Interestingly, 14% of subjects met criteria for mild cognitive impairment based on the eQmci, even if they did not have symptoms consistent with acute mountain sickness. Further assessment of cognitive impairment as a method to detect altitude illness is worthy of further investigation.

Introduction

Acute mountain sickness (AMS) is a common problem with exposure to high altitude.[1,2] AMS is characterized by headache, nausea and vomiting, difficulty sleeping and fatigue. Hypoxic conditions can also impair cognition, including executive, memory and language processes.[3] Despite these known deficits at high altitude, there are not any reliable objective tests to diagnosis AMS. Vital signs, physical examination and laboratory testing can fall within normal range comparable to others at high altitude.[2] Currently there are a few diagnostic scoring systems including the Lake Louise Self report (LLS) and the Environmental Symptoms Questionnaire (ESQ) that can assist with diagnosis. In 1983, the second revision of the environmental symptoms questionnaire was published.[4] In 1993 the Lake Louise hypoxia symposium proposed diagnostic criteria for altitude illness based on a self-assessment questionnaire or this questionnaire plus a clinical assessment.[5] The sensitivity for the LLS was 78% with LLS >4).[6] However, these tests rely on subjective rating amongst regarding their symptoms. In addition, the sensitivity and specificity of the LLS varies with altitude.[6]

Currently, there lacks an objective method to diagnose AMS. There is evidence that test for short term and working memory, cognitive flexibility and selective attention and executive functioning may be useful for screening for acute symptoms of hypoxia. [3] The goal of this study was to create a screening test for AMS based off of these known deficits that occur at high altitude. As AMS is on a continuum with high altitude cerebral edema (HACE), the hope is to catch cognitive impairment early enough to prevent progression to HACE, or more commonly, before lapses in judgment occur. High altitude mountaineering can carry significant risks and impaired intellectual function can lead to disastrous outcomes.

One test that has potential for detection of mild cognitive impairment in acute mountain sickness is the Quick Mild Cognitive Impairment (Qmci) screen. The Qmci screen is test developed to rapidly and reliably detect early mild cognitive impairment and dementia.[7] It is based on ABCS 135 screening tool.[8] It has been showed to be more sensitive and better at discriminating between mild cognitive impairment and normal cognition as compared with the Standardized Mini Mental State Exam.[7]

Our goal is to test the a slightly modified version of the Qmci, which we will refer to as the Environmental Quick Mild Cognitive Impairment Screen (eQmci), and determine if it is an appropriate screening test for AMS. We will compare it to the LLS.

Methods

Study Population

We performed data collection of ascents >8000ft (2438m). Fluent adult English speaking subjects visiting the Himalayan Rescue Association Aid Post in Manang, Nepal at 11,548ft (3520m) and Thorong Phedi, Nepal at 14,927ft (4550m) would be offered enrollment into the study. Surveys were only offered to medical stable subjects, after clearance from the health professional caring for them, at the end of their medical visit. Inclusion criteria included fluent English speaking adults between the ages of 18 and 65 years old who were trekking in Manang or Thorong Phedi. Exclusion criteria included history of dementia, non-fluent in English or outside the age range.

Study Procedures

Ninety subjects were enrolled in the study and all subjects enrolled completed the study. A consent document with information about the study was presented to each volunteer and written consent was obtained. Conveniences sample of patients who present to aid post were recruited. A source document was collected for each subject including questions of age, years of education, history of dementia, fluency in English, rate of ascent, medication use, and high altitude experience. Each subject enrolled was administered the LLS and the eQmci by a single investigator. These tests were compared to each other using a scatter plot and summarized using Pearson or Spearman correlation coefficient. This study was IRB approved (Protocol number 2014P001803) and approved by the Nepali Health Research Council.

Screening Tests

The LLS is based on a 5-item scale, which surveys a climber's subjective feelings of headache, dizziness or lightheadedness, fatigue or weakness, gastrointestinal distress, and difficulty sleeping. Each symptom is graded on a scale of 0 to 3. A total score of greater than or equal to 3 meet criteria for AMS.[5] However, studies have suggested that a score greater than four or even five should be used.[6,9]

Permission to use the Qmci test as the basis of our screening test was granted by Dr. William Molloy. The Qmci tests orientation, registration, clock drawing, delayed recall, verbal fluency and logical memory. It has a medium administration time of 4.24 minutes.[10] It is scored out of 100. A few modifications were made to better apply this screen in wilderness settings. Firstly, we removed the clock drawing task given the difficulty writing while in gloves as one would want to avoid exposing their hands to the cold environment. Although the clock drawing test is useful to assess visuospacial cognition, it clinically a less useful subtest when compared to the others in the Qmci.[10] Instead, in order to maintain a distracting task before the verbal recall, subjects were asked to count backwards from 100 by sevens. This task, as well as spelling words backwards, has been used to test attention. Serial sevens was used instead of words since it has been suggested that serial seven's may be more appropriate in a population where English is not necessarily the first language.[11] Secondly, repetition and recall of common names were replaced with proper names matched for frequency. High altitude seems to have a more dramatic effect on the recall of proper names while recall of common names is relatively resistant to hypoxia.[12] To meet a criteria of cognitive impairment, once must score less or equal to 62 out of 100.[13]

Results

A total of 90 subjects were enrolled in the study. All subjects that were enrolled completed the surveys. There were 27 (30%) subjects that met criteria for AMS based on the LLS and 13 subjects that met criteria for mild cognitive impairment based on the eQmci (14%). One subject enrolled had been diagnosed with high altitude cerebral edema. In this particular patient, their LLS was 9 on arrival. Because of their critical condition, they were not enrolled in the study until medically stable. Several hours after treatment, they were enrolled in the study. Their eQmci score was 53, meeting criteria for cognitive impairment. The patient's LLS at the time of enrollment has reduced to 3.

Basic demographics were collected for each subject (see Table 1). There was a significant difference in acetazolamide use between groups. Specifically, more subjects diagnosed with AMS by the LLS had taken acetazolamide in the last 24 hours than those that did not meet criteria (p=0.050). Similarly, more subjects with mild cognitive impairment diagnosed by the eQmci had taken acetazolamide in the last 24 hours than those that did not meet criteria (p = 0.0008). There were no other significant differences in group characteristics in those that met and did not meet criteria for AMS based on the LLS. However, there were group differences in the subjects that met and did not meet criteria for cognitive impairment based on the eQmci. Specifically, subjects that were cognitively impaired were more likely to be male (p=0.026) and speak English as a second learner (p=0.027).

Table 1: Summary of demographics

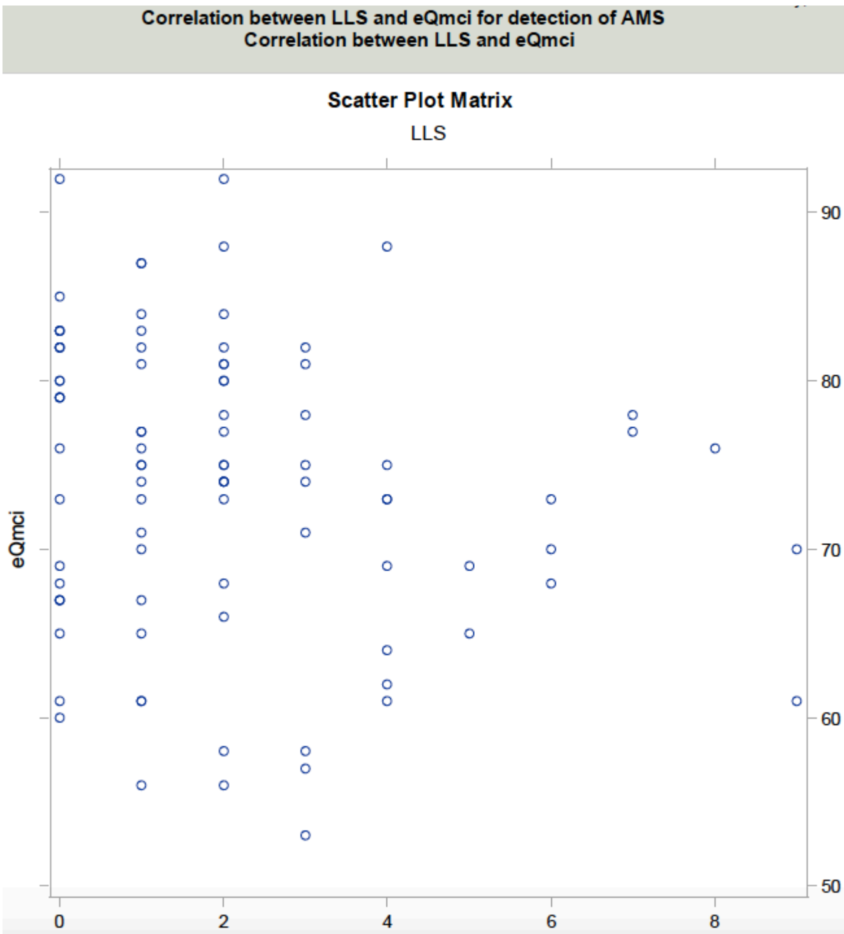
	LLS < 3	LLS ≥ 3	eQmci > 62	eQmci ≤ 62	Total
N	63	27	77	13	90
Average Age (years)	31	32	30	34	31
Sex					

Male	40 (63%)	13 (48%)	49 (64%)	9 (69%)	53 (59%)
Female	23 (37%)	14 (52%)	28 (36%)	4 (31%)	37 (41%)
Native English speaker	57 (91%)	22 (82%)	70 (91%)	9 (62%)	79 (88%)
Education					
High School	3 (5%)	3 (11%)	5 (7%)	1 (8%)	6 (7%)
Undergraduate	41 (65%)	19 (70%)	52 (68%)	8 (61%)	60 (67%)
Postgraduate	19 (30%)	5 (19%)	20 (25%)	4 (31%)	24 (26%)
Experience at high altitude					
Beginner	49 (78%)	23 (85%)	60 (78%)	12 (92%)	72 (80%)
Intermediate	13 (21%)	4 (15%)	16 (21%)	1 (8%)	17 (19%)
Expert	1 (1%)	0	1 (1%)	0	1 (1%)
Avg. days above 8000ft (2438m)	3.6	3.4	3.5	3.8	3.6
Location					
Manang	51(81%)	20 (74%)	61 (79%)	10 (77%)	71 (79%)
Thorong Phedi	12 (19%)	7 (26%)	16 (21%)	3 (23%)	19 (21%)
Nationality					
American	28 (44%)	7 (26%)	31 (40%)	4 (31%)	35 (39%)
Australian	6 (10%)	3 (11%)	8 (10%)	1 (8%)	9 (10%)
Bulgarian	1 (2%)	0	1 (1%)	0	1 (1%)
Canadian	4 (6%)	0	4 (5%)	0	4 (4%)
Chinese	0	1 (4%)	1 (1%)	0	1 (1%)
Danish	0	1 (4%)	1 (1%)	0	1 (1%)
Dutch	2 (3%)	2 (7%)	3 (4%)	1 (8%)	4 (4%)
Irish	2 (3%)	1 (4%)	3 (4%)	0	3 (3%)
Israeli	1 (2%)	3 (11%)	3 (4%)	1 (8%)	4 (4%)
New Zealand	4 (6%)	1 (4%)	3 (4%)	2 (15%)	5 (6%)
South African	0	1 (4%)	0	1 (8%)	1 (1%)
Spanish	1 (2%)	1 (4%)	0	2 (15%)	2 (2%)
United Kingdom	13 (21%)	6 (22%)	19 (25%)	0	19 (21%)
Unknown	1 (2%)	0	0	1 (8%)	1 (1%)
Medication (last 24 hrs)					

Acetazolamide	15 (24%)	12 (44%)	18 (23%)	9 (69%)	27 (30%)
NSAIDs	8 (13%)	5 (19%)	12 (16%)	1 (8%)	13 (15%)
Acetaminophen	4 (6%)	2 (7%)	4 (5%)	2 (15%)	6 (7%)

The mean LLS between all subjects was 2.1 (Std ±2.1). The mean score for subjects that met criteria for AMS (LLS ≥ 3) was 4.7 (Std ±1.9) and 1.0 (Std ±0.8) for those that did not meet criteria (LLS <3). The mean eQmci score for all subjects was 73.8 (Std ±8.8). The mean score for subjects that met criteria for cognitive impairment (eQmci ≤ 62) was 58.8 (Std±2.7) and 76.3 (Std ±6.7) for those with normal cognition (eQmci > 62).

Figure 1: Scatter plot of LLS to eQmci



There was poor correlation between the eQmci score and the LLS based on the Pearson (-0.20) and spearman (-0.22) correlation coefficients.

Discussion

Even ascent to altitudes to 2400m is enough to impair central nervous system functions (cite Petra). The goal of this study was to find an objective test based on early cognitive impairment to help detect AMS as current scoring systems are based mainly on subjective measures. This study did not find a clear correlation between scoring systems for acute mountain sickness and cognitive impairment. However, interestingly, 14% of subjects met criteria for mild cognitive impairment, even if they did not have symptoms consistent with acute mountain sickness.

There are several possibilities as to why there was only poor correlation between the eQmci and LLS. Firstly, there may be no true relationship between acute mountain sickness and cognitive impairment. AMS is considered on a continuum with HACE, which would argue against this. Secondly, perhaps only subjects with severe AMS would have shown cognitive impairment. Most subjects in this study had mild AMS (LLS 3-5) as opposed to severe AMS (LLS ≥6). Notably, the one patient with HACE did have cognitive impairment as well, though their LLS at the time of testing was only 3. Thirdly, the LLS may be labeling individuals with AMS who suffer from other conditions. For example, a trekker may present with moderate headache that may or may not be associated with mild brain swelling and cognitive changes. A moderate headache only scores a 2 on the LLS and therefore does not meet criteria for AMS. However, if the trekker had a traveler’s associated gastrointestinal illness which caused them to have poor sleep the night prior, they would score at least a 3 on the LLS and therefore meet criteria for AMS. The underlying gastrointestinal illness has the potential to change the LLS, while the eQmci would still target cognition as the primary variable. It may be that the eQmci would be a more appropriate test to differentiate a benign headache from a headache associated with minor behavioral changes and potentially impaired judgment.

The way we view mild altitude illness as a precursor to HACE maybe more appropriate to think of in terms of cognitive function rather than a constellation of various symptoms. The tragedy surrounding the 1996 Mount Everest Expedition illustrated how potential lapses in judgment can contribute to devastating consequences. Much like an athletic trainer would not allow a football player return to play with a concussion, we must re-evaluate if a “return to ascent” is appropriate. It is curious that we found a significant portion of young healthy subjects with impaired cognition that did not necessarily have AMS based on the LLS. Studies using MRI have found that vasogenic edema is present in subjects with and without symptoms of AMS at high altitude (cite Bailey 2009). Perhaps it is these individuals that should be screened as being potentially “high risk” for altitude illness. Cognitive tests are sensitive and have the potential to screen for hypoxic impairment at early presymptomatic stages (cite Stepanek 2013).

Another interesting finding is that more subjects on acetazolamide that met criteria with AMS than those who were not on acetazolamide. One possibility is that patients can self treat when symptoms occur. They often seek medical attention in the clinic after they are still symptomatic.

There are several limitations in this investigation. First, there is no real “gold standard” to diagnose acute mountain sickness. This makes comparing sensitivity and specificity between scoring systems difficult. Some studies have used physician evaluation as a gold standard to compare scoring systems as an alternative (cite Margioini). Second, the subjects with cognitive impairment were more likely to speak English as a second language. This may suggest that these subjects would have more difficulty on a test given in English, however, this was controlled for as subjects who did not speak English fluently were excluded from the study. Third, the cut-off between normal cognition and mild cognitive impairment were taken from the Qmci screen. The eQmci had slight modifications (the clock drawing task was replaced by reciting serial sevens and the repetition and recall of names were changed from common to proper). This potentially could have a subtle effect on the cut-off values originally tested for the Qmci. Fourth, trends may be been seen with a more robust sample. Unfortunately, recruitment was limited secondary to an earthquake in Nepal resulting in termination of the study.

In summary, cognitive impairment can occur at moderate altitude. Those individuals may or may not be diagnosed with acute mountain sickness. While there was little correlation between the LLS and the eQmci, screening of individuals with cognitive impairment for the development of altitude illness maybe more relevant and therefore worthy of future studies.

Acknowledgement: Thank you Dr. Marjorie Nicolas, Dr. William Molloy, Dr. Ronan O'Caoimh, Anthony Brohan, Dr. Sagar Panthi, Dr. Remi Drozd, Dr. Allison Mulcahy, and Emily Ledingham.

Table and Figure Legend

Table 1: Basic demographics were collected for each subject and summarized. Percentages are reported with respect to different subgroups (LLS <3, LLS ≥ 3, eQmci > 62, eQmci ≤ 62).

Figure 1: A scatter plot was created between LLS and eQmci scores. There was poor correlation between the eQmci score and the LLS based on the Pearson (-0.20) and spearman (-0.22) correlation coefficients.

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